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Studies of Ocular Heat Transfer using the Boundary Element Method

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List of Symbols

Geometrical variables

x, y, z	Cartesian coordinates
r, z	axisymmetrical coordinates
ξ, η, ζ	coordinates of source point
R	domain
C	exterior boundary
$\mathcal{R}$	Euclidean distance
Γ	boundary enclosing domain
λ	geometrical coefficient

Physical variables

T	temperature
q	heat flux
t	time
p	pressure
$\vec{v}$	velocity vector
u, v	velocity components
$\vec{\omega}$	vorticity vector
ω	vorticity component
Δt	time step
Ω	degree of thermal damage

Material properties

α	thermal diffusivity
β	thermal expansion coefficient
c	specific heat
ε	corneal surface emissivity
κ	thermal conductivity
μ	dynamic viscosity
σ	Stefan-Boltzmann constant
ρ	density
ϱ	absorption coefficient

Physical parameters

d_p	penetration depth
g	gravitational acceleration
h	convection coefficient
w	laser beam diameter
D_T	tumor doubling time
$E(r, z)$	incident irradiance
E_o	peak irradiance
E_{vap}	heat loss due to tears evaporation
Q_m	metabolic heat generation
ΔT	thermal gradient inside the anterior chamber
$\mathbb{F}$	Fresnel reflectance of the corneal surface
ϖ	blood perfusion rate

Mathematical symbols

K	elliptic integral of the first kind
E	elliptic integral of the second kind
Φ	fundamental solution

ϕ	radial basis function
φ	interpolation function in Orz and Oxy
$\overline{\varphi}$	interpolation function in $Oxyz$
$\varkappa$	particular solution

Miscellaneous

s	free parameter
Nu	Nusselt number
Pr	Prandtl number
Ra	Rayleigh number
SNR	signal to noise ratio
Θ	relaxation parameter

Subscripts

2D	two-dimensional
3D	three-dimensional
axis	axisymmetric
axis-time	axisymmetric and time-dependent
amb	ambient
bl	blood

Publications

The following are publications from the work carried out in this thesis.

1. Ooi, E.H., Ang, W.T. and Ng, E.Y.K., Bioheat transfer in the human eye: A boundary element approach. *Engineering Analysis with Boundary Elements*, vol. 31 (6), pp. 494-500, 2007.
2. Ooi, E.H., Ang, W.T. and Ng, E.Y.K., An axisymmetric boundary element model for bioheat transfer in the human eye. In: Acharya, R., Ng, E.Y.K. and Suri, J. (eds), *Image Modeling of the Human Eye*, Artech House, Massachusetts, 2008.
3. Ang, W.T. and Ooi, E.H., A dual-reciprocity boundary element approach for solving axisymmetric heat equation subject to specification of energy. *Engineering Analysis with Boundary Elements*, vol. 32 (3), pp. 210-215, 2008.
4. Ooi, E.H., Ang, W.T. and Ng, E.Y.K., A boundary element model of the human eye undergoing laser-thermokeratoplasty. *Computers in Biology and Medicine*, vol. 38 (6), pp. 727-737, 2008.
5. Ooi, E.H., Ang, W.T. and Ng, E.Y.K., A boundary element model for investigating the effects of eye tumor on the temperature distribution inside the human eye. *Computers in Biology and Medicine*, vol. 39 (8), pp. 667-677, 2009.
6. Ooi, E.H. and Ng, E.Y.K., Ocular surface temperature: A mathematical perspective. *Journal of Mechanics in Medicine and Biology*, vol. 9 (2), pp. 199-227, 2009.

ABSTRACT

Ocular heat transfer is a promising area of research. The continual fascination with ocular temperature may be attributed to its potential use in monitoring the physiological and health conditions of the human eye. Mathematical modeling has proven to be a reliable technique in the studies of ocular heat transfer. This has been attributed to the advancement of computational technology that enables complex mathematical problems to be modeled accurately. The incapability of infrared thermography (which is the current method in ocular thermometry) to measure intraocular temperatures in particular, may also contribute to the rising popularity of mathematical modeling.

Majority of the ocular heat transfer studies in the past have been carried out using the finite element method. The boundary element method, which has been established as a leading alternative to the commonly used finite element method in engineering analysis, is rarely used. Since some aspects of the boundary element method have been found to be advantageous over the finite element method, it may be worth exploring the performance and feasibility of the boundary element method in the studies of ocular heat transfer. For this purpose, four specific problems involving heat transfer inside the human eye are investigated.

The first problem deals with sensitivity analysis, which is a study that investigates the effects of various factors on the human eye temperature. Six parameters, namely ambient convection coefficient, ambient temperature, blood convection coefficient, blood temperature, tears evaporation rate and lens thermal conductivity are examined. The second problem investigates the effects of aqueous humor flow inside the anterior chamber on the overall heat transfer inside the human eye. Effects of thermal gradient and orientation of the anterior chamber are analyzed. Studies of the transient temperature changes inside the human eye during treatment of laser-thermokeratoplasty (LTKP) is

considered as the third problem. In addition to the thermal analysis, an assessment of thermal damage during LTKP is carried out using the damage model of Henriques and Moritz based on the predicted transient temperature profile of the cornea. The last problem looks into the thermal effects of eye tumor on the ocular temperature distribution. A parametric optimization study based on analysis of variance (ANOVA) and the Taguchi method is also carried out to determine the optimal setting of parameters that amplifies the thermal signal from the eye tumor.

Various techniques of the boundary element method have been employed to solve each of the four specific problems considered. The domain decomposition technique and the cell integration approach are adopted when solving the natural convection flow inside the anterior chamber. Numerical simulations of the transient temperature changes inside the eye during LTKP are executed using the time-stepping dual reciprocity boundary element method, while the dual reciprocity method has been exclusively used in the studies of thermal effects of eye tumor. Although each problem has been successfully solved, the various numerical schemes of the boundary element method that have been developed in this thesis are not free from drawbacks. These shortcomings are acknowledged and alternatives that may help to overcome these limitations are recommended.

Chapter 1

General Introduction

1.1 Opening Remarks

The temperature of the human eye has been an interesting area of research. One of the earliest works that documented the temperature of the human eye was published in 1876 by Dohnberg (cited by Holmberg [1]). Since then, literature pertaining to the study of ocular temperature distribution has progressed and with ongoing research being carried out, the number of published articles is expected to increase further. The continual fascination with the ocular temperature may be due to heat being a unique property in human physiology.

According to the Greek physician Hippocrates in 400 B.C, disease is likely to be found in parts of the human body with excess of heat or cold. This fundamental idea, which was proposed more than 2,000 years ago, is still being applied in the medical field today. Among the diseases that have been successfully detected based on the thermal physiology of the human body, include breast cancer [2, 3], rheumatic diseases [4] and vascular disorders [5, 6]. Although no attempts have been made to extend this application to ocular diseases, the use of ocular temperature to monitor the physiological and health conditions of the human eye is certainly promising [7, 8].

From the mathematical point of view, the human eye is a unique biological structure

that presents a host of bioengineering problems to be investigated. Many of the biological functions as well as the physiological conditions of the human eye may be described using fundamental principles of heat transfer [9]. Moreover, various medical treatments of the human eye are based on the thermal responses of the ocular media towards heat. Therefore, a proper mathematical description may improve our understanding of the various conditions in the human eye, which may be of great medical relevance. Furthermore, mathematical simulations provide alternative sources of information that may be of practical interest.

Mathematical investigations of the ocular temperature distribution have received considerable amount of attention over the past two decades. This may have been encouraged by the development of numerical methods and the advancement of computational technology that allow simulations to be carried out with relative ease. The ability of existing principles of bioheat transfer to accurately describe the heat transfer phenomena inside the human eye may also be a contributing factor [10]. Above all, mathematical modeling manages to overcome some of the limitations of infrared (IR) thermography¹, such as the inability to measure intraocular temperatures and to carry out investigations on some of the cases that are deemed too hazardous to be experimentally performed on human subjects.

This thesis examines mathematically some specific problems involving ocular heat transfer. To study these problems, various numerical models, based on the boundary element method, are developed.

1.2 Anatomy of the Human Eye

A large part of ocular heat transfer may depend on the anatomy of the human eye. Hence, a good understanding of the anatomical features of the human eye helps to ensure an accurate model description of the ocular heat transfer phenomena. This section presents

¹IR thermography is the primary experimental technique in ocular temperature measurement

an overview of the anatomical and physiological characteristics of the human eye.

Figure 1-1 illustrates the anatomical structure of a typical human eye in the mid-sagittal plane. Anatomical components that surround the eyeball such as eyelids, orbital fat, orbital muscles and bones are not shown. The shape of the eyeball resembles roughly that of a sphere. The human eye may be assumed to be bounded by the exterior surfaces of the cornea and sclera. The horizontal line that stretches from the center of the corneal surface to the back of the human eye is known as the pupillary axis. By ignoring the optic nerve, the human eye may be considered geometrically, to be symmetrical about the pupillary axis.

Figure 1-1: Anatomy of a typical human eye

The human eye may be divided into two segments, namely the *anterior segment* and the *posterior segment*. The anterior segment is occupied by regions such as cornea, anterior and posterior chambers, iris, lens, zonular fibers and ciliary body. Ocular regions such as the vitreous, layers of the retina, choroid and sclera and the optic nerve occupy the posterior segment.

1.2.1 Anterior segment

Cornea

The cornea is the anterior-most region of the human eye. It is a transparent medium with a water content of approximately 78% [11]. The anterior surface of the cornea is exposed to the environment while its posterior surface forms the interface with the anterior chamber. The cornea has a non-uniform thickness. It is approximately $600\mu\text{m}$ thick at the center, which increases as it approaches the limbus (the location where the cornea is attached to the sclera). The cornea may be divided into three layers, namely the epithelium, the stroma and the endothelium, such as shown in Figure 1-2. The epithelium is the top layer and is approximately $50\mu\text{m}$ thick. The stroma forms the middle layer and has a thickness of roughly $500\mu\text{m}$. The bottom layer is given by the endothelium and is approximately 30 to $50\mu\text{m}$ thick. It forms the interface between the cornea and the anterior chamber. One of the main functions of the cornea is to reflect light onto the retina, which accounts for almost 80% of the eye's optical power [12].

Figure 1-2: Layers of epithelium, stroma and endothelium inside the cornea (figure not to scale)

On top of the corneal surface, one may find a layer of tears known as the tear film. The functions of the tear film include to protect the eye from foreign debris and to ensure that the corneal surface is sufficiently lubricated [11]. It is approximately $10\mu\text{m}$ thick and is commonly referred to as the tear film. Since the tear film is exposed to the

environment, it is constantly evaporated when the eye is opened. A layer of oil known as the lipid layer covers the surface of the tear film to help prevent excessive evaporation. The loss of tears is replenished following each eye blink.

Anterior and posterior chambers

The anterior and posterior chambers are cavities inside the eye that are filled with aqueous humor. Although they may appear to be separate components, inside the actual eye, the anterior chamber is connected to the posterior chamber via a small gap of $10\mu\text{m}$ between the iris and lens. The anterior chamber of a healthy adult eye has a depth along the pupillary axis of 2.5 to 3mm. The depth of the anterior chamber increases as the individual ages [13].

The aqueous humor is essentially a liquid with properties that are similar to saline solution. Composition-wise, the aqueous humor is 99% water while the remaining 1% is made up of nutrients such as protein, amino acids and glucose, that are supplied to the cornea and lens [14]. The aqueous humor is produced by the ciliary body and is secreted into the posterior chamber. It drains from the anterior chamber through the trabecular meshwork that is located near the base of the cornea.

Iris and ciliary body

The iris is a thin muscular tissue that gives color to the eye. It is shaped like a disc with a hollow section in the middle. One of the main functions of the iris is to control the amount of light that enters the eye by changing the size of the pupil.

The ciliary body is located at the base of the iris (see Figure 1-1). It is composed of the ciliary processes and the ciliary muscles. One of the main functions of the ciliary body, as pointed out earlier, is to produce aqueous humor. Since both the iris and the ciliary body are muscle tissues, they are generally vascularized to ensure ample blood supply for carrying out tissue metabolism. Blood flow into the iris and ciliary body originates from the anterior ciliary arteries [11].

Lens

The human lens is a biconvex, avascular structure that is suspended inside the eye by zonular fibers. The thickness of the lens along the pupillary axis is approximately 3.5mm in a healthy adult eye [15]. The thickness and the radii of curvature of the human lens have been found to increase with age [16]. The human lens is composed of approximately 65% water and 35% protein. The percentage of water content depends on the individual's age however [17]. The function of the lens is to focus light that is refracted from the cornea onto the retina.

1.2.2 Posterior segment

Vitreous

The vitreous occupies the largest portion inside the eye. It is made up of almost 98% water. Despite the extremely high percentage of water content, the vitreous is essentially a gelatinous structure that allows the eye to return to its original shape if compressed. In an adult human eye, the length of the vitreous along the pupillary axis is approximately 16.5mm [18]. One of the main functions of the vitreous is to store metabolites that are supplied to the retina and choroid. It also helps to transmit and refract light by focusing light rays onto the retina [19].

Retina

The retina is the innermost coat of the eye [19]. It is a very thin layer that encapsulates the surface of the vitreous. Light that is focused by the lens onto the retina is converted into electrical impulse by the abundance of light sensitive cells. The electrical signal is then transmitted into the brain via the optic nerve. The thickness of the retina is less than 0.3mm. It is a vascularized structure and receives its blood supply from the central retinal artery. Blood flow here is slow to ensure efficient oxygenation [20].

Choroid

The choroid is located next to the retina and has a thickness of approximately 0.5mm. It is a highly vascularized structure and contains a complex network of arteries and veins known as the choriocapillaries. Blood flow inside the choroid originates from the ophthalmic artery that branches into the posterior ciliary arteries. Unlike the retina, blood flow inside the choroid is strong and it accounts for almost 85% of the total blood flow inside the human eye [20]. One of the functions of the choroid is to provide sufficient nutrients to various parts of the eye without interfering with the visual pathway [20]. Blood flow inside the choroid is highly regulated to adapt to the changing metabolic needs, compensate for varying perfusion pressures and to ensure a constant temperature at the back of the eye through thermoregulation [21].

Sclera

Sclera is usually referred to as the white part of the human eye. It covers the entire surface of the eyeball except for the corneal surface. The sclera is an avascular structure and is made up of collagen and elastic fibers that helps to protect the eye from physical damage. The thickness of the sclera varies with location. The thickest part of the sclera is at the posterior-most region, which is approximately 1mm thick (more than twice the thickness of the retina and choroid). The thinnest part of the sclera is at the limbus.

Optic nerve

The optic nerve is connected to the retina and helps to transmit the visual information in the form of electrical pulses into the brain.

1.3 Problems Involving Ocular Heat Transfer

Various problems involving heat transfer inside the human eye have been investigated in the past. Most of these problems, which have been mentioned in Section 1.1, may

be directly or indirectly related to the various ocular conditions, physiological state and medical treatments of the human eye. In this thesis, four specific problems, namely sensitivity analysis, aqueous humor hydrodynamics, laser-thermokeratoplasty (LTKP) and thermal effects of ocular tumor are investigated. These problems are discussed next. For brevity, only a general description of each problem is given. Specific details are presented in subsequent chapters.

1.3.1 Sensitivity analysis

Sensitivity analysis investigates the response of a model towards changes in governing parameters in the mathematical model. Various factors are known to affect the temperature distribution inside the human eye. Generally, these factors may be categorized into three groups, namely environmental factors, physiological factors and individual variation.

The main purpose of carrying out sensitivity analysis is to investigate how parameters of each of these factors influence the temperature distribution inside the human eye. Since these factors not only affect the temperature in a normal human eye, but also various other ocular conditions, it is necessary to have a good understanding of how the human eye thermally responds towards changes in these factors. To perform such a sensitivity analysis, a model that simulates the thermal conditions of a normal human eye has to be firstly developed. The temperatures obtained from this study are established as baseline temperatures that represent the conditions of a normal human eye. By establishing the ocular temperatures of a normal eye, results obtained from the investigations of the other problems can be compared to and analyzed.

1.3.2 Aqueous humour hydrodynamics

A watery substance known as the aqueous humor fills the anterior and posterior chambers. In most of the human eye models that have been developed, the aqueous humor has been assumed to be stagnant such that heat is only conducted across the anterior and posterior chambers [22–24]. In reality, this is not true. Clinical observations carried out on mice

and humans revealed that the aqueous humor is in constant circulation inside the anterior chamber [25]. It has been widely acknowledged that the flow of aqueous humor is driven primarily by the temperature gradient inside the anterior chamber.

One of the consequences of the aqueous humor flow inside the anterior and posterior chambers is the presence of natural convection. As a result, models that were developed based on a stagnant aqueous humor assumption may not represent accurately the actual condition inside the human eye. Thus, a particular problem of interest is to study the effects of aqueous humor circulation on the heat transfer inside the human eye. This study is aimed at examining the significance of natural convection flow inside the anterior chamber on the overall heat transfer inside the human eye.

1.3.3 Laser-thermokeratoplasty (LTKP)

Thermokeratoplasty is a corneal refractive surgery technique whereby temperature of the cornea is increased to induce shrinkages to the corneal collagen [26]. LTKP is basically another form of thermokeratoplasty, where laser is utilized as the heating mechanism. Shrinkages of the cornea generally lead to changes in the curvature that ultimately alters the refractive power of the cornea. By correlating parameters such as corneal temperature, degree of shrinkage, corneal curvature and corneal refractive power with the laser properties, heating may be calibrated accordingly to treat specific cases of impaired vision.

In vitro experimental studies revealed that the threshold for shrinkages occur when the cornea is heated to temperatures between 55 and 65°C [27]. In clinical practice however, it is common for the cornea to be heated to temperatures beyond this range. In fact, corneal temperatures exceeding 90°C have been observed in clinical trials [28, 29]. One of the risks involved in subjecting the cornea to such extreme heat is irreversible thermal damage that may produce permanent scarring on the cornea. Hence, it is important for ophthalmologists to have an in-depth knowledge of the thermal behavior of the cornea when subjected to intense heat. This may help in designing proper treatment procedure

that reduces the risk of thermal damage while achieving the desired level of corneal shrinkage.

1.3.4 Thermal effects of ocular tumor

Some of the diseases that have been successfully detected based on the abnormal temperature profile have been briefly mentioned in Section 1.1. Recently, there have been suggestions for such thermal detection system to be extended into the field of ophthalmology [8, 30]. Preliminary experimental investigations revealed that diseases such as acute inflammation and dry eyes produce abnormal ocular surface temperatures that are characterized by the warmer ocular surfaces and abnormal corneal isotherms when compared to a healthy eye [7, 31].

The use of mathematical models to investigate the effects of diseases on the temperature of biological bodies is an area of research that shows enormous potential. In many cases, numerical predictions obtained may help to complement the results obtained from experimental studies. Temperature changes caused by the growth of tumor inside the human breast and skin have been successfully investigated using mathematical models [32–36]. In most of these studies, numerical predictions were found to agree well with the data obtained from experimental measurements. Abnormality inside the human body is usually simulated by relating the symptoms and anatomical and physiological characteristics of the disease with the heat transfer phenomena inside the affected tissue. For instance, tumor is usually modeled as a region that has higher metabolic heat generation and blood perfusion rate than the surrounding healthy tissues. This observation is well-documented in literature [37, 38].

Hence, it is of interest to extend the modeling approach in the aforementioned to investigate the thermal effects of ocular diseases on the human eye. One of the major obstacles in such studies however, is the lack of relevant information that can be used to mathematically describe ocular diseases such as glaucoma, cataract and diabetic retinopathy in terms of ocular heat transfer. Since studies of the thermal effects of tumor

on the human breast and skin have been successful [32–36], it may be more appropriate to consider cases of ocular tumors as a preliminary investigation.

1.4 Previous Eye Models

Models of the human eye developed in the 1960s' were among the earliest works that mathematically investigated the temperature distribution inside the human eye [39–44]. Since computational technology and numerical methods during this period were still at their infancies, it is not surprising that these models were crude and in most cases, overly simplified. As computational technology and numerical methods progressed, researchers have been able to develop more sophisticated and realistic eye models that allow numerical simulations to be carried out more accurately. From the numerous eye models that have been published in literature, it is possible to distinguish them into three categories based on the modeling approach used. These three approaches are defined as the simplified model approach, the isolated model approach and the comprehensive model approach.

1.4.1 Simplified model approach

The simplified model approach is the simplest modeling technique used in the studies of ocular heat transfer. In this approach, only regions that are of specific interests are modeled. For instance, one may choose to model only the cornea if temperature changes at that particular region are of main concern. The model region is usually assumed to have simple geometries such as cylinder or cubic slab. This is illustrated in Figure 1-3.

One of the main disadvantages of the simplified model approach is the lack of diversity. This makes the approach applicable only to a few cases. In general, the simplified model approach is often used to investigate problems that involve localized temperature changes. Typical examples include laser and radio-frequency heating where temperature increases are confined to the heated area [45–47]. Another limitation associated with the simplified model approach is the use of simple geometries to represent the model region.

Figure 1-3: Illustration of the model region commonly used in the simplified model approach

Consequently, assumptions have to be made when specifying the boundary conditions of the problem. This may not represent accurately the actual condition inside the human eye.

1.4.2 Isolated model approach

The isolated model approach is perhaps the most commonly used technique in the mathematical studies of ocular heat transfer. Examples include the models developed by Scott [22, 48], Amara [23], Okuno [49] and Cvetković et al. [50]. In this approach, the human eye is modeled as an organ that is isolated from the human head, i.e. the model consists only of the eyeball. Ocular components such as cornea, anterior and posterior chambers, lens and vitreous are treated as part of the solution domain. Models developed based on the isolated model approach are more realistic and represents more accurately the anatomical structure of the human eye. This makes the approach better suited for investigating the temperature distribution inside the human eye. A sketch of the hu-

man eye model developed by Cvetković et al. [50] using the isolated model approach is illustrated in Figure 1-4.

Figure 1-4: Model developed based on the isolated model approach

From Figure 1-4, it is apparent that the model developed using the isolated model approach is more complicated than the models developed using the simplified model approach. This may increase the computer memory needed to perform the numerical computations. Nevertheless, this has become less of an issue due to the availability of computers with superior memory capacity and computing speed. One of the limitations of the isolated model approach concerns the assumption that the eye is separated from the human head. This assumption effectively ignores the effects of the anatomical components surrounding the eyeball on the heat transfer inside the human eye. In most cases, this assumption does not introduce significant errors to the simulated results. However, when dealing with problems involving heating that extends beyond the region defined by the human eye, investigations based on the isolated model approach may no longer be appropriate.

1.4.3 Comprehensive model approach

In the comprehensive model approach, anatomical components that surround the eye such as orbital fat, orbital muscles and bones are modeled together with the eye and

are collectively treated as the solution domain. Generally, this approach overcomes the limitation of the isolated model approach mentioned in the previous section. Figure 1-5 illustrates a sketch of the solution domain of a model developed using the comprehensive model approach. Models developed based on this approach are usually used for investigating the temperature increase inside the human eye during exposure to microwave radiation [51–53]. Some isolated cases may be found however, such as in the work by Tompkins et al. [54], where temperature distribution inside the eye during thermoradiotherapy was simulated.

Figure 1-5: A sketch of the model based on the comprehensive model approach

Although models developed using the comprehensive model approach simulate more accurately the anatomical and physiological structure of the human eye, the inclusion of other extra-ocular anatomical components means that more details have to be omitted from the structure of the eyeball. This is evident from Figure 1-5. The lack of details in the human eye structure is presumably to conserve the computer memory needed for solving the relatively large problem that involve most of the human head. With a less

intricate eye model, it may not be possible to carry out detailed analysis on the temperature changes at specific locations inside the eye. Hence, the use of the comprehensive model approach seems to be appropriate only when the primary concern is the ocular temperature changes as a whole.

1.5 The Boundary Element Method

1.5.1 Preamble

The boundary element method is a class of numerical methods that employ boundary-like discretization for solving integral equations [55]. In a broader sense, the boundary element method may be viewed as a numerical technique for solving integral equations regardless of whether discretization is used or not [56].

There have been conflicting beliefs as to the origins of the boundary element method. Some researchers have credited the work of Fredholm [57] in 1903 as the starting point of the boundary element method when he adopted a discretization procedure to establish the existence of solutions to the boundary integral equation of the Laplace equation. On the other hand, Jawson [58] and Symm [59], who in 1963, solved the boundary integral equation of the Laplace equation using discretization and computational techniques have been considered by many as the pioneer of the boundary element method.

The idea of solving partial differential equations based on the values at the boundary had been known to researchers since the early 18th century based on the work of a British mathematician named George Green. Back then, Green derived solutions of Dirichlet and Neumann problems of the Laplace equation that were expressed in the form of boundary integral equations². Although the boundary integral formulations were not solved, it provided an indication of the possibility of solving Laplace equation based on the values at the boundary.

²The work by Green may be found in ‘An Essay on the Application of Mathematical Analysis to the Theories of Electricity and Magnetism’ Printed for the Author by Wheelhouse T. Nottigham; 1828.

Developments of the boundary element method had been rather slow during the early 1960s' to the late 1980s'. By the late 1990s', the boundary element method began to show signs of significant progress and in the last decade or so, has established itself as a powerful numerical tool for solving various partial differential equations. While the boundary element method remains a less popular technique than the finite element method, its reputation as a leading alternative in numerical analysis has remained unchallenged [60].

1.5.2 Characteristics of the boundary element method

Unlike finite element and finite difference methods that are classified as *domain methods*, i.e. numerical methods that employ a full domain discretization, the boundary element method is categorized as a *boundary method*, i.e. the numerical scheme requires only the boundary of the solution domain to be discretized. Discretization that is now carried out at a reduced spatial dimension helps to lessen the requirement of computer memory, which eventually leads to a more efficient numerical scheme. Data preparation is also much simpler, which is particularly useful when solving problems with complex geometries.

One of the unique features of the boundary element method is that it sets up a system of linear algebraic equations that solves for the unknowns at the boundary. Domain values if required, are usually calculated as a post-processing step. Since half of the boundary data in well-posed problems is already known from the boundary conditions, the resulting system of linear algebraic equation is much smaller than those generated from domain methods. This feature offers a less time consuming and more memory efficient technique for solving problems where solutions at the boundary are of priority.

It is worth pointing out that the numerical solution obtained using the boundary element method is more accurate than the finite element method for the same level of discretization [61]. In other words, the boundary element method requires a less fine discretization than the finite element method in order to produce numerical results that are of the same degree of accuracy. The boundary element method is also known to compute secondary variables more accurately than the finite element method [62].

1.5.3 Motivation for the present thesis

Human eye models that have been developed in the past for investigating the ocular temperature distribution were mainly based on the finite element method [22, 23, 48, 50]. Finite difference and finite volume methods have been occasionally used [24, 49, 63]. Models that employ the boundary element method to numerically simulate the temperature distribution inside the human eye have yet to be encountered. Although successful implementations of the boundary element method in human eye studies have been reported, they were mainly developed for investigating the current density distribution inside the eye during electromagnetic wave radiation [64].

Based on the discussions on the various advantages of the boundary element method over other domain methods presented in Section 1.5.2, it is worth exploring the feasibility of the boundary element method in numerically simulating the temperature distribution inside the human eye. It is thus, the objective of this thesis to extensively use the various techniques of the boundary element method to solve the four specific problems of the ocular heat transfer described in Section 1.3. The results obtained from each investigation may not only benefit researchers from a biological standpoint, but also from a computational perspective, where the boundary element models offer other researchers with alternatives that may be computationally more viable for investigating the various heat transfer problems of the human eye.

For the numerical results presented in this thesis, self-written codes based on the boundary element method are programmed using the computing software, Matlab [65].

1.6 Organization of this Thesis

This thesis is organized into eight chapters. In Chapter 2, a preliminary investigation is carried out to examine the temperature distribution inside a normal human eye. Steps involved in the development of the human eye model are presented. It will be shown in this chapter that a model developed in the axisymmetric (Orz) coordinate system suffices

for simulating the heat transfer phenomena inside the human eye. Details such as the dimensions of the model, the thermal properties of each ocular region and the governing equation and boundary conditions that describe the heat flow are presented. Some of the assumptions made to simplify the problem are discussed. A numerical scheme based on the boundary element method is developed. This chapter establishes parameters and the ocular temperature distribution that represents condition of a normal human eye.

Investigations carried out on the first specific problem considered, i.e. sensitivity analysis, is presented in Chapter 3. Governing parameters that are examined, are identified. Values of each parameter are varied from the control based on information retrieved from literature. Numerical results obtained are critically discussed and the clinical significance of the results are deliberated.

Chapter 4 investigates the effects of natural convection inside the anterior chamber on the overall heat transfer inside the human eye. Various hypotheses that have been put forward to explain the mechanism of the aqueous humor flow are presented. Mathematical models proposed by various researchers in the past that dealt with the flow of aqueous humor are reviewed. In this thesis, only the thermally driven flow of aqueous humor is considered. Additionally, natural convection is assumed to exist only inside the anterior chamber. In carrying out the numerical simulation, only the region of the anterior chamber is modeled. This helps to reduce the amount of computer memory required to obtain a numerical solution. The Navier-Stokes equations are used to describe the natural convection flow, thus resulting in a non-linear problem. A detailed outline of the numerical scheme developed for solving the non-linear problem is presented.

The transient temperature changes inside the cornea during LTKP are investigated in Chapter 5. Investigations are carried out for both pulsed and continuous-wave lasers. The axisymmetric model of the whole human eye is used for the purpose of this study. Heat that is generated inside the cornea due to absorption of laser energy is described using the Beer-Lambert law [66]. The time-dependent problem is solved using the time-stepping dual reciprocity method. In addition to the investigation of the temperature

changes inside the eye, the degree of thermal damage induced onto the cornea during LTKP is estimated using the Henriques and Moritz [67] model for thermal injury.

Chapter 6 investigates the effects of an eye tumor on the ocular temperature distribution. The presence of tumor generally destroys the axisymmetrical characteristics of the human eye. Therefore, the axisymmetrical model developed in Chapter 2 cannot be used. For the purpose of this study, a three-dimensional model of the human eye is developed. The tumor is modeled as a separate homogeneous region that has a higher metabolic heat generation and blood perfusion rate than the surrounding ocular tissues [37, 38]. Simulations are carried out for two different locations of tumor growth. Numerical results obtained are examined and the clinical implications are discussed.

A critical discussion of the models that have been developed to solve each specific problem is presented in Chapter 7. The versatility of the models and the feasibility of the boundary element method in predicting the temperature distribution inside the eye are examined. Additionally, some of the limitations of the numerical techniques that are employed together with the boundary element method throughout this thesis are identified. Methods and alternatives for resolving these issues are recommended.

This thesis is concluded in Chapter 8. This chapter summarizes all the works that have been done in this thesis. Advantages and disadvantages encountered in this thesis are outlined. Methods for improving the accuracy of the models developed and areas for future research are proposed.

Chapter 2

Preliminary Investigation

2.1 Introduction

In this chapter, a preliminary study is carried out to investigate the temperature distribution inside a normal human eye. The phrase ‘normal human eye’ refers to a healthy eye at normo-thermal condition and is not exposed to external heat sources. The purpose of carrying out this preliminary investigation is two-fold:

1. to establish baseline temperatures (control temperatures) of a normal human eye so that numerical predictions obtained from each of the specific problem investigated in the upcoming chapters can be compared to, and
2. to verify the accuracy of the model developed by comparing the numerical predictions to those found in literature.

In the next section, the mechanisms of ocular heat transfer inside a normal eye are discussed. Section 2.3 presents the steps involved in the development of the human eye model that will be used in this chapter as well as in some of the later chapters. Details such as the dimensions of each region of the human eye are presented. Governing equations and boundary conditions that mathematically describe the heat flow inside the normal human eye are outlined in Section 2.4. Sections 2.5 and 2.6 highlight the values

of the thermal properties and control parameters respectively. The values used here are considered to represent the conditions of a normal human eye. The numerical scheme based on the boundary element method and the numerical results obtained are presented in Sections 2.7 and 2.8 respectively.

2.2 Ocular Heat Transfer

Heat transfer inside the human eye is driven primarily by a heat source and a heat sink. These are respectively given by the blood flow inside the eye and the exposure of the corneal surface to the environment. Despite playing an important role in the thermoregulation of the human body, metabolic heat generation does not appear to have any significant effect on the ocular heat transfer [22]. This may be due to regions such as the iris, ciliary body and choroid, i.e. regions that are metabolically active, that account for only a very small percentage of the volume of the entire eyeball.

It is well-acknowledged that blood is a major source of heat inside the human eye [31]. Blood that enters the eye is generally at a temperature that is close to that of the body core, while the surrounding ocular tissues have temperatures that are slightly lower. Given that choroidal blood flow accounts for almost 85% of the total ocular blood flow [20], it is reasonable to assume that the primary source of heat inside the human eye comes from the blood flow inside the choroid. Contributions from blood perfusion inside the iris and ciliary body are not expected to be significant since blood flow in these tissues are relatively small when compared to the choroid [11].

The corneal surface is exposed to the environment. When the ambient temperature is lower than the corneal surface temperature, a thermal gradient is created that causes heat to be transferred from the eye to the environment via convection and radiation. Cooling of the corneal surface is aided by the evaporation of tears. Blinking has been found to induce dynamic changes in the temperature on the corneal surface [68, 69]. According to Mapstone [31], blinking produces four different effects on the corneal surface. These

effects are summarized as follows.

1. a passive prevention of heat loss when eyelids are closed,
2. heat gained from the micro-blood vessels lining the conjunctiva of the eyelids,
3. spreading of warm tears during opening of eyelids and
4. an air-conditioning effect induced by the movement of eyelids.

Although the net contribution of these effects is difficult to assess, the spreading of warm tears is widely believed to be the dominant factor that induces changes in the corneal surface temperature during blinking [68, 69].

2.3 Model Development

In Chapter 1, three approaches that may be adopted when developing models of the human eye for the purpose of heat transfer studies have been introduced. Since the temperature distribution throughout the human eye is of primary concern here, the isolated model approach appears to be the best choice.

The model of the human eye is developed based on dimensions that may be found in literature [13, 15, 70]. While a three-dimensional model provides the best geometrical representation of the human eye, for computational convenience, the eye shall be assumed to be geometrically symmetrical about the pupillary axis by ignoring the optic nerve. It follows that the problem may now be formulated in the cylindrical coordinate system ($Orz\theta$) with the pupillary axis represented by the z -axis. Assuming that all the parameters inside the human eye are independent of the coordinate θ such that the temperature inside the human eye is only a function of r and z , the three-dimensional model may then be reduced into a two-dimensional one, which is now defined in the Orz coordinate system.

With reference to the Orz coordinate system, Figure 2-1 shows one half of the cross-section of the human eye in the mid-sagittal plane. The model comprises six regions, namely cornea, anterior chamber, lens, posterior chamber, vitreous and sclera, which are respectively denoted by R_1 , R_2 , R_3 , R_4 , R_5 and R_6 . The exterior boundaries of the human eye are defined by the exterior surfaces of the cornea, C_1 and sclera, C_2 . Note that in the axisymmetrical model, the axis of symmetry, which is given by the z -axis, does not form part of the boundary of the model. To obtain a complete model of the human eye, the geometry shown in Figure 2-1 may be rotated 360° about the z -axis.

Figure 2-1: Model of the human eye in the axisymmetrical coordinate system

In the model illustrated in Figure 2-1, the iris has been modeled together with the sclera as one homogeneous region due to the similarity in their thermal properties [71]. In reality, in between the sclera and the vitreous, one may find layers of the retina and choroid. For simplicity, since these layers are relatively thin, they are modeled together with the sclera as a single homogeneous region. The zonular fibres that hold the lens in place such as shown in Figure 1-1 has also been treated as part of the sclera.

The cornea is assumed to have a uniform thickness of $588\mu\text{m}$ and a diameter of 13.2mm . Variation of the corneal thickness in the actual human eye that changes from $500\mu\text{m}$ at the limbus to $600\mu\text{m}$ at the center is assumed to be too small to produce

any significant effect on the heat flow through the cornea. The radii of curvature of the anterior and posterior surfaces of the cornea are approximately 9.84 and 9.25mm respectively. A gap of $10\mu\text{m}$ separates the anterior chamber from the posterior chamber. For mathematical convenience, this gap is assumed to be non-existence, i.e. the anterior and posterior chambers are treated as separate components. The anterior chamber has a depth along the pupillary axis of 2.8mm and a diameter of 13.8mm. These dimensions are within the range of values found for a healthy adult eye [13].

The human lens is modeled based on the measurements obtained by Charles and Brown [15]. In an unaccommodated eye, the lens has a thickness of 4.2mm and a diameter of 9.8mm. The radii of curvature of the anterior and posterior surfaces are approximately 12.5 and 8mm respectively. The iris is modeled based on the dimensions of the model presented by Heys et al. [70]. It has a uniform thickness of approximately 0.4mm and a length of about 4.6mm. This produces a pupil diameter of roughly 5mm. The vitreous and sclera occupy the posterior segment of the human eye. The vitreous, which resembles roughly the shape of a sphere, has a diameter of 21mm and a depth along the pupillary axis of 17mm. The sclera encapsulates a large portion of the vitreous. It has a thickness of approximately 1mm at the posterior segment.

Dimensions of each of the ocular region are illustrated in Figure 2-2.

2.4 Mathematical Model

2.4.1 Governing equation

The human eye is assumed to be a solid such that heat is conducted inside the entire eyeball. In this preliminary investigation, the aqueous humor that fills the anterior and posterior chambers is assumed to be stagnant such that no convectonal flow occurs. Since the steady-state temperature distribution inside the human eye is of interest here, the dynamic changes in temperature induced by blinking are not considered.

Assuming that each region inside the human eye is homogeneous and thermally

Figure 2-2: Dimensions of the human eye in mm (figure not to scale)

isotropic, the steady-state heat flow with reference to the model of the human eye shown in Figure 2-1 may be expressed using the Pennes bioheat equation [72], which is given by

$$\begin{aligned} \nabla_{\text{axis}}(\kappa_i \nabla_{\text{axis}} T_i(r, z)) &= \rho_{\text{bl}} c_{\text{bl}} \varpi_{\text{bl}} (T_i(r, z) - T_{\text{bl}}) - Q_{\text{m}}, \\ &\text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \end{aligned} \quad (2.1)$$

where the first and second terms on the right hand side represent the thermal effects due to blood perfusion and metabolic activity respectively, T_i and κ_i are the temperature and thermal conductivity of region R_i respectively, ρ_{bl} , c_{bl} and ϖ_{bl} are density, specific heat and perfusion rate of blood respectively, T_{bl} is blood temperature, which is assumed to be the same as the body core temperature and Q_{m} is metabolic heat generation. Subscript ‘axis’ implies that the gradient operator is defined in the Orz coordinate system such that

$$\nabla_{\text{axis}} = \tilde{e}_r \frac{\partial}{\partial r} + \tilde{e}_z \frac{\partial}{\partial z},$$

where $\tilde{e}_r$ and $\tilde{e}_z$ are the base vectors in the polar coordinate system.

The thermal effects of blood perfusion are effective only in the region defined by the sclera (which includes the iris). Since blood flow inside the iris is relatively smaller than the blood flow inside the choroid, its contribution to the overall ocular heat transfer may be assumed to be negligible [73]. Meanwhile, heat that enters the eye from the blood flow inside the choroid may be modeled as part of the boundary condition on the surface of the sclera [63]. This will be discussed in the subsequent section. With these assumptions, the blood perfusion term in Equation (2.1) may be eliminated. Since contribution from the metabolic heat generation inside the eye is also negligible (see Section 2.2), the term Q_m may also be omitted from Equation (2.1).

Equation (2.1) thus reduces to

$$\nabla_{\text{axis}} (\kappa_i \nabla_{\text{axis}} T_i(r, z)) = 0, \text{ for } i = 1, 2, 3, 4, 5 \text{ and } 6, \quad (2.2)$$

which is essentially the steady-state heat diffusion equation.

2.4.2 Boundary conditions

To solve Equation (2.2), appropriate boundary conditions have to be specified on the exterior surfaces of the cornea, C_1 and sclera, C_2 . These boundary conditions are derived based on the anatomical and physiological observations of the human eye.

For an ambient temperature that is smaller than the corneal surface temperature, heat flows from the corneal surface to the environment via convection, radiation and tears evaporation (see Section 2.2). Mathematically, this may be written as

$$-\kappa_1 \frac{\partial T_1}{\partial n} = h_{\text{amb}} (T_1 - T_{\text{amb}}) + \varepsilon \sigma (T_1^4 - T_{\text{amb}}^4) + E_{\text{vap}} \text{ on } C_1, \quad (2.3)$$

where the first, second and third terms on the right hand side correspond to the heat loss due to convection, radiation and tears evaporation respectively, h_{amb} is the ambient convection coefficient, T_{amb} is ambient temperature, ε is emissivity on the corneal surface,

σ is Stefan-Boltzmann constant, E_{vap} is the amount of heat loss due to tears evaporation and $\partial T_1/\partial n$ is the rate of change of T_1 in the outward unit vector, normal to the external corneal surface, C_1 .

To model the thermal interaction between the blood and the eye, the approach suggested by Lagendijk [63] is adopted. In this approach, the entire human eye except for the corneal surface, is assumed to be embedded in an anatomically homogeneous surrounding that is at body core temperature. Heat transfer between the artificial surrounding and the eye may be described using a single heat transfer coefficient, such that

$$-\kappa_6 \frac{\partial T_6}{\partial n} = h_{\text{bl}}(T_6 - T_{\text{bl}}) \text{ on } C_2, \quad (2.4)$$

where h_{bl} is the heat transfer coefficient between the artificial surrounding and the human eye (also known as the blood convection coefficient), T_{bl} is the temperature of the artificial surrounding, which simulates the temperature of blood, and $\partial T_6/\partial n$ is the rate of change of T_6 in the outward unit vector, normal to the external scleroid surface, C_2 .

The boundary conditions specified on the surfaces of the cornea and sclera are illustrated in Figure 2-3.

Figure 2-3: Illustration of the boundary conditions specified on the surfaces of cornea, C_1 and sclera, C_2

To complete the formulation of the problem, the variation of temperature and heat flux at the interface between two contiguous ocular regions has to be defined. Here, the continuity principle applies, that is,

$$\begin{aligned} T_i &= T_j \text{ and,} \\ \kappa_i \frac{\partial T_i}{\partial n} &= \kappa_j \frac{\partial T_j}{\partial n}, \text{ on } I_{ij}, \end{aligned} \quad (2.5)$$

where I_{ij} denotes the interface between regions R_i and R_j (in Figure 2-1) and $\partial T_i / \partial n$ and $\partial T_j / \partial n$ are the rate of change of T_i and T_j respectively in the direction of a normal vector to the interface.

2.5 Thermal Properties

A proper selection of thermal properties is one of the criteria that determines the accuracy of the model developed. In this thesis, the thermal properties of each ocular region are obtained from data that can be found in literature. Although most of the values that are reported in literature are only estimations based on animal subjects and properties of water or saline solution, investigations carried out by other researchers in the past using these values had managed to obtain realistic ocular temperatures [22–24, 48]

Values of thermal conductivity, density and specific heat of each of the six ocular regions illustrated in Figure 2-1 are tabulated in Table 2.1 along with the references where they are obtained.

2.6 Control Parameters

This section presents values of the various parameters that are used to describe Equations (2.3) and (2.4), namely ambient temperature, ambient convection coefficient, blood temperature, blood convection coefficient and heat loss due to tears evaporation. The values presented here are treated as the control, i.e. values that represent the conditions

Table 2.1: Thermal properties of the human eye

Region	Thermal conductivity, κ ($\text{Wm}^{-1}\text{K}^{-1}$)	Density, ρ (kgm^{-3})	Specific heat, c ($\text{Jkg}^{-1}\text{K}^{-1}$)
Cornea, R_1	0.58^e	1050^a	4178^f
Anterior chamber, R_2	0.58^c	996^b	3997^g
Lens, R_3	0.40^d	1050^a	3000^d
Posterior chamber, R_4	0.58^c	996^b	3997^g
Vitreous, R_5	0.60^f	1000^f	4178^f
Sclera, R_6	1.00^b	1100^b	3180^b

^aNeelakantaswamy and Ramakrishnan [74]; ^bCicekli [71]; ^cEmery et al. [75];

^dLagendijk [63]; ^eScott [22]; ^faccepted as water; ^gaccepted as saline solution

of a normal human eye.

The ambient temperature is chosen to be 25°C based on the average temperature of an air-conditioned laboratory in Singapore. A value of $10\text{Wm}^{-2}\text{K}^{-1}$ is selected as the control for the ambient convection coefficient. This value, which represents conditions of free convection, was estimated by Emery et al. [75] based on a laminar flow over a vertical flat plate. Blood temperature is assumed to be the same as that of the body core, which for a healthy subject, is given approximately by 37°C. The value of blood convection coefficient was estimated by Lagendijk [63] to be roughly $65\text{Wm}^{-2}\text{K}^{-1}$ based on experimental data found on rabbit eyes. This value has since been used by numerous models of the human eye where reasonable predictions of the ocular temperature have been reported [22, 23, 48].

Tears evaporation rate inside a normal human eye varies between individuals. Based on the different measurements compiled by Mathers [104], values of 15.6×10^{-7} , 14.7×10^{-7} , 14.8×10^{-7} , 13.0×10^{-7} and $15.1 \times 10^{-7}\text{g}\cdot\text{cm}^{-2}\text{s}^{-1}$ have been found for a normal human eye [77–81]. These values yield an average of $14.6 \times 10^{-7}\text{g}\cdot\text{cm}^{-2}\text{s}^{-1}$, which is assumed to be the control. Assuming that the latent heat of evaporation of tears is similar to water, which is given by 2427.6kJkg^{-1} [82], the corresponding average heat loss is calculated to be 35.5Wm^{-2} . For convenience purposes, this value is rounded up to 40Wm^{-2} and is chosen as the control. This is similar to the value chosen by Scott [22].

Table 2.2 summarizes the control values chosen for this study along with the values of the corneal surface emissivity and the Stefan-Boltzmann constant. Value of the corneal surface emissivity is obtained from the estimation made by Mapstone [76].

Table 2.2: Values of the control parameters

Parameter	Value
Ambient temperature, T_{amb} ($^{\circ}\text{C}$)	25
Ambient convection coefficient, h_{amb} ($\text{Wm}^{-2}\text{K}^{-1}$)	10
Blood temperature, T_{bl} ($^{\circ}\text{C}$)	37
Blood convection coefficient, h_{bl} ($\text{Wm}^{-2}\text{K}^{-1}$)	65
Heat loss due to tears evaporation, E_{vap} (Wm^{-2})	40
Emissivity of the cornea surface, ε	0.97
Stefan-Boltzmann constant, σ ($\text{Wm}^{-2}\text{K}^{-4}$)	5.67×10^{-8}

2.7 Boundary Element Model

The numerical solution of Equation (2.2) subjected to the conditions given in Equations (2.3) to (2.5) is obtained using the boundary element method. To do so, the integral representation of Equation (2.2) has to be derived. Since the detailed steps involved in the derivation of the boundary integral equation can be found in most of the boundary element method textbooks available in literature, they shall not be repeated here. Instead, one may refer to Brebbia et al. [55], Wrobel [83] and Ang [84] for more information.

Following the procedures outlined by Brebbia et al. [55], the integral representation of Equation (2.2) is given by

$$\begin{aligned}
 \lambda(\xi_i, \eta_i)T_i(\xi_i, \eta_i) &= \int_{\Gamma_i} T_i(r, z) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z) \\
 &\quad - \int_{\Gamma_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \frac{\partial}{\partial n} [T_i(r, z)] \cdot r \cdot ds(r, z) \\
 &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6,
 \end{aligned} \tag{2.6}$$

where Γ_i denotes the boundary of the region R_i , $ds(r, z)$ denotes the length of an infinitesimal portion of curve Γ_i , $\lambda(\xi_i, \eta_i)$ is a geometrical coefficient such that $\lambda(\xi_i, \eta_i) = 1$, if (ξ_i, η_i) lies inside the region R_i and $\lambda(\xi_i, \eta_i) = \frac{1}{2}$, if (ξ_i, η_i) lies on a smooth part of Γ_i , and Φ_{axis} and $\partial\Phi_{\text{axis}}/\partial n$ are the axisymmetrical fundamental solution of the Laplace equation and its normal derivative respectively, which are given by

$$\begin{aligned}\Phi_{\text{axis}}(r, z; \xi, \eta) &= -\frac{K(m(r, z; \xi, \eta))}{\pi\sqrt{a(r, z; \xi, \eta) + b(r; \xi)}}, \\ \frac{\partial}{\partial n}[\Phi_{\text{axis}}(r, z; \xi, \eta)] &= -\frac{1}{\pi\sqrt{a(r, z; \xi, \eta) + b(r; \xi)}} \\ &\times \left\{ \frac{n_r}{2r} \left[\frac{\xi^2 - r^2 + (\eta - z)^2}{a(r, z; \xi, \eta) - b(r; \xi)} E(m(r, z; \xi, \eta)) \right. \right. \\ &\quad \left. \left. - K(m(r, z; \xi, \eta)) \right] \right. \\ &\quad \left. + n_z \frac{\eta - z}{a(r, z; \xi, \eta) - b(r; \xi)} E(m(r, z; \xi, \eta)) \right\}, \quad (2.7)\end{aligned}$$

where n_r and n_z are the components of the outward unit normal vector on Γ_i in the r and z direction respectively, K and E denote the complete elliptic integral of the first and second kind respectively as given by Abramowitz and Stegun [85] and the variables m , a and b are expressed as

$$m(r, z; \xi, \eta) = \frac{2b(r; \xi)}{a(r, z; \xi, \eta) + b(r; \xi)},$$

$$a(r, z; \xi, \eta) = \xi^2 + r^2 + (\eta - z)^2,$$

$$b(r; \xi) = 2r\xi.$$

Steps involved in the derivation of Equation (2.7) may be found in the book by Brebbia et al. [55].

For a numerical procedure based on Equation (2.6), the boundary Γ_i is discretized into N_i straight line segments known as boundary elements, such that $\Gamma_i = \Gamma_i^{(1)} \cup \Gamma_i^{(2)} \dots$

$\Gamma_i^{(N_i-1)} \cup \Gamma_i^{(N_i)}$. Suppose that the starting and ending points of each boundary element, $\Gamma_i^{(k)}$ are denoted by $(r_i^{(k)}, z_i^{(k)})$ and $(r_i^{(k+1)}, z_i^{(k+1)})$ respectively. Two points on $\Gamma_i^{(k)}$ denoted by $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ may then be selected, such that

$$\begin{aligned} (\xi_i^{(k)}, \eta_i^{(k)}) &= (r_i^{(k)}, z_i^{(k)}) + \tau(r_i^{(k+1)} - r_i^{(k)}, z_i^{(k+1)} - z_i^{(k)}), \\ (\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)}) &= (r_i^{(k)}, z_i^{(k)}) + (1 - \tau)(r_i^{(k+1)} - r_i^{(k)}, z_i^{(k+1)} - z_i^{(k)}), \end{aligned} \quad (2.8)$$

where τ is a pre-defined number, which has a value in the range of $0 < \tau < \frac{1}{2}$. An optimal value of τ that produces the least numerical error depends on the type of problem solved and the level of boundary discretization used [84]. For the purpose of obtaining the results presented in Section 2.8, the value of τ is taken here to be $\frac{1}{4}$.

With the boundary nodes $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ selected, variation of temperature and heat flux across each boundary element may now be approximated using linear interpolation functions, such that

$$T_i(r, z) \approx \varphi_1(r, z)T_i^{(k)} + \varphi_2(r, z)T_i^{(k+N_i)}, \text{ for } (r, z) \in \Gamma_i^{(k)}, \quad (2.9)$$

and

$$\frac{\partial}{\partial n} [T_i(r, z)] \approx \varphi_1(r, z)q_i^{(k)} + \varphi_2(r, z)q_i^{(k+N_i)}, \text{ for } (r, z) \in \Gamma_i^{(k)}, \quad (2.10)$$

where $\varphi_1(r, z)$ and $\varphi_2(r, z)$ are linear interpolation functions, $T_i^{(k)}$ and $T_i^{(k+N_i)}$ are temperatures at nodes $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ respectively and $q_i^{(k)}$ and $q_i^{(k+N_i)}$ are heat flux at nodes $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ respectively. Details on the linear interpolation functions, $\varphi_1(r, z)$ and $\varphi_2(r, z)$ may be found in Appendix A.

Note that the linear approximations in Equations (2.9) and (2.10) do not guarantee continuity of $T_i(r, z)$ and $\partial T_i(r, z)/\partial n$ between two neighbouring elements. This is attributed to the selection of boundary nodes that are placed inside each boundary element. Boundary elements that are based on such approximations are known as the discontinuous linear elements [86].

Substituting Equations (2.9) and (2.10) into (2.6) yields

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) T_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{F}_3^{(k)}(\xi_i, \eta_i) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{F}_4^{(k)}(\xi_i, \eta_i) T_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{F}_1^{(k)}(\xi_i, \eta_i) q_i^{(k)} - \sum_{k=1}^{N_i} \mathcal{F}_2^{(k)}(\xi_i, \eta_i) q_i^{(k+N_i)} \\
 &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \tag{2.11}
 \end{aligned}$$

where

$$\begin{aligned}
 \mathcal{F}_1^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_1(r, z) \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \cdot r \cdot ds(r, z), \\
 \mathcal{F}_2^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_2(r, z) \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \cdot r \cdot ds(r, z), \\
 \mathcal{F}_3^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_1(r, z) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z), \\
 \mathcal{F}_4^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_2(r, z) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z). \tag{2.12}
 \end{aligned}$$

The integrals in Equation (2.12) can be evaluated numerically using the Gaussian quadrature.

By letting (ξ_i, η_i) be given by $(\xi_i^{(n)}, \eta_i^{(n)})$, for $n = 1, 2, \dots, 2N_i - 1, 2N_i$, one obtains

$$\begin{aligned}
 \lambda_i^{(n)} T_i^{(n)} &= \sum_{k=1}^{N_i} \mathcal{F}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{F}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) T_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{F}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) q_i^{(k)} - \sum_{k=1}^{N_i} \mathcal{F}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) q_i^{(k+N_i)} \\
 &\quad \text{for } n = 1, 2, \dots, 2N_i - 1, 2N_i \text{ and} \\
 &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \tag{2.13}
 \end{aligned}$$

where $\lambda_i^{(n)} = \lambda(\xi_i^{(n)}, \eta_i^{(n)})$ and $T_i^{(n)} = T_i(\xi_i^{(n)}, \eta_i^{(n)})$.

Collocations of $(\xi_i^{(n)}, \eta_i^{(n)})$ at all the $2N_i$ boundary nodes in each of the six ocular region yield six sets of system of algebraic equations. Each set of equations may be related to the other by using the continuity condition given in Equation (2.5). This results in a global system of algebraic equations that is block-banded, where each block corresponds to the set of equations generated for each ocular region. When $(\xi_i^{(n)}, \eta_i^{(n)})$ is collocated at the exterior boundaries, i.e. $C_1 \cup C_2$, the unknown heat flux may be expressed in terms of the unknown temperatures using the boundary conditions given in Equations (2.3) and (2.4).

It follows that a system of algebraic equation that consists of $2 \times (N_1 + N_2 + N_3 + N_4 + N_5 + N_6)$ equations and $2 \times (N_1 + N_2 + N_3 + N_4 + N_5 + N_6)$ unknowns can be set up from Equation (2.13). The system of equations may be solved for the unknown temperatures at the exterior boundaries $C_1 \cup C_2$, and the unknown temperatures and heat flux at the interface between two matching regions.

2.7.1 Treatment of non-linear boundary condition

In most of the studies carried out in the past, the non-linear radiation term appearing in the boundary condition on the corneal surface is usually ignored or approximated using a linear expression. In these models, the system of linear algebraic equations assembled presents no difficulty and can be solved directly for the unknowns T_i at all exterior boundaries, $C_1 \cup C_2$ and the interfaces, and the unknown $\partial T_i / \partial n$ at the interfaces. If the radiation term is considered, the non-linearity may be easily dealt with using a simple iterative scheme that basically solves T_i through consecutive approximations of $T_i^{(m-1)}$, where $m = 1, 2, 3, \dots$. By making an initial guess ($m = 1$) of the temperature at C_1 say, $T_1^{(0)} = T_{\text{amb}}$, and substituting this in place of the non-linear term in Equation (2.3), one arrives at

$$-\kappa_1 \frac{\partial T_1}{\partial n} = h_{\text{amb}} (T_1 - T_{\text{amb}}) + \varepsilon \sigma \left\{ \left[T_1^{(0)} \right]^4 - T_{\text{amb}}^4 \right\} + E_{\text{vap}}, \quad (2.14)$$

which is now a linear approximation of the unknown T_1 . By carrying out the boundary discretization as described earlier, a system of linear algebraic equation can be set up to solve for the unknown $T_i^{(1)}$ and $\partial T_i^{(1)}/\partial n$ at the exterior boundaries $C_1 \cup C_2$ and the interfaces. If the same procedure is repeated for successive approximations $T_i^{(1)}$, $T_i^{(2)}$, $T_i^{(3)}$, ..., higher and higher order approximations of T may be obtained until the convergence criteria

$$\left| T_1^{(m)} - T_1^{(m-1)} \right| < \delta, \quad (2.15)$$

where δ is a pre-selected small positive number, is satisfied. For the purpose here, δ is chosen to be 1×10^{-5} .

2.8 Numerical Results

2.8.1 Mesh-independent study

A mesh-independent study is carried out to determine the number of boundary elements that is necessary to produce numerical results that are mesh insensitive. When discretizing the boundaries of the solution domain, steps are taken to ensure that regions that are thin, such as the cornea and the posterior chamber, are sufficiently refined. This is crucial in order to guarantee that the temperature gradients over these thin regions are modeled accurately. Seven sets of boundary meshes that vary from coarse to fine are examined. The total number of boundary elements used in each set is specifically given by 63, 103, 152, 202, 243, 290 and 336, which are denoted by M_1 , M_2 , M_3 , M_4 , M_5 , M_6 and M_7 respectively. Temperature at the center of the corneal surface, i.e. $(r, z) = (0, 0)$, is used to check for the convergence of the numerical solution.

Figure 2-4 shows the results obtained from the mesh-independent study. The bars indicate the temperature at the center of the corneal surface obtained for each set of mesh. The line plot shows the percentage difference of the numerical result between each

consecutive set of mesh, which is calculated using

$$\% \text{ difference} = \frac{|T_1^{(m)}(0,0) - T_1^{(m-1)}(0,0)|}{T_1^{(m)}(0,0)} \times 100\%,$$

for $m = 1, 2, 3, 4, 5, 6$ and 7 ,

where $T_1^{(m)}$ denotes the temperature calculated at mesh M_m .

From Figure 2-4, it is apparent that the numerical solution may be considered to have achieved convergence as the number of boundary elements increases. It is thus, reasonable to conclude that the numerical scheme developed in the previous section produces solutions that are mesh-independent.

Figure 2-4: Results obtained from mesh-independent study

2.8.2 Results and analysis

Figure 2-5 shows the temperature distribution inside the human eye obtained using the boundary element model developed in Sections 2.4 to 2.7. Isotherms are defined by the

solid lines across the human eye. Temperatures at the corneal surface appear to be the coolest. The ocular regions get progressively warmer towards the posterior segment of the eye. Temperatures at points closer to the surface of the sclera approach that of the body core, i.e. 37°C . From a biological standpoint, such an observation is to be expected, since heat is transferred by blood to the eye through the exterior surfaces of the sclera.

Figure 2-5: Temperature profile inside the normal human eye

Temperature at the center of the corneal surface is calculated to be approximately 34.19°C , which happens to be the point inside the human eye with the lowest temperature. This is not surprising, given that the center of the corneal surface is furthest from the heat source inside the eye, i.e. the blood flow on the surface of the sclera. The temperature obtained at the center of the corneal surface is compared in Table 2.3 with the values obtained by other researchers using IR thermography. The numerical prediction is found to lie within the range of the experimentally obtained values ($32.9\text{--}34.8^{\circ}\text{C}$). This implies good agreement between the numerical prediction and the experimentally obtained results. Discrepancies may be due to differences in the control parameters such as environmental condition and individual variation.

Table 2.3: Values of temperature at the center of the corneal surface

Author(s)	Temperature ($^{\circ}\text{C}$)
Present model	34.19
Mapstone [76]	34.80
Rysä and Sarvaranta [87]	34.80
Aliò and Padron [88]	32.90
Efron et al [68]	34.30
Morgan et al [7]	33.50
Girardin et al [89]	33.70
Gugleta et al [92]	33.65
Craig et al [92]	33.82
Purslow et al [92]	35.00

To further validate the numerical results obtained from the present model, the temperature at the center of the corneal surface is compared to the predictions obtained by other researchers using various numerical models. This is tabulated in Table 2.4. There appears to be reasonable agreement between the results obtained from the current study and the other models in literature. The temperatures obtained by Ridouane and Campo [24] and Cvetković et al. [50] using two-dimensional models are smaller than the other temperatures presented in Table 2.4. This is only to be expected since a two-dimensional model generally underestimates the heat flow inside the actual eye.

From Table 2.4, it is also found that the temperature calculated from the present model is slightly warmer than the values obtained by other researchers. This may be attributed to factors such as the differences in the geometry of the models developed and the values of thermal properties specified for each region inside the human eye model. In previous models, the thermal conductivities of the iris and sclera were assumed to be the same as the anterior chamber, which is given by $0.58\text{Wm}^{-1}\text{K}^{-1}$. In the present study, thermal conductivities of these regions are chosen to be $1\text{Wm}^{-1}\text{K}^{-1}$. This is based on the data given by Cicekli [71], which is almost twice the thermal conductivity of the anterior chamber. A larger thermal conductivity encourages more heat to be conducted through these regions, thus increasing the temperature of the surrounding ocular tissues.

Figure 2-6 plots the variation of the ocular temperature along the pupillary axis. For

Table 2.4: Numerical predictions of the ocular surface temperature made by previous investigators

Author(s)	Model	^a Method	Corneal surface temperature (°C)
Present model	Axisymmetric	BEM	34.19
Lagendijk [63]	Axisymmetric	FDM	34.2
Scott [22]	Axisymmetric	FEM	33.3
Amara [23]	Axisymmetric	FEM	33.7
El-Ridouane and Campo [24]	Two-dimensional	FVM	30.0
Cvetković et al [50]	Two-dimensional	FEM	30.0

^aBEM: Boundary element method; FDM: Finite difference method;

FEM: Finite element method; FVM: Finite volume method

comparison purposes, data extracted from the results presented by Scott [22] and Amara [23] is also shown. The vertical lines in Figure 2-6 separate the pupillary axis into regions occupied by the cornea, anterior chamber, lens, vitreous and sclera. These lines apply only to the results obtained from the present model however. At the region defined by the lens, the thermal gradient appears to be slightly greater than those observed in other parts of the human eye. Similar observations may be found in the lines plotted from the data presented by Scott [22] and Amara [23]. The larger thermal gradient inside the lens may be due to its thermal conductivity, which is the smallest among the ocular regions. Good qualitative agreement between the profiles obtained from the present model and the models proposed by Scott [22] and Amara [23] is observed. The higher temperature at the anterior segment observed from the present model may be explained by the larger thermal conductivities specified for the iris and sclera, as previously discussed.

Figure 2-7 plots the differences in the temperature between various points along boundary C_1 and the center of the corneal surface. The mirror image about the z -axis is also displayed for a clearer illustration. As a comparison, the experimental data

Figure 2-6: Temperature distribution along the pupillary axis

measured by Efron et al. [68] using IR thermography is also shown in Figure 2-7. From Figure 2-7, one may observe that the temperature gradient across the corneal surface for both the present model and the experimental result share the same thermal characteristics. A larger thermal gradient is predicted by the present model however. Generally, the plot obtained from the present model may be characterized as being less ‘widespread’ than the one obtained from the experimental data.

The temperature at the limbus of the present model is estimated to be approximately 1.4°C warmer than the temperature at the center of the corneal surface. This is greater than the observation made by Efron et al. [68] using IR thermography, where the limbus was found to be about 0.4°C warmer than the center of the corneal surface. Nevertheless, it has to be pointed out that the temperature measured by Efron et al. [68] is relatively smaller than the observations made by other researchers. According to Purslow and Wolffsohn [8], the limbus can be as high as 1°C warmer than the temperature at the center of the corneal surface.

Figure 2-7: Temperature difference between points along the corneal surface and the center of the cornea

2.9 Discussion

One of the main features of the model in the present study that is different from most of the other models presented in literature, is the inclusion of the radiation term as part of the boundary condition specified on the corneal surface. While some researchers have acknowledged the significance of heat radiation by introducing an additional heat transfer coefficient to account for the heat loss due to radiation [22, 48, 75, 93], others have chosen to ignore this term [50, 63]. From the boundary condition specified on the corneal surface (see Equation (2.3)), the heat flux due to radiation, q_{rad} is simply given by the expression

$$q_{\text{rad}} = \varepsilon \sigma (T_1^4 - T_{\text{amb}}^4), \quad (2.16)$$

where T_1 is the temperature at the corneal surface. Assuming a mean corneal surface temperature of 34°C and using the values of ε , σ and T_{amb} listed in Table 2.2, the heat

flux due to radiation is calculated to be approximately 55Wm^{-2} .

Similarly, from Equation (2.3), the heat loss due to convection, q_{conv} can be described using

$$q_{\text{conv}} = h_{\text{amb}} (T_1 - T_{\text{amb}}). \quad (2.17)$$

Using values of h_{amb} and T_{amb} listed in Table 2.2 and a mean corneal surface temperature of 34°C , the value of q_{conv} is calculated to be 90Wm^{-2} . By comparing the values of q_{rad} and q_{conv} calculated, the heat loss due to convection appears to be only 1.6 times the amount due to heat radiation. This implies that the effects of radiation are not negligible.

The emissivity of the corneal surface used in this study has been selected to be 0.97. This value is obtained from the estimation carried out by Mapstone [76]. According to Mapstone [76], the emissivity of the corneal surface ranges from 0.97 to 1. By using Equation (2.16), changes in the corneal surface emissivity from 0.97 to 1 are found to yield values of q_{rad} that range from 55.1 to 56.8Wm^{-2} . This shows a variation of less than 5%. Hence, it may be concluded that the choice of 0.97 as the emissivity of the corneal surface introduces no significant error to the analysis carried out in this study.

In the present model, the blood flow inside the iris have been assumed to have insignificant effects on the ocular heat transfer. This assumption is made based solely on the magnitude of blood flow inside the iris, which has been found to be relatively smaller than the blood flow inside the choroid [73]. If the effects of blood perfusion inside the iris are taken into consideration, a warmer ocular temperature distribution, particularly at the anterior segment of the human eye, is expected. The significance of the blood perfusion inside the iris on the ocular heat transfer is open for future studies.

The tendency of the present model to produce temperatures that are higher than the experimentally obtained temperatures is evident in some of the cases presented in Table 2.3. This may be explained by the way the heat transfer between the blood and the eye is modeled. In the present study, the human eye has been assumed to be embedded in an anatomically homogeneous surrounding that is at a constant body core temperature. Heat transfer between the artificial surrounding and the eye is modeled using a constant

heat transfer coefficient. This generally assumes the blood flow inside the choroid to be uniform, which in reality, is not true. In the actual eye, blood enters the eye via the ophthalmic artery, which then branches into a network of arteries that stretches across the layer of choroid before entering the iris via the posterior ciliary arteries. Naturally, the blood flow rate inside the ophthalmic artery is the strongest. As the ophthalmic artery separates into smaller blood vessels and into the posterior ciliary arteries, the flow rate decreases [11]. The different blood flow rates at different segments of the scleroid surface yield a non-uniform heat transfer coefficient. At present, the effects of non-uniform heat transfer coefficient remain difficult to assess. Further investigations may be carried out in future to improve our understanding of this issue.

A network of veins that drains the blood from the eye interweave with the arteries inside the choroidal layer. Since temperature of the venous blood is smaller than the arterial blood [72], a thermal gradient is created between the arterial and venous blood. This induces counter-current heat transfer, which have not been considered in the present study. Without taking into account the effects of counter-current heat transfer and the heterogeneity of the capillary bed inside the choroid, the present model may have overestimated the heat transfer between blood flow and eye. Nonetheless, accounting for the counter-current heat transfer may not be feasible due to the complexity of the problem. Perhaps one of the better option to model the effects of ocular blood flow is to use the discrete vasculature (DIVA) model proposed by Flyckt et al. [94]. In the DIVA model, the blood vessels inside the choroid are constructed as part of the solution domain, thus giving rise to an accurate representation of the blood flow inside the eye. Such models however, are extremely complicated and may require enormous computational memory.

An important feature that has not been considered in the present study is the effects of eyelids. In the human eye, eyelids cause the isotherms on the corneal surface to have a profile that is slightly elliptical, with the major axis oriented along the lateral geometrical center of the cornea [7,68]. This is shown in Figure 2-8. According to Efron et al. [68], the elliptical isotherms are caused by the naturally elliptical shape of the palpebral aperture

Figure 2-8: Isotherms of the corneal surface in an actual human eye and a human eye model

produced by the eyelids. Without the eyelids, the elliptical pattern disappears and the isotherms take a profile that is more circular [7]. The temperature distribution of the human eye in the mid-sagittal plane has been shown in Figure 2-5. Since the model is axisymmetrical, it is possible to obtain a surface plot of the corneal surface by revolving the temperature plot in Figure 2-5, 360° about the pupillary axis. This is shown in Figure 2-8.

The absence of eyelids from the present model also affects the accuracy of the boundary condition specified on the corneal surface. Cooling on the corneal surface via convection, radiation and tears evaporation have been assumed to take place at the entire surface of the cornea. In reality, not all of the corneal surface is exposed to the environment. The palpebral aperture created by the eyelids shields a small portion of the top and bottom surfaces of the cornea from the environment. Without considering this effect, the boundary condition specified using Equation (2.3) may have overestimated the amount of heat loss from the corneal surface. It may also be possible for the micro-blood vessels lining the inner conjunctiva of the eyelids to induce heat transfer from blood to the cornea in a manner similar to the choroidal blood flow. Nonetheless, the significance

of the blood flow inside the eyelids in ocular heat transfer remains speculative and more investigations are required before a definite conclusion can be drawn.

Blinking plays a part in governing the temperature distribution on the corneal surface. According to Purslow and Wolffsohn [69], blinking produces a dynamic response in the corneal surface temperature. The effects of blinking on the corneal surface temperature, as deduced by Mapstone [31], have been mentioned in Section 2.2. Using IR thermography, Efron et al. [68] discovered that the process of blinking over an extended period of time causes a cyclic variation of $\pm 0.033^\circ\text{C}$ on the corneal surface temperature. The dynamic changes in the corneal surface temperature immediately after a blink were investigated by Purslow and Wolffsohn [95] using a more advanced system of IR thermography. A mean decrease of approximately 0.9°C during post-blink was found at the center of the corneal surface. It was suggested that the changes in the temperature profile on the corneal surface after each blink reflect the flow of tears as it is being spread across the corneal surface [95].

Of the four possible effects of blinking hypothesized by Mapstone [31] (see Section 2.2), the spreading of warm tears has been suggested to be the primary factor that produces changes to the corneal surface temperature [95]. To include such thermal effect into the present model, one may need to have a precise knowledge on the deposition and thinning of the tear film during blinking [96]. This is not a straightforward task. The prevention of heat loss during the period when the eyelids completely cover the eye may be simulated by specifying an insulated boundary condition on the corneal surface. Alternatively, one may choose to replicate the heat flow from the blood inside the conjunctiva of the eyelids to the corneal surface by specifying a convective boundary condition such as the one used for describing the heat exchange on the surface of the sclera. These approaches however, are mere suggestions and further developments are necessary to determine the feasibility of the aforementioned methodology.

Perhaps the best way to model the thermal effects of blinking at present, is to consider the average frequency and the total duration of blinking during waking period when the

eyelids completely covers the corneal surface. Blinking may then be incorporated into the model by specifying a smaller percentage of heat transfer from the corneal surface to the environment. This is to account for the prevention of heat loss when the eyelids are closed during blinking [48]. Nonetheless, this approach considers only the effects of blinking over an extended period and does not model the dynamic changes in the corneal temperature during post-blink.

2.10 Concluding Remarks

A model of the human eye has been successfully developed to predict the temperature distribution inside the eye during normal ocular condition. Although the human eye is essentially three-dimensional, it is possible to reduce it into a two-dimensional problem defined in the Orz coordinate system by ignoring the optic nerve and assuming the geometry of the human eye to exhibit axisymmetrical characteristics. This assumption remains valid as long as the governing equation and the boundary conditions that describe the heat transfer inside the eye are also axisymmetrical. The model of the human eye has been developed based on the dimensions that can be found in literature. Efforts have been made to ensure that the geometrical shape of the model resembles closely the anatomical structure of the actual human eye. The bioheat equation has been adopted to describe the heat flow inside the human eye. As a consequence of some of the assumptions made, the final expression used essentially becomes the steady-state heat diffusion equation. Boundary conditions that are specified at the exterior surfaces of the cornea and sclera have been derived based on the anatomical and physiological observations of the actual human eye.

To facilitate with the objective of obtaining temperatures that represents the conditions of a normal human eye, thermal properties of each ocular region and values of control parameters such as ambient convection coefficient, blood convection coefficient and tears evaporation rate that are practically realistic, have been selected. Using these

values, the temperatures obtained from the numerical model have been found to lie within the range of the numerically and experimentally obtained temperatures reported in literature. The results obtained in this chapter are established as a baseline, where results obtained for each problem in subsequent chapters are compared to and analyzed.

Chapter 3

Sensitivity Analysis

3.1 Introduction

In Chapter 2, a model of the human eye has been successfully developed to simulate the ocular temperature distribution. Investigations are carried out using an axisymmetrical boundary element analysis. Values of thermal properties and control parameters that are regarded as representing the conditions inside a normal human eye have been used. Under these normal circumstances, a temperature of 34.19°C at the center of the corneal surface has been found. In this chapter, the boundary element model is used to carry out sensitivity analysis to investigate how changes in some of these thermal properties and control parameters may affect the temperature distribution inside the human eye. The results obtained from this study may provide a useful insight on how the temperature inside the human eye may change, should any of the thermal properties and control parameters vary from those presented in Chapter 2.

Various factors are known to affect the temperature distribution inside the human eye. These factors may be categorized into three groups, namely environmental conditions, individual variations and physiological factors. Parameters associated with environmental conditions include ambient temperature, presence of air draft (wind) and humidity. In the present analysis, only the effects of ambient temperature and the presence of air

draft are investigated. Effects of humidity are not considered due to the difficulty in incorporating the effects into the present model. Moreover, Schwartz [97] discovered from an experimental study that humidity does not have a strong influence on the ocular temperature.

Parameters affiliated with individual variations include the shape of the cornea, such as thickness and curvature, gender and left or right eye. Experimental studies in the past had shown that the shape of the cornea has no significant effect on the ocular temperature distribution [7, 98, 99]. Likewise, differences that are not statistically significant have been observed between the left and right eyes and between male and female subjects [7, 31, 88, 100]. These parameters are thus, not considered in the present study.

Body temperature, blood convection coefficient and tears evaporation rate are parameters that concern the physiological factors. The effects of these parameters shall be examined here. Additionally, effects of the changes in lens thermal conductivity are also investigated for reasons that will be discussed subsequently.

Based on the aforementioned, six parameters are investigated in the sensitivity analysis carried out in this chapter. They are ambient temperature, presence of air draft, body temperature, blood convection coefficient, tears evaporation rate and lens thermal conductivity. To carry out the sensitivity analysis, values of each of these six parameters are varied from the control (see Tables 2.1 and 2.2) based on data that may be found in literature. Investigations are performed numerically using the model of the human eye developed in Chapter 2.

Observations are made at six points along the pupillary axis. These points, are denoted by O, A, B, C, D and E such as shown in Figure 3-1, are specifically given by the coordinates $(0, 0)$, $(5.88 \times 10^{-4}, 0)$, $(0.0034, 0)$, $(0.0076, 0)$, $(0.0244, 0)$ and $(0.0254, 0)$ respectively. For each parameter examined, values of the other parameters are retained at the control level. In the results tabulated in Tables 3.1 to 3.7, numbers in **bold** represent temperatures when all parameters are at the control level.

Figure 3-1: Six points selected along the pupillary axis

3.2 Effects of Ambient Temperature, T_{amb}

In Chapter 2, a control value of 25°C has been specified as the control to represent the ambient temperature of a typical laboratory condition in Singapore. To investigate how the human eye responds towards changes in the environmental temperature, four different values, namely 15, 20, 30 and 35°C are considered. These temperatures are generally values at 60, 80, 120 and 140% of the control temperature respectively. It is also of interest to examine the temperature inside the human eye during conditions of cold stress [87]. For this purpose, simulation is carried out for the case when the ambient temperature is at -15°C [87]. Table 3.1 tabulates the temperatures at each of the six pre-selected points along the pupillary axis that are obtained for each set of ambient temperature investigated.

Table 3.1: Effects of ambient temperature on the pupillary axis

T_{amb} (°C)	Temperature (°C)					
	O	A	B	C	D	E
-15	27.11	27.79	30.55	34.11	36.61	36.62
15	32.33	32.65	33.95	35.64	36.82	36.82
20	33.25	33.51	34.55	35.91	36.85	36.86
25	34.19	34.39	35.17	36.18	36.88	36.89
30	35.15	35.28	35.79	36.46	36.93	36.93
35	36.12	36.18	36.43	36.75	36.96	36.97

From Table 3.1, it appears that temperatures at the anterior segment of the human eye (O-C) are strongly affected by the changes in the ambient temperature. Temperature changes at the posterior segment are less significant. Generally, temperatures inside the human eye are found to increase with ambient temperature. This may be mathematically explained by the boundary condition specified at C_1 , which is given in Equation (2.3). When ambient temperature increases, less heat is being transferred away from the corneal surface due to the decreasing thermal gradient between the eye and the environment.

Based on the measurements carried out on rabbits, Schwartz [97] found a change of 0.23°C on the corneal surface for every 1°C change in ambient temperature. Mapstone [31] and Horven [100] who carried out similar investigations on human eyes reported a change of 0.15 and 0.37°C respectively for every 1°C change in ambient temperature. Interpolating the results given in Table 3.1, a change of 1°C in the ambient temperature is found to induce a change of approximately 0.19°C at the corneal surface. This is well within the range of the experimentally obtained values.

During cold stress, temperature at the center of the corneal surface is found to decrease to 27.11°C . This indicates a drop of about 7°C from the control temperature. For the same ambient temperature, Rysä and Sarvaranta [87] found a drop of 4°C based on measurements carried out on human eyes. A larger drop in temperature in the present model is only to be expected since the effects of thermoregulation such as vasoconstriction and shivering when the human body is subjected to low ambient temperature conditions have not been considered.

3.3 Effects of Ambient Convection Coefficient, h_{amb}

Changes in the ambient convection coefficient may be used to describe the presence of air drafts on the corneal surface. A larger ambient convection coefficient typically implies a stronger air draft. Assuming that the convection coefficient across the corneal surface can be represented by the coefficient across a vertical flat plate (for a human in standing

position) [75], the ambient convection coefficient may be related to the velocity of air flow by the following mathematical expression [82]:

$$h_{\text{amb}} = 0.664 \cdot Pr^{\frac{1}{3}} \cdot \left[\frac{\rho_{\text{air}} L_c}{\mu_{\text{air}}} \right]^{\frac{1}{2}} \cdot \sqrt{u_{\infty}}, \quad (3.1)$$

where Pr is the Prandtl number of air, which is given by 0.71 at 25°C, ρ_{air} and μ_{air} are the density and dynamic viscosity of air, which are respectively given by 1.16kgm^{-3} and $1.85 \times 10^{-5}\text{Nsm}^{-2}$ at 25°C, L_c is the characteristic length, which is selected to be the same as the diameter of the cornea, i.e. 0.0132m and u_{∞} is velocity of the air flow. To investigate the effects of air drafts, five different values of air flow velocity are considered. These values are given by 0, 1.25, 2.5, 3.75 and 5ms^{-1} [101]. The corresponding values of ambient convection coefficient calculated using Equation (3.1) are approximately given by 0, 20, 30, 35 and $40\text{Wm}^{-2}\text{K}^{-1}$ respectively. A value of $20\text{Wm}^{-2}\text{K}^{-1}$ represents free convection while values of 30, 35 and $40\text{Wm}^{-2}\text{K}^{-1}$ depict forced convection [82].

Table 3.2 tabulates the temperatures at points O, A, B, C, D and E for the various ambient convection coefficients investigated. A larger ambient convection coefficient (air flow velocity) is found to produce a cooler ocular temperature distribution. Again, it is observed that only the temperatures at the anterior segment (O-C) are severely affected by the changes in the ambient convection coefficient.

Table 3.2: Effects of ambient convection coefficient on the pupillary axis

h_{amb} ($\text{Wm}^{-2}\text{K}^{-1}$)	Temperature ($^{\circ}\text{C}$)					
	O	A	B	C	D	E
0	35.46	35.57	36.00	36.56	36.94	36.94
10	34.19	34.39	35.17	36.18	36.88	36.89
20	33.16	33.42	34.48	35.87	36.84	36.85
30	32.31	32.63	33.91	35.61	36.81	36.82
35	31.94	32.28	33.66	35.50	36.79	36.80
40	31.60	31.96	33.43	35.39	36.78	36.79

Temperatures at the center of the corneal surface are compared in Table 3.3 with the results obtained by Rosenbluth and Fatt [101] based on experimental and numerical

investigations carried out on rabbits. The results obtained from the present model appear to be in good agreement with those obtained by Rosenbluth and Fatt [101]. It is observed that the temperatures obtained experimentally (via contact thermometry) are slightly smaller than those predicted using numerical models. This may be attributed to heat loss from the corneal surface via the measuring probe, which causes the measured temperature to be smaller than the actual value [102].

Table 3.3: Comparisons of results obtained for the ambient convection coefficient

h_{amb} ($\text{Wm}^{-2}\text{K}^{-1}$)	Present model ($^{\circ}\text{C}$)	*Experimental value ($^{\circ}\text{C}$)	*Numerical value ($^{\circ}\text{C}$)
0	35.46	35.71	35.00
20	33.16	32.57	33.25
30	32.31	31.29	32.38
35	31.94	30.57	31.75
40	31.60	30.00	31.44

*Data found by Rosenbluth and Fatt [101]

3.4 Effects of Body Temperature, T_{bl}

Temperature of blood entering the eye has been assumed to be the same as the temperature of the body core. The temperature of a healthy human body is generally accepted to be 37°C . This is chosen in Chapter 2 to be the control. Abnormal physiological conditions such as fever may increase the temperature inside the human body. To examine the thermal effects of different body temperatures on the human eye, values of body temperature of 37.5 , 38 and 38.5°C are considered. For a more complete study, body temperatures that are lower than the control are also considered. For this purpose, values of 36 and 36.5°C are chosen. Numerically predicted temperatures at points O, A, B, C, D and E are tabulated in Table 3.4.

Significant variation in the human eye temperature is found when temperature of the human body changes. This is observed at all the six points along the pupillary axis. Based on the data presented in Table 3.4, an increase of 1°C in the body temperature is

Table 3.4: Effects of body temperature on the pupillary axis

T_{bl} ($^{\circ}\text{C}$)	Temperature ($^{\circ}\text{C}$)					
	O	A	B	C	D	E
36.0	33.38	33.57	34.30	35.24	35.89	35.90
36.5	33.79	33.98	34.73	35.71	36.39	36.40
37.0	34.19	34.39	35.17	36.18	36.88	36.89
37.5	34.59	34.79	35.60	36.65	37.38	37.39
38.0	34.99	35.20	36.04	37.12	37.88	37.89
38.5	35.39	35.61	36.47	37.60	38.37	38.38

found to produce an increase of 0.8°C at the corneal surface. This is rather close to the experimental results obtained by Horven [100] (0.93°C per 1°C increase in body temperature) and Purslow and Wolffsohn [69] (0.98°C per 1°C increase in body temperature).

3.5 Effects of Blood Convection Coefficient, h_{bl}

Blood convection coefficient is related to the blood flow inside the choroid. A larger blood convection coefficient implies a stronger ocular blood flow. In Chapter 2, a value of $65\text{Wm}^{-2}\text{K}^{-1}$ has been chosen as the control value of the blood convection coefficient. This value was proposed by Lagendijk [63] using a numerical model of the human eye and temperature measured on rabbit eyes. In addition to the value of $65\text{Wm}^{-2}\text{K}^{-1}$, Lagendijk [63] also estimated a value of $110\text{Wm}^{-2}\text{K}^{-1}$ based on the blood flow rates of rabbit and monkey eyes measured by O'Day et al. [103]. More recently, Flyckt et al. [94] suggested that values between 250 and $300\text{Wm}^{-2}\text{K}^{-1}$ better describe the heat transfer between ocular blood flow and the human eye. Based on the aforementioned, values of 110, 250, 275 and $300\text{Wm}^{-2}\text{K}^{-1}$ are investigated. For a value that is lower than the control, a value of $20\text{Wm}^{-2}\text{K}^{-1}$ is chosen.

Table 3.5 lists the numerically obtained temperatures at the six pre-selected points along the pupillary axis. From Table 3.5, it is apparent that a larger blood convection coefficient produces a warmer ocular temperature distribution. Changes in the blood convection coefficient appear not to have any significant effect on the temperatures at

Table 3.5: Effects of blood convection coefficient on the pupillary axis

h_{bl} ($\text{Wm}^{-2}\text{K}^{-1}$)	Temperature ($^{\circ}\text{C}$)					
	O	A	B	C	D	E
20	33.55	33.73	34.48	35.49	36.37	36.38
65	34.19	34.39	35.17	36.18	36.88	36.89
110	34.36	34.56	35.35	36.35	36.95	36.96
250	34.56	34.77	35.56	36.51	36.99	36.99
275	34.58	34.79	35.58	36.53	36.99	36.99
300	34.60	34.80	35.60	36.54	36.99	36.99

the posterior segment of the eye. At the anterior segment, considerable changes in the ocular temperature are observed when the blood convection coefficient varies from 20 to $250\text{Wm}^{-2}\text{K}^{-1}$. However, as the value increases to $300\text{Wm}^{-2}\text{K}^{-2}$, the effects appear to have become relatively insignificant.

This phenomena may be explained by using Equation (2.4), which describes the heat transfer between blood and the eye. One may observe that the temperatures at the posterior segment (points D and E) approach the body core temperature when value of the blood convection coefficient increases. As temperature at the surface of the sclera increases, the thermal gradient between blood and the eye decreases. Hence, while a larger blood convection coefficient may imply a greater rate of heat transfer, the corresponding decrease of thermal gradient may contribute to a reduced heat transfer into the eye.

3.6 Effects of Tears Evaporation Rate, E_{vap}

A value of 40Wm^{-2} has been chosen in Chapter 2 as the control to represent value of the tears evaporation rate of a normal human eye. According to Scott [22], normal rate of tears evaporation may range from 20 to 100Wm^{-2} . As described in Chapter 2, evaporation rate of tears is controlled by the lipid layer that covers the surface of the tear film. Deficiency in the production of lipid layer observed in patients with dry eyes and the inhibition of the evaporative control of the lipid layer due to Meibomian gland disease are among the ocular abnormalities that are known to cause abnormally high tears

evaporation rates [104]. An evaporation rate of $59 \times 10^{-7} \text{g} \cdot \text{cm}^{-2} \text{s}^{-1}$ in patients with dry eyes and Meibomian gland diseases was measured by Mathers [79]. This translates to a value of approximately 140Wm^{-2} (see Section 2.5 for more details). In the case when the lipid layer is completely destroyed, Scott [22] estimated an evaporation rate of 320Wm^{-2} .

Five different values of tears evaporation rate, namely 20, 60, 100, 140 and 320Wm^{-2} are thus, considered here. Results obtained are presented in Table 3.6. As expected, a larger evaporation rate yields a cooler ocular temperature. This is due to the greater loss of heat from the corneal surface. In eyes with dry eye syndrome and meibomian gland diseases ($E_{\text{vap}} = 140 \text{Wm}^{-2}$), a drop of 1.2°C at the corneal surface from the control is found. When the lipid layer is completely destroyed ($E_{\text{vap}} = 320 \text{Wm}^{-2}$), the corneal surface temperature drops to 30.84°C .

Table 3.6: Effects of tears evaporation rate on the pupillary axis						
E_{vap} (Wm^{-2})	Temperature ($^\circ\text{C}$)					
	O	A	B	C	D	E
20	34.43	34.61	35.32	36.25	36.90	36.90
40	34.19	34.39	35.17	36.18	36.88	36.89
60	33.95	34.16	35.01	36.11	36.88	36.88
100	33.47	33.72	34.70	35.97	36.86	36.87
140	32.99	33.27	34.39	35.83	36.84	36.85
320	30.84	31.26	32.98	35.20	36.75	36.77

Using IR thermography, Craig et al. [91] found that the corneal surface temperature in patients with dry eyes is lower than the healthy eye. This agrees with the numerical predictions presented in Table 3.6. Conflicting results have been reported by Morgan et al. [105, 106] however, where corneal surface temperature in dry eye patients is found to be greater than the normal eye. This has been attributed to hyperaemia, a symptom associated with dry eye that increases the eye temperature [106]. A larger cooling rate on the corneal surface has also been found in patients with dry eyes [105]. Perhaps a more appropriate approach for studying the effects of tears evaporation rate on the ocular heat transfer is to consider a transient analysis, where cooling rate of the cornea can be quantified.

3.7 Effects of Lens Thermal Conductivity, κ_3

Lahm et al. [107] found that the water content inside the human lens decreases as age of the individual increases. According to Spells [108], the decrease in water content causes the thermal conductivity of the lens to drop. The effects of different lens thermal conductivity are examined here. In Chapter 2, the value of $0.4\text{Wm}^{-1}\text{K}^{-1}$, which is based on the value estimated by Lagendijk [63], has been selected to be the control. Although this value has been adopted by most of the human eye models developed in the past, some studies have opted for values obtained from different sources.

Emery and his co-investigators [75, 93] adopted the thermal conductivity of bovine lens in their rabbit eye models, which was given by $0.21\text{Wm}^{-1}\text{K}^{-1}$ [109]. Meanwhile, Neelakantaswamy and Ramakrishnan [74], assumed the thermal conductivity of the lens to be similar to that of tissue medium, which is given by $0.54\text{Wm}^{-1}\text{K}^{-1}$. To investigate the effects of different lens thermal conductivity on the human eye temperature, three values that are different from the control are considered, namely 0.21, 0.30 and $0.54\text{Wm}^{-1}\text{K}^{-1}$. The value of $0.30\text{Wm}^{-1}\text{K}^{-1}$ is included for a more complete study. Numerical results obtained are tabulated in Table 3.7.

Table 3.7: Effects of lens thermal conductivity on the pupillary axis						
κ_3 ($\text{Wm}^{-1}\text{K}^{-1}$)	Temperature ($^{\circ}\text{C}$)					
	O	A	B	C	D	E
0.21	34.03	34.22	34.91	36.28	36.89	36.90
0.30	34.12	34.31	35.05	36.23	36.89	36.89
0.40	34.19	34.39	35.17	36.18	36.88	36.89
0.54	34.26	34.46	35.29	36.14	36.88	36.89

From Table 3.7, it is found that the corneal surface temperature increases with lens thermal conductivity. The same may be said for the temperatures at points A and B. However, at points C, D and E, an increase in the lens thermal conductivity causes the temperature to drop. This may be explained by the region defined by the lens along the pupillary axis, which is given by the region between points B and C. When the thermal conductivity of the lens is high, heat transfer across this region is enhanced.

This encourages heat from the posterior segment of the eye to be conducted to the anterior segment, thus warming the anterior surface of the lens (point B). When the thermal conductivity decreases, the rate of heat transfer across the lens drops. This produces greater warming effects at the posterior surface of the lens (point C). Meanwhile, cooling that is taking place at the corneal surface causes the temperature at point B to drop. For a better illustration of the results in Table 3.7, variation of the differences in temperature along the pupillary axis between the results obtained for each set of lens thermal conductivity and the control are plotted. This is shown in Figure ??.

Figure 3-2: Temperature difference from the control along the pupillary axis

3.8 Significance of Study

Results obtained in Section 3.2 show that the temperature on the corneal surface is sensitive towards changes in the ambient temperature. One of the implications of this finding is that it is important to maintain a constant ambient temperature during measurements of the corneal surface temperature. This is essential to reduce uncertainties in the measured data. Temperature on the corneal surface has also been found to be

sensitive towards the presence of air draft. As in the case with the ambient temperature, the presence of air drafts during experimental measurement of the corneal surface temperature should be maintained constant or eliminated altogether. Simulations on the temperature distribution inside the human eye during cold stress have also been performed. These investigations are only preliminary however. Future works may be carried out to correlate the drop in temperature with the thickness of the cornea and depth of the anterior chamber. Information of the thermal behavior of the eye during cold stress may help researchers understand the various ocular diseases that are often associated with people residing in arctic climates, such as pterygium, pinguecula and band shaped keratopathy [87].

Temperature on the corneal surface has been found to increase with body temperature. This result opens up the possibility of fever detection based on the ocular surface temperature. Nevertheless, more studies especially in clinical trials, have to be carried out before such a proposal can be put into practice. Blood convection coefficient, which correlates with the blood flow inside the eye, has been found to cause changes to the corneal surface temperature when the value decreases from the control. Similar observations were reported by Mapstone [31], where patients with carotid artery disease (a condition that decreases blood flow into the eye) were found to exhibit a cooler corneal surface than the normal eye. Since ocular physiology is related to the vascular condition of the eye, this raises the possibility of detecting vascular disorders of the eye based on the temperature at the corneal surface [8, 31]. This hypothesis may benefit from future investigations.

Effects of different tears evaporation rate have been examined in Section 3.6. Significant changes in the corneal surface temperature due to changes in the tears evaporation rate suggest that corneal surface temperature may be used for detecting ocular abnormalities such as dry eye syndrome and obtrusive meibomian gland disease. This argument is supported by the results obtained from the preliminary experimental investigations carried out by Morgan et al. [7, 105] and Chiang et al. [110]. From a mathematical

point of view, investigations on the effects of dry eye on the ocular temperature distribution still require further developments. The effects of hyperaemia on the corneal surface temperature have to be considered for a more accurate representation of dry eyes.

Changes in the thermal conductivity of the lens have been found to affect the human eye temperature, where a larger thermal conductivity produces a warmer corneal surface. According to Lahm et al. [107], water content inside the human lens decreases with increasing age. Spells [108] meanwhile, found that the thermal conductivity of biological tissues increases with its water content. Assuming that the human lens behaves in a manner similar to that of biological tissues, it may be deduced that the thermal conductivity of the lens decreases with age. From the results presented in Table 3.7, it is found that a smaller lens thermal conductivity (increasing age) causes the corneal surface temperature to drop. This implies that the corneal surface temperature decreases with increasing age. Changes in lens thermal conductivity as an individual ages offer an alternative explanation to the commonly accepted hypothesis of atherosclerosis for describing the relationship between corneal surface temperature and age [88,111].

3.9 Concluding Remarks

A sensitivity analysis that examines the thermal responses of the human eye towards changes in various governing parameters have been successfully performed. Six parameters have been investigated, namely ambient temperature, ambient convection coefficient, body temperature, blood convection coefficient, tears evaporation rate and thermal conductivity of the human lens. Each of these parameters has been found to affect the temperature distribution inside the human eye to some extent.

The use of ocular surface temperature to monitor ocular physiology is well-recognized [7, 8, 31]. This has been demonstrated from the sensitivity analysis carried out in this chapter, particularly in the investigations carried out on the effects of body temperature, blood convection coefficient and tears evaporation rate on the human eye temperature.

Chapter 4

Natural Convection inside the Anterior Chamber

4.1 Introduction

In the numerical investigations carried out in the previous two chapters, the aqueous humor that occupies the anterior and posterior chambers has been assumed to be stagnant. The same assumption has been made in most of the models of the human eye proposed in the past by other researchers (see references [22, 23, 63] for example). With this assumption, the aqueous humor is generally treated as a solid such that only heat conduction takes place inside the anterior and posterior chambers. In reality, this is not true since aqueous humor has been found to flow inside the anterior and posterior chambers [25]. Although flow exists in both the anterior and posterior chambers, the flow inside the posterior chamber is usually very small. As a result, it is usually ignored in most cases [114].

Various hypotheses such as the thermally driven flow, production and drainage of aqueous humor, mixing and stirring during rapid eye movement (REM) sleep and phakodonesis, have been proposed to explain the mechanism behind the flow of aqueous humor inside the anterior chamber. Of the four hypotheses mentioned, thermally driven flow is

widely believed to be the primary cause of aqueous humor flow inside the anterior chamber. Although production and drainage of aqueous humor are acknowledged to play a part in the aqueous humor hydrodynamics [14], the flow generated by these phenomena is weaker than the thermally driven one. Flow of aqueous humor created during REM sleep was suggested by Maurice [112] as a way for the human eye to compensate for the lack of thermally driven flow during sleep. Nevertheless, in a theoretical study carried out by Fitt and Gonzalez [113], the movement of the eyeball during REM sleep was found to produce no flow of aqueous humor. Phakodensis is defined as the vibration sustained by the lens when the eye or the head moves. It has been suggested that the pumping action of the lens during phakodensis is sufficient to propel the aqueous humor across the anterior chamber. Numerical investigations have found that the flow generated due to phakodensis is smaller than the thermally driven flow [113] however.

The importance of the aqueous humor flow is well-acknowledged. From a biological perspective, the flow of aqueous humor plays an important role in ensuring a continual supply of nutrients and metabolites to the cornea. This is vital for maintaining an adequate corneal respiration [11]. Furthermore, some of the symptoms observed in various ocular abnormalities such as Krukenberg spindle, hypopyons, hyphemas and keratic precipitates have been attributed to the flow of particulate matter due to the movement of aqueous humor inside the anterior chamber [114, 115].

From a heat transfer point of view, the flow of aqueous humor produces natural convection inside the anterior chamber. This may have a significant impact on the overall heat transfer inside the human eye. The presence of convective flow inside the anterior chamber may raise some doubts over the accuracy of the models that have been developed based on a stagnant aqueous humor assumption [22–24, 49]. Although numerical results obtained from these models have shown rather good agreement with the experimental results found in literature, it has to be noted that these comparisons have been limited to the temperatures on the corneal surface. Questions remain over the accuracy of the predictions of the intraocular temperatures, particularly inside the anterior chamber,

where natural convection occurs.

This chapter examines the effects of natural convection inside the anterior chamber on the heat transfer inside the human eye. Investigations are confined to flow inside the anterior chamber, which is assumed to be thermally driven. Some of the factors that may affect the thermally driven flow such as the magnitude of temperature difference inside the anterior chamber and the orientation of the human eye are also examined.

4.2 The Thermally Driven Flow

4.2.1 Flow description

This section describes the mechanisms involved in the thermally driven flow inside the anterior chamber. Figure 4-1 shows a sketch of an enlarged portion of the anterior chamber and some of the ocular components that surround it.

Figure 4-1: A sketch of the anterior segment of the human eye

The anterior chamber may be considered to be enclosed by the inner surface of the cornea and the surfaces of the iris and lens. Temperatures at the surfaces of the iris and lens are naturally higher than the temperatures at the inner surface of the cornea. This

is due to the proximity of the lens and iris to the source of heat (blood) inside the eye. Consequently, fluid that is closer to the lens and iris is expected to be warmer than the fluid that is nearer to the cornea. This creates buoyancy, where warmer aqueous humor tends to rise due to its smaller density, while the cooler aqueous humor, that has a larger density, descends. The rise and fall of aqueous humor creates a constant circulation inside the anterior chamber, as depicted by the red arrows in Figure 4-1.

The thermally driven flow inside the anterior chamber, as described in the aforementioned, was first hypothesized by Türk in 1906 (cited by Canning et al. [114]). One of the earliest mathematical studies that examined the thermally driven flow of aqueous humor was carried out by Wyatt [116] in 1996. Investigations were performed using a purely analytical approach. For simplicity, the anterior chamber was modeled to be a rectangular cavity. Using this simple analytical model, Wyatt [116] predicted an average velocity of the aqueous humor of 1mms^{-1} inside the anterior chamber.

A more proper study was carried out by Canning et al. [114] in 2002. Investigations were confined to the anterior chamber, which comprised of a flat disk and a curved surface. Using this model, they noted that the flow of aqueous humor inside the anterior chamber takes place in a single convection cell, where very little or no lateral flows are expected. This essentially describes a *two-dimensional flow*. In other words, if the anterior chamber is assumed to be dissected into several individual slices that are parallel to the sagittal plane, each slice would then have flow profiles that are independent of the other slices. Canning et al. [114] found that the maximum velocity, u_{max} achieved inside the anterior chamber may be mathematically expressed as

$$u_{\text{max}} \approx \Delta T \times 1.98 \times 10^{-4} \text{ms}^{-1} \text{K}^{-1}, \quad (4.1)$$

where ΔT is the temperature difference between the anterior and posterior surfaces of the anterior chamber³. Assuming that ΔT may vary from 2 to 4°C [117], the corresponding

³Temperatures at the surfaces of the anterior chamber have been assumed by Canning et al [114] to be constant

range of $u_{\max}$ calculated from Equation (4.1) is given approximately by 0.4 to 0.8mms⁻¹. The simplicity of the model developed by Canning et al. [114] has led other researchers such as El-Shahed and El-Maboud [118] and Avtar and Srivastava [119] to adopt the same approach in their subsequent investigations of the thermally driven flow inside the anterior chamber.

Some studies have investigated the contributions of production and drainage of aqueous humor to the thermally driven flow inside the anterior chamber [113,115,117,120]. As described in Chapter 1, aqueous humor is produced inside the ciliary body. It is secreted into the posterior chamber by the ciliary epithelium lining the ciliary processes [11]. The aqueous humor then flows into the anterior chamber through the small gap of 10 μ m between the iris and the lens. It exits the anterior chamber through the trabecular meshwork located at the angle of the anterior chamber and into the Schlemm's canal. This is graphically represented by the blue arrows in Figure 4-1.

In the numerical investigations carried out by Heys and Barocas [115], the inlet flow of aqueous humor from the 10 μ m gap between the iris and lens was found to produce no significant effect on the thermally driven flow inside the anterior chamber. Likewise, the inflow and outflow of aqueous humor at the ciliary body and trabecular meshwork respectively, were found to contribute insignificantly to the thermally driven flow. Wyatt [120] estimated the maximum velocity achieved inside the anterior chamber due to the secretion of aqueous humor to be 0.02mms⁻¹. On the other hand, the flow produced by the buoyant forces was found to be 0.33mms⁻¹, which is about 16 times the flow caused by the secretion of aqueous humor. Kumar et al. [117] found that buoyancy causes the velocity of the aqueous humor flow to be nearly 500 times the flow produced by the production and drainage of aqueous humor.

4.2.2 Navier-Stokes equations

Natural convection inside the anterior chamber presents a coupled field problem involving thermal-fluid interaction. The flow and thermal fields may be mathematically described

using the Navier-Stokes equations. For a steady incompressible flow, these equations are given by

$$\text{(continuity equation)} \quad \nabla \cdot \vec{v} = 0, \quad (4.2)$$

$$\text{(momentum equation)} \quad \rho (\vec{v} \cdot \nabla \vec{v}) = -\nabla p + \mu \nabla^2 \vec{v} + \rho g \vec{j}, \quad (4.3)$$

$$\text{(energy equation)} \quad \alpha \nabla^2 T = \vec{v} \cdot \nabla T, \quad (4.4)$$

where $\vec{v}$ is velocity vector, p and T are pressure and temperature distribution respectively, ρ is density, μ is dynamic viscosity, α is thermal diffusivity, g is gravitational acceleration and $\vec{j}$ is a unit vector in the direction where gravity is acting. In Equation (4.4), it is assumed that the viscous dissipation effect and heat generation due to external sources are negligible. Equations (4.2) to (4.4), which are expressed in terms of the velocity, pressure and temperature, are known as the Navier-Stokes equations in the primitive variables.

The last term on the right hand side of Equation (4.3) is associated with the body force. In natural convection flow, the body force term is represented by the buoyant forces created due to the thermal gradient inside the anterior chamber. The relationship between the buoyant forces and the thermal gradient may be described using the Boussinesq approximation, which states that the density of fluid changes significantly with temperature but negligibly with pressure. Mathematically, the Boussinesq approximation is given by [82]

$$\rho = \rho_{\text{ref}} \beta (T - T_{\text{ref}}), \quad (4.5)$$

where β is the thermal expansion coefficient and ρ_{ref} is the density of fluid at a reference temperature, T_{ref} .

Substituting Equation (4.5) into the body force term in Equation (4.3) yields

$$\rho_{\text{ref}} (\vec{v} \cdot \nabla \vec{v}) = -\nabla p + \mu \nabla^2 \vec{v} + \rho_{\text{ref}} \beta (T - T_{\text{ref}}) g \vec{j}.$$

Solutions of Equations (4.2) to (4.5) along with appropriate boundary conditions lead to the distribution of velocity, pressure and temperature of the aqueous humor inside the anterior chamber.

4.2.3 Velocity-vorticity formulation

One of the difficulties associated with the use of the Navier-Stokes equations in the primitive variables is the presence of the pressure term p , which is usually an unknown. In most problems, there are no proper equation that solves for the unknown pressure distribution. Additionally, the presence of the pressure term requires the pressure boundary condition to be specified. This is not a straightforward task, particularly in problems that are bounded by solid walls.

In 1976, Fasel [121] introduced an alternative form of the Navier-Stokes equations known as the velocity-vorticity formulation to replace the set of equations in the primitive variables. In the velocity-vorticity formulation, the Navier-Stokes equations in the primitive variables are expressed in terms of velocity, vorticity and temperature. By doing so, the flow field is computationally partitioned into the kinetics and kinematics aspects. This eventually leads to the elimination of the pressure variable from the original formulation.

To derive the velocity-vorticity formulation of the Navier-Stokes equations, let us first define the vorticity of a flow field, $\vec{\omega}$, which is given by the curl of the velocity vector

$$\vec{\omega} = \nabla \times \vec{v}. \quad (4.6)$$

The kinetics aspect of the flow may be obtained by taking the curl of the momentum equation, i.e. Equation (4.3). This yields

$$\rho [\nabla \times (\nabla \cdot \nabla \vec{v})] = \nabla \times (-\nabla p) + \mu(\nabla \times \nabla^2 \vec{v}) + \rho g(\nabla \times \vec{j}),$$

which upon using some vector identities and making use of the expressions in Equations

(4.2) and (4.6), give rise to the vorticity transport equation

$$\rho \nabla^2 \vec{\omega} = \mu (\vec{v} \cdot \nabla \vec{\omega}) + \rho g (\nabla \times \vec{j}). \quad (4.7)$$

Equation (4.7) generally describes the distribution of the vorticity vector in a fluid flow field [122].

The kinematics aspect of the flow may be derived by taking the curl of Equation (4.6), such that

$$\nabla \times \vec{\omega} = \nabla \times (\nabla \times \vec{v}).$$

By using vector identities, the expression above reduces to the elliptic Poisson equation of the velocity vector, which is given by

$$\nabla^2 \vec{v} = -\nabla \times \vec{\omega}. \quad (4.8)$$

Details on the derivation of Equations (4.7) and (4.8) are presented in Appendix D.

Equations (4.7) and (4.8) describe respectively the kinetics and kinematics aspects of flow and are collectively known as the velocity-vorticity formulation of the Navier-Stokes equations. The Navier-Stokes equations expressed in the velocity-vorticity formulation may be simpler to solve than the one in the primitive variables, since the pressure term has been eliminated from the original formulation. Along with appropriate boundary conditions, solutions of Equations (4.7), (4.8) and (4.4) yield the distribution of vorticity, velocity and temperature respectively in a natural convection problem.

4.3 Mathematical Model

4.3.1 Model description

Although flow of aqueous humor exists in both the anterior and posterior chambers, only flow in the anterior chamber will be considered in the present study. The secretion of

aqueous humor from the ciliary body into the posterior chamber is assumed to produce negligible effects on the flow inside the anterior chamber. Investigations are restricted to the region defined by the anterior chamber. Although it is acknowledged that a complete model of the eye may be a better choice for the purpose of this study, it is not considered in this chapter since it requires intensive computational efforts.

The mechanisms involved in the natural convection flow inside the anterior chamber have been presented in Section 4.2. According to Canning et al. [114], the natural convection flow inside the anterior chamber takes place in a single, two-dimensional convective cell. Investigations in the present study are therefore, confined to a two-dimensional region.

Figure 4-2 illustrates the model of the anterior chamber at the mid-sagittal plane with reference to the Oxy coordinate system. The dimensions are obtained from the model

Figure 4-2: Model of the anterior chamber in the mid-sagittal plane with reference to Oxy coordinate system

of the human eye developed in Chapter 2. The model, which is denoted here by R , is enclosed by two surfaces that are defined by the inner surface of the cornea, C_1 (dotted line in Figure 4-2) and the surfaces of the iris and lens, C_2 (solid line in Figure 4-2). The

orientation of the anterior chamber illustrated in Figure 4-2 is assumed to represent an individual that is in a standing position. In this case, gravity (g) pulls in the direction orthogonal to the pupillary axis (negative y -direction).

4.3.2 Governing equations

The distributions of vorticity, velocity and temperature inside the anterior chamber during natural convection are described by the velocity-vorticity formulation of the Navier-Stokes equations and the energy equation presented in Section 4.2.

Using the following change of variables:

$$\begin{aligned} x^* &= \frac{x}{L}, \quad y^* = \frac{y}{L}, \quad u^* = \frac{uL}{\alpha}, \quad v^* = \frac{vL}{\alpha}, \quad \omega^* = \frac{\omega L^2}{\alpha}, \\ T^* &= \frac{T - T_c}{T_h - T_c}, \quad \frac{\partial T^*}{\partial n^*} = \frac{\partial T}{\partial n} \frac{L}{T_h - T_c}, \\ Pr &= \frac{\mu}{\rho\alpha}, \quad Ra = \frac{\rho g \beta (T_h - T_c) L^3}{\mu\alpha}, \end{aligned} \quad (4.9)$$

Equations (4.7), (4.8) and (4.4) may be non-dimensionalized to give

$$\begin{aligned} \nabla^2 \omega^*(x^*, y^*) &= \frac{1}{Pr} \left\{ u^*(x^*, y^*) \frac{\partial}{\partial x^*} [\omega^*(x^*, y^*)] \right. \\ &\quad \left. + v^*(x^*, y^*) \frac{\partial}{\partial y^*} [\omega^*(x^*, y^*)] \right\} + Ra \frac{\partial}{\partial x^*} [T^*(x^*, y^*)], \\ &\quad \text{in } R \cup C, \end{aligned} \quad (4.10)$$

$$\nabla^2 u^*(x^*, y^*) = -\frac{\partial}{\partial y^*} [\omega^*(x^*, y^*)], \text{ in } R \cup C, \quad (4.11)$$

$$\nabla^2 v^*(x^*, y^*) = \frac{\partial}{\partial x^*} [\omega^*(x^*, y^*)], \text{ in } R \cup C, \quad (4.12)$$

and

$$\begin{aligned} \nabla^2 T^*(x^*, y^*) &= u^*(x^*, y^*) \frac{\partial}{\partial x^*} [T^*(x^*, y^*)] + v^*(x^*, y^*) \frac{\partial}{\partial y^*} [T^*(x^*, y^*)], \\ &\text{in } R \cup C, \end{aligned} \quad (4.13)$$

respectively, where $C = C_1 \cup C_2$, L is the characteristic length, u and v are the velocity components in the x - and y -directions respectively and u^* and v^* are their dimensionless counterparts, T_c and T_h are pre-selected temperatures such that $T_h > T_c$, ω and ω^* are the vorticity and its dimensionless counterpart respectively⁴ and Pr and Ra are the Prandtl and Rayleigh numbers respectively.

4.3.3 Boundary conditions

Boundary conditions are specified on boundaries C_1 and C_2 for both the flow and thermal fields. Let us first consider the boundary conditions in the flow field. The surfaces of the anterior chamber, i.e. the surfaces of the cornea, iris and lens are assumed to be solids that remain stationary inside the human eye. Consequently, the no slip condition applies, which is given by

$$\left. \begin{aligned} u^*(x^*, y^*) \\ v^*(x^*, y^*) \end{aligned} \right\} = 0 \text{ on } C_1 \text{ and } C_2. \quad (4.14)$$

To solve the vorticity transport equation, either the vorticity or the vorticity flux has to be specified at the boundaries. These variables are not always known however. In the present study, the only proper boundary condition associated with the vorticity transport equation is the definition of vorticity given in Equation (4.6). This may be expressed in the dimensionless variables, with reference to the Ox^*y^* coordinate system, as

$$\omega^*(x^*, y^*) = \frac{\partial}{\partial x^*} [v^*(x^*, y^*)] - \frac{\partial}{\partial y^*} [u^*(x^*, y^*)] \text{ on } C_1 \text{ and } C_2. \quad (4.15)$$

⁴In two-dimensional flow, only one component of vorticity exist, which we simply denote by ω

Boundary conditions specified in the thermal field merit some discussion. According to Heys and Barocas [115], the cornea may be treated as a layer of insulation that shields the anterior chamber from the environment. Assuming that the cornea forms a section of a solid spherical shell and is a thin enough structure such that heat flow in the tangential direction is negligible, heat flux that flows from the anterior chamber into the cornea may be mathematically expressed as [115]

$$\frac{\partial}{\partial n} [T(x, y)] = -\frac{T(x, y) - T_{\text{cornea}}}{r_p \left(1 - \frac{r_p}{r_c}\right)} \text{ on } C_1, \quad (4.16)$$

where $T(x, y)$ is the temperature at point (x, y) along boundary C_1 , T_{cornea} is the temperature at the surface of the cornea and r_p and r_c are the radii of curvature of the inner and outer surfaces of the cornea respectively.

In reality, T_{cornea} is a spatially-dependent function. However, for the sake of simplicity, the spatial variation of temperature across the corneal surface is assumed to be very small such that T_{cornea} may be represented by a constant. Using the change of variables in Equation (4.9) and selecting $T_c = T_{\text{cornea}}$, the boundary condition at C_1 may be expressed in the dimensionless variables as

$$\frac{\partial}{\partial n^*} [T^*(x^*, y^*)] = h_{\text{ac}} T^*(x^*, y^*) \text{ on } C_1, \quad (4.17)$$

where

$$h_{\text{ac}} = -\frac{L}{r_p \left(1 - \frac{r_p}{r_c}\right)}.$$

On boundary C_2 , it is assumed that the arterial blood flow inside the iris is sufficient to maintain the temperature here at the body core level [114, 115, 117]. By selecting $T_h = T_{\text{bl}}$, the boundary condition at C_2 may be expressed in the dimensionless variables as

$$T^*(x^*, y^*) = 1 \text{ on } C_2. \quad (4.18)$$

4.4 Numerical Scheme

4.4.1 Integro-differential equations

To solve Equations (4.10) to (4.13) subjected to the boundary conditions in Equations (4.14) to (4.18), the integro-differential representations of Equations (4.10) to (4.13) have to be derived. Following the procedures highlighted by Ang [84], the integro-differential equations derived from Equations (4.10) to (4.13), with reference to the model of the anterior chamber illustrated in Figure 4-2, are respectively given by

$$\begin{aligned}
 \lambda(\xi, \eta)\omega(\xi, \eta) &= \int_C \omega(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [\omega(x, y)] ds(x, y) \\
 &\quad + \frac{1}{Pr} \iint_R \Phi_{2D}(x, y; \xi, \eta) \left\{ u(x, y) \frac{\partial}{\partial x} [\omega(x, y)] \right. \\
 &\quad \left. + v(x, y) \frac{\partial}{\partial y} [\omega(x, y)] \right\} dA(x, y) \\
 &\quad - Ra \iint_R \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial y} [T(x, y)] dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C, \tag{4.19}
 \end{aligned}$$

$$\begin{aligned}
 \lambda(\xi, \eta)u(\xi, \eta) &= \int_C u(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [u(x, y)] ds(x, y) \\
 &\quad - \iint_R \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial y} [\omega(x, y)] dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C, \tag{4.20}
 \end{aligned}$$

$$\begin{aligned}
 \lambda(\xi, \eta)v(\xi, \eta) &= \int_C v(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [v(x, y)] ds(x, y) \\
 &\quad + \iint_R \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial x} [\omega(x, y)] dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C, \tag{4.21}
 \end{aligned}$$

and

$$\begin{aligned}
 \lambda(\xi, \eta)T(\xi, \eta) &= \int_C T(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [T(x, y)] ds(x, y) \\
 &\quad + \iint_R \Phi_{2D}(x, y; \xi, \eta) \left\{ u(x, y) \frac{\partial}{\partial x} [T(x, y)] \right. \\
 &\quad \left. + v(x, y) \frac{\partial}{\partial y} [T(x, y)] \right\} dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C, \tag{4.22}
 \end{aligned}$$

where $ds(x, y)$ denotes the length of an infinitesimal portion of curve C , $dA(x, y)$ denotes the area of an infinitesimal portion of region R , $\lambda(\xi, \eta)$ is a coefficient, which has a value of $\frac{1}{2}$ when (ξ, η) lies on a smooth path of C and 1 when (ξ, η) lies at the interior of R , and $\Phi_{2D}(x, y; \xi, \eta)$ and $\partial\Phi_{2D}(x, y; \xi, \eta)/\partial n$ are the fundamental solution of the two-dimensional Laplace equation and its normal derivative respectively, which are

mathematically expressed as [84]

$$\begin{aligned}\Phi_{2D}(x, y; \xi, \eta) &= \frac{1}{4\pi} \ln [(x - \xi)^2 + (y - \eta)^2], \\ \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] &= \frac{1}{2\pi} \left[\frac{n_x(x - \xi) + n_y(y - \eta)}{(x - \xi)^2 + (y - \eta)^2} \right],\end{aligned}\quad (4.23)$$

where n_x and n_y are the components of the outward unit normal vector on C in the x - and y -directions respectively. In Equations (4.19) to (4.22) and in all the variables presented in this chapter hereafter, the asterisk denoting dimensionless variables are dropped for convenience.

The integro-differential equations defined in Equations (4.19) to (4.22) contain domain integrals that are expressed in terms of the first order derivatives of the unknown variables. These domain integrals may be further transformed using the steps outlined in Appendix E to give

$$\begin{aligned}\lambda(\xi, \eta)\omega(\xi, \eta) &= \int_C \omega(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\ &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [\omega(x, y)] ds(x, y) \\ &\quad + \int_C \Phi_{2D}(x, y; \xi, \eta) \left\{ \frac{1}{Pr} [n_x u(x, y) + n_y v(x, y)] \omega(x, y) \right. \\ &\quad \left. - Ra [n_y T(x, y)] \right\} ds(x, y) \\ &\quad - \frac{1}{Pr} \iint_R \omega(x, y) \left\{ u(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] \right. \\ &\quad \left. + v(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi, \eta)] \right\} dA(x, y) \\ &\quad + Ra \iint_R T(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] dA(x, y) \\ &\quad \text{for } (\xi, \eta) \in R \cup C,\end{aligned}\quad (4.24)$$

$$\begin{aligned}
 \lambda(\xi, \eta)u(\xi, \eta) &= \int_C u(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \left\{ \frac{\partial}{\partial n} [u(x, y)] + n_y \omega(x, y) \right\} ds(x, y) \\
 &\quad + \iint_R \omega(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi, \eta)] dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C,
 \end{aligned} \tag{4.25}$$

$$\begin{aligned}
 \lambda(\xi, \eta)v(\xi, \eta) &= \int_C v(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \left\{ \frac{\partial}{\partial n} [v(x, y)] - n_x \omega(x, y) \right\} ds(x, y) \\
 &\quad - \iint_R \omega(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C,
 \end{aligned} \tag{4.26}$$

and

$$\begin{aligned}
 \lambda(\xi, \eta)T(\xi, \eta) &= \int_C T(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [T(x, y)] ds(x, y) \\
 &\quad + \int_C \Phi_{2D}(x, y; \xi, \eta) [n_x u(x, y) + n_y v(x, y)] T(x, y) ds(x, y) \\
 &\quad - \iint_R T(x, y) \left\{ u(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] \right. \\
 &\quad \left. + v(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi, \eta)] \right\} dA(x, y) \\
 &\quad \text{for } (\xi, \eta) \in R \cup C,
 \end{aligned} \tag{4.27}$$

respectively, where the first order derivatives of the unknown variables in the domain

integrals of the original formulation have been transferred to the fundamental solution.

Equations (4.24) to (4.27) are to be solved numerically using the boundary element method.

4.4.2 Domain decomposition technique

The domain decomposition technique (also known as the subdomain technique and the multi-domain method) is a technique that is usually employed together with other numerical methods for solving partial differential equations. In the domain decomposition technique, the original solution domain is divided into a series smaller domains known as subdomains. In principle, there are no restrictions on the shape of the subdomains generated. Each subdomain may have different arbitrary polygonal shape such as triangle and quadrilateral in two-dimensions, and tetrahedral and hexahedral in three-dimensions. Inside each subdomain, the governing equation describing the physical problem holds.

Numerical investigations carried out by researchers in the past have discovered that the domain decomposition technique can significantly improve the performance of the boundary element method when solving large-scale problems such as fluid flow problems [122, 124–126]. Some of the established boundary element approaches that utilize the domain decomposition technique include the boundary-domain integral method [122, 124, 128] and the multi-domain dual reciprocity boundary element method [125, 126]. Both approaches have been successfully implemented for solving problems involving natural convection inside closed cavities.

In the present study, the domain decomposition technique is used together with the boundary element method to solve Equations (4.24) to (4.27). In carrying out the domain decomposition technique, the region occupied by the anterior chamber R , is divided into N_d subdomains denoted by R_i , such that $R = R_1 \cup R_2 \dots R_{N_d-1} \cup R_{N_d}$. The boundary enclosing each subdomain R_i is given by Γ_i . Since the integro-differential equations satisfy the governing equations and the governing equations hold in each subdomain, it can be deduced that the integro-differential equations also hold in each subdomain.

The division of the original solution domain into a series of subdomains introduces additional unknowns that are defined at the interfaces between two adjacent subdomains. To account for these additional unknowns, one may impose the continuity condition, which is given by

$$\omega_i = \omega_j \text{ and } \frac{\partial \omega_i}{\partial n} = \frac{\partial \omega_j}{\partial n}, \text{ at } I_{ij}, \quad (4.28)$$

for the kinematics aspect of flow,

$$\begin{aligned} u_i &= u_j \text{ and } \frac{\partial u_i}{\partial n} = \frac{\partial u_j}{\partial n}, \text{ at } I_{ij}, \\ v_i &= v_j \text{ and } \frac{\partial v_i}{\partial n} = \frac{\partial v_j}{\partial n}, \text{ at } I_{ij}, \end{aligned} \quad (4.29)$$

for the kinematics aspect of flow, and

$$T_i = T_j \text{ and } \frac{\partial T_i}{\partial n} = \frac{\partial T_j}{\partial n}, \text{ at } I_{ij}, \quad (4.30)$$

for the energy equation, where I_{ij} denotes the interface between subdomains R_i and R_j . Equations (4.28) to (4.30) are essentially the same as the continuity condition specified in Chapter 2 for describing the variation of temperature and heat flux at the interface between two neighbouring ocular regions.

4.4.3 Boundary discretization

Upon dividing the original domain into a series of smaller subdomains, the boundaries of each subdomain, Γ_i is discretized into N_i straight line segments known as boundary elements. Each boundary element is denoted by $\Gamma_i^{(k)}$ such that $\Gamma_i = \Gamma_i^{(1)} \cup \Gamma_i^{(2)} \dots \Gamma_i^{(N_i-1)} \cup \Gamma_i^{(N_i)}$. If $(x_i^{(k)}, y_i^{(k)})$ and $(x_i^{(k+1)}, y_i^{(k+1)})$ represent the starting and ending points of $\Gamma_i^{(k)}$ respectively, two points, $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ may then be chosen inside $\Gamma_i^{(k)}$

such that

$$\begin{aligned}(\xi_i^{(k)}, \eta_i^{(k)}) &= (x_i^{(k)}, y_i^{(k)}) + \tau(x_i^{(k+1)} - x_i^{(k)}, y_i^{(k+1)} - y_i^{(k)}), \\(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)}) &= (x_i^{(k)}, y_i^{(k)}) + (1 - \tau)(x_i^{(k+1)} - x_i^{(k)}, y_i^{(k+1)} - y_i^{(k)}),\end{aligned}\quad (4.31)$$

where τ is a pre-defined positive number selected here to be $\frac{1}{4}$.

Using the boundary nodes selected in Equation (4.31), variation of the vorticity, velocity and temperature and their corresponding normal derivatives inside each boundary element may be approximated using linear interpolation functions, $\varphi_1(x, y)$ and $\varphi_2(x, y)$ (see Appendix A for more details), such that

$$\begin{aligned}\omega_i(x, y) &\approx \varphi_1(x, y)\omega_i^{(k)} + \varphi_2(x, y)\omega_i^{(k+N_i)}, \\u_i(x, y) &\approx \varphi_1(x, y)u_i^{(k)} + \varphi_2(x, y)u_i^{(k+N_i)}, \\v_i(x, y) &\approx \varphi_1(x, y)v_i^{(k)} + \varphi_2(x, y)v_i^{(k+N_i)}, \\T_i(x, y) &\approx \varphi_1(x, y)T_i^{(k)} + \varphi_2(x, y)T_i^{(k+N_i)},\end{aligned}\quad \text{for } (x, y) \in \Gamma_i^{(k)}, \quad (4.32)$$

and

$$\begin{aligned}\frac{\partial}{\partial n} [\omega_i(x, y)] &\approx \varphi_1(x, y)\frac{\partial \omega_i^{(k)}}{\partial n} + \varphi_2(x, y)\frac{\partial \omega_i^{(k+N_i)}}{\partial n}, \\ \frac{\partial}{\partial n} [u_i(x, y)] &\approx \varphi_1(x, y)\frac{\partial u_i^{(k)}}{\partial n} + \varphi_2(x, y)\frac{\partial u_i^{(k+N_i)}}{\partial n}, \\ \frac{\partial}{\partial n} [v_i(x, y)] &\approx \varphi_1(x, y)\frac{\partial v_i^{(k)}}{\partial n} + \varphi_2(x, y)\frac{\partial v_i^{(k+N_i)}}{\partial n}, \\ \frac{\partial}{\partial n} [T_i(x, y)] &\approx \varphi_1(x, y)\frac{\partial T_i^{(k)}}{\partial n} + \varphi_2(x, y)\frac{\partial T_i^{(k+N_i)}}{\partial n},\end{aligned}\quad \text{for } (x, y) \in \Gamma_i^{(k)}, \quad (4.33)$$

where $\omega_i^{(k)}$ and $\omega_i^{(k+N_i)}$ are values of $\omega_i(x, y)$ at $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ respectively and $\partial \omega_i^{(k)} / \partial n$ and $\partial \omega_i^{(k+N_i)} / \partial n$ are values of $\partial \omega_i(x, y) / \partial n$ at $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$,

$\eta_i^{(k+N_i)})$ respectively. The same argument applies for the other variables $u_i^{(k)}$ and $u_i^{(k+N_i)}$, $v_i^{(k)}$ and $v_i^{(k+N_i)}$, and $T_i^{(k)}$ and $T_i^{(k+N_i)}$, and their respective normal derivatives.

Substituting Equations (4.32) and (4.33) into Equations (4.24) to (4.27) accordingly, yields

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) \omega_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) \omega_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) \omega_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_{1,i}^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [\omega_i^{(k)}] - \sum_{k=1}^{N_i} \mathcal{G}_{2,i}^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [\omega_i^{(k+N_i)}] \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \left[\frac{1}{Pr} (n_{x,i}^{(k)} u_i^{(k)} + n_{y,i}^{(k)} v_i^{(k)}) \omega_i^{(k)} \right. \\
 &\quad \left. - Ra (n_{y,i}^{(k)} T_i^{(k)}) \right] \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \left[\frac{1}{Pr} (n_{x,i}^{(k)} u_i^{(k+N_i)} + n_{y,i}^{(k)} v_i^{(k+N_i)}) \omega_i^{(k+N_i)} \right. \\
 &\quad \left. - Ra (n_{y,i}^{(k)} T_i^{(k+N_i)}) \right] \\
 &\quad - \frac{1}{Pr} \iint_{R_i} \omega_i(x, y) \left\{ u_i(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] \right\} dA(x, y) \\
 &\quad - \frac{1}{Pr} \iint_{R_i} \omega_i(x, y) \left\{ v_i(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi_i, \eta_i)] \right\} dA(x, y) \\
 &\quad - Ra \iint_{R_i} T_i(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y) \\
 &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.34}
 \end{aligned}$$

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) u_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) u_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) u_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [u_i^{(k)}] + n_{y,i}^{(k)} \omega_i^{(k)} \right\} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [u_i^{(k+N_i)}] + n_{y,i}^{(k)} \omega_i^{(k+N_i)} \right\} \\
 &\quad + \iint_{R_i} \omega_i(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y), \\
 &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.35}
 \end{aligned}$$

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) v_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) v_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) v_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [v_i^{(k)}] - n_{x,i}^{(k)} \omega_i^{(k)} \right\} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [v_i^{(k+N_i)}] - n_{x,i}^{(k)} \omega_i^{(k+N_i)} \right\} \\
 &\quad - \iint_{R_i} \omega_i(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y) \\
 &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.36}
 \end{aligned}$$

and

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) T_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) T_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [T_i^{(k)}] - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [T_i^{(k+N_i)}] \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) [n_{x,i}^{(k)} u_i^{(k)} + n_{y,i}^{(k)} v_i^{(k)}] T_i^{(k)} \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) [n_{x,i}^{(k)} u_i^{(k+N_i)} + n_{y,i}^{(k)} v_i^{(k+N_i)}] T_i^{(k+N_i)} \\
 &\quad - \iint_{R_i} T_i(x, y) \left\{ u(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] \right\} dA(x, y) \\
 &\quad - \iint_{R_i} T_i(x, y) \left\{ v(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi_i, \eta_i)] \right\} dA(x, y) \\
 &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.37}
 \end{aligned}$$

respectively, where

$$\begin{aligned}
 \mathcal{G}_1^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_1(x, y) \Phi_{2D}(x, y; \xi_i, \eta_i) ds(x, y), \\
 \mathcal{G}_2^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_2(x, y) \Phi_{2D}(x, y; \xi_i, \eta_i) ds(x, y), \\
 \mathcal{G}_3^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_1(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi_i, \eta_i)] ds(x, y), \\
 \mathcal{G}_4^{(k)}(\xi_i, \eta_i) &= \int_{\Gamma_i^{(k)}} \varphi_2(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi_i, \eta_i)] ds(x, y). \tag{4.38}
 \end{aligned}$$

Unlike the boundary integrals defined in the *Orz* coordinate system (see Equation (2.12)), the integrals in Equation (4.38) may be evaluated analytically. This may be accomplished by using the mathematical software, Maple. One of the benefits of evaluating analytically the integrals in Equation (4.38) is the reduced total computational time of the numerical scheme.

4.4.4 Treatment of domain integrals

The domain integrals appearing in Equations (4.34) to (4.37) are expressed in terms of unknown variables that are to be solved. As a result, these integrals may not be evaluated directly using either analytical or numerical approaches. It is possible however, to approximate these unknown variables using interpolation functions such that the integrand reduces to known functions. By doing so, a straightforward evaluation of the domain integrals can be executed using numerical integration formulae.

For illustration purposes, let us consider the first domain integral in the right hand side of Equation (4.34), which is defined by I such that

$$I = \iint_{R_i} \omega_i(x, y) u_i(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y), \quad (4.39)$$

where the unknown variables are given by $\omega_i(x, y) u_i(x, y)$. The objective here is to approximate $\omega_i(x, y) u_i(x, y)$ using a series of radial basis functions that are centered about a set of selected points. To do so, M_i nodes denoted by $(a_i^{(1)}, b_i^{(1)})$, $(a_i^{(2)}, b_i^{(2)})$, ..., $(a_i^{(M_i-1)}, b_i^{(M_i-1)})$, $(a_i^{(M_i)}, b_i^{(M_i)})$ are selected on the boundary and interior of each sub-domain, such that $(a_i^{(m)}, b_i^{(m)}) \in R_i \cup \Gamma_i$. Using the M_i selected nodes, the following approximation is carried out:

$$\omega_i(x, y) u_i(x, y) \approx \sum_{m=1}^{M_i} \gamma_i^{(m)} \phi_{2D}(x, y; a_i^{(m)}, b_i^{(m)}), \quad (4.40)$$

where $\phi_{2D}(x, y; a_i^{(m)}, b_i^{(m)})$ is the radial basis function defined in the *Oxy* coordinate sys-

tem centered about the point $(a_i^{(m)}, b_i^{(m)})$ and $\gamma_i^{(m)}$ are unknown coefficients to be determined.

Substituting Equation (4.40) into (4.39) leads to

$$I \approx \sum_{m=1}^{M_i} \gamma_i^{(m)} \iint_{R_i} \phi_{2D}(x, y; a_i^{(m)}, b_i^{(m)}) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] dA(x, y), \quad (4.41)$$

where the domain integral is now expressed in terms of ϕ_{2D} and $\partial\Phi_{2D}/\partial x$, both which are known functions.

To obtain the unknown coefficients $\gamma_i^{(m)}$, the point (x, y) in Equation (4.40) is collocated at the M_i selected nodes, such that $(x, y) = (a_i^{(m)}, b_i^{(m)})$, for $m = 1, 2, \dots, M_i - 1, M_i$. This leads to a system of M_i equations

$$\omega(a_i^{(j)}, b_i^{(j)})u(a_i^{(j)}, b_i^{(j)}) = \sum_{m=1}^{M_i} \gamma_i^{(m)} \phi_{2D}(a_i^{(j)}, b_i^{(j)}; a_i^{(m)}, b_i^{(m)}), \quad (4.42)$$

for $j = 1, 2, \dots, M_i - 1, M_i$,

which may be inverted to give

$$\gamma_i^{(j)} = \sum_{j=1}^{M_i} W_i^{(mj)} \omega_i^{(j)} u_i^{(j)}, \quad \text{for } m = 1, 2, \dots, M_i - 1, M_i, \quad (4.43)$$

where $\omega_i^{(j)} u_i^{(j)} = \omega(a_i^{(j)}, b_i^{(j)})u(a_i^{(j)}, b_i^{(j)})$ and the coefficients $W_i^{(mj)}$ are given by

$$\sum_{j=1}^{M_i} W_i^{(kj)} \phi_{2D}(a_i^{(j)}, b_i^{(j)}; a_i^{(m)}, b_i^{(m)}) = \begin{cases} 1, & \text{if } k = m, \\ 0, & \text{if } k \neq m, \end{cases}$$

for $k, m = 1, 2, \dots, M_i - 1, M_i$.

Replacing Equation (4.43) into (4.41) leads to

$$I \approx \sum_{j=1}^{M_i} \omega_i^{(j)} u_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \iint_{R_i} \phi_{2D}(x, y; a_i^{(m)}, b_i^{(m)}) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y).$$

For computational convenience, the M_i selected nodes are taken to be $M_i = 2N_i + L_i$, where the $2N_i$ nodes are chosen to coincide with the $2N_i$ nodes selected on the boundary, while the remaining L_i nodes are selected to be well-spaced out inside R_i . Repeating the steps in Equations (4.40) to (4.43) for the remaining domain integrals in Equations (4.34) to (4.37), and substituting the resulting approximations into Equations (4.34) to (4.37) accordingly, yields

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) \omega_i(\xi_i, \eta_i) = & \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) \omega_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) \omega_i^{(k+N_i)} \\
 & - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [\omega_i^{(k)}] - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [\omega_i^{(k+N_i)}] \\
 & + \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \left[\frac{1}{Pr} (n_{x,i}^{(k)} u_i^{(k)} + n_{y,i}^{(k)} v_i^{(k)}) \omega_i^{(k)} - Ra (n_{y,i}^{(k)} T_i^{(k)}) \right] \\
 & + \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \left[\frac{1}{Pr} (n_{x,i}^{(k)} u_i^{(k+N_i)} + n_{y,i}^{(k)} v_i^{(k+N_i)}) \omega_i^{(k+N_i)} \right. \\
 & \left. - Ra (n_{y,i}^{(k)} T_i^{(k+N_i)}) \right] \\
 & - \frac{1}{Pr} \sum_{j=1}^{M_i} \omega_i^{(j)} u_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i, \eta_i) \\
 & - \frac{1}{Pr} \sum_{j=1}^{M_i} \omega_i^{(j)} v_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_2^{(m)}(\xi_i, \eta_i) \\
 & - Ra \sum_{j=1}^{M_i} T_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i, \eta_i), \\
 & \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\
 & \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.44}
 \end{aligned}$$

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) u_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) u_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) u_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [u_i^{(k)}] + n_{y,i}^{(k)} \omega_i^{(k)} \right\} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [u_i^{(k+N_i)}] + n_{y,i}^{(k)} \omega_i^{(k+N_i)} \right\} \\
 &\quad + \sum_{j=1}^{M_i} \omega_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_2^{(m)}(\xi_i, \eta_i),
 \end{aligned}$$

for $(\xi_i, \eta_i) \in R_i \cup \Gamma_i$ and

for $i = 1, 2, \dots, N_d - 1, N_d$, (4.45)

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) v_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) v_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) v_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [v_i^{(k)}] - n_{x,i}^{(k)} \omega_i^{(k)} \right\} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \left\{ \frac{\partial}{\partial n} [v_i^{(k+N_i)}] - n_{x,i}^{(k)} \omega_i^{(k+N_i)} \right\} \\
 &\quad - \sum_{j=1}^{M_i} \omega_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i, \eta_i),
 \end{aligned}$$

for $(\xi_i, \eta_i) \in R_i \cup \Gamma_i$ and

for $i = 1, 2, \dots, N_d - 1, N_d$, (4.46)

and

$$\begin{aligned}
 \lambda(\xi_i, \eta_i) T_i(\xi_i, \eta_i) &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i, \eta_i) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i, \eta_i) T_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [T_i^{(k)}] - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [T_i^{(k+N_i)}] \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i, \eta_i) [n_{x,i}^{(k)} u_i^{(k)} + n_{y,i}^{(k)} v_i^{(k)}] T_i^{(k)} \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i, \eta_i) [n_{x,i}^{(k)} u_i^{(k+N_i)} + n_{y,i}^{(k)} v_i^{(k+N_i)}] T_i^{(k+N_i)} \\
 &\quad - \sum_{j=1}^{M_i} T_i^{(j)} u_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i, \eta_i) \\
 &\quad - \sum_{j=1}^{M_i} T_i^{(j)} v_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_2^{(m)}(\xi_i, \eta_i)
 \end{aligned}$$

for $(\xi_i, \eta_i) \in R_i \cup \Gamma_i$ and

for $i = 1, 2, \dots, N_d - 1, N_d$, (4.47)

respectively, where

$$\begin{aligned}
 \mathcal{P}_1^{(m)}(\xi_i, \eta_i) &= \iint_{R_i} \phi_{2D}(x, y; \xi_i^{(m)}, \eta_i^{(m)}) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y), \\
 \mathcal{P}_2^{(m)}(\xi_i, \eta_i) &= \iint_{R_i} \phi_{2D}(x, y; \xi_i^{(m)}, \eta_i^{(m)}) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi_i, \eta_i)] dA(x, y). \quad (4.48)
 \end{aligned}$$

The domain integrals which are now expressed in terms of the radial basis functions and the first order derivatives of the fundamental solution may be evaluated numerically by applying the trapezoidal rule twice.

4.4.5 Numerical procedure

For a numerical procedure, the point (ξ_i, η_i) in Equations (4.44) to (4.47) is selected to be given by $(\xi_i^{(n)}, \eta_i^{(n)})$, for $n = 1, 2, \dots, M_i - 1, M_i$, such that

$$\begin{aligned}
\lambda_i^{(n)} \omega_i^{(n)} &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \omega_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \omega_i^{(k+N_i)} \\
&\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \frac{\partial}{\partial n} [\omega_i^{(k)}] - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \frac{\partial}{\partial n} [\omega_i^{(k+N_i)}] \\
&\quad + \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \left\{ \frac{1}{Pr} [n_{x,i}^{(k)} u_i^{(k)} + n_{y,i}^{(k)} v_i^{(k)}] \omega_i^{(k)} - Ra [n_{y,i}^{(k)} T_i^{(k)}] \right\} \\
&\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \left\{ \frac{1}{Pr} [n_{x,i}^{(k)} u_i^{(k+N_i)} + n_{y,i}^{(k)} v_i^{(k+N_i)}] \omega_i^{(k+N_i)} \right. \\
&\quad \left. - Ra [n_{y,i}^{(k)} T_i^{(k+N_i)}] \right\} \\
&\quad - \frac{1}{Pr} \sum_{j=1}^{M_i} \omega_i^{(j)} u_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i^{(n)}, \eta_i^{(n)}) \\
&\quad - \frac{1}{Pr} \sum_{j=1}^{M_i} \omega_i^{(j)} v_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_2^{(m)}(\xi_i^{(n)}, \eta_i^{(n)}) \\
&\quad - Ra \sum_{j=1}^{M_i} T_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i^{(n)}, \eta_i^{(n)})
\end{aligned}$$

for $n = 1, 2, \dots, M_i - 1, M_i$ and

for $i = 1, 2, \dots, N_d - 1, N_d$, (4.49)

$$\begin{aligned}
 \lambda_i^{(n)} u_i^{(n)} &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) u_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) u_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \left\{ \frac{\partial}{\partial n} [u_i^{(k)}] + n_{y,i}^{(k)} \omega_i^{(k)} \right\} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \left\{ \frac{\partial}{\partial n} [u_i^{(k+N_i)}] + n_{y,i}^{(k)} \omega_i^{(k+N_i)} \right\} \\
 &\quad + \sum_{j=1}^{M_i} \omega_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_2^{(m)}(\xi_i^{(n)}, \eta_i^{(n)}), \\
 &\quad \text{for } n = 1, 2, \dots, M_i - 1, M_i \text{ and} \\
 &\quad \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.50}
 \end{aligned}$$

$$\begin{aligned}
 \lambda_i^{(n)} v_i^{(n)} &= \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) v_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) v_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \left\{ \frac{\partial}{\partial n} [v_i^{(k)}] - n_{x,i}^{(k)} \omega_i^{(k)} \right\} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \left\{ \frac{\partial}{\partial n} [v_i^{(k+N_i)}] - n_{x,i}^{(k)} \omega_i^{(k+N_i)} \right\} \\
 &\quad - \sum_{j=1}^{M_i} \omega_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i^{(n)}, \eta_i^{(n)}), \\
 &\quad \text{for } n = 1, 2, \dots, M_i - 1, M_i \text{ and} \\
 &\quad \text{for } i = 1, 2, \dots, N_d - 1, N_d, \tag{4.51}
 \end{aligned}$$

and

$$\begin{aligned}
\lambda_i^{(n)} T_i^{(n)} = & \sum_{k=1}^{N_i} \mathcal{G}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{G}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) T_i^{(k+N_i)} \\
& - \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \frac{\partial}{\partial n} [T_i^{(k)}] - \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) \frac{\partial}{\partial n} [T_i^{(k+N_i)}] \\
& + \sum_{k=1}^{N_i} \mathcal{G}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) [n_{x,i}^{(k)} u_i^{(k)} + n_{y,i}^{(k)} v_i^{(k)}] T_i^{(k)} \\
& + \sum_{k=1}^{N_i} \mathcal{G}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) [n_{x,i}^{(k)} u_i^{(k+N_i)} + n_{y,i}^{(k)} v_i^{(k+N_i)}] T_i^{(k+N_i)} \\
& - \sum_{j=1}^{M_i} T_i^{(j)} u_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_1^{(m)}(\xi_i^{(n)}, \eta_i^{(n)}) \\
& - \sum_{j=1}^{M_i} T_i^{(j)} v_i^{(j)} \sum_{m=1}^{M_i} W_i^{(mj)} \mathcal{P}_2^{(m)}(\xi_i^{(n)}, \eta_i^{(n)})
\end{aligned}$$

for $n = 1, 2, \dots, M_i - 1, M_i$ and

for $i = 1, 2, \dots, N_d - 1, N_d$, (4.52)

where $\lambda_i^{(n)} = \lambda(\xi_i^{(n)}, \eta_i^{(n)})$, $\omega_i^{(n)} = \omega_i(\xi_i^{(n)}, \eta_i^{(n)})$, $u_i^{(n)} = u_i(\xi_i^{(n)}, \eta_i^{(n)})$, $v_i^{(n)} = v_i(\xi_i^{(n)}, \eta_i^{(n)})$ and $T_i^{(n)} = T_i(\xi_i^{(n)}, \eta_i^{(n)})$.

Equation (4.49) generates in each subdomain, a set of M_i algebraic equations containing M_i unknowns, that are expressed in terms of unknown vorticity and vorticity flux. Since there are N_d subdomains, a total of N_d sets of linear algebraic equations, each with the size of $(M_i \times M_i)$ are produced. Each set of equations which corresponds to one subdomain, may be related to the other subdomains using the continuity condition described in Equation (4.28). Along with the vorticity boundary condition specified in Section 4.3.3, a block banded system of algebraic equations containing $(M_i \times N_d)$ equations and $(M_i \times N_d)$ unknowns are generated. Likewise, Equations (4.50) to (4.52) along with the corresponding continuity conditions and boundary conditions generates three additional block banded system of algebraic equations containing $(M_i \times N_d)$ equations

and $(M_i \times N_d)$ unknowns that are expressed in terms of the unknown velocities and temperatures and their corresponding fluxes respectively. Solutions of the four system of algebraic equations generated from Equations (4.49) to (4.52) lead to the distribution of vorticity, velocities in the x - and y -directions and temperature and their respective fluxes inside the anterior chamber.

4.5 Solution Procedure

4.5.1 Iterative solver

According to Škerget et al. [122], solution of the kinematics described by Equations (4.50) and (4.51) subjected to the prescribed velocity boundary condition (Equation (4.14)) produces a velocity distribution inside the anterior chamber that does not guarantee solenoidality of the velocity field for an arbitrary vorticity distribution. In order to satisfy the solenoidality constraints, Škerget et al. [122] proposed that the kinetics aspect of flow has to be coupled with the kinematics aspect to set up a system of non-linear equations. Hence, Equation (4.49) is coupled with Equations (4.50), (4.51) and (4.52) to set up a non-linear system of equations that has to be solved iteratively.

To obtain a numerical solution, an iterative solver based on a sequential routine that solves Equations (4.49), (4.50), (4.51) and (4.52) separately is developed. The algorithm is described as follows.

1. Start with an initial guess ($s = 0$) of the vorticity distribution over the solution domain, say $^{(s)}\omega_i$, for $i = 1, 2, \dots, N_d - 1, N_d$.
2. With the initial guess $^{(s)}\omega_i$, solve Equations (4.50) and (4.51) for $^{(s+1)}u_i$ and $^{(s+1)}v_i$ respectively, subjected to the velocity boundary condition (Equation (4.14)) and kinematics continuity condition (Equation (4.29)).
3. Using values of $^{(s+1)}u_i$ and $^{(s+1)}v_i$ obtained from Step 2, solve Equation (4.52) for

$^{(s+1)}T_i$ subjected to the temperature boundary conditions in Equations (4.17) and (4.18) and the continuity condition in Equation (4.30).

4. Calculate vorticity distribution at boundaries C_1 and C_2 based on the values of $^{(s+1)}u_i$ and $^{(s+1)}v_i$ obtained from Step 2 using Equation (4.15).
5. Solve Equation (4.49) for $^{(s+1)}\omega_i$ using values of $^{(s+1)}u_i$, $^{(s+1)}v_i$ and $^{(s+1)}T_i$ subjected to the boundary vorticities calculated from Step 4 and the kinetics continuity condition in Equation (4.28).
6. Relax vorticity values using

$$^{(s+1)}\omega_i = \Theta \left(^{(s+1)}\omega_i \right) + (1 - \Theta) \left(^{(s+1)}\omega_i \right), \quad (4.53)$$

where Θ is the relaxation parameter. In the present study, Θ is selected to be in the range of $0 < \Theta < 0.5$.

7. Check for convergence by calculating [127]

$$\delta = \frac{\sum_{i=1}^{N_d} \sum_{j=1}^{M_i} \left[^{(s+1)}\omega_i^{(j)} - ^{(s)}\omega_i^{(j)} \right]^2}{\sum_{i=1}^{N_d} \sum_{j=1}^{M_i} \left[^{(s+1)}\omega_i^{(j)} \right]^2}. \quad (4.54)$$

If $\delta < 10^{-6}$, then stop iteration. Otherwise, repeat Steps 2 to 7 for higher orders of s until the criteria, $\delta < 10^{-6}$ is satisfied.

4.5.2 Calculation of boundary vorticities

One of the more crucial steps involved in the algorithm presented in the preceding section is the calculation of boundary vorticities using Equation (4.15), i.e. Step 4. According to Equation (4.15), vorticity at the boundaries may be calculated if the first order derivatives of the velocity distribution are known. Škerget et al. [122, 128] suggested three methods

that may be used to calculate the boundary vorticities for general flow problems. These methods are described as follow.

1. Derivation of the interpolation functions used in approximating the velocity distribution, as typically carried out in the finite element method. Although the method is straightforward and easy to implement, the accuracy of the approximation is poor and may severely affect the performance of the numerical scheme [122, 128].
2. Estimation based on the velocity derivatives calculated at points close to the boundary. The velocity derivatives are obtained by differentiating the kinematic integral equations (Equations (4.20) and (4.21)). Significant errors may be introduced if the sampled points are too far from the boundaries. Coarse boundary discretization may also lead to inaccurate approximations.
3. Development of higher order singular integral kinematic equations for solving the unknown velocity derivatives at the boundaries. This approach has been regarded by Škerget et al. [122, 128] to be the most consistent and promising. Nonetheless, solution of the singular integral equations is mathematically very challenging and may not be a feasible option.

For flow problems that are bounded by stationary solid walls such as in the present study, values of the normal derivatives of velocity ($\partial u/\partial n$ and $\partial v/\partial n$) at boundaries C_1 and C_2 provide the necessary information for calculating the boundary vorticity [128]. Mathematically, the normal derivatives of velocity may be expressed as

$$\begin{aligned}\frac{\partial}{\partial n} [u(x, y)] &= n_x \frac{\partial}{\partial x} [u(x, y)] + n_y \frac{\partial}{\partial y} [u(x, y)], \\ \frac{\partial}{\partial n} [v(x, y)] &= n_x \frac{\partial}{\partial x} [v(x, y)] + n_y \frac{\partial}{\partial y} [v(x, y)].\end{aligned}\tag{4.55}$$

Likewise, the tangential derivatives of velocity ($\partial u/\partial \mathbf{t}$ and $\partial v/\partial \mathbf{t}$) are given by

$$\begin{aligned}\frac{\partial}{\partial \mathbf{t}} [u(x, y)] &= t_x \frac{\partial}{\partial x} [u(x, y)] + t_y \frac{\partial}{\partial y} [u(x, y)], \\ \frac{\partial}{\partial \mathbf{t}} [v(x, y)] &= t_x \frac{\partial}{\partial x} [v(x, y)] + t_y \frac{\partial}{\partial y} [v(x, y)],\end{aligned}\tag{4.56}$$

where t_x and t_y are the components of the unit tangential vector at the boundary. Components of the unit tangential vector are related to the components of the unit normal vector by

$$t_x = -n_y \text{ and } t_y = n_x.\tag{4.57}$$

Substituting Equations (4.55) and (4.56) into Equation (4.15) and using the relationship described in Equation (4.57) leads to

$$\omega(x, y) = n_x \left(\frac{\partial}{\partial n} [v(x, y)] - \frac{\partial}{\partial \mathbf{t}} [u(x, y)] \right) - n_y \left(\frac{\partial}{\partial n} [u(x, y)] + \frac{\partial}{\partial \mathbf{t}} [v(x, y)] \right).\tag{4.58}$$

Since velocities at boundaries C_1 and C_2 are zero (as a consequence of the no slip condition), tangential derivatives here are also zero. Therefore, Equation (4.58) reduces to

$$\omega(x, y) = n_x \frac{\partial}{\partial n} [v(x, y)] - n_y \frac{\partial}{\partial n} [u(x, y)], \text{ at } C_1 \cup C_2.\tag{4.59}$$

Equation (4.59) presents a simpler and more accurate approach for calculating boundary vorticities since solutions of the kinematics alone yield the normal derivatives of u and v everywhere inside the anterior chamber.

4.5.3 Choice of radial basis functions

This section describes some of the radial basis functions that may be used for the treatment of domain integrals. A proper selection of radial basis function is crucial for an accurate approximation of the unknown variables. One of the most commonly used radial

basis functions between the late 1980s' and early 1990s' is given by

$$\phi_{2D}(x, y; \xi, \eta) = 1 + \mathcal{R}(x, y; \xi, \eta), \quad (4.60)$$

where $\mathcal{R}(x, y; \xi, \eta)$ is the Euclidean distance between points (x, y) and (ξ, η) . Although the radial basis function described in Equation (4.60) is simple and easy to implement, it is plagued by its relatively poor accuracy when compared to other more recent radial basis functions [129, 130].

The radial basis function of the form

$$\phi_{2D}(x, y; \xi, \eta) = 1 + \mathcal{R}^2(x, y; \xi, \eta) + \mathcal{R}^3(x, y; \xi, \eta), \quad (4.61)$$

was proposed by Zhang and Zhu [130] as a more accurate and versatile alternative to the radial basis function expressed in Equation (4.60). According to Partridge [131] however, the $\mathcal{R}^2(x, y; \xi, \eta)$ term in Equation (4.61) does not introduce significant improvements to the accuracy of the approximation. He further suggested that the radial basis function of the form

$$\phi_{2D}(x, y; \xi, \eta) = 1 + \mathcal{R}^3(x, y; \xi, \eta), \quad (4.62)$$

suffices in producing approximations that are of reasonable accuracy.

The performance of the radial basis function in Equation (4.62) may be significantly improved by introducing a scale factor $\mathcal{R}_{\max}$, such that

$$\phi_{2D}(x, y; \xi, \eta) = 1 + \left(\frac{\mathcal{R}(x, y; \xi, \eta)}{\mathcal{R}_{\max}} \right)^3, \quad (4.63)$$

where $\mathcal{R}_{\max}$ is the maximum value of $\mathcal{R}(x, y; \xi, \eta)$. The importance of introducing $\mathcal{R}_{\max}$ into Equation (4.62) will be discussed in Chapter 7.

The thin plate spline (TPS), which is expressed in the Oxy coordinate system as

$$\phi_{2D}(x, y; \xi, \eta) = \mathcal{R}^2(x, y; \xi, \eta) \ln [\mathcal{R}(x, y; \xi, \eta)], \quad (4.64)$$

has been found to exhibit optimal interpolation properties [132]. To further improve the accuracy of the TPS, one may choose to augment Equation (4.64) with the first three terms of the Pascal triangle, i.e. $a_1 + a_2x + a_3y$ [132], such that

$$f(x, y) \approx \sum_{m=1}^{M_i} \gamma^{(m)} \{ \mathcal{R}^2(x, y; \xi_i, \eta_i) \ln [\mathcal{R}(x, y; \xi_i, \eta_i)] \} + a_1 + a_2x + a_3y, \quad (4.65)$$

subjected to the conditions

$$\sum_{m=1}^{M_i} \gamma^{(m)} = \sum_{m=1}^{M_i} \gamma^{(m)} x = \sum_{m=1}^{M_i} \gamma^{(m)} y = 0, \quad (4.66)$$

where $f(x, y)$ is the unknown function to be approximated and $\gamma^{(m)}$, a_1 , a_2 and a_3 are unknown coefficients to be determined.

The multiquadrics was introduced by Golberg et al. [133] in 1996 and is mathematically expressed as

$$\phi_{2D}(x, y; \xi, \eta) = \sqrt{\mathcal{R}^2(x, y; \xi, \eta) + s^2}, \quad (4.67)$$

where s is a free parameter such that $s^2 \geq 0$.

The compactly supported-positive definite-radial basis function (CS-PD-RBF) was introduced by Wendland [134] in 1995 for multivariate surface reconstruction. It was first used in the context of the boundary element method in 1999 by Chen et al. [135]. Different types of CS-PD-RBF of various smoothness, C^{2k} (for $k \geq 0$) have since been formulated (see references [135, 136] for examples). An example of the CS-PD-RBF of smoothness C^2 proposed by Wendland [134] is given by

$$\phi_{2D}(x, y; \xi, \eta) = \begin{cases} \left(1 - \frac{\mathcal{R}(x, y; \xi, \eta)}{s\mathcal{R}_{\max}}\right)^4 \left(1 + \frac{4\mathcal{R}(x, y; \xi, \eta)}{s\mathcal{R}_{\max}}\right), & \text{for } 0 \leq \frac{\mathcal{R}(x, y; \xi, \eta)}{s\mathcal{R}_{\max}} \leq 1, \\ 0, & \text{otherwise,} \end{cases} \quad (4.68)$$

where s is a free parameter such that $s > 0$ [136]. Note that the free parameter, s in the multiquadrics and the CS-PD-RBFs are independent of one another.

Of all the radial basis functions that have been mentioned, it is generally agreed that the multiquadrics and the CS-PD-RBFs produce numerical results that have the best degree of accuracy [133, 136]. The accuracy of the approximation however, depends on the proper selection of the value of the free parameter, s . Since the optimum value of s is problem-dependent and no proper guidelines for selecting s are yet available, the multiquadrics and the CS-PD-RBFs are rarely used. Instead, the augmented TPS (ATPS) has become the preferred choice among researchers. This is largely attributed to its simplicity and good accuracy [131, 132, 139].

4.6 Benchmarking of Numerical Solver

4.6.1 Benchmark problem

Before solving the natural convection flow inside the anterior chamber, it is important for the numerical scheme developed in Sections 4.4 and 4.5 to be verified with test problems where benchmark solutions are easily available. For this purpose, the thermally driven flow inside a unit square cavity, such as illustrated in Figure 4-3, is solved [137, 138].

The flow and thermal fields inside the anterior chamber are governed by Equations (4.10) to (4.13) and are subjected to the following boundary conditions:

$$\begin{aligned} u(x, y) &= v(x, y) = 0, \text{ on all boundaries,} \\ T(0, y) &= 1, \text{ for } 0 \leq y \leq 1, \\ T(1, y) &= 0, \text{ for } 0 \leq y \leq 1, \\ \frac{\partial}{\partial n} [T(x, 0)] &= \frac{\partial}{\partial n} [T(x, 1)] = 0, \text{ for } 0 \leq x \leq 1. \end{aligned}$$

The square cavity is assumed to be filled with air such that $Pr = 0.71$ [137]. Flows at $Ra = 1,000$ and $Ra = 10,000$ are solved.

Figure 4-3: Thermally driven flow inside a square cavity

4.6.2 Results

To implement the numerical scheme developed in the preceding sections, the square cavity shown in Figure 4-3 is discretized into smaller subdomains. Although it is not necessary for each subdomain to have the same geometrical shape, for mathematical and computational convenience, each subdomain here is selected to be a triangle. Each side of the triangle is taken to be represented by one boundary element such that each subdomain consists of three boundary elements ($N_i = 3$). For the treatment of the domain integrals, four well-spaced out interior points ($L_i = 4$) are selected inside each subdomain (see Appendix B). These are shown in Figure 4-4.

Figure 4-4: Geometrical, boundary and interior collocation nodes of a triangular subdomain (figure not to scale)

The numerical scheme is tested for two sets of subdomain meshes, namely Mesh 1 and Mesh 2. Mesh 1 consists of 200 subdomains ($N_d = 200$) while Mesh 2 consists of 800 subdomains ($N_d = 800$). These are shown in Figure 4-5. Each set of mesh is examined using the radial basis function of the form ‘ $1 + \mathcal{R}^3$ ’ (Equation (4.63)) and the ATPS (Equation (4.65)).

Figure 4-5: Subdomain discretization used in the benchmark problem

Tables 4.1 and 4.2 summarize the maximum velocity in the x - and y -directions for flows at $Ra = 1,000$ and $Ra = 10,000$ respectively. The values presented in Tables 4.1 and 4.2 represent the maximum velocity at the collocation nodes (boundary and interior). The Nusselt numbers at $x = 0$ ($Nu_{(x=0)}$) in the last row of Tables 4.1 and 4.2 are obtained by numerically calculating the expression

$$Nu_{(x=0)} = \int_0^1 \frac{\partial}{\partial n} [T(0, y)] dy, \quad (4.69)$$

using the trapezoidal rule.

Generally, the numerical results obtained using the numerical scheme developed show very good agreement when compared to the benchmark solutions. The numerical predictions approach the benchmark solution as the number of subdomains increases from

Table 4.1: Results obtained for flow at $Ra=1,000$

$Ra = 1,000$	Mesh 1 ($N_d = 200$)		Mesh 2 ($N_d = 800$)		Benchmark [137]
	$1 + \mathcal{R}^3$	ATPS	$1 + \mathcal{R}^3$	ATPS	
$u_{\max}$ (x, y)	3.748 (0.53, 0.80)	3.742 (0.53, 0.80)	3.728 (0.50, 0.81)	3.689 (0.50, 0.81)	3.649 (0.50, 0.81)
$v_{\max}$ (x, y)	3.810 (0.18, 0.50)	3.794 (0.18, 0.50)	3.791 (0.18, 0.49)	3.771 (0.18, 0.49)	3.697 (0.18, 0.50)
$Nu_{(x=0)}$	1.077	1.077	1.108	1.080	1.117

200 to 800. This indicates convergence in the numerical scheme. For the same number of subdomains used, the results obtained using the ATPS are much closer to the benchmark solution than the results obtained using the radial basis function of the form $1 + \mathcal{R}^3$. Similar observations have been reported in the numerical experiments carried out by other researchers [131, 132, 139].

Table 4.2: Results obtained for flow at $Ra=10,000$

$Ra = 10,000$	Mesh 1 ($N_d = 200$)		Mesh 2 ($N_d = 800$)		Benchmark [137]
	$1 + \mathcal{R}^3$	ATPS	$1 + \mathcal{R}^3$	ATPS	
$u_{\max}$ (x, y)	15.992 (0.48, 0.82)	16.026 (0.50, 0.83)	15.928 (0.47, 0.83)	16.190 (0.49, 0.83)	16.178 (0.50, 0.82)
$v_{\max}$ (x, y)	20.093 (0.12, 0.48)	19.925 (0.12, 0.48)	20.048 (0.12, 0.48)	19.728 (0.12, 0.48)	19.617 (0.12, 0.50)
$Nu_{(x=0)}$	2.189	2.138	2.251	2.120	2.238

Figure 4-6 shows the distribution of velocities, u and v at $y = 0.5$ and $x = 0.5$ respectively for flows at $Ra = 1,000$ and $Ra = 10,000$. Only results obtained using the ATPS with 800 subdomains are presented. For comparison purposes, the results obtained by Florez et al. [140] using the multi-domain boundary element method are included. There appears to be reasonably good agreement between the numerical results obtained from the present model and those computed by Florez et al. [140], which further supports the accuracy of the present numerical scheme.

Figure 4-6: Distribution of velocity in the a) x -direction at $y = 0.5$ and b) y -direction at $x = 0.5$, for flows at $Ra = 1,000$ and $10,000$

4.7 Natural Convection inside the Anterior Chamber

4.7.1 Material properties

Values of the thermal properties used for simulating the natural convection phenomena inside the anterior chamber are obtained from literature. The thermal expansion coefficient, β and the dynamic viscosity, μ of the aqueous humor are assumed to be the same as water [115]. These values are given by $3.37 \times 10^{-4} \text{K}^{-1}$ and $7.4 \times 10^{-4} \text{Nsm}^{-2}$ respectively [82]. The thermal diffusivity of the aqueous humor is calculated using

$$\alpha = \frac{\kappa}{\rho c},$$

where values of κ (thermal conductivity), ρ (density) and c (specific heat) of the aqueous humor have been presented in Chapter 2. A value of $1.46 \times 10^{-7} \text{m}^2 \text{s}^{-1}$ is found.

The values of T_h and T_c are represented by the temperature of the body core and the corneal surface respectively. Temperature of the healthy human body is given by 37°C . Temperature on the corneal surface, which have been assumed to be spatially-independent (see Section 4.3.3), is obtained from the average of the experimentally obtained values listed in Table 2.3. A value of 34°C is found.

The characteristic length L , is chosen to be 0.0068m based on the vertical distance from the pupillary axis to the tip of the anterior chamber. The radii of curvature of the anterior and posterior surfaces of the cornea are respectively given by 0.00925 and 0.00984m . The gravitational acceleration, g has a value of 9.81ms^{-2} .

Table 4.3 summarizes the values of thermal properties and various geometrical parameters used in this study. Based on the data tabulated in Table 4.3, values of Pr and Ra calculated from the expressions in Equation (4.9) are found to be approximately 5.1 and $30,000$ respectively. These values represent the conditions inside a normal human eye.

Table 4.3: Properties of the aqueous humor and the anterior chamber

Parameter	Value
Characteristic length, L (m)	0.0068
Thermal expansion coefficient, β (K^{-1})	3.37×10^{-4}
Dynamic viscosity, μ (Nsm^{-2})	7.4×10^{-4}
Thermal diffusivity, α (m^2s^{-1})	1.46×10^{-7}
Density, ρ (kgm^{-3})	996
Hot temperature, T_h ($^\circ\text{C}$)	37
Cold temperature, T_c ($^\circ\text{C}$)	34
Gravitational acceleration, g (ms^{-2})	9.81
Radius of curvature of posterior corneal surface, r_p (m)	0.00984
Radius of curvature of anterior corneal surface, r_c (m)	0.00925

4.7.2 Results

To carry out the numerical scheme developed, the model of the anterior chamber illustrated in Figure 4-2 is discretized into small triangular subdomains. Meshing of the

anterior chamber model is accomplished by using the mesh generator of the partial differential equation calculator, COMSOL Multiphysics [141]. A total of 1,648 triangular subdomains are generated. This is shown in Figure 4-7. The numbers of boundary elements and interior points used here are similar to the one used in the benchmark problem, i.e. $N_i = 3$ and $L_i = 4$. In Section 4.6, the numerical scheme based on the ATPS has been demonstrated to produce results that are more accurate than the radial basis function of the form ‘ $1 + \mathcal{R}$ ’. Hence, simulations in this section are carried out using only the numerical scheme based on the ATPS.

Figure 4-7: Model of the anterior chamber with 1,648 triangular subdomains

Figure 4-8 shows the distribution of the resultant velocity inside the anterior chamber during natural convection for an eye in the standing position. The contour and arrow plots indicate the velocity field and the flow profile inside the anterior chamber respec-

tively. Generally, the warmer aqueous humor that is closer to the surfaces of the iris and lens is less dense than the cooler aqueous humor near the inner surface of the cornea. Consequently, the warmer aqueous humor rises, while the cooler aqueous humor descends in the direction of gravity. This creates a constant circulation of aqueous humor inside the anterior chamber. The flow of aqueous humor represented by the arrow plot in Figure 4-8 agrees with the predictions obtained by other researchers using various mathematical models [113–115,117].

Figure 4-8: Resultant velocity distribution inside the anterior chamber for flow at $Ra = 30,000$

From the contour plot shown in Figure 4-8, it appears that the velocity of the flow in the downwards directions is greater than the flow in the upwards direction. This may be due to gravity that accelerates the downwards motion of aqueous humor, while opposing

the upwards motion.

The maximum resultant velocity achieved inside the anterior chamber is found to be 0.86mms^{-1} . This value is compared in Table 4.4 with the predictions obtained by other researchers using theoretical and various different numerical models. From Table 4.4, it is found that the numerical prediction obtained from the present model is in the same order of magnitude as those obtained by other researchers. The numerical prediction of the present model is slightly larger than the predictions obtained by other researchers however.

Table 4.4: Maximum resultant velocity obtained from the present model and other models in literature

Author(s)	Maximum velocity (mms^{-1})	Remarks
Present study	0.86	$N_d = 1,648$
Fitt and co-worker [113,114]	0.59	Based on a simplified model of the anterior chamber
Wyatt [120]	0.33	Maximum velocity in the y -direction
Heys and Barocas [115]	0.77	Model used included the inflow from the posterior chamber and the outflow at the trabecular meshwork
Kumar et al. [117]	0.79	Predictions made based on a temperature difference inside the anterior chamber of 2°C

Discrepancies between the numerical results obtained from the present study and those found by other researchers may be explained by the differences in the geometry of the anterior chamber models. In the present study, the anterior chamber has been modeled based on the dimensions of an actual human eye (see Chapter 2). Meanwhile, Canning et al. [114] and Fitt and Gonzalez [113] modeled the anterior chamber using a flat surface to represent the surfaces of the iris and lens and a curved surface to represent

the inner surface of the cornea. The curved surface is generally described by a simple mathematical function such as shown in Figure 4-9. In the work carried out by Kumar et al. [117], the model was developed based on the anterior chamber of a rabbit eye, which is geometrically defined by a hemisphere. This is illustrated in Figure 4-9.

Figure 4-9: Models of the anterior chamber developed by (a) Canning et al [114] and (b) Kumar et al [117]

Different thermal boundary conditions specified on the inner surface of the cornea may also contribute to the discrepancies in the results tabulated in Table 4.4. In the present study, a boundary condition describing the relationship between the temperature and heat flux, i.e. a mixed boundary condition, have been specified on the inner surface of the cornea. Other researchers such as Canning et al. [114], Fitt and Gonzalez [113] and Kumar et al. [117] have specified a constant temperature boundary condition. A constant temperature boundary condition generally assumes the temperature difference between the surfaces of the cornea and iris and lens to be uniform. On the other hand, the use of a mixed boundary condition allows the temperature difference between the two surfaces of the anterior chamber to vary according to location. Although it may not be possible to determine whether which approach is better for simulating the conditions inside the

Figure 4-10: Temperature distribution inside the anterior chamber with and without natural convection

actual human eye, the use of the mixed boundary condition in the present study provides an alternative for other researchers who may be interested in investigating the flow of aqueous humor inside the anterior chamber.

Figure 4-10 illustrates the temperature distribution inside the anterior chamber during natural convection. As a comparison, the temperature distribution when no natural convection exists is also shown. Unlike the anterior chamber without natural convection, the isotherms inside the anterior chamber appear to be slightly asymmetrical in the presence of natural convection. This may be explained by the convectonal currents inside the anterior chamber. As the aqueous humor flows upwards, it gains heat from the ocular blood flow inside the iris. In the downwards motion, heat transfer from the

aqueous humor to the inner corneal surface occurs. Consequently, aqueous humor in the lower portion of the anterior chamber has a smaller temperature than the aqueous humor that is in the upper portion. Without natural convection, heat transfer inside the anterior chamber occurs purely by conduction and is not affected by the actions of gravity. Hence, the isotherms inside the anterior chamber are naturally symmetrical about the pupillary axis.

It is of interest to determine the magnitude of temperature difference across the anterior chamber that gives rise to the flow of aqueous humor shown in Figure 4-8. To do so, the largest temperature difference, which occurs along the pupillary axis, is taken as the reference. This is denoted by ΔT . From the numerical results obtained, a value of $\Delta T = 2.52^\circ\text{C}$ is found when natural convection is present inside the anterior chamber. This agrees well with the results obtained by Heys and Barocas [115], where a value of 2.6°C was reported. When no natural convection is present, a value of $\Delta T = 2.53^\circ\text{C}$ is obtained. This suggests that the presence of natural convection has no significant effect on the magnitude of temperature inside the anterior chamber despite producing an asymmetrical temperature profile.

4.7.3 Significance of natural convection

From the analysis carried out in the preceding section, it has been shown that the convective flow of aqueous humor causes the isotherms inside the anterior chamber to be asymmetrical about the pupillary axis. No significant difference in the magnitude of temperature difference inside the anterior chamber is found however. In this section, the issue concerning the significance of natural convection on the heat transfer inside the anterior chamber is addressed. To do so, the dimensionless heat flux ($\partial T^*/\partial n^*$) that flows through boundary C_1 for cases with and without natural convection are compared.

Figure 4-11 plots the variation of the dimensionless heat flux along boundary C_1 for cases with and without natural convection. Both cases show magnitudes of dimensionless heat flux that are not significantly different from one another. Not surprisingly, the curve

observed in the case with natural convection shows a slight asymmetrical profile.

Figure 4-11: Dimensionless heat flux along the inner surface of the cornea

For a quantitative comparison, the total rate of heat transfer that flows through the inner surface of the cornea is calculated. When no natural convection is present, the total rate of heat transfer is estimated to be 223.98. The presence of natural convection increases the total dimensionless heat flux to approximately 225.03, which shows an increment of less than 0.5%. The lack of enhanced heat flux suggests that the heat transfer inside the anterior chamber is not significantly affected by the flow of aqueous humor. The same conclusion was reached by Heys and Barocas [115] based on a similar analysis using a numerical model of the anterior chamber.

Results obtained from the present analysis suggest that it suffices to carry out analyses of ocular heat transfer without considering the natural convection flow inside the anterior chamber. This supports the models of the human eye developed in Chapters 2 and 3 and by other researchers in the past [22, 23, 48, 49, 63], where aqueous humor inside the

anterior chamber has been assumed to be stagnant. The presence of natural convection causes the isotherms inside the anterior chamber to be slightly asymmetrical however.

4.8 Effects of Temperature Difference inside the Anterior Chamber

One of the factors that affect the natural convection flow inside the anterior chamber is the magnitude of temperature difference, ΔT . Since the flow is thermally driven, a larger temperature difference is expected to produce a stronger flow. From the numerical results presented in Section 4.7.2, flow at $Ra = 30,000$, which represents conditions inside a normal human eye, has been found to correspond to a temperature difference inside the anterior chamber of 2.52°C . Therefore, the effects of temperature difference inside the anterior chamber may be investigated by repeating the simulations for different values of Ra . For the purpose of this study, four different values of Ra are considered, namely 10,000, 20,000, 40,000 and 50,000.

The distribution of resultant velocity inside the anterior chamber for flows at $Ra = 10,000, 20,000, 40,000$ and $50,000$ are displayed in Figure 4-12. For a better visualization of the effects of different Ra on the velocity distribution inside the anterior chamber, flow at $Ra = 30,000$ is also included. From Figure 4-12, it is found that the velocity achieved by the aqueous humor inside the anterior chamber becomes larger as Ra increases from 10,000 to 50,000. Specifically, the maximum resultant velocity is found to be 0.25, 0.57, 0.86, 1.10 and 1.36mms^{-1} for flows at $Ra = 10,000, 20,000, 30,000, 40,000$ and $50,000$ respectively. Despite showing an increased in the magnitude of resultant velocity, the velocity profile inside the anterior chamber does not appear to be significantly affected by the increase in Ra .

Figure 4-13 shows the temperature profiles inside the anterior chamber for flows at $Ra = 10,000, 20,000, 40,000$ and $50,000$. The temperature profile obtained for flow at $Ra = 30,000$ is also presented for a better comparison. For each value of Ra investigated,

Figure 4-12: Resultant velocity field inside the anterior chamber at $Ra = 10,000, 20,000, 30,000, 40,000$ and $50,000$.

Figure 4-13: Isotherms inside the anterior chamber at $Ra = 10,000$, $20,000$, $30,000$, $40,000$ and $50,000$.

asymmetrical isotherms can be observed inside the anterior chamber. As the value of Ra increases from 10,000 to 50,000, the degree of thermal asymmetry also increases. This may be due to the stronger flow produced when values of Ra become larger (see Figure 4-12). As expected, flow at a larger Ra yields a larger temperature difference inside the anterior chamber. Values of ΔT of 0.84, 1.68, 2.52, 3.33 and 4.14°C have been found for flows at $Ra = 10,000, 20,000, 30,000, 40,000$ and 50,000 respectively.

Table 4.5 summarizes the values of ΔT and the maximum resultant velocities achieved inside the anterior chamber for flows at $Ra = 10,000, 20,000, 30,000, 40,000$ and 50,000. It is observed that the maximum resultant velocity increases with the temperature difference inside the anterior chamber. This is not surprising given that the flow is thermally driven. Hence, a greater temperature difference creates larger buoyancy forces that drive the flow of aqueous humor at a higher velocity. From Table 4.5, an increase in ΔT from 1.68 to 4.14°C is found to produce an increase in the maximum resultant velocity of 0.57 to 1.67mms⁻¹. This shows an increment of approximately 2.4 times. Using the data presented by Canning et al. [114] (see Equation (4.1)), the same increase in temperature is found to produce an increase in the maximum resultant velocity of approximately two times. Kumar et al. [117] estimated an increase in the maximum resultant velocity of approximately 1.5 times when ΔT increases from 2 to 4°C. Comparisons between the results obtained from the present model and those found by Canning et al. [114] and Kumar et al. [117] generally yield good qualitative agreement.

Table 4.5: Values of the thermal gradient and maximum resultant velocity inside the anterior chamber for flows at different values of Ra

Ra	Temperature difference, ΔT (°C)	Maximum resultant velocity (mms ⁻¹)
10,000	0.84	0.25
20,000	1.68	0.57
30,000	2.52	0.86
40,000	3.33	1.10
50,000	4.14	1.36

From Table 4.5, it is apparent that the strongest flow is produced when the aqueous

humor flows at $Ra = 50,000$. It is thus of specific interest to determine if the stronger flow increases the heat transfer inside the anterior chamber. At $Ra = 50,000$, the total dimensionless heat flux that flows into the cornea is calculated to be 227.52. This shows an increment of only 1.5% from the case when no natural convection exists inside the anterior chamber (223.98). It is important to note that the temperature difference inside the anterior chamber of a normal human eye is unlikely to be greater than 2°C , such as those seen in flows at $Ra > 20,000$. From the results of the preliminary investigation carried out in Chapter 2, the temperature difference along the pupillary axis between the anterior and posterior surfaces of the anterior chamber is found to be 1.04°C . Based on the experimental results obtained by Schwartz [142] using invasive measuring techniques, the temperature difference inside the anterior chamber of rabbit eyes was found to be less than 1°C . Given that the thermal gradient inside the anterior chamber is unlikely to be as high as 4.14°C as seen in the case when $Ra = 50,000$, it may be convincingly deduced that the flow of aqueous humor does not increase the amount of heat flow inside the anterior chamber.

4.9 Effects of eye orientation

Different orientations of the anterior chamber may affect the natural convection flow of aqueous humor inside the anterior chamber. This is due to gravity, which pulls at different directions of the anterior chamber. So far, investigations of the natural convection flow have been limited to the case when the human eye is in the standing position. In this case, gravity pulls in the direction orthogonal to the pupillary axis (see Figure 4-2). When the anterior chamber is in the supine position, gravity pulls in the direction parallel to the pupillary axis. This is illustrated in Figure 4-14. Changes in the directions of gravity pull as a result of different orientations of the human eye are expected to produce changes in the flow profiles. This section investigates the effects of different eye orientations on the natural convection flow inside the anterior chamber.

Figure 4-14: Orientation of the anterior chamber in the supine position

The governing equations and the boundary conditions describing the thermally driven flow with reference to the orientation of the anterior chamber shown in Figure 4-14 are similar to the ones used for describing the flow in the standing position. These have been presented in Sections 4.3.2 and 4.3.3. As in the case of the anterior chamber in the standing position, investigations here are carried out using 1,648 triangular subdomains. Each subdomain consists of three boundary elements and four interior points. Values of parameters used for describing the governing equations and boundary conditions are the same as those used in the earlier investigations. These are tabulated in Table 4.3. Using these values, flow at $Ra = 30,000$ is simulated.

Figure 4-15 presents the temperature profile inside the anterior chamber of an eye in the supine position. Unlike the isotherms obtained for the anterior chamber in the standing position (see Figure 4-10), the isotherms shown in Figure 4-15 is symmetrical about the pupillary axis. In fact, the temperature profile shown in Figure 4-15 is generally similar to the temperature profile inside the anterior chamber when no natural convection exists (see Figure 4-10). The lack of thermal asymmetry inside the anterior chamber in a supine position has also been observed by Kumar et al. [117].

The distribution of the resultant velocity and the flow profile inside the anterior chamber are illustrated in Figure 4-16 and are represented by the contour and arrow plots respectively. From the contour plot presented in Figure 4-16, the distribution of

Figure 4-15: Temperature distribution inside the anterior chamber in a supine position for flow at $Ra = 30,000$

resultant velocity is found to be slightly symmetrical about the pupillary axis. The flow profile presented in Figure 4-16 appears to be counter-intuitive. Since the largest temperature difference inside the anterior chamber occurs along the pupillary axis, flow in the upwards direction is expected to take place here [117]. This is not the case however. Instead, flow in the opposite direction is obtained, such as illustrated in Figure 4-16.

The maximum resultant velocity achieved by the aqueous humor inside the anterior chamber in the supine position is found to be 0.09mm s^{-1} . This is approximately 0.1 times the value in the standing position. The smaller flow produced in the supine position as found from the present study contradicts the results obtained by Kumar et al. [117], where the maximum velocity of flow in the supine position was found to be 1.5 times the flow in the standing position. The conflicting results may be explained by the use of a two-dimensional geometry in the present study. While a two-dimensional model may be used to describe the natural convection flow inside the anterior chamber in a standing position [114], the same may not apply for flows inside the anterior chamber in the supine orientation. Without a strong basis for assuming the flow inside the anterior chamber in a supine position to be two-dimensional, the results presented in this section should be treated purely as a theoretical study, where different orientations of the anterior chamber are acknowledged to produce different flow profiles.

Figure 4-16: Resultant velocity distribution inside the anterior chamber in the supine position for flow at $Ra = 30,000$

4.10 Discussion

The thermally driven flow inside the anterior chamber has been successfully simulated using the boundary element method. The natural convection flow inside the anterior chamber is described using the Navier-Stokes equations, which consist of the continuity, momentum and energy equations. Difficulty associated with the unknown pressure term in the momentum equation is alleviated by partitioning the Navier-Stokes equations in the primitive variables into the kinetics and kinematics aspect of flow. This leads to the velocity-vorticity formulation of the Navier-Stokes equations.

When deriving the integro-differential equations of the Navier-Stokes equations, the presence of non-linear terms gives rise to domain integrals. These domain integrals are dealt with using an approach that is similar to the boundary-domain integral method developed by Škerget et al. [122]. One of the differences between the numerical scheme developed in the present study and the boundary-domain integral method lies in the approximation of the unknown variables in the domain integrals. In the boundary-domain

integral method, the approximation is carried out using polynomial interpolation functions such as linear and quadratic. In the present numerical scheme, an approximation based on a series of radial basis functions is adopted. Numerical experiments carried out to validate the accuracy of the numerical scheme have found that the approximation based on a series of radial basis functions yield results that conform with the benchmark solutions. At present, it may not be possible to determine if the approximation based on a series of radial basis functions is more accurate than the polynomial interpolation functions. Nevertheless, the approach adopted in the present study provides other researchers with an alternative for treating the domain integrals when solving fluid flow problems. Comparisons between the accuracy of the approximation using the radial basis functions and polynomial interpolation functions may be investigated in future studies.

One may observe that the discretization carried out on the boundaries of each subdomain is coarse, where only three boundary elements have been used. Likewise, the number of interior points that has been selected for the treatment of domain integral is very small. The use of very few boundary elements and interior points in each subdomain is compensated by employing a large number of subdomains in the domain decomposition technique. In addition to setting up a system of linear algebraic equations that is very sparse, the use of large number of subdomains enables numerical evaluation of the domain integrals to be performed more efficiently. When the number of subdomains used increases, the size of each subdomain decreases. Each subdomain may then be treated as a single cell, where numerical integration can be carried out directly. On the other hand, if only a few subdomains are used, each subdomain may have to be further discretized into smaller cells, in order for the numerical calculation of the domain integrals to be performed more accurately. This introduces additional computational labour that reduces the performance of the numerical scheme.

An iterative solver that solves each integral equation in a sequential algorithm has been developed to obtain a numerical solution of the non-linear problem. When executing the iterative solver, a proper choice of the initial vorticity distribution helps to ensure

convergence of the numerical scheme. Ideally, the initial assumption has to be close to the actual solution. However, since this is not possible without making random estimations, a zero vorticity field has been selected as the initial guess. To guarantee convergence of the iterative solver, an approach that solves the numerical scheme for consecutive increments of Ra has been adopted. Using the initial guess of zero vorticity distribution, flow at $Ra = 1,000$ is initially solved. Solutions obtained for the flow at $Ra = 1,000$ are then used as the initial guess to solve for the flow at $Ra = 2,000$. The same procedure is then repeated for solutions at $Ra = 3,000, 4,000, 5,000, \dots$, in a consecutive manner until the desired Ra is reached. One of the drawbacks of such an approach is the extended computational time needed to obtain the final solution.

In order to speed up the convergence of the iterative solver developed, relaxation is carried out on the values of vorticity obtained in each iteration step. In doing so, values of the relaxation parameter Θ , have been selected to be in the range of 0 to 0.5. Specifically, values of Θ between 0.3 and 0.5 are used when flows at $Ra \leq 30,000$ are solved, while values in the range between 0 and 0.3 have been used when $Ra > 30,000$. The iterative solver fails to converge if value of Θ is chosen to be greater than 0.5 ($\Theta > 0.5$) or when relaxation is not carried out.

Generally, the numerical results obtained for the anterior chamber in the standing position show good agreement when compared to the predictions obtained by other researchers using various theoretical and numerical models. The magnitude of the maximum resultant velocity achieved inside the anterior chamber of the present study has been found to be in the same order of magnitude as those predicted by other researchers. Discrepancies may be explained by the differences in the geometries of the model and the boundary conditions specified on the inner surface of the cornea. In the case of the anterior chamber in the supine position, the results obtained using the present model is found to be unreliable. This is due to the use of a two-dimensional model, which does not accurately simulate the natural convection flow inside an anterior chamber in the supine position.

One of the limitations of the present model lies in the specification of the boundary condition at the surfaces of iris and lens. In the present study, the surfaces of the iris and lens have been assumed to be at a constant body core temperature. This boundary condition, which is similar to those specified by other researchers in the past [113–115, 117], generally assumes the blood flow inside the iris to be sufficient to maintain the temperature at these surfaces at the body core level. From the numerical investigations carried out in Chapters 2 and 3, temperatures at the surfaces of the iris and lens have been found to be lower than the body core temperature. These numerical predictions are supported by the experimentally obtained temperatures presented by Schwartz [142].

One of the consequences of assuming a constant body core temperature at the surfaces of the iris and lens is the overestimation of the heat flow inside the anterior chamber. In the present model, the average heat flux that flows through the inner surface of the cornea is estimated to be approximately 770Wm^{-2} (based on a thermal conductivity of the anterior chamber of $0.58\text{Wm}^{-1}\text{K}^{-1}$). From the preliminary investigation carried out in Chapter 2, the average heat flux that flows from the anterior chamber into the cornea in the absence of natural convection is calculated to be approximately 300Wm^{-2} . By comparing the values of heat flux obtained from the present model and the model of the human eye in Chapter 2, it is apparent that the model of the anterior chamber used here predicts heat flow that is nearly 2.6 times the heat flow inside the human eye model. Therefore, it may be deduced that the model developed in the present study may have overestimated the convectational flow inside the anterior chamber.

The investigations carried out in this chapter may be further improved by repeating the analysis using a complete model of the human eye. By doing so, errors that originate from the assumptions made when specifying boundary conditions on the walls of the anterior chamber may be avoided. Furthermore, the complete model of the human eye presents a more realistic thermal environment for the thermally driven flow of aqueous humor to be simulated. Nevertheless, the use of a complete human eye model may not be computationally feasible due to the increased computational cost, both in memory

and execution time.

Investigations of the natural convection flow inside the anterior chamber in the supine position may be repeated in future using a three-dimensional model. Results obtained using a three-dimensional model are more reliable and provides a better comparison with the results found by Kumar et al. [117]. One has to take note however, that a three-dimensional flow is generally more complex to solve. In addition to the increased in the dimension of the problem, flow in three-dimensional problems are complicated by the three components of vorticity. This increases the number of non-linear terms of the governing equations, which results in a flow problem that is mathematically more challenging than a two-dimensional flow. These are open for future studies.

In the present study, the inner surface of the cornea has been assumed to be a solid wall. According to Ethier et al. [14], the surface of the cornea is porous such that aqueous humor inside the anterior chamber is able to permeate into the cornea. The effects of a permeable corneal surface on the flow of aqueous humor may also be investigated as an extension to the work presented in this chapter. This may be accomplished by using the slip condition of Beavers and Joseph, which describes the boundary condition of a porous surface. This is mathematically given by

$$\begin{aligned} u &= -\frac{\sqrt{k}}{s} \frac{\partial u}{\partial x}, \\ v &= 0, \end{aligned} \tag{4.70}$$

where k and s are the permeability of the corneal surface and slip parameter respectively.

In addition to the lack of relevant information on the values of parameters associated with the permeability of the cornea, other issues that have to be taken into account when considering the porous boundary condition include the technique for calculating boundary vorticity using Equation (4.59). In the present study, the no slip condition enables the boundary vorticity to be evaluated using only values of the normal derivatives of velocity. However, if Equation (4.70) is specified as the boundary condition on C_1 , one

may require the knowledge of both the normal and tangential derivatives of velocity in order to calculate Equation (4.59).

4.11 Concluding Remarks

The thermally driven flow inside the anterior chamber has been successfully simulated in this chapter using the boundary element method. A two-dimensional model of the anterior chamber is developed based on the dimensions of an actual human eye for simulating the natural convection flow. One of the major conclusions than can be drawn from this chapter is that the thermally driven flow inside the anterior chamber has no significant effect on the heat transfer inside the human eye. This implies that analysis of the ocular heat transfer can be carried out by neglecting the flow of aqueous humor inside the anterior chamber without introducing significant errors. The results obtained from this chapter generally uphold the numerical results presented in Chapters 2 and 3, where aqueous humor inside anterior chamber has been assumed to be stagnant.

Chapter 5

Laser Thermokeratoplasty

5.1 Introduction

Laser thermokeratoplasty (LTKP) is a corneal refractive surgery that is intended for vision correction. It is a subset of the thermokeratoplasty technique that involves heating of the cornea via laser treatment for the purpose of inducing corneal shrinkages. When the cornea is subjected to heat, the collagen bonds inside the stroma break, leading to contractions (shrinkages) of the collagen fibrillae [143]. Shrinkages of the cornea cause the curvature to change, which ultimately affect the refractive power of the cornea. Based on the aforementioned behavior, ophthalmologists have been able to correlate the amount of corneal shrinkages due to heat, with parameters such as heating duration and laser energy to produce the desired level of changes in the corneal refractive power. Although LTKP is a less popular method than other laser surgery techniques such as laser in-situ keratomileusis (LASIK), it is still used in clinical practice today, especially in the treatment of presbyopia and astigmatism.

One of the main concerns of LTKP is the risk of causing irreversible thermal damage. This may induce permanent scarring to the cornea. LTKP also suffers from poor predictability and repeatability, which usually lead to clinical outcomes that are often not very reliable. A proper understanding of the thermal behavior of the cornea during

LTKP is therefore, essential in the designing of treatment procedures that may help to reduce the risk of thermal injury and to improve the predictability and repeatability of clinical results. Mathematical modeling plays a key role in the studies of corneal temperature changes during LTKP. This is largely due to the hazardous nature of the treatment procedure that makes experimental studies on human subjects difficult. In fact, most of the experimental studies of LTKP have been performed *in vitro* using samples of animal cornea [29,143].

One of the earliest mathematical models that was developed for investigating the corneal temperature changes during LTKP was presented by Mainster [144] in 1979. Although various other studies of the thermal interaction between lasers and cornea have been reported prior to the work of Mainster [144], these investigations were mainly focused on the thermal effects of lasers that were not associated with the treatment of LTKP [44,145]. In the investigation carried out by Mainster [144], the cornea was modeled as a semi-infinite region where a one-dimensional heat transfer was assumed. By the early 1990s', numerical models that investigated the thermal profile of the cornea during LTKP began to emerge. Most of the models developed during this period considered only the cornea as the solution domain [146,147]. The cornea was modeled as a cylinder in the *Orz* coordinate system. Numerical solutions were largely obtained using the finite difference method.

Between the early 1990s' and early 2000s', studies of LTKP were eagerly pursued by Brinkmann and co-worker [28,148,149] from both the experimental and numerical perspectives. The models, which comprised of the cornea and anterior chamber, were assumed as a two-layered cylinder and were developed in the *Orz* coordinate system. The finite element method was used to obtain a numerical solution. One of the unique features of the models developed by Brinkmann and co-worker [28,148,149] was the inclusion of intracorneal focusing of the laser beam, i.e. the distribution of laser energy within the cornea. Various types of lasers used in LTKP such as Er:Glass, Ho:YAG and CO₂ lasers have been investigated. In most cases, the numerical predictions showed

results that were comparable to those observed during in vitro experiments.

Since the early 2000s', numerical investigation of LTKP have been actively carried out by Manns and co-investigator [150–152]. Unlike the models developed by Brinkmann and co-worker [28, 148, 149], the model region consisted only of the cornea and was modeled as a single-layered tissue slab in the $Oxyz$ coordinate system. Analytical solutions that were expressed in terms of summations of an infinite series were derived based on the Green's function approach. The transient temperature profile of the cornea was found to be reasonable from a biological standpoint. No comparisons with experimental data have been performed however. In addition to the investigations on the transient temperature changes of the cornea, Manns and co-investigator [150, 152] predicted the thermal damage and corneal shrinkages inside the cornea during LTKP using the Arrhenius equation, the damage integral and the second order kinetic model of corneal shrinkage.

One of the common features shared by most of the studies of LTKP in the past is the use of the simplified model approach (see Chapter 1) when developing the mathematical models. The choice of using the simplified model approach may be due to the need for maintaining mathematical simplicity. This approach remains valid since temperature changes inside the cornea during LTKP are localized to the area where the laser beam is applied. One of the limitations of the simplified model approach however, concerns the assumptions that have to be made when specifying the boundary conditions. In most cases, these assumptions may not be physiologically correct.

In this chapter, the model of the human eye developed in Chapter 2 is used to investigate changes in the temperature distribution inside the human cornea during treatment of LTKP. In addition to improving our understanding of the thermal behavior of the cornea when subjected to heat, this study aims to examine the feasibility of using an anatomically more realistic eye model for the studies of ocular heat transfer during LTKP. Problems associated with the increase of computer memory due to the use of a more complex model are avoided by numerically solving the model using the boundary element method (see Chapter 1 for some of the characteristics of the boundary element method).

Investigations are carried out for treatments of LTKP using pulsed and continuous-wave lasers. Additionally, the degree of thermal damage induced onto the cornea during laser radiation is estimated based on the transient temperature profile of the cornea using the thermal damage model of Henriques and Moritz [67].

5.2 Characteristics of Laser-Thermokeratoplasty

The premise behind the treatment of LTKP is the shrinkages experienced by the corneal collagen when the cornea is subjected to heating. According to Stringer and Parr [27], the corneal collagen shrinks when the cornea is heated to a temperature between 55 and 65°C. However, this observation was made without considering the factors involved in ensuring a successful treatment of LTKP. Subsequent investigations carried out by other researchers discovered that the cornea has to be heated to a minimum temperature of 64°C in order to produce permanent corneal shrinkages [153]. Likewise, Brinkmann et al. [148] found that the deep stromal tissues have to be heated to temperatures beyond the shrinkage threshold to guarantee long term effects of corneal shrinkage.

One of the important steps involved during LTKP is the need to maintain the corneal temperature below 100°C. This is essential in order to avoid corneal relaxation [154]. Relaxation generally causes the bonds between the collagen molecules inside the cornea to break, thus countering the intended corneal shrinkage. Another important issue during treatment of LTKP concerns the temperature at the corneal endothelium, which is highly sensitive towards heat [155]. According to Wirbelauer [155], endothelial cell deaths occur when the temperature at the endothelium increases to 65°C. Therefore, an ideal treatment of LTKP is expected to produce the desired amount of permanent shrinkage while minimizing the amount of corneal relaxation and thermal damage inside the cornea.

In a typical clinical treatment of LTKP, eight equally-distanced laser spots that are arranged concentrically around the center of the corneal surface are applied onto the cornea. Each spot has a radial distance of 3 to 5mm from the center of the corneal

surface. In some cases, 16 spots are applied, where the additional eight spots are located on an outer ring at a radial distance of approximately 7mm from the center. Although the threshold for corneal shrinkage has been found to be in the range of 55 to 65°C, it is common for the cornea to be heated beyond this threshold. The temperature that the cornea is eventually heated to, depends on the type of lasers used. Two types of laser, namely pulsed and continuous-wave lasers, can be used for the purpose of LTKP.

5.2.1 Pulsed laser

Pulsed laser refers to the type of laser with output that is irregular [66]. Each laser pulse delivers a relatively large amount of energy at a duration that is usually less than 0.25s. One of the most commonly used pulsed laser in the treatment of LTKP is the Ho:YAG laser, which emits laser beam at a wavelength of $2.1\mu\text{m}$ [147,153]. Other types of pulsed lasers that have been used in LTKP include the Er:Glass and the Tm:YAG laser. In a typical LTKP procedure using pulsed laser, seven laser pulses, each with a duration of $200\mu\text{s}$, are applied onto the corneal surface at a repetition rate of 5Hz [151].

5.2.2 Continuous-wave laser

Continuous-wave lasers are lasers that produce a steady continuous output [66]. Radiation is usually carried out at a low energy rate. Among the type of continuous-wave lasers that have been used in LTKP include laser diodes, CO_2 lasers and the CoMgF_2 lasers. Laser diodes are usually preferred over CO_2 and CoMgF_2 lasers due to its tunability. This allows the laser beam to be emitted at different wavelengths, hence making it a more versatile choice for LTKP. Common wavelengths used range from 1.85 to $1.87\mu\text{m}$ [28]. LTKP treatment using continuous-wave lasers may be carried out using two different approaches, namely the 10s coagulation, where the cornea is heated continuously for 10s at a laser power of 0.125W, and the minute coagulation, where a continuous heating of 60s is carried out using a 0.10W laser [149].

5.3 Mathematical Model

5.3.1 Model description

The model of the human eye developed in Chapter 2 is used for the investigations carried out in this chapter. The model, which consists of six separate regions, is reproduced here as Figure 5-1. The regions defined by R_1 , R_2 , R_3 , R_4 , R_5 and R_6 are respectively the cornea, anterior chamber, lens, posterior chamber, vitreous and sclera. The exterior surfaces of the cornea and sclera are denoted by boundaries C_1 and C_2 respectively.

Figure 5-1: Model of the human eye used in the study of laser-thermokeratoplasty

5.3.2 Governing equations

The transient temperature distribution inside the human eye during LTKP may be described using

$$\begin{aligned} \rho_i c_i \frac{\partial}{\partial t} [T_i(r, z, t)] &= \nabla_{\text{axis}} (\kappa_i \nabla_{\text{axis}} T_i(r, z, t)) + S_i(r, z, t) \\ &\text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \\ &\text{for } t > 0, \end{aligned} \quad (5.1)$$

where ρ_i , c_i and κ_i are the density, specific heat and thermal conductivity of region R_i respectively, T_i is the temperature distribution in R_i , t is time and S_i is the heat generated inside region R_i due to the absorption of laser energy. Note that the temperature distribution is now a function of space and time. The expression in Equation (5.1) follows the assumptions made in Chapter 2, where blood perfusion and metabolic heat generation terms in the bioheat equation are omitted. Additionally, aqueous humor inside the anterior and posterior chambers is assumed to be stagnant (see Chapter 4). Each region inside the human eye is assumed to be homogeneous and thermally isotropic.

Heat that is generated inside the eye due to the absorption of laser energy, S_i may be described using the Beer-Lambert law [66]. For the typical range of laser wavelengths used in LTKP (1.85 to $2.1\mu\text{m}$), S_i may be mathematically expressed as

$$S_i(r, z, t) = \begin{cases} \psi(t)\varrho(1 - \mathbb{F})E(r, z)\exp(-\varrho z), & \text{for } i = 1, \\ 0 & \text{, for } i = 2, 3, 4, 5 \text{ and } 6, \end{cases} \quad (5.2)$$

where ϱ is the corneal absorption coefficient, which is dependent on the wavelength of the laser (unit of m^{-1}), $\mathbb{F}$ is the Fresnel reflectance of the corneal surface, $E(r, z)$ is the incident irradiance at the center of the corneal surface and $\psi(t)$ is given by

$$\psi(t) = \begin{cases} 1, & \text{if laser is on,} \\ 0, & \text{if laser is off,} \end{cases} \quad (5.3)$$

which dictates the time when laser is being applied onto the cornea. When laser is off, $\psi(t)$ has a value of zero. Consequently, value of S_i becomes zero; implying that no heat generation takes place inside the human eye.

Equation (5.2) implies that the laser beam that is incident on the corneal surface causes heat to be generated only inside the cornea. This is largely attributed to the penetration depth of laser, d_p inside the cornea. Penetration depth generally describes the depth inside the ocular media where radiation from the laser approaches zero as it decreases exponentially from the irradiated surface [66]. Mathematically, the penetration

depth is given by

$$d_p = \rho^{-1}. \quad (5.4)$$

In Section 5.2, it is mentioned that typical laser wavelengths used in the treatment of LTKP ranges from 1.87 to $2.1\mu\text{m}$ (for both pulsed and continuous-wave lasers). These correspond to values of corneal absorption coefficient from 1900 to 2000m^{-1} [149, 151]. Using Equation (5.4), the range of d_p corresponding to the range of corneal absorption coefficient is calculated to be 0.48 to 0.50mm . This suggests that if a laser with a wavelength of $1.87\mu\text{m}$ is applied onto the corneal surface, the laser radiation approaches zero at a depth of 0.50mm . Similarly, if a laser with a wavelength of $2.1\mu\text{m}$ is used, radiation at regions beyond the depth of 0.48mm from the corneal surface becomes negligible. Since thickness of the cornea in the present model is approximately 0.588mm , no radiation is expected in the ocular regions located beyond the cornea.

The mathematical expression of the incident irradiance, $E(r, z)$ in Equation (5.2) depends on the profile of the laser beam that arrives on the corneal surface. Ideally, the laser beam may be assumed to have a flat profile such that the distribution of irradiance is uniform. In most practical cases, the laser beam has a distribution that follows closely the profile of a Gaussian-type equation [66]. This is shown in Figure 5-2. For laser beams

Figure 5-2: Distribution of the gaussian laser beam

that are centered about the center of the corneal surface, $(r, z) = (0, 0)$, the expression

of $E(r, z)$ for a Gaussian beam profile is mathematically given by

$$E(r, z) = E_o \exp\left(-\frac{2r^2}{w^2}\right), \quad (5.5)$$

where E_o denotes the peak irradiance and w denotes the radius of the laser beam where the laser irradiance decreases to $\exp(-1)$ times its maximum value [66].

5.3.3 Initial-boundary conditions

Boundary conditions are specified on both the surfaces of the cornea, C_1 and sclera, C_2 . Laser radiation during LTKP is assumed to produce no significant effect on the heat transfer between the environment and the corneal surface. Similarly, heat transfer between blood flow and the eye is assumed not to be affected by the treatment of LTKP. Therefore, the boundary conditions specified on C_1 and C_2 in this study are similar to those used in Chapter 2. These boundary conditions are given by

$$\begin{aligned} -\kappa_1 \frac{\partial T_1}{\partial n} &= h_{\text{amb}} (T_1 - T_{\text{amb}}) + \varepsilon \sigma (T_1^4 - T_{\text{amb}}^4) + E_{\text{vap}}, \\ &\text{on } C_1 \text{ and for } t > 0, \end{aligned} \quad (5.6)$$

and

$$-\kappa_6 \frac{\partial T_6}{\partial n} = h_{\text{bl}} (T_6 - T_{\text{bl}}), \text{ on } C_2 \text{ and for } t > 0, \quad (5.7)$$

respectively.

Variation of the temperature and heat flux at the interfaces between two contiguous ocular regions, I_{ij} may be described using the continuity condition given in Equation (2.5), which for simplicity, is reproduced here as

$$T_i = T_j \text{ and } \kappa_i \frac{\partial T_i}{\partial n} = \kappa_j \frac{\partial T_j}{\partial n}, \text{ on } I_{ij}. \quad (5.8)$$

Since the problem in the present study is a transient one, an initial condition is

required to complete the formulation of the problem. For this purpose, the temperature distribution inside the normal unexposed human eye during steady-state, which is obtained by solving

$$\nabla_{\text{axis}} (\kappa_i \nabla_{\text{axis}} T_i(r, z)) = 0, \text{ for } i = 1, 2, 3, 4, 5 \text{ and } 6, \quad (5.9)$$

subjected to Equations (5.6) to (5.8), is specified as the initial condition.

5.4 Numerical Scheme

5.4.1 Integro-differential equation

Following the steps outlined by Brebbia et al. [55], the integro-differential representation of Equation (5.1) is given by

$$\begin{aligned} \lambda(\xi_i, \eta_i) T_i(\xi_i, \eta_i, t) = & \int_{\Gamma_i} T_i(r, z, t) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z) \\ & - \int_{\Gamma_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \frac{\partial}{\partial n} [T_i(r, z, t)] \cdot r \cdot ds(r, z) \\ & + \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(r, z, t)] \right. \\ & \left. - \frac{1}{\kappa_i} S_i(r, z, t) \right] \cdot r \cdot dA(r, z) \\ & \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\ & \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \end{aligned} \quad (5.10)$$

where α_i is the thermal diffusivity of region R_i ($\alpha_i = \kappa_i / \rho_i c_i$), Γ_i denotes the curve boundary of the region R_i , $ds(r, z)$ denotes the length of an infinitesimal portion of curve Γ_i , $dA(r, z)$ denotes the area of an infinitesimal portion of the region R_i , λ is a geometrical coefficient that depends on the location of (ξ_i, η_i) (see Chapter 2) and Φ_{axis}

and $\partial\Phi_{\text{axis}}/\partial n$ are the axisymmetric fundamental solution of the Laplace equation and its normal derivatives respectively. The mathematical expressions of Φ_{axis} and $\partial\Phi_{\text{axis}}/\partial n$ have been presented in Chapter 2 and are thus, not repeated here.

5.4.2 The dual reciprocity method

The domain integral in Equation (5.10) may be approximated into an equivalent boundary integral using the dual reciprocity method introduced by Nardini and Brebbia [156] in 1983. The method generally involves the approximation of the terms in the governing partial differential equation that contribute to the domain integral using a series of interpolations functions..

To carry out the dual reciprocity method, M_i points denoted by $(a_i^{(1)}, b_i^{(1)})$, $(a_i^{(2)}, b_i^{(2)})$, ..., $(a_i^{(M_i-1)}, b_i^{(M_i-1)})$ and $(a_i^{(M_i)}, b_i^{(M_i)})$ are selected inside $R_i \cup \Gamma_i$. Using the M_i selected points, the following approximation is carried out:

$$\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(r, z, t)] - \frac{1}{\kappa_i} S_i(r, z, t) \approx \sum_{m=1}^{M_i} \gamma_i^{(m)}(t) \phi_{\text{axis}}(r, z; a_i^{(m)}, b_i^{(m)})$$

for $i = 1, 2, 3, 4, 5$ and 6 , (5.11)

where $\phi_{\text{axis}}(r, z; a_i^{(m)}, b_i^{(m)})$ is the radial basis function in the Orz coordinate system centered about the point $(a_i^{(m)}, b_i^{(m)})$ and $\gamma_i^{(m)}(t)$ are unknown coefficients to be determined. The approximation in Equation (5.11) is similar to the one carried out for the treatment of domain integrals in Chapter 4. Substituting Equation (5.11) into the domain integral in Equation (5.10) leads to

$$\begin{aligned} & \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(r, z, t)] - \frac{1}{\kappa_i} S_i(r, z, t) \right] \cdot r \cdot dA(r, z) \\ & \approx \sum_{m=1}^{M_i} \gamma_i^{(m)}(t) \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \phi_{\text{axis}}(r, z; a_i^{(m)}, b_i^{(m)}) \cdot r \cdot dA(r, z). \end{aligned} \quad (5.12)$$

Suppose that there exists a particular solution, $\varkappa_{\text{axis}}$ such that it satisfies

$$\nabla_{\text{axis}}^2 [\varkappa_{\text{axis}}(r, z; a, b)] = \phi_{\text{axis}}(r, z; a, b). \quad (5.13)$$

Substituting Equation (5.13) into (5.12) results in

$$\begin{aligned} & \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(r, z, t)] - \frac{1}{\kappa_i} S_i(r, z, t) \right] \cdot r \cdot dA(r, z) \\ & \approx \sum_{m=1}^{M_i} \gamma_i^{(m)}(t) \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \nabla_{\text{axis}}^2 [\varkappa_{\text{axis}}(r, z; a_i^{(m)}, b_i^{(m)})] \cdot r \cdot dA(r, z), \end{aligned}$$

where upon using the reciprocal theorem, leads to

$$\begin{aligned} & \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(r, z, t)] - \frac{1}{\kappa_i} S_i(r, z, t) \right] \cdot r \cdot dA(r, z) \\ & \approx \sum_{m=1}^{M_i} \gamma_i^{(m)}(t) \left\{ \lambda(\xi_i, \eta_i) \varkappa_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) \right. \\ & \quad - \int_{\Gamma_i} \varkappa_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z) \\ & \quad \left. + \int_{\Gamma_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \frac{\partial}{\partial n} [\varkappa_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)})] \cdot r \cdot ds(r, z) \right\}. \quad (5.14) \end{aligned}$$

The unknown coefficients $\gamma_i^{(m)}(t)$ can be determined by letting the point (r, z) in Equation (5.14) be given by the M_i points, $(a_i^{(1)}, b_i^{(1)})$, $(a_i^{(2)}, b_i^{(2)})$, ..., $(a_i^{(M_i-1)}, b_i^{(M_i-1)})$, $(a_i^{(M_i)}, b_i^{(M_i)})$. This generates a system of M_i equations, such that

$$\begin{aligned} & \frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(a_i^{(m)}, b_i^{(m)}, t)] - \frac{1}{\kappa_i} S_i(a_i^{(m)}, b_i^{(m)}, t) \\ & \approx \sum_{m=1}^{M_i} \gamma_i^{(m)}(t) \phi_{\text{axis}}(a_i^{(j)}, b_i^{(j)}; a_i^{(m)}, b_i^{(m)}), \\ & \quad \text{for } j = 1, 2, \dots, M_i - 1, M_i, \end{aligned} \quad (5.15)$$

which may be inverted to give

$$\gamma_i^{(m)}(t) = \sum_{j=1}^{M_i} W_i^{(mj)} \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(a_i^{(j)}, b_i^{(j)}, t)] - \frac{1}{\kappa_i} S_i(a_i^{(j)}, b_i^{(j)}, t) \right],$$

for $m = 1, 2, \dots, M_i - 1, M_i$, (5.16)

where the coefficients $W^{(mj)}$ are given by

$$\sum_{j=1}^{M_i} W_i^{(kj)} \phi_{\text{axis}}(a_i^{(j)}, b_i^{(j)}; a_i^{(m)}, b_i^{(m)}) = \begin{cases} 1, & \text{if } k = m, \\ 0, & \text{if } k \neq m, \end{cases}$$

for $k, m = 1, 2, \dots, M_i - 1, M_i$.

Substituting Equations (5.14) and (5.16) into (5.10) leads to

$$\begin{aligned} \lambda(\xi_i, \eta_i) T_i(\xi_i, \eta_i, t) &= \int_{\Gamma_i} T_i(r, z, t) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z) \\ &\quad - \int_{\Gamma_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \frac{\partial}{\partial n} [T_i(r, z, t)] \cdot r \cdot ds(r, z) \\ &\quad + \sum_{j=1}^{M_i} \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(a_i^{(j)}, b_i^{(j)}, t)] - \frac{1}{\kappa_i} S_i(a_i^{(j)}, b_i^{(j)}, t) \right] \\ &\quad \times \sum_{m=1}^{M_i} W_i^{(mj)} \left[\lambda(\xi_i, \eta_i) \chi_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) \right. \\ &\quad \left. - \int_{\Gamma_i} \chi_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi_i, \eta_i)] \cdot r \cdot ds(r, z) \right. \\ &\quad \left. + \int_{\Gamma_i} \Phi_{\text{axis}}(r, z; \xi_i, \eta_i) \frac{\partial}{\partial n} [\chi_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)})] \cdot r \cdot ds(r, z) \right] \\ &\quad \text{for } (\xi_i, \eta_i) \in R_i \cup \Gamma_i \text{ and} \\ &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \end{aligned} \quad (5.17)$$

where the original domain integral has now been approximated into an equivalent boundary integral. A numerical procedure based on the boundary element method can now be developed based on Equation (5.17).

5.4.3 Boundary discretization

For a numerical procedure based on Equation (5.17), boundary Γ_i of each ocular region, R_i is discretized into small straight line segments known as boundary elements. Two points denoted by $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ that serve as collocation nodes are selected inside each boundary element. Following the steps outlined in Section 2.7 for the approximation based on the discontinuous linear element, Equation (5.17) may be expressed in the discretized form as

$$\begin{aligned} \lambda(\xi_i, \eta_i) T_i(\xi_i, \eta_i, t) = & \sum_{k=1}^{N_i} \mathcal{F}_3^{(k)}(\xi_i, \eta_i) T_i^{(k)}(t) + \sum_{k=1}^{N_i} \mathcal{F}_4^{(k)}(\xi_i, \eta_i) T_i^{(k+N_i)}(t) \\ & - \sum_{k=1}^{N_i} \mathcal{F}_1^{(k)}(\xi_i, \eta_i) q_i^{(k)}(t) - \sum_{k=1}^{N_i} \mathcal{F}_2^{(k)}(\xi_i, \eta_i) q_i^{(k+N_i)}(t) \\ & + \sum_{j=1}^{M_i} \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i(a_i^{(j)}, b_i^{(j)}, t)] - \frac{1}{\kappa_i} S_i(a_i^{(j)}, b_i^{(j)}, t) \right] \\ & \times \sum_{m=1}^{M_i} W_i^{(mj)} \Psi_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) \end{aligned}$$

for $(\xi_i, \eta_i) \in R_i \cup \Gamma_i$ and
for $i = 1, 2, 3, 4, 5$ and 6 , (5.18)

where $T_i^{(k)}(t)$ and $T_i^{(k+N_i)}(t)$ are values of $T(r, z, t)$ at points $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ respectively, $q_i^{(k)}(t)$ and $q_i^{(k+N_i)}(t)$ are values of $\partial T(r, z, t)/\partial n$ at points $(\xi_i^{(k)}, \eta_i^{(k)})$ and $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)})$ respectively, $\mathcal{F}_1^{(k)}(\xi_i, \eta_i)$, $\mathcal{F}_2^{(k)}(\xi_i, \eta_i)$, $\mathcal{F}_3^{(k)}(\xi_i, \eta_i)$ and $\mathcal{F}_4^{(k)}(\xi_i, \eta_i)$ are boundary integrals of the fundamental solution and its normal derivative, such as given

in Equation (2.12) and $\Psi_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)})$ is given by

$$\begin{aligned}
 \Psi_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) &= \lambda(\xi_i, \eta_i) \mathcal{K}_{\text{axis}}(\xi_i, \eta_i; a_i^{(m)}, b_i^{(m)}) \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{F}_3^{(k)}(\xi_i, \eta_i) \mathcal{K}_{\text{axis}}^{(k)}(a_i^{(m)}, b_i^{(m)}) \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{F}_4^{(k)}(\xi_i, \eta_i) \mathcal{K}_{\text{axis}}^{(k+N_i)}(a_i^{(m)}, b_i^{(m)}) \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{F}_1^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [\mathcal{K}_{\text{axis}}^{(k)}(a_i^{(m)}, b_i^{(m)})] \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{F}_2^{(k)}(\xi_i, \eta_i) \frac{\partial}{\partial n} [\mathcal{K}_{\text{axis}}^{(k+N_i)}(a_i^{(m)}, b_i^{(m)})]. \quad (5.19)
 \end{aligned}$$

For computational convenience, M_i is selected such that $M_i = 2N_i + L_i$, where the first $2N_i$ nodes are selected such that in coincide with the $2N_i$ nodes on the boundary. The remaining L_i nodes are chosen to be at the interior of each ocular region, R_i . If the point (ξ_i, η_i) is selected to be given by $(\xi_i^{(n)}, \eta_i^{(n)})$, for $n = 1, 2, \dots, M_i - 1, M_i$, Equation (5.18) reduces to

$$\begin{aligned}
 \lambda_i^{(n)} T_i^{(n)}(t) &= \sum_{k=1}^{N_i} \mathcal{F}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) T_i^{(k)}(t) + \sum_{k=1}^{N_i} \mathcal{F}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) T_i^{(k+N_i)}(t) \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{F}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) q_i^{(k)}(t) - \sum_{k=1}^{N_i} \mathcal{F}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) q_i^{(k+N_i)}(t) \\
 &\quad + \sum_{j=1}^{M_i} \left[\frac{1}{\alpha_i} \frac{\partial}{\partial t} [T_i^{(j)}(t)] - \frac{1}{\kappa_i} S_i^{(j)}(t) \right] \\
 &\quad \times \sum_{m=1}^{M_i} W_i^{(mj)} \Psi_{\text{axis}}(\xi_i^{(n)}, \eta_i^{(n)}; \xi_i^{(m)}, \eta_i^{(m)}) \\
 &\quad \text{for } n = 1, 2, \dots, M_i - 1, M_i \\
 &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \quad (5.20)
 \end{aligned}$$

where $\lambda_i^{(n)} = \lambda(\xi_i^{(n)}, \eta_i^{(n)})$, $T_i^{(n)}(t) = T(\xi_i^{(n)}, \eta_i^{(n)}, t)$ and $S_i^{(j)}(t) = S_i(\xi_i^{(j)}, \eta_i^{(j)}, t)$.

5.4.4 Time-stepping approach

The functions $T_i^{(p)}(t)$ and its first order derivative, $\partial T_i^{(p)}(t)/\partial t$ in Equation (5.20) may be approximated using

$$T_i^{(p)}(t) \approx \frac{1}{2} \left[T_i^{(p)}(t + \frac{1}{2}\Delta t) + T_i^{(p)}(t - \frac{1}{2}\Delta t) \right], \quad (5.21)$$

and

$$\frac{d}{dt}[T_i^{(p)}(t)] \approx \frac{1}{\Delta t} \left[T_i^{(p)}(t + \frac{1}{2}\Delta t) - T_i^{(p)}(t - \frac{1}{2}\Delta t) \right], \quad (5.22)$$

respectively, where Δt is a small positive number. Note that the magnitudes of the errors in the approximations above are $O([\Delta t]^2)$.

Substituting the approximation in Equations (5.21) and (5.22) into (5.20) gives

$$\begin{aligned} & \frac{1}{2} \lambda_i^{(n)} [T_i^{(n)}(t + \frac{1}{2}\Delta t) + T_i^{(n)}(t - \frac{1}{2}\Delta t)] \\ = & \frac{1}{2} \sum_{k=1}^{N_i} \mathcal{F}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) [T_i^{(k)}(t + \frac{1}{2}\Delta t) + T_i^{(k)}(t - \frac{1}{2}\Delta t)] \\ & + \frac{1}{2} \sum_{k=1}^{N_i} \mathcal{F}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) [T_i^{(k+N_i)}(t + \frac{1}{2}\Delta t) + T_i^{(k+N_i)}(t - \frac{1}{2}\Delta t)] \\ & - \sum_{k=1}^{N_i} \mathcal{F}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) q_i^{(k)}(t) - \sum_{k=1}^{N_i} \mathcal{F}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}) q_i^{(k+N_i)}(t) \\ & + \sum_{j=1}^{M_i} \left\{ \frac{1}{\alpha_i \Delta t} [T_i^{(j)}(t + \frac{1}{2}\Delta t) - T_i^{(j)}(t - \frac{1}{2}\Delta t)] - \frac{1}{\kappa_i} S_i^{(j)}(t) \right\} \\ & \times \sum_{m=1}^{M_i} W_i^{(mj)} \Psi_{\text{axis}}(\xi_i^{(j)}, \eta_i^{(j)}; \xi_i^{(m)}, \eta_i^{(m)}) \\ & \text{for } n = 1, 2, \dots, M_i - 1, M_i \text{ and} \\ & \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6. \end{aligned} \quad (5.23)$$

To obtain a numerical solution, a time-stepping scheme that solves Equation (5.23) for consecutive time levels is developed. Assuming that $T_i^{(m)}(t - \frac{1}{2}\Delta t)$ is known, Equation

(5.23) together with Equations (5.6) to (5.8) reduces to a system of $(M_1 + M_2 + M_3 + M_4 + M_5 + M_6)$ algebraic equations in $(M_1 + M_2 + M_3 + M_4 + M_5 + M_6)$ unknowns of $T_i^{(m)}(t + \frac{1}{2}\Delta t)$ at boundaries C_1 and C_2 and $T_i^{(m)}(t + \frac{1}{2}\Delta t)$ and $q_i^{(m)}(t)$ at the interfaces. By letting $t = \frac{1}{2}\Delta t$, values of $T_i^{(m)}(0)$ can be determined by using the initial condition given in Equation (5.9). Unknown values of $T_i^{(m)}(\Delta t)$ and $q_i^{(m)}(\frac{1}{2}\Delta t)$ at the boundaries and the interfaces may then be obtained by solving the system of linear algebraic equations. With $T_i^{(m)}(\Delta t)$ known, values of $T_i^{(m)}(2\Delta t)$ at the boundaries and the interfaces and $q_i^{(m)}(\frac{3}{2}\Delta t)$ at the interfaces can be obtained. This procedure may be repeated for $t = \frac{5}{2}\Delta t, \frac{7}{2}\Delta t, \frac{9}{2}\Delta t, \dots$ in a consecutive manner to solve for $T_i^{(m)}(t + \frac{1}{2}\Delta t)$ and $q_i^{(m)}(t)$ at the boundaries and interfaces for higher and higher time levels until the desired time level is reached. When solving the system of linear algebraic equations, the non-linear boundary condition in Equation (5.6) is dealt with using the same iterative procedure as described in Chapter 2.

5.4.5 Axisymmetric radial basis function

The accuracy of the dual reciprocity method depends on the type of radial basis function chosen. When the dual reciprocity method was first used to solve diffusion problems in the Orz coordinate system [157], the axisymmetric radial basis function of the form

$$\phi_{\text{axis}}(r, z; \xi, \eta) = \mathcal{R}(r, z; \xi, \eta) \left(1 - \frac{\xi}{4r}\right), \quad (5.24)$$

have been employed, where $\mathcal{R}(r, z; \xi, \eta)$ is the Euclidean distance between the source point (ξ, η) and the field point (r, z) .

More recently, Wang et al. [158] introduced an alternative expression of the axisymmetric radial basis function, which is given by

$$\phi_{\text{axis}}(r, z; \xi, \eta) = 4E(m(r, z; \xi, \eta)) \sqrt{a(r, z; \xi, \eta) + b(r, z; \xi, \eta)}, \quad (5.25)$$

where E is the complete elliptic integral of the second kind and m , a and b are given by

$$\begin{aligned} m(r, z; \xi, \eta) &= \frac{2b(r; \xi)}{a(r, z; \xi, \eta) + b(r; \xi)}, \\ a(r, z; \xi, \eta) &= \xi^2 + r^2 + (\eta - z)^2, \\ b(r; \xi) &= 2r\xi. \end{aligned} \tag{5.26}$$

One of the advantages of the radial basis function in Equation (5.25) is that it is expressed in a closed form. This helps to simplify the evaluation of the particular solution, $\varkappa_{\text{axis}}$ [158]. The expression of $\varkappa_{\text{axis}}$ obtained from the solution of Equation (5.13) is given by

$$\begin{aligned} \varkappa_{\text{axis}}(r, z; \xi, \eta) &= \frac{1}{9} [a(r, z; \xi, \eta) + b(r, z; \xi, \eta)] \sqrt{a(r, z; \xi, \eta) + b(r, z; \xi, \eta)} \\ &\quad \times \{[(m(r, z; \xi, \eta)) - 1]K(m(r, z; \xi, \eta))\} \\ &\quad + [4 - 2m(r, z; \xi, \eta)] E(m(r, z; \xi, \eta))\}, \end{aligned} \tag{5.27}$$

where K is the complete elliptic integral of the first kind and m , a and b are such as given in Equation (5.26).

5.5 Transient Temperature Changes during LTKP

5.5.1 Numerical Model

Investigations on the transient temperature distribution inside the cornea during LTKP are carried out for both the pulsed and continuous-wave lasers. Only laser with a Gaussian beam profile is considered. Values of the laser parameters used in the present study are selected based on the values used in a typical clinical LTKP treatment. Although a minimum of eight laser spots are usually applied onto the corneal surface (see Section 5.2), in the present study, only a single laser spot is considered, which is assumed to be applied onto the center of the corneal surface. This assumption is necessary in order to maintain the axisymmetric features of the human eye, which is of great computational

advantage. With the laser spot placed at the center of the corneal surface, an increase in the temperature here is expected.

To capture accurately the large thermal variation over the small heated area around the center of the corneal surface, the number of boundary elements and interior points chosen here has to be sufficiently large. The model of the human eye is discretized into a total of 253 boundary elements, with 72 of them located on the boundary of the cornea. A total of 316 interior points are selected inside the human eye model, with 53 and 142 of them placed inside the cornea and anterior chamber respectively. The interior points selected inside each region of the human eye model are illustrated in Figure 5-3. All simulations are performed using the axisymmetric radial basis function suggested by Wang et al. [158], which is given in Equation (5.25).

Figure 5-3: Interior points selected inside each region of the human eye

Values of the thermal conductivity, density and specific heat of each region inside the human eye have been presented in Chapter 2 and are tabulated in Table 2.1. Similarly, values of the control parameters such as the ambient convection coefficient, blood convection coefficient and tears evaporation rate used for describing the boundary conditions in Equations (5.6) and (5.7) have been presented in Chapter 2. These are given in Table

2.2. Value of the Fresnel reflectance, $\mathbb{F}$ used in the simulations for both the pulsed and continuous-wave lasers is chosen here to be 0.024 [151].

5.5.2 Pulsed laser

Table 5.1 summarizes the values of laser parameters of a typical LTKP treatment using pulsed laser. These values are obtained from Manns et al. [151]. Energy per pulse

Table 5.1: Typical laser parameters chosen for the pulsed laser

Parameter	Value
Energy per pulse, E_{pp} (mJ)	30
Pulse duration, t_p (μ s)	200
Pulse repetition rate (Hz)	5
Number of pulse	7
Wavelength (μ m)	2.1
Laser beam radius, w (mm)	0.3
Laser absorption coefficient, ϱ (m^{-1})	2000
Peak irradiance, E_o (Wm^{-2})	5.31×10^8

describes the amount of laser energy that is delivered onto the corneal surface during each laser pulse. The laser absorption coefficient of the cornea is obtained by assuming the cornea to have optical properties that are similar to water. The value of peak irradiance, E_o in Table 5.1 is obtained using the following expression [150]

$$E_o = \frac{E_{pp}}{\pi w^2 t_p},$$

where E_{pp} is energy per pulse and t_p is pulsed duration.

Based on the values given in Table 5.1, the function $\psi(t)$ in Equation (5.3) describing the period when the laser is on and off may be expressed as

$$\psi(t) = \begin{cases} 1, & \text{if } t \in J, \\ 0, & \text{if } t \notin J, \end{cases} \quad (5.28)$$

where t is time taken to be in seconds here and J is the time interval defined by

$$J = \bigcup_{m=0}^6 \{t : 0.2002m \leq t \leq 0.2002m + 0.0002\}. \quad (5.29)$$

In carrying out the time-stepping scheme, the time step, Δt is chosen to be

$$\Delta t = \begin{cases} 0.0002\text{s}, & \text{if } t \in J, \\ 0.05\text{s} & , \text{if } t \notin J. \end{cases}$$

Figure 5-4 plots the transient temperature changes along the pupillary axis ($r = 0$) at various depths of the cornea during treatment of pulsed LTKP. The seven temperature peaks correspond to the seven laser pulses that are applied onto the corneal surface. Cooling is observed at intervals between laser pulses where heat that is absorbed inside the cornea is diffused into the environment via convection and radiation and into the other ocular regions inside the eye. Throughout the treatment of LTKP, the corneal surface experiences the largest increase in temperature. At the end of the seventh laser pulse, temperature as high as 111°C is reached, albeit for only a very short duration. At the corneal endothelium, i.e. at $z = 588\mu\text{m}$, temperature at the seventh laser pulse is found to be approximately 53°C . Temperature at the corneal stroma, which is represented by the curves between $z = 100$ and $z = 500\mu\text{m}$, increases beyond the threshold for corneal shrinkages after the third laser pulse.

Figure 5-5 illustrates the temperature profile along the pupillary axis at various depths of the cornea during each laser pulse, i.e. for $t = 0.0002, 0.2002, 0.4006, 0.6008, 0.801, 1.0012$ and 1.2014s . The vertical lines separate the z -axis into regions occupied by the epithelium, stroma and endothelium, while the horizontal lines represent the lower threshold for corneal shrinkages ($T = 55^\circ\text{C}$) and corneal relaxation ($T = 90^\circ\text{C}$). A large part of the corneal stroma, where the corneal collagens are located, are found to have temperatures that are greater than the threshold for corneal shrinkages. This indicates the occurrences of corneal shrinkages. At the corneal epithelium, temperature increases beyond the re-

Figure 5-4: Transient temperature changes along the pupillary axis at various depth inside the cornea during pulsed LTKP with a Gaussian beam profile

laxation threshold. However, this may not severely affect the overall shrinkages of the cornea since the collagens that are responsible for the contraction and relaxation of the cornea are not found in the corneal epithelium. At the end of the seventh laser pulse, the maximum temperature achieved by the corneal endothelium is smaller than 65°C ; implying an absence of endothelial cell deaths.

The spatial temperature profiles over a small cross-section of the cornea and the anterior chamber on the rz plane are shown in Figure 5-6. The cross-section is selected in such a way that significant variation of the temperature can be observed. For a clearer visualization, the temperature plots in Figure 5-6 are presented with the mirror images about the z -axis. The dotted lines denote the interface between the cornea and the anterior chamber.

Figure 5-5: The corneal temperature along the pupillary axis (against z at $r = 0$) at the end of each laser pulse

There appears to be a large temperature gradient at the depth of approximately 0.5mm from the corneal surface. This may be attributed to the penetration depth of laser inside the cornea, which according to Equation (5.4) and using the properties of pulsed laser given in Table 5.1, is calculated to be 0.5mm. Temperature increase at regions defined by $z < 0.5\text{mm}$ is thus, caused by the absorption of laser energy, while temperature increase at $z > 0.5\text{mm}$ is due to the diffusion of heat from the regions at $z < 0.5\text{mm}$.

5.5.3 Continuous-wave laser

The transient temperature changes inside the eye during treatment of LTKP using continuous-wave laser are examined in this section. Both the 10s coagulation and the minute coagulation (see Section 5.2) are investigated. Parameters of the continuous-wave laser used in a typical treatment of LTKP are tabulated in Table 5.2. These values are obtained from Brinkmann et al. [149]. Wavelengths of laser used in the treatment of LTKP using continuous-wave lasers may vary between 1.85 and 1.87 μm . However, in the

Figure 5-6: Spatial temperature profiles over a selected cross-section of the eye subject to pulsed laser irradiation.

present study, only laser that is emitted at a wavelength of $1.87\mu\text{m}$ is considered [149].

Values of peak irradiance, E_o are obtained using the expression

$$E_o = \frac{P}{\pi w^2},$$

where P is laser power. The expressions of $\psi(t)$ for the 10s and minute coagulations are given by

$$\psi(t) = \begin{cases} 1, & \text{if } t \leq 10\text{s}, \\ 0, & \text{if } t > 10\text{s}, \end{cases} \quad (5.30)$$

and

$$\psi(t) = \begin{cases} 1, & \text{if } t \leq 60\text{s}, \\ 0, & \text{if } t > 60\text{s}, \end{cases} \quad (5.31)$$

respectively. When executing the time stepping scheme, values of Δt of 0.1 and 0.5s are chosen for the 10s and minute coagulations respectively.

Table 5.2: Typical laser parameters chosen for the continuous-wave laser

Parameter	10s coagulation	Minute coagulation
Laser power, P (W)	0.125	0.10
Peak irradiance, E_o (Wm^{-2})	4.42×10^5	3.54×10^5
Heating duration, t (s)	10	60
Time step, Δt (s)	0.1	0.5
Wavelength (μm)	1.87	1.87
Laser absorption coefficient, ρ (m^{-1})	1900	1900

Figure 5-7 illustrates the transient temperature profiles along the pupillary axis ($r = 0$) at various depths of the cornea during treatment of LTKP for both the 10s and minute coagulations. Both approaches show uniform increase in the corneal temperature. These are unlike the temperature profiles observed in Figure 5-4 for the pulsed laser radiation. At the end of the laser treatment, a sharp decrease in temperature is found. This is a result of the rapid dissipation of heat to the environment and the adjacent regions inside the human eye.

The largest temperature reached inside the cornea during the 10s and the minute coagulations are given by 75.6 and 70.1°C respectively. The higher temperature observed in the 10s coagulation may be attributed to the larger laser power used when compared to the minute coagulation (0.125 vs. 0.10W). A large portion of the corneal stroma, defined by depths between 50 and 550 μm , are heated beyond the threshold for corneal shrinkages. This is true for both the 10s and minute coagulations. In both coagulations, no corneal relaxation occurs since the largest temperatures achieved are not greater than 90°C.

Figure 5-8 shows the temperature profiles along the pupillary axis ($r = 0$) of the cornea at various time levels for both the 10s and minute coagulations. During the course of radiation, temperatures at the endothelium ($z > 550\mu\text{m}$) are found to be lesser than 55°C. This is true for both the 10s and minute coagulations. These results imply

Figure 5-7: Transient temperature profiles at various depths of the cornea in the 10s coagulation and minute coagulation

Figure 5-8: Temperature distribution inside the cornea at various time levels for both the 10s and minute coagulations

that no endothelial cell deaths occur during continuous-wave laser radiation.

The spatial temperature distribution over a small cross-section of the cornea and anterior chamber at $t = 2, 4, 6, 8$ and 10s for the 10s coagulation and at $t = 12, 24, 36, 48$ and 60s for the minute coagulation are illustrated in Figure 5-9. These times are selected to highlight the spatial temperature distribution throughout the course of laser radiation. The dotted lines denote the interface between cornea and anterior chamber. The temperature plots in Figure 5-9 have been presented with the mirror images about the z -axis. The isotherms observed in Figure 5-9 appear to be more uniformly distributed than the isotherms observed during pulsed laser radiation. A large thermal gradient is observed at about $z = 0.52\text{mm}$, which is approximately the point defined by the penetration depth of the continuous-wave laser.

5.6 Thermal Damage Assessment

One of the major concerns of LTKP, as pointed out in Section 5.1, is the risk of inducing thermal damage onto the cornea. This is due to the heat that the cornea is exposed to, which can be extremely large [28, 149, 151]. This has been shown by the numerical results obtained from the preceding section, where temperatures as high as 111°C have been predicted during pulsed laser treatment (see Figures 5-4, 5-5 and 5-6).

Based on the magnitude of temperature rise inside the cornea alone, pulsed laser appears to produce a greater amount of thermal damage than the continuous-wave laser. Nonetheless, it has to be pointed out that the degree of thermal damage inflicted onto human tissues is dependent not only on the magnitude of temperature, but also the duration of heating [67]. In this section, a thermal damage assessment is carried out to estimate the degree of thermal damage experienced by the cornea during treatment of LTKP. Investigations are carried out using the thermal damage model of Henriques and Moritz [67].

In 1947, Henriques and Moritz [67] developed a mathematical model to predict the

Figure 5-9: Spatial temperature profiles over a selected cross-section of the eye subject to continuous-wave laser irradiation.

degree of thermal damage inside the human skin during burn. The thermal damage of the human skin was assumed to be a biochemical process defined by the thermal denaturation of proteins. Hence, this process may be described using the Arrhenius relationship [159]. Assuming that the same biochemical process takes place inside the cornea during LTKP, the degree of thermal damage inside the cornea, Ω at $r = 0$ may then be expressed using the Arrhenius integral, which is given by [67]

$$\Omega(z, t)_{r=0} = \int_0^{t_f} A \exp \left(-\frac{\Delta E_a}{\mathbb{R}T(0, z, t)} \right) dt, \quad (5.32)$$

where ΔE_a is the activation energy, $\mathbb{R}$ is the universal gas constant, t_f is the time when the thermal damage is evaluated and A is an empirically-valued coefficient given by

$$A = \frac{k_b T(0, z, t)}{h} \exp \left(\frac{\Delta S}{\mathbb{R}} \right), \quad (5.33)$$

where k_b is the Boltzmann constant, h is the Planck constant and ΔS is the entropy of activation. Values of the parameters used for calculating Equations (5.32) and (5.33) are obtained from Kampmeier et al. [160] and Incropera and DeWitt [82]. These are summarized in Table 5.3.

Table 5.3: Values of the parameters used in estimating the damage integral

Parameter	Value
^a Activation energy, E_a (Jmol ⁻¹)	106×10^3
^a Entropy of activation, ΔS (Jmol ⁻¹ K ⁻¹)	39
^b Universal gas constant, $\mathbb{R}$ (Jmol ⁻¹ K ⁻¹)	8.314
^b Boltzmann constant, k_b (kgm ² s ⁻¹ K ⁻¹)	1.38×10^{-23}
^b Planck constant, h (kgm ² s ⁻¹)	6.63×10^{-34}
^a Values obtained from reference [160];	
^b Values obtained from reference [82]	

Using the values tabulated in Table 5.3, the degree of thermal damage at various depths inside the cornea are estimated by evaluating numerically Equation (5.32) using the trapezoidal rule.

Figure 5-10 shows the thermal damage profile of the cornea during pulsed laser radiation. The largest thermal damage is observed at the surface of the cornea where the increase in temperature is maximum. The ‘step’ profile observed in Figure 5-10 is due to the irregular radiation of pulsed laser. A large increase in thermal damage occurs only when there is an increase in the corneal temperature, i.e. during application of each laser pulse.

Figure 5-10: Variation of thermal damage inside the cornea with time during pulsed laser radiation

In order to assess the severity of the thermal damage illustrated in Figure 5-10, the thermal damage characterization for human skin is assumed to be applicable in the case of the human cornea. Using the description given by Henriques and Moritz [67], a value of $\Omega < 0.53$ describes reversible thermal damage, while $0.53 \leq \Omega < 1$ defines the range of irreversible thermal damage. Complete tissue necrosis occurs when $\Omega \geq 1$. From Figure 5-10, it is found that pulsed laser radiation produces no irreversible thermal damage since the largest value of Ω is lesser than 0.53.

The thermal damage inflicted onto the cornea during continuous-wave laser radiation is illustrated in Figure 5-11 for both 10s and minute coagulations. Both plots show profiles that are rather similar. The sharp increase in thermal damage observed in the first 10 and 60s in the 10s and minute coagulations respectively, are attributed to the continuous heating of the cornea. Once the laser radiation is removed, no significant changes in the thermal damage are observed. The thermal damage induced onto the cornea during the 10s coagulation appears to be smaller than the minute coagulation. This is rather surprising given that the increase in corneal temperature during the 10s coagulation is higher than the minute coagulation. Similarly the larger thermal damage experienced by the cornea during continuous-wave laser radiation when compared to pulsed laser radiation is not anticipated since temperature increase during pulsed laser treatment are greater than the continuous-wave laser.

From Figure 5-11, it is established that the 10s coagulation produces irreversible thermal damage inside the cornea. The irreversible thermal damage occurs only at depths of up to $200\mu\text{m}$ from the corneal surface however. In the minute coagulation, complete necrosis is found at depths of $0 \leq z \leq 300\mu\text{m}$.

5.7 Discussion

The numerical results obtained from the present study are validated with the experimental and numerical data obtained by other researchers that can be found in literature. Generally, the temperature profiles of the cornea during pulsed laser radiation shown in Figures 5-4 and 5-6 agree well with those predicted by Manns et al. [151]. The transient variation of the maximum ($z = 0$) and minimum temperatures ($z = 588\mu\text{m}$) shown in Figure 5-4 agrees qualitatively with the experimental results presented by Papaioannou et al. [29]. The corneal temperatures measured by Papaioannou et al. [29] are smaller than the predictions obtained from the present study however.

In the continuous-wave laser radiation, the temperature distribution in Figure 5-9

Figure 5-11: Variation of thermal damage inside the cornea with time during continuous-wave laser radiation

shows isotherms that agree well with the predictions obtained by Brinkmann et al. [149]. Differences in the magnitude of temperature increase are found however. In the present study, the largest corneal temperature achieved during the 10s and minute coagulations is found to be 75.6 and 70.1°C respectively. On the other hand, Brinkmann et al. [149] predicted values of 110 and 90°C respectively. Discrepancies may be due to the absence of intracorneal focusing in the present study, which was taken into account by Brinkmann et al. [149]. Differences in the mathematical models used may also be a contributing factor.

One of the main differences between the models developed in the present study and those by other researchers lies in the geometry of the cornea. In earlier studies, the assumption that the cornea can be modeled as a cylinder or a tissue slab with finite thickness is highly idealized. In the present study, the model is anatomically and physiologically more complete and realistic, where various components of the human eye have been taken into consideration. The use of a complete model provides a more accurate anatomical representation of the human cornea. Furthermore, boundary conditions can be specified based on the physical observation of the actual human eye.

In maintaining the axisymmetrical feature of the human eye model, only one laser spot has been assumed, which is applied on the center of the corneal surface. While this does not represent the actual treatment of LTKP, this assumption is not expected to introduce significant errors to our analysis. This is due to the corneal temperature changes that are localized to the area where heating occurs. In other words, the thermal response of the cornea in each laser spot is not affected by the temperature changes in the other parts of the cornea where the other laser spots are applied.

From the numerical results presented in Section 5.5, pulsed laser has been found to produce an increase in corneal temperature that is greater than the continuous-wave laser. In particular, temperature at the corneal epithelium as high as 111°C has been predicted. This may imply a complete destruction of the epithelial layer. Based on the corneal temperature alone, one may be inclined to deduce that pulsed laser produces a

greater corneal thermal damage than the continuous-wave laser. On the contrary, the assessment of thermal damage carried out using the Arrhenius integral appear to suggest otherwise. In Section 5.6, the amount of thermal damage suffered by the cornea during continuous-wave laser radiation is found to be greater than the pulsed laser radiation. One of the reasons for such an observation may be due to the extended duration of heating in the continuous-wave laser radiation.

From the expression given in Equation (5.32), the degree of thermal damage inside the cornea is found to depend on both the temperature and duration of heating. In the treatment of LTKP using pulsed laser, the duration when heating actually takes place is only in the order of milliseconds. Consequently, while the cornea is subjected to intense heat during each laser pulse, the period when heating actually takes place is extremely short. On the other hand, the continuous exposure of cornea towards heat during continuous-wave laser radiation makes it more susceptible to thermal damage. This explanation is further supported by the results presented in Figure 5-11, where the minute coagulation is found to yield a more severe thermal damage than the 10s coagulation, despite the latter producing a larger increase in corneal temperature. Results from the thermal damage assessment suggest that the duration of heating plays a more important role than the magnitude of temperature increase in determining the degree of thermal damage inside the cornea during LTKP.

According to Jean et al. [153], continuous-wave lasers are better suited for the treatment of LTKP than pulsed lasers. This has been attributed to the smaller corneal temperature, which helps to avoid overheating and corneal relaxation. The ability of continuous-wave lasers to produce various coagulation depths (due to the tunability of the laser wavelength) and the consumption of less energy than pulsed laser also makes the continuous-wave laser a much preferred choice. If the temperature profile of the cornea is used as the criterion for determining the type of laser that is best suited for LTKP, the temperature profiles presented in Section 5.5 would then support the conclusion drawn by Jean et al. [153]. However, if one considers the degree of thermal damage to be a more

important criterion, results from the thermal damage assessment in Section 5.6 would suggest that pulsed laser serves as a better choice, since the thermal damage induced onto the cornea is less severe.

Nonetheless, any conclusion drawn from the present study on the type of laser that is best suited for the treatment of LTKP may be premature, since the degree of corneal shrinkage experienced by the cornea has not been taken into consideration. Additionally, accuracy of the thermal damage estimated in the present study depends on how well the Arrhenius damage integral models the thermal damage inside the human cornea. It is also worth pointing out that the analysis of the severity of the thermal damage inside the cornea has been carried out based on the thermal damage classification of the human skin [159]. More studies have to be carried out in future to determine if such a classification can represent accurately the severity of the thermal damage inside the cornea.

The model in the present study can be further improved by taking into account the effects of intracorneal focussing such as in the work carried out by Brinkmann and co-worker [28, 148, 149]. Some issues regarding the eye model presented here should be addressed in future studies. During LTKP, shrinkages alter the dimension and shape of the cornea. This aspect has not been considered in the present study. Inclusion of this feature, which involves a moving boundary problem, may produce results that are different from those presented in Section 5.5.

The absorption coefficient of the cornea has been taken to be the same as water which have been assumed to be constant. Previous studies however, have shown this assumption to be misleading [162]. According to Ith et al. [162], the absorption coefficient of water is subjected to dynamic changes during laser-tissue interaction. Some studies have found the accuracy of simulated results to be severely affected by the assumption of constant optical properties [163, 164]. Variation of the thermal conductivity of the cornea with temperature has also been reported. According to Bhattacharya and Mahajan [165], the thermal conductivity of the cornea increases linearly with temperature. This has not been

considered in the present study since the relationship was obtained using sheep cornea and is only valid for heating temperatures up to 55°C. More research has to be carried out in future studies to examine the effects of these factors on the thermal response of the cornea during LTKP.

5.8 Concluding Remarks

The model of the human eye developed in Chapter 2 has been successfully used for simulating the temperature changes inside the cornea during LTKP. This has been demonstrated by the good qualitative agreement between the numerical predictions of our model and those obtained from the literature. The use of the boundary element method helps to alleviate the high computational cost required for solving a complete eye model by allowing discretization to be carried out only at the boundaries. In the axisymmetric formulation, the boundary is given by a set of curves that are easily discretized into straight line elements.

Numerical results show that temperature increase during pulsed laser radiation is greater than continuous-wave laser radiation. The duration that the corneal temperature exceeds 100°C is very small however. Intuitively, one may consider the thermal damage induced onto the cornea during pulsed laser radiation to be greater than continuous-wave laser radiation due to the higher increase in temperature. Assessment of the thermal damage has shown this to be otherwise. It appears that duration of heating plays a more dominant role than temperature increase in determining the amount of thermal damage induced onto the cornea during LTKP.

Chapter 6

Thermal Effects of Eye Tumor

6.1 Introduction

The temperature of the human body depends strongly on its physiological condition. In Chapter 1, it has been mentioned that diseases are likely to be detected in parts of the human body where an excess of heat or cold is found; a proposition pioneered by Hippocrates more than 2,000 years ago. A typical example of the use of temperature for monitoring the health of the human body today, can be seen when physicians measure the body temperature to determine if a patient is healthy or otherwise. In fact, application of thermal diagnostics extends beyond the confinements of general practitioners. In the studies of breast cancer, medical researchers have been able to make successful diagnosis based on the abnormal thermal patterns of the infected breast using IR thermography [2, 3]. Application of such thermal diagnostics system have also been demonstrated in other diseases such as vascular disorders [5, 6], rheumatism [4] and fever causing diseases such as SARS [166] and bird flu [167].

The use of ocular temperature in monitoring ocular physiology is well-acknowledged [7, 8]. Ocular abnormalities such as dry eye syndrome and acute inflammation have been found to produce ocular surface temperatures that are different from the temperature of a normal human eye [7, 31, 110]. In more severe ocular diseases such as cataract, glau-

coma, diabetic retinopathy and eye tumors, there has yet to be any conclusive evidence to suggest that abnormal ocular surface temperature may be used as a means for detection. Nonetheless, this area is currently undergoing extensive research and preliminary experimental investigations carried out on patients with glaucoma have revealed results that are rather promising [168, 169].

In this chapter, a mathematical investigation is carried out to examine the thermal effects of eye diseases on the temperature distribution inside the human eye. This study seeks to determine the changes in ocular temperature distribution, in particular, the corneal surface temperature and the likelihood of these temperature changes to be detected using the current method of ocular thermometry.

Various ocular diseases may infect the human eye. However, in the present study, only the effects of eye tumor will be examined. One of the main reasons eye tumor is selected for the investigations carried out in this study is the availability of a well-established method for simulating the thermal behavior of tumors in biological tissues [32, 33]. According to Gautherie [37, 38], tumor tissues have a higher rate of metabolic activity that leads to the production of a greater amount of metabolic heat. Additionally, blood perfusion rate inside tumor tissues has been found to be in general, greater than the blood perfusion rate of the surrounding healthy tissues [170]. These characteristics of tumor enable the thermal effects of tumors to be simulated without much difficulty.

Despite the growing number of mathematical models that investigate the temperature distribution inside the human eye during various ocular circumstances, to the best of our knowledge, there has yet to be any mathematical studies that looked into the effects of an eye tumor on the human eye temperature. On the other hand, investigations of the thermal effects of tumors that grow on other parts of the human body, such as the human breast and skin, have been carried out by various other researchers. Ng and co-worker [32, 33] developed a finite element model of the human breast to simulate the changes in temperature caused by the growth of breast tumor. Similar studies have been reported by Hu et al. [34] using the finite volume method. Models of the human skin

with a tumor growing inside have been developed by Deng and Liu [35,36] using various numerical approaches such as the dual reciprocity method and the Monte-Carlo method.

In the models of the human breast and skin developed by Ng and co-worker [32,33], Hu et al. [34] and Deng and Liu [35,36], tumors were modeled as a homogeneous region that has distinguishable thermal properties characterized by the larger metabolic heat generation and blood perfusion rate when compared to the healthy surrounding tissues. Using these modeling approaches, temperatures of the infected tissues were found to be 0.5 to 2°C greater than the temperatures of healthy tissues.

In this chapter, the same approach used for simulating the thermal behavior of tumors in human breast and skin is adopted to investigate the thermal effects of eye tumors on the ocular temperature distribution. Simulations are carried out using a three-dimensional model of the human eye. As in all previous chapters, the boundary element method is used to obtain a numerical solution. The presence of terms associated with the metabolic heat generation and blood perfusion rate of tumor in the governing bioheat equation give rise to domain integrals in the integral representation derived. These are dealt with using the dual reciprocity method [156].

A parametric optimization based on the Analysis of Variance (ANOVA) [171] and the Taguchi method [172] is carried out to identify the precedence and importance of the various factors that may affect the ocular surface temperature and to determine the optimal setting of factors that maximizes the signal from the eye tumor, while isolating the other effects that may be classified as *noise*.

6.2 Classification of Eye Tumors

Various type of eye tumors such as ocular melanoma (melanoma of the iris, ciliary body and choroid), retinoblastoma and secondary intraocular tumors (tumors that have spread to the eye from other parts of the body) may grow inside the human eye. Focus of this study is limited to choroidal melanoma. Choroidal melanoma grows on the highly

vascularized choroid, where the large supply of blood flow makes it ideal for tumor cells to grow and metastasize. When tumor grows on the choroid, it roughly takes the shape of a dome or a mushroom [173,174]. Dome-shaped choroidal melanomas are usually associated with the early stages of tumor growth, while the mushroom-shaped melanomas often take shape during the later stages [175].

According to the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), choroidal melanoma can be classified according to its size (T), degree of lymph nodes (N) and the presence of metastasis (M), or the TNM classification in short. In 2006, the sixth edition of the TNM classifications (TNM6) was published by AJCC and UICC. According to TNM6, four categories of choroidal melanoma can be distinguished based on the T category, namely categories T1, T2, T3 and T4. These categories generally describe the largest basal diameter (LBD) and thickness (t) of the tumor. LBD defines the diameter of the tumor at the base where it is attached to the choroidal surface, while thickness refers to the apical height of the tumor, i.e. the distance from the base to the tip of the tumor [176].

Table 6.1 summarizes the range of LBD and t of categories T1, T2, T3 and T4 choroidal melanoma [177]. Throughout this chapter, unless otherwise stated, the phrase ‘eye tumor’ is used to refer to choroidal melanoma.

6.3 Mathematical Model

6.3.1 The human eye

The three dimensional model of the human eye in this chapter is developed based on the axisymmetrical model presented in Chapter 2. Suppose that the model of the human eye shown in Figure 2-1 represents one half of the cross-section of the human eye in the mid-sagittal plane with reference to the Oxy coordinate system. The x -axis is taken to be given by the pupillary axis.

To obtain a three dimensional model, the geometry shown in Figure 2-1 is rotated by

Table 6.1: Classification of choroidal melanoma based on the T category

Category	Description	
	LBD	t
T1	$\leq 10\text{mm}$	$\leq 2.5\text{mm}$
T2	$\leq 15\text{mm}$	$\leq 5.0\text{mm}$
T3	$> 15\text{mm}$	$> 5.0\text{mm}$
T4	tumor grows beyond the eyeball	

an angle of 360° about the x -axis (pupillary axis). The three-dimensional model of the human eye generated from the aforementioned step with a view of its interior structure is shown in Figure 6-1. As in earlier chapters, the regions occupied by the cornea, anterior chamber, lens, posterior chamber, vitreous and sclera are denoted by R_1 , R_2 , R_3 , R_4 , R_5 and R_6 respectively. The exterior boundaries of the model are defined by the surfaces of the cornea, C_1 and sclera, C_2 .

6.3.2 The eye tumor

The region occupied by the eye tumor is constructed using the same approach as described by Yoriyaz et al. [178]. A sphere of a particular diameter with its center placed at a specific point on the interface between the vitreous and sclera is firstly generated. The region of the sphere that is cut by the interfaces between the sclera and the vitreous is then taken as the region occupied by the tumor, which is denoted by R_7 . A sketch of the steps involved in the development of the eye tumor model is illustrated in Figure 6-2. An example of an eye tumor growing at the upper region inside the human eye, developed using the aforementioned steps, is shown in Figure 6-1.

The model of the eye tumor generated using the steps illustrated in Figure 6-2 is categorized based on the diameter of the sphere that is used for generating the model. Suppose that a model is created using a sphere of diameter 13mm. Based on the classifications tabulated in Table 6.1, the tumor model may then be categorized as a category T2 eye tumor.

Figure 6-1: Three-dimensional model of a left human eye with a view of its interior structure

6.3.3 Governing equations

The equation governing the steady state temperature distribution inside the regions of the normal (healthy) human eye is similar to the one used in Chapter 2, which is given with reference to the model shown in Figure 6-1, by

$$\nabla(\kappa_i \nabla T_i(x, y, z)) = 0, \text{ for } i = 1, 2, 3, 4, 5 \text{ and } 6, \quad (6.1)$$

where κ_i and T_i denote the thermal conductivity and temperature of region R_i respectively. Equation (6.1) generally assumes each region of the human eye to be homogeneous

Figure 6-2: Steps involved in constructing the model of the eye tumor

and thermally isotropic. Furthermore, metabolic heat generation, blood perfusion rate and natural convection inside the anterior chamber are all assumed to have negligible effects on the heat flow inside the human eye.

For simplicity, the region occupied by the eye tumor is also assumed to be homogeneous and thermally isotropic. To account for the metabolic heat generation and the blood perfusion rate inside the eye tumor, heat flow inside region R_7 is taken to be given by the Pennes bioheat equation [72], which may be mathematically expressed as:

$$\begin{aligned} \nabla(\kappa_i \nabla T_i(x, y, z)) &= \rho_{bl} c_{bl} \varpi_{bl} (T_i(x, y, z) - T_{bl}) - Q_m, \\ &\text{for } i = 7, \end{aligned} \quad (6.2)$$

where ρ_{bl} and c_{bl} are the density and specific heat of blood respectively, T_{bl} is arterial blood temperature which is assumed to be the same as the body core temperature, ϖ_{bl} is the blood perfusion rate inside the eye tumor and Q_m denotes the volumetric heat generated from the metabolic activity inside the eye tumor.

6.3.4 Boundary conditions

A few assumptions have to be made prior to the specification of the boundary conditions on the surfaces of the cornea, C_1 and sclera, C_2 . Firstly, the presence of eye tumor inside the human eye is assumed to have no significant effect on the heat transfer between the corneal surface and the environment. Secondly, blood flow inside the choroid is assumed not to be affected by the growth of tumor inside the human eye. Therefore, the boundary conditions specified on C_1 and C_2 in this chapter are similar those used in Chapter 2. These are reproduced here as

$$-\kappa_1 \frac{\partial T_1}{\partial n} = h_{\text{amb}}(T_1 - T_{\text{amb}}) + \varepsilon\sigma(T_1^4 - T_{\text{amb}}^4) + E_{\text{vap}}, \text{ on } C_1, \quad (6.3)$$

and

$$-\kappa_6 \frac{\partial T_6}{\partial n} = h_{\text{bl}}(T_6 - T_{\text{bl}}), \text{ on } C_2, \quad (6.4)$$

respectively. The variation of temperature and heat flux at the interfaces between two contiguous ocular regions, I_{ij} may be described using the continuity condition such that

$$T_i = T_j \text{ and } \kappa_i \frac{\partial T_i}{\partial n} = \kappa_j \frac{\partial T_j}{\partial n}, \text{ on } I_{ij}. \quad (6.5)$$

6.4 Material Properties

The thermal conductivity of each region inside the human eye shown in Figure 6-1 and the values of control parameters used for describing the boundary conditions in this chapter are presented in Tables 2.1 and 2.2. While the thermal properties of each ocular region can be easily obtained from literature, the same may not be said of the eye tumor. A search in the literature yields no relevant information regarding the thermal properties of the eye tumor. On the other hand, thermal properties of various other types of tumor have been measured and reported. To enable simulations to be carried out in the present study, values of the unknown thermal properties of the eye tumor, specifically the thermal

conductivity, blood perfusion rate and metabolic heat generation, are chosen to be given over a range of values that are derived based on the experimental data measured from the different types of tumors that grow inside the human body.

Based on the measurements compiled by Jain [179], the thermal conductivities of various tumors that grow on different parts of the human body are found to be in the range of 0.35 to $0.67 \text{Wm}^{-1}\text{K}^{-1}$. The types of tumors that were measured included the tumor of the breast, colon, liver, lungs and pancreas. No significant differences in the values of thermal conductivity between normal and metastatic tumors of the same kind are observed. Values of the tumor blood perfusion rate that were measured by various researchers using different measuring techniques were compiled and published by Fieldman et al. [180]. Based on the data measured on breast tumors, lymphomas, anaplastic carcinoma and differentiated tumors, the tumor blood perfusion rate was found to be in the range of 0.0014 to $0.0072 \text{m}^3\text{s}^{-1}\text{m}^{-3}$.

Unlike the thermal conductivity and blood perfusion rate, the metabolic heat generation remains an elusive term in the bioheat equation, where experimental data remains scarce [179]. One of the more established studies that quantified the values of the tumor metabolic heat generation is perhaps the work carried out by Gautherie [37] on breast tumors. According to Gautherie [37], the metabolic heat generation of breast tumors remain constant during the phase of exponential growth. Experimental data collected from patients diagnosed with breast tumors revealed that the volumetric metabolic heat generated by the tumor is related to the tumor doubling time by [37]

$$Q_m = \frac{\Lambda}{D_T}, \quad (6.6)$$

where Λ is a constant that has a value of $3.27 \times 10^6 \text{W.day.m}^{-3}$ and D_T is the tumor doubling time in days. The tumor doubling time is defined as the time needed for the tumor to double its volume [181].

Suppose that Equation (6.6) is valid for all types of tumor. Assuming that the doubling time is a unique property of tumors, the only variable in Equation (6.6) that

may change to account for different types of tumor is the constant Λ . Instead of using the range of metabolic heat generation of breast tumor to represent the values of eye tumor, it may be more appropriate to allow the value of Λ to vary within a certain range. In this study, Λ is assumed to have a value that ranges from 1×10^6 to $5 \times 10^6 \text{ W} \cdot \text{day} \cdot \text{m}^{-3}$. For an average eye tumor doubling time of 63 days [182], the corresponding range of volumetric metabolic heat calculated using Equation (6.6) is found to be approximately 15,000 to $80,000 \text{ Wm}^{-3}$.

Table 6.2 summarizes the range of values of the thermal conductivity, blood perfusion rate and metabolic heat generation of the various types of tumors that grow inside the human body.

Table 6.2: Thermal properties of the eye tumor used in this study

Parameter	Range
Thermal conductivity, κ_T ($\text{Wm}^{-1}\text{K}^{-1}$)	0.35-0.67
Blood perfusion rate, ϖ_{bl} ($\text{m}^3\text{s}^{-1}\text{m}^{-3}$)	0.0014-0.0072
Metabolic heat generation, Q_m (Wm^{-3})	15,000-80,000

By establishing the range of thermal conductivity, blood perfusion rate and metabolic heat generation of various tumors of the human body, the thermal properties of eye tumor may now be assumed to lie within the corresponding range of values given in Table 6.2. Since the values given in Table 6.2 have been obtained for different types of tumor that grow on various parts of the human body, this assumption is likely to remain valid, as the thermal properties of the tumors in general, are not expected to be significantly different from one another.

6.5 Numerical Scheme

6.5.1 Integro-differential equations

The boundary element method begins with the derivation of the integral representations of the governing equations. Following the steps outlined by Ang [84], the integral

representations of Equations (6.1) and (6.2) are respectively given by

$$\begin{aligned} \lambda(\xi_i, \eta_i, \zeta_i) T_i(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i} T_i(x, y, z) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z) \\ &\quad - \iint_{\Gamma_i} \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [T_i(x, y, z)] dA(x, y, z) \\ &\quad \text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \text{ and} \\ &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \end{aligned} \quad (6.7)$$

and

$$\begin{aligned} \lambda(\xi_i, \eta_i, \zeta_i) T_i(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i} T_i(x, y, z) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z) \\ &\quad - \iint_{\Gamma_i} \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [T_i(x, y, z)] dA(x, y, z) \\ &\quad + \iiint_{R_i} \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) [\alpha T_i(x, y, z) - \beta] dV(x, y, z), \\ &\quad \text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \text{ and} \\ &\quad \text{for } i = 7, \end{aligned} \quad (6.8)$$

where $\alpha = \frac{\rho_{bl} c_{bl} \varpi_{bl}}{\kappa_i}$, $\beta = \frac{1}{\kappa_i} (\rho_{bl} c_{bl} \varpi_{bl} T_{bl} + Q_m)$, Γ_i denotes the curve boundary of region R_i , $dA(x, y, z)$ denotes the area of an infinitesimal portion of surface Γ_i , $dV(x, y, z)$ denotes the volume of an infinitesimal portion of region R_i , $\lambda(\xi_i, \eta_i, \zeta_i) = 1$ if point (ξ_i, η_i, ζ_i) lies at the interior of region R_i , $\lambda(\xi_i, \eta_i, \zeta_i) = \frac{1}{2}$ if point (ξ_i, η_i, ζ_i) lies on the smooth part of surface Γ_i and $\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)$ and $\partial \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) / \partial n$ are the fundamental solution of the three-dimensional Laplace equation and its normal derivative respectively, which are given by

$$\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) = -\frac{1}{4\pi} [(x - \xi_i)^2 + (y - \eta_i)^2 + (z - \zeta_i)^2]^{-\frac{1}{2}}, \quad (6.9)$$

and

$$\frac{\partial}{\partial n}[\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] = \frac{1}{4\pi} \left\{ \frac{n_x(x - \xi_i) + n_y(y - \eta_i) + n_z(z - \zeta_i)}{[(x - \xi_i)^2 + (y - \eta_i)^2 + (z - \zeta_i)^2]^{\frac{3}{2}}} \right\}, \quad (6.10)$$

where n_x , n_y and n_z are the components of the outward unit normal vector on Γ_i in the direction of x , y and z respectively.

6.5.2 The dual reciprocity method

Equation (6.8) contains a domain integral that can be approximated into equivalent boundary integrals using the dual reciprocity method [156]. Since the steps involved in carrying out the dual reciprocity method have been presented in Chapter 5, a detailed description shall be avoided here. Following the selection of M collocation points in $R_7 \cup \Gamma_7$, which are denote by $(a^{(1)}, b^{(1)})$, $(a^{(2)}, b^{(2)})$, ..., $(a^{(M-1)}, b^{(M-1)})$ and $(a^{(M)}, b^{(M)})$, and letting ϕ_{3D} and $\varkappa_{3D}$ define the three-dimensional radial basis function and the corresponding particular solution respectively, the domain integral in Equation (6.8) may be reduced into an equivalent boundary integral, such that

$$\begin{aligned} & \iiint_{R_i} \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) [\alpha T_i(x, y, z) - \beta] dV(x, y, z) \\ & \approx \sum_{j=1}^M [\alpha T_i(a^{(j)}, b^{(j)}, c^{(j)}) - \beta] \sum_{m=1}^M W^{(mj)} \\ & \quad \times \left\{ \lambda(\xi_i, \eta_i, \zeta_i) \varkappa_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) \right. \\ & \quad - \iint_{\Gamma_i} \varkappa_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z) \\ & \quad + \iint_{\Gamma_i} \{ \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) \\ & \quad \times \frac{\partial}{\partial n} [\varkappa_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)})] \} dA(x, y, z) \left. \right\}, \end{aligned} \quad (6.11)$$

where the coefficients $W^{(mj)}$ are expressed as

$$\sum_{j=1}^M W^{(kj)} \phi_{3D}(a^{(j)}, b^{(j)}, c^{(j)}; a^{(m)}, b^{(m)}, c^{(m)}) = \begin{cases} 1, & \text{if } k = m, \\ 0, & \text{if } k \neq m, \end{cases}$$

for $k, m = 1, 2, \dots, M-1, M$.

Substituting the approximation in Equation (6.11) into (6.8) leads to an expression that consists of boundary only integrals:

$$\begin{aligned} & \lambda(\xi_i, \eta_i, \zeta_i) T_i(\xi_i, \eta_i, \zeta_i) \\ &= \iint_{\Gamma_i} T_i(x, y, z) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z) \\ & - \iint_{\Gamma_i} \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [T_i(x, y, z)] dA(x, y, z) \\ & + \sum_{j=1}^M [\alpha T_i(a^{(j)}, b^{(j)}, c^{(j)}) - \beta] \sum_{m=1}^M W^{(mj)} \\ & \times \left\{ \lambda(\xi_i, \eta_i, \zeta_i) \varkappa_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) \right. \\ & - \iint_{\Gamma_i} \varkappa_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z) \\ & \left. + \iint_{\Gamma_i} \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [\varkappa_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)})] dA(x, y, z) \right\} \\ & \text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \text{ and} \\ & \text{for } i = 7. \end{aligned} \tag{6.12}$$

6.5.3 Boundary discretization

For a numerical method based on Equations (6.7) and (6.12), the surface of each region R_i is discretized into N_i boundary elements denoted by $\Gamma_i^{(1)}, \Gamma_i^{(2)}, \dots, \Gamma_i^{(N_i-1)}, \Gamma_i^{(N_i)}$. Each boundary element is taken to be a triangle. Across each boundary element, $\Gamma_i^{(k)}$ the temperature and heat flux are assumed to vary linearly. This can be accom-

plished by selecting three points denoted by $(\xi_i^{(k)}, \eta_i^{(k)}, \zeta_i^{(k)})$, $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)}, \zeta_i^{(k+N_i)})$ and $(\xi_i^{(k+2N_i)}, \eta_i^{(k+2N_i)}, \zeta_i^{(k+2N_i)})$ inside each boundary element. Details on the selection of the three boundary collocation points are presented in Appendix B.

Once the three nodes on $\Gamma_i^{(k)}$ have been selected, variation of the temperature and heat flux across each boundary element may be mathematically expressed as

$$\begin{aligned} T_i(x, y, z) &\approx \bar{\varphi}_1(x, y, z)T_i^{(k)} + \bar{\varphi}_2(x, y, z)T_i^{(k+N_i)} + \bar{\varphi}_3(x, y, z)T_i^{(k+2N_i)}, \\ -\kappa_i \frac{\partial}{\partial n}[T_i(x, y, z)] &\approx \bar{\varphi}_1(x, y, z)q_i^{(k)} + \bar{\varphi}_2(x, y, z)q_i^{(k+N_i)} + \bar{\varphi}_3(x, y, z)q_i^{(k+2N_i)}, \end{aligned} \quad \text{for } (x, y, z) \in \Gamma_i^{(k)}, \quad (6.13)$$

where $\bar{\varphi}_1(x, y, z)$, $\bar{\varphi}_2(x, y, z)$ and $\bar{\varphi}_3(x, y, z)$ are linear interpolation functions in the $Oxyz$ coordinate system, $T_i^{(k)}$, $T_i^{(k+N_i)}$ and $T_i^{(k+2N_i)}$ are values of $T_i(x, y, z)$ at points $(\xi_i^{(k)}, \eta_i^{(k)}, \zeta_i^{(k)})$, $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)}, \zeta_i^{(k+N_i)})$ and $(\xi_i^{(k+2N_i)}, \eta_i^{(k+2N_i)}, \zeta_i^{(k+2N_i)})$ respectively and $q_i^{(k)}$, $q_i^{(k+N_i)}$ and $q_i^{(k+2N_i)}$ are values of $\partial T_i(x, y, z)/\partial n$ at points $(\xi_i^{(k)}, \eta_i^{(k)}, \zeta_i^{(k)})$, $(\xi_i^{(k+N_i)}, \eta_i^{(k+N_i)}, \zeta_i^{(k+N_i)})$ and $(\xi_i^{(k+2N_i)}, \eta_i^{(k+2N_i)}, \zeta_i^{(k+2N_i)})$ respectively. Details on the linear interpolation functions $\bar{\varphi}_1(x, y, z)$, $\bar{\varphi}_2(x, y, z)$ and $\bar{\varphi}_3(x, y, z)$ are presented in Appendix C.

Substituting the approximation in Equation (6.13) into Equations (6.7) and (6.12) leads to

$$\begin{aligned} \lambda(\xi_i, \eta_i, \zeta_i)T_i(\xi_i, \eta_i, \zeta_i) &= \sum_{k=1}^{N_i} \mathcal{H}_4^{(k)}(\xi_i, \eta_i, \zeta_i)T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{H}_5^{(k)}(\xi_i, \eta_i, \zeta_i)T_i^{(k+N_i)} \\ &\quad + \sum_{k=1}^{N_i} \mathcal{H}_6^{(k)}(\xi_i, \eta_i, \zeta_i)T_i^{(k+2N_i)} - \sum_{k=1}^{N_i} \mathcal{H}_1^{(k)}(\xi_i, \eta_i, \zeta_i)q_i^{(k)} \\ &\quad - \sum_{k=1}^{N_i} \mathcal{H}_2^{(k)}(\xi_i, \eta_i, \zeta_i)q_i^{(k+N_i)} - \sum_{k=1}^{N_i} \mathcal{H}_3^{(k)}(\xi_i, \eta_i, \zeta_i)q_i^{(k+2N_i)} \end{aligned} \quad \begin{aligned} &\text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \text{ and} \\ &\text{for } i = 1, 2, 3, 4, 5 \text{ and } 6, \end{aligned} \quad (6.14)$$

and

$$\begin{aligned}
 \lambda(\xi_i, \eta_i, \zeta_i) T_i(\xi_i, \eta_i, \zeta_i) &= \sum_{k=1}^{N_i} \mathcal{H}_4^{(k)}(\xi_i, \eta_i, \zeta_i) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{H}_5^{(k)}(\xi_i, \eta_i, \zeta_i) T_i^{(k+N_i)} \\
 &+ \sum_{k=1}^{N_i} \mathcal{H}_6^{(k)}(\xi_i, \eta_i, \zeta_i) T_i^{(k+2N_i)} - \sum_{k=1}^{N_i} \mathcal{H}_1^{(k)}(\xi_i, \eta_i, \zeta_i) q_i^{(k)} \\
 &- \sum_{k=1}^{N_i} \mathcal{H}_2^{(k)}(\xi_i, \eta_i, \zeta_i) q_i^{(k+N_i)} - \sum_{k=1}^{N_i} \mathcal{H}_3^{(k)}(\xi_i, \eta_i, \zeta_i) q_i^{(k+2N_i)} \\
 &+ \sum_{j=1}^M [\alpha T_i(a^{(j)}, b^{(j)}, c^{(j)}) - \beta] \\
 &\times \sum_{m=1}^M W^{(mj)} \Psi_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) \\
 &\quad \text{for } (\xi_i, \eta_i, \zeta_i) \in R_i \cup \Gamma_i \text{ and} \\
 &\quad \text{for } i = 7,
 \end{aligned} \tag{6.15}$$

respectively, where

$$\begin{aligned}
 \mathcal{H}_1^{(k)}(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i^{(k)}} \bar{\varphi}_1(x, y, z) \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) dA(x, y, z), \\
 \mathcal{H}_2^{(k)}(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i^{(k)}} \bar{\varphi}_2(x, y, z) \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) dA(x, y, z), \\
 \mathcal{H}_3^{(k)}(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i^{(k)}} \bar{\varphi}_3(x, y, z) \Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i) dA(x, y, z), \\
 \mathcal{H}_4^{(k)}(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i^{(k)}} \bar{\varphi}_1(x, y, z) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z), \\
 \mathcal{H}_5^{(k)}(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i^{(k)}} \bar{\varphi}_2(x, y, z) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z), \\
 \mathcal{H}_6^{(k)}(\xi_i, \eta_i, \zeta_i) &= \iint_{\Gamma_i^{(k)}} \bar{\varphi}_3(x, y, z) \frac{\partial}{\partial n} [\Phi_{3D}(x, y, z; \xi_i, \eta_i, \zeta_i)] dA(x, y, z),
 \end{aligned} \tag{6.16}$$

and

$$\begin{aligned}
\Psi_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) &= \lambda(\xi_i, \eta_i, \zeta_i) \mathcal{W}_{3D}(\xi_i, \eta_i, \zeta_i; a^{(m)}, b^{(m)}, c^{(m)}) \\
&- \sum_{k=1}^{N_i} \mathcal{H}_4^{(k)}(\xi_i, \eta_i, \zeta_i) \mathcal{W}_{3D}^{(k)}(a^{(m)}, b^{(m)}, c^{(m)}) \\
&- \sum_{k=1}^{N_i} \mathcal{H}_5^{(k)}(\xi_i, \eta_i, \zeta_i) \mathcal{W}_{3D}^{(k+N_i)}(a^{(m)}, b^{(m)}, c^{(m)}) \\
&- \sum_{k=1}^{N_i} \mathcal{H}_6^{(k)}(\xi_i, \eta_i, \zeta_i) \mathcal{W}_{3D}^{(k+2N_i)}(a^{(m)}, b^{(m)}, c^{(m)}) \\
&+ \sum_{k=1}^{N_i} \mathcal{H}_1^{(k)}(\xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [\mathcal{W}_{3D}^{(k)}(a^{(m)}, b^{(m)}, c^{(m)})] \\
&+ \sum_{k=1}^{N_i} \mathcal{H}_2^{(k)}(\xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [\mathcal{W}_{3D}^{(k+N_i)}(a^{(m)}, b^{(m)}, c^{(m)})] \\
&+ \sum_{k=1}^{N_i} \mathcal{H}_3^{(k)}(\xi_i, \eta_i, \zeta_i) \frac{\partial}{\partial n} [\mathcal{W}_{3D}^{(k+2N_i)}(a^{(m)}, b^{(m)}, c^{(m)})].
\end{aligned}$$

Although the integrals in Equation (6.16) may be evaluated numerically using numerical integration formulae, in the present study, a semi-analytical evaluation is performed. In the semi-analytical calculation, the inner integral of each expression in Equation (6.16) is first performed analytically. Integration of the resulting analytical expression is then performed numerically using the Gaussian integration formulae. By carrying out a semi-analytical integration, the amount of error that may be introduced when performing numerical integration is minimized.

To implement the dual reciprocity method, M is chosen such that $M = 3N_7 + L$, where the $3N_7$ points are taken to coincide with the $3N_7$ boundary nodes selected on the boundary of region R_7 . The remaining L points are chosen to be well-spaced out at the interior of region R_7 . For a numerical procedure, point (ξ_i, η_i, ζ_i) in Equations (6.14) and (6.15) are collocated at $(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)})$, for $n = 1, 2, \dots, 3N_i - 1, 3N_i$, and $(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)})$,

for $n = 1, 2, \dots, M - 1, M$, respectively, such that

$$\begin{aligned}
 \lambda_i^{(n)} T_i^{(n)} &= \sum_{k=1}^{N_i} \mathcal{H}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{H}_5^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) T_i^{(k+N_i)} \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{H}_6^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) T_i^{(k+2N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{H}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) q_i^{(k)} - \sum_{k=1}^{N_i} \mathcal{H}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) q_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{H}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) q_i^{(k+2N_i)} \\
 &\quad \text{for } n = 1, 2, \dots, 3N_i - 1, 3N_i \text{ and} \\
 &\quad \text{for } i = 1, 2, 3, 4, 5 \text{ and } 6,
 \end{aligned} \tag{6.17}$$

and

$$\begin{aligned}
 \lambda_i^{(n)} T_i^{(n)} &= \sum_{k=1}^{N_i} \mathcal{H}_4^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) T_i^{(k)} + \sum_{k=1}^{N_i} \mathcal{H}_5^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) T_i^{(k+N_i)} \\
 &\quad + \sum_{k=1}^{N_i} \mathcal{H}_6^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) T_i^{(k+2N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{H}_1^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) q_i^{(k)} - \sum_{k=1}^{N_i} \mathcal{H}_2^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) q_i^{(k+N_i)} \\
 &\quad - \sum_{k=1}^{N_i} \mathcal{H}_3^{(k)}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}) q_i^{(k+2N_i)} \\
 &\quad + \sum_{j=1}^M \left[\alpha T_i^{(j)} - \beta \right] \sum_{m=1}^M W^{(mj)} \times \Psi_{3D}(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)}; \xi_i^{(m)}, \eta_i^{(m)}, \zeta_i^{(m)}) \\
 &\quad \text{for } n = 1, 2, \dots, M - 1, M \text{ and} \\
 &\quad \text{for } i = 7,
 \end{aligned} \tag{6.18}$$

where $\lambda_i^{(n)} = \lambda(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)})$ and $T_i^{(n)} = T_i(\xi_i^{(n)}, \eta_i^{(n)}, \zeta_i^{(n)})$.

Equations (6.17) and (6.18) along with the boundary conditions and continuity condition described in Section 6.3.4 generate a system of $(3N_1 + 3N_2 + 3N_3 + 3N_4 + 3N_5 +$

$3N_6 + 3N_7 + L$) algebraic equations with $(3N_1 + 3N_2 + 3N_3 + 3N_4 + 3N_5 + 3N_6 + 3N_7 + L)$ unknowns that can be solved for the unknown temperatures at boundaries C_1 and C_2 and the unknown temperatures and heat flux at the interfaces. The non-linear boundary condition in Equation (6.3) is treated using the iterative procedure as described in Chapter 2.

6.6 Choice of Radial Basis Function

In the present study, the radial basis function used in the implementation of the dual reciprocity method is chosen to be

$$\phi_{3D}(x, y, z; \xi, \eta, \zeta) = 1 + \left(\frac{\mathcal{R}(x, y, z; \xi, \eta, \zeta)}{\mathcal{R}_{\max}} \right)^3, \quad (6.19)$$

where $\mathcal{R}(x, y, z; \xi, \eta, \zeta)$ denotes the Euclidean distance between point (x, y, z) and (ξ, η, ζ) and $\mathcal{R}_{\max}$ is the maximum value of $\mathcal{R}(x, y, z; \xi, \eta, \zeta)$. Numerical investigations carried out by Partridge et al. [131] discovered that the radial basis function in Equation (6.19) yield results that are generally accurate. The corresponding particular solution, $\varkappa_{3D}$ obtained from solving $\nabla^2 \varkappa_{3D} = \phi_{3D}$ is given by

$$\varkappa_{3D}(x, y, z; \xi, \eta, \zeta) = \frac{\mathcal{R}^2(x, y, z; \xi, \eta, \zeta)}{6} + \frac{\mathcal{R}^5(x, y, z; \xi, \eta, \zeta)}{30\mathcal{R}_{\max}^3}. \quad (6.20)$$

6.7 Results

6.7.1 Numerical model

Three categories of eye tumor, namely T1, T2 and T3 are examined in the present study. Category T4 is not considered since the tumor has grown beyond the region defined by the model of the human eye (see Table 6.1). Based on the range of values given in Table 6.1, values of 10 and 15mm are selected to be the diameter of the sphere used for

generating the model of the eye tumor of categories T1 and T2 respectively. A value of 17mm is assumed for category T3 since the largest value of LBD is not explicitly defined.

For each category of eye tumor examined, investigations are carried out for two different locations of tumor growth. In the first location, the tumor is assumed to grow at the positive y region of the human eye. Specifically, the center of the sphere used in generating the eye tumor is placed at coordinates $(0.013, 0.0105, 0)$. This is defined as Case 1. In the second location, which is defined as Case 2, the tumor is assumed to grow at the back of the human eye such that it is symmetrical about the pupillary axis. In this case, the center of the sphere is placed at coordinates $(0.0244, 0, 0)$. Locations of the eye tumors inside the human eye in Cases 1 and 2 viewed in the mid-sagittal plane are illustrated in Figure 6-3.

Figure 6-3: Locations of the eye tumor in Cases 1 and 2

In carrying out the numerical scheme outlined in Section 6.5, the boundaries of each region of the human eye are discretized into small triangular elements. In Case 1, a total of 2,212, 2,362 and 2,306 elements are generated in the model of the human eye with categories T1, T2 and T3 eye tumors respectively, while in Case 2, a total of 2,388, 2,316 and 2,332 elements are generated respectively. Discretization of the boundaries are carried out using the build-in mesh generator of the partial differential equation calculator, COMSOL Multiphysics [141]. To implement the dual reciprocity method, 100

interior points are selected inside the region occupied by the eye tumor for both Cases 1 and 2 and for each category of eye tumor investigated. The discretized structures of each ocular region and a category T2 eye tumor are displayed in Figure 6-4.

Simulations are carried out by varying the eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation over five different values that are defined within the range given in Table 6.2. The five values considered for the thermal conductivity are 0.3, 0.4, 0.5, 0.6 and $0.7\text{Wm}^{-1}\text{K}^{-1}$, while values of tumor blood perfusion rate are selected to be 0.002, 0.004, 0.006, 0.008 and $0.01\text{m}^3\text{s}^{-1}\text{m}^{-3}$. The metabolic heat generation of the eye tumor is chosen to be given by 15,000, 30,000, 45,000, 60,000 and $75,000\text{Wm}^{-3}$. When carrying out simulations for the variation of a specific thermal property of the eye tumor, values of the other two are remained as constants, which are simply denoted as the control. Specifically, the control values of the eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation are chosen to be $0.50\text{Wm}^{-1}\text{K}^{-1}$, $0.006\text{m}^3\text{s}^{-1}\text{m}^{-3}$ and $45,000\text{Wm}^{-3}$ respectively.

6.7.2 Case 1

Effects of eye tumors of categories T1, T2 and T3 on the temperature distribution along the pupillary axis are plotted in Figures 6-5, 6-6 and 6-7 respectively. Values of the temperature difference shown in Figures 6-5 to 6-7 represent the increase in temperature from the case when no tumor grows inside the eye.

An increase in the temperature along the pupillary axis is apparent when tumor grows inside the human eye. The ‘bell-shaped’ curves seen in Figures 6-5 to 6-7 imply that the thermal effects of eye tumor are greater at the vicinity of the tumor region. Similar thermal characteristics have been reported by other researchers who carried out investigations on the human breast and skin [32,33,35,36]. Comparing the temperature plots in Figures 6-5 to 6-7, it is found that a category T3 eye tumor produces the largest increase in temperature. This is followed by categories T2 and T1. The observed results imply that a larger-sized tumor produces greater warming effects than a smaller-sized

Figure 6-4: The discretized structure of the cornea, anterior chamber, lens, posterior chamber, vitreous, sclera and eye tumor (figures are not to scale)

Figure 6-5: Temperature variations along the pupillary axis of an eye with a category T1 eye tumor in Case 1

Figure 6-6: Temperature variations along the pupillary axis of an eye with a category T2 eye tumor in Case 1

Figure 6-7: Temperature variations along the pupillary axis of an eye with a category T3 eye tumor in Case 1

tumor. This may be attributed to the larger amount of metabolic heat generated by the larger-sized tumor.

In each category of eye tumor examined, changes in the metabolic heat generation produce the largest variation in the temperature along the pupillary axis. The effects of the thermal conductivity and blood perfusion rate are roughly the same and in both cases, they are found to be very small when compared to the effects of the metabolic heat generation.

From Figures 6-5 to 6-7, the temperatures along the pupillary axis are found to increase with the eye tumor thermal conductivity and metabolic heat generation. A larger thermal conductivity generally encourages more heat transfer between the eye tumor and the surrounding ocular regions. Likewise, a larger metabolic heat generation implies that more heat is generated by the eye tumor, thus increasing the temperature of the surrounding ocular regions. From Figures 6-5 to 6-7, it is also found that a larger blood perfusion rate produces a smaller increase in the temperatures along the pupillary axis. This may be explained by the role of blood perfusion inside the tumor. In biological tissues, blood flow acts as a medium for transferring away excessive heat. In the case of the human eye, the larger blood perfusion rate inside the tumor suggests that larger amount of metabolic heat is transferred away from the eye. This eventually leads to a cooler ocular surrounding.

In the eye with a category T1 eye tumor (Figure 6-5), variation in the tumor thermal conductivity and blood perfusion rate appear to have minimal effects on the temperature distribution inside the human eye when compared to the metabolic heat generation. The largest increase in temperature is found to be approximately 0.16°C , which occurs when value of the tumor metabolic heat generation is the highest ($75,000\text{Wm}^{-3}$). Similar results are observed in eyes with categories T2 and T3 eye tumors (see Figures 6-6 and 6-7). The effects of blood perfusion rate in eyes with categories T2 and T3 eye tumors are much stronger than the category T1 eye tumor however. This is a further indication of the importance of tumor size in the temperature increase inside the human eye. The

largest increase in temperature caused by the categories T2 and T3 eye tumors are found to be approximately 0.5 and 0.7°C respectively. These values are well within the range of temperature rise predicted by the models of the human breast and skin [32,33,35,36].

Table 6.3 summarizes the increase in the temperature at the corneal surface from caused by the growth of eye tumor from the case when no tumor grows inside the human eye. The location of the central, superior, inferior, nasal and temporal are defined by

Table 6.3: Increase in temperature on the corneal surface in Case 1

Location	Normal	Temperature increase (°C)		
		Tumor category		
		T1	T2	T3
Central (A)	34.274	0.068	0.206	0.285
Superior (B)	35.477	0.101	0.298	0.404
Inferior (C)	35.472	0.042	0.128	0.181
Nasal (D)	35.474	0.058	0.174	0.243
Temporal (E)	35.473	0.060	0.182	0.253
Average		0.066	0.198	0.273

points A, B, C, D and E respectively. This is shown in Figure 6-1. In particular, the coordinates of these points are given by (0, 0, 0), (0.0025, 0.0064, 0), (0.0025, -0.0064, 0), (0.0025, 0, -0.0064) and (0.0025, 0, 0.0064) respectively. Points B, C, D and E are generally located at the periphery of the corneal surface. Values in the second column of Table 6.3 represent the temperatures at points A, B, C, D and E of a normal human eye. Results presented in Table 6.3 are obtained for values of eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation at their respective control level.

Out of the five points analyzed, the increase in temperature at the superior is found to be the largest. This is true for all three categories of eye tumor examined. This may be credited to the location of the superior, which is closest to the eye tumor. Consequently, the warming effects from the metabolic heat generated by the eye tumor are much greater here than the other points on the corneal surface. At the inferior, which is the point on the corneal surface farthest from the eye tumor, the increase in temperature is found to be the smallest. This further supports the argument given above. As expected, a larger

sized tumor is found to produce a larger increase in the corneal surface temperature.

In the second column of Table 6.3, points at the periphery of the corneal surface in a normal eye are found to have temperatures that are not significantly different from one another. Temperature at the center meanwhile, is approximately 0.2°C lower than the points at the periphery. Such a temperature distribution suggests that the thermal profile on the corneal surface is symmetrical about the geometrical center of the cornea. When an eye tumor grows inside the human eye, the temperature at the superior is found to be approximately 50% and 60% higher than the central and inferior respectively. This indicates thermal asymmetry along the vertical geometrical center of the cornea.

An average increase of 0.066, 0.198 and 0.273°C are found on the corneal surface of eyes with categories T1, T2 and T3 eye tumor respectively.

6.7.3 Case 2

The temperature increase along the pupillary axis caused by eye tumors of categories T1, T2 and T3 in Case 2 are plotted in Figures 6-8, 6-9 and 6-10 respectively. Unlike the ‘bell-shaped’ curves seen in Figures 6-5 to 6-7 in Case 1, the profiles observed in Figures 6-8 to 6-10 show a warmer temperature distribution at the posterior region of the human eye. This is a consequence of the eye tumor being oriented along the pupillary axis. Variation of the temperature at the anterior regions of the human eye appear to be very small. This may be explained by the location of the eye tumor in Case 2, which is positioned at the back of the eye. As distance from the eye tumor increases, the warming effect of the metabolic heat generated by the eye tumor diminishes.

Table 6.4 tabulates the magnitude of temperature rise on the corneal surface due to the growth of eye tumor in Case 2. As in Case 1, the results presented in Table 6.4 are obtained using the control values of eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation.

Contrary to the results obtained in Case 1, the point on the corneal surface where the largest increase in temperature occurs is located at the center. This is not surprising since

Figure 6-8: Temperature variations along the pupillary axis of an eye with a category T1 eye tumor in Case 2

Figure 6-9: Temperature variations along the pupillary axis of an eye with a category T2 eye tumor in Case 2

Figure 6-10: Temperature variations along the pupillary axis of an eye with a category T3 eye tumor in Case 2

Table 6.4: Increase in temperature on the corneal surface in Case 2

Location	Normal	Temperature increase ($^{\circ}\text{C}$)		
		Tumor category		
		T1	T2	T3
Central (A)	34.274	0.036	0.091	0.121
Superior (B)	35.477	0.025	0.077	0.107
Inferior (C)	35.472	0.029	0.082	0.113
Nasal (D)	35.474	0.027	0.080	0.110
Temporal (E)	35.473	0.025	0.079	0.108
Average		0.028	0.082	0.112

the center of the corneal surface is now closer to the eye tumor than the superior, inferior, nasal and temporal. While the increase in temperature at the center of the corneal surface is the largest, no significant differences in the temperatures at the periphery of the corneal surface are found. This indicates a lack of thermal asymmetry, which is to be expected since the eye tumor is positioned in such a way that it is symmetrical about the pupillary axis. Consequently, warming effects of the eye tumor are evenly dispersed into adjacent regions of the human eye, thus leading to a uniform increase in the temperature at the corneal periphery.

Comparing the results in Table 6.4 with those in Table 6.3, the eye tumor in Case 1 is found to produce temperature rise that is on average (average of all the five points and the three categories of eye tumor), 2.4 times greater than the temperature increase in Case 2. This may be attributed to the greater distance between the eye tumor and the corneal surface in Case 2 than in Case 1 (see Figure 6-3).

6.7.4 Discussion

From the numerical results presented in Sections 6.7.2 and 6.7.3, the growth of tumor inside the human eye is found to produce a warmer ocular temperature distribution than a normal healthy eye. For the location of eye tumor in Case 1, a thermal asymmetry on the corneal surface is detected. Although simulations have not been carried out for eye tumors that grow at the negative y region of the human eye, results from our present

study suggest that such a case will yield the largest increase in temperature at the inferior. Future studies may include investigations of the ocular temperature changes for locations of eye tumor that are different from the two cases considered here.

In the present study, the region occupied by the eye tumor has been assumed to be homogeneous. This assumption does not accurately depict the actual anatomical structure of tumors however. In reality, the tumor may be divided into two zones, namely a necrotic zone at the center of the tumor and a regionally vascularized zone at the periphery [170]. As a result of the tissue inhomogeneity, thermal properties of the tumor such as blood perfusion rate and metabolic heat generation may not be uniform throughout the entire tumor region. Instead, the vascularized periphery is expected to have larger blood perfusion rate and metabolic heat generation than the necrotic center. Although it is not known whether such inhomogeneity may cause any significant difference to the simulated results, the present model may be reworked in future to deal with these issues, provided that sufficient information is available.

Investigations in the present study have been limited to choroidal melanoma. For eye tumors that grow on the iris (iris melanoma) and ciliary body (ciliary body melanoma), similar investigations may be performed by making minor modifications to the present model. These are open for future studies.

To verify the accuracy of the model developed in this study, the numerical results obtained are qualitatively compared with the experimental observations reported by other researchers that can be found in literature. Bourjat and Gautherie [183] used IR thermography to observe the temperature profile of the corneal surface in patients with unilateral exophthalmos. A marked orbital hyperthermy was found in the infected eye. Bogdasarov et al. [184] discovered that IR thermography is a feasible choice in the diagnosis of retinoblastoma in children. Furthermore, they established that the intensity and the extent of the temperature increase inside the eye are related to the stages of tumor growth. Wittig et al. [185] observed warmer corneal surfaces and slight thermal asymmetries in patients with malignant uveal and conjunctival melanoma. The numer-

ical predictions obtained from the present study generally agrees with the experimental results obtained by Bourjat and Gautherie [183], Bogdasarov et al. [184] and Wittig et al. [185].

Along with the experimental results found by other researchers [183–185], the numerical results obtained from the present study suggest that the growth of tumor inside the human eye may be detected using IR thermography. The presence of eye tumor is generally defined by the thermal abnormality displayed on the corneal surface. From the results presented in Sections 6.7.2 and 6.7.3, the average increase in the corneal surface temperature for categories T1, T2 and T3 eye tumors are found to be 0.066, 0.198 and 0.273°C respectively for Case 1 and 0.028, 0.082 and 0.112°C respectively for Case 2. Except for the category T1 eye tumor in Case 2, the increase in the corneal surface temperature are well within the range of thermal sensitivity of a highly sensitive IR camera [186]. This suggests the potential use of the corneal surface temperature in the detection of eye tumor. The thermal asymmetry on the corneal surface may also indicate the location of tumor growth. For instance, a larger temperature at the superior of the corneal surface may imply that the tumor is growing at the positive y region inside the human eye (see Case 1).

It is worth pointing out that the corneal surface temperature is sensitive towards factors such as the environmental condition (ambient temperature and ambient convection coefficient) and physiological variation between individuals (age, blood convection coefficient and tears evaporation rate). From the results of the sensitivity analysis carried out in Chapter 3, these factors have been found to produce changes in the corneal surface temperature that are of the same order of magnitude as those caused by the eye tumor. Therefore, if the effects of the eye tumor on the corneal surface are to be effectively measured, it is important to ensure that changes in the corneal surface temperature recorded using an IR camera are solely caused by the eye tumor and are free from the effects of other factors that are classified as ‘noise’. A parametric optimization based on ANOVA and the Taguchi method may thus be carried out to better explain the precedence and

the importance of the various factors that may affect the corneal surface temperature. These are presented next.

6.8 Parametric Optimization

The effects of eye tumor on the ocular temperature distribution have been demonstrated in the previous section using a numerical model of the human eye. The presence of eye tumor inside the human eye has been found to produce a warmer ocular surrounding. Depending on the location, the eye tumor has also been found to produce a small degree of thermal asymmetry on the corneal surface. Of particular interest, is the increase in the corneal surface temperature caused by the eye tumor, which has been found to be in the same order of magnitude as those caused by factors such as environmental conditions and individual variation.

In this section, a statistical analysis based on the ANOVA is carried out to identify the precedence and importance of various factors that may affect the corneal surface temperature of an eye that is infected with eye tumor. An optimization procedure based on the Taguchi method is then performed to determine the optimal setting of factors that maximizes the thermal signal from the eye tumor, while isolating the effects of noise factors. The statistical study carried out in this section assumes that the use of IR thermography for detecting eye tumors is already a well-established technique.

6.8.1 Analysis of Variance (ANOVA)

ANOVA is a statistical tool that is often applied in the design of experiments. It is generally used for deciding whether and which factor(s) or interaction(s) has significant effect on the response of a system. In the context of the numerical investigation carried out in this chapter, ANOVA may be used to determine the factors or interaction of factors that have dominant effects on the corneal surface temperature.

From the results obtained in Section 6.7, it is found that the metabolic heat gen-

eration, size and location are among the factors of the eye tumor that determine the magnitude of temperature increase on the corneal surface. Effects of the tumor blood perfusion rate and thermal conductivity are found to be very small. From the results of the sensitivity analysis carried out in Chapter 3, the corneal surface temperature has been found to be sensitive towards factors such as ambient temperature, body temperature, ambient and blood convection coefficients and tears evaporation rate.

Five factors are considered in this study, namely ambient convection coefficient, blood convection coefficient, tears evaporation rate, tumor size and tumor metabolic heat generation. These factors are denoted by A, B, C, D and E respectively. Effects of ambient and body temperatures are not considered. It is assumed that the ambient temperature remains constant during the period when measurements of the corneal surface temperature are carried out. Likewise, the growth of eye tumor is assumed to have no significant effect on the temperature of the human body. Although location of the tumor growth has been found to play a major role in the thermal abnormality on the corneal surface, it is not considered in the present analysis due to the irregular shape of the choroidal surface. As a result, a consistent establishment of distance between the eye tumor and the corneal surface is difficult to obtain. In the present study, ANOVA is carried out only for the location of eye tumor in Case 1.

A 2^n factorial design is used, where n represents the number of factors considered, i.e. five. Each of the five factors has two levels defined by low and high. This leads to a total of 32 (2^5) runs. Selections of the low and high values of each factor are described as follow.

In Chapter 2, a value of $10\text{Wm}^{-2}\text{K}^{-1}$ has been selected to represent the value of the ambient convection coefficient at the control level. It is assumed that the value of the ambient convection coefficient may fluctuate as much as $\pm 20\%$ from the control during the period when measurements are carried out. Values of 80 and 120% of the control are thus, considered as the low and high values of the ambient convection coefficient respectively. These values are given by 8 and $12\text{Wm}^{-2}\text{K}^{-1}$. The control value of the blood convection

coefficient is given by $65\text{Wm}^{-2}\text{K}^{-1}$. More recently, Flyckt et al. [94] discovered that values between 250 and $300\text{Wm}^{-2}\text{K}^{-1}$ better represent the blood convection coefficient inside the actual human eye. Based on this, values of $65\text{Wm}^{-2}\text{K}^{-1}$ and $300\text{Wm}^{-2}\text{K}^{-1}$ are selected to be the low and high values of the blood convection coefficient respectively. The heat loss due to tears evaporation of a normal human eye is represented by 40Wm^{-2} (see Chapter 2). According to Mishima and Maurice [187], the tears evaporation rate of a normal human eye may range from 2.8 to $14.7\text{mg.hr}^{-1}\text{cm}^{-2}$. This corresponds to a heat loss of 20 to 100Wm^{-2} . The low and high values of the heat loss due to tears evaporation rate are thus, chosen to be 20 and 100Wm^{-2} respectively.

Eye tumors of categories T1 and T3 are selected to represent sizes of the eye tumors at low and high levels respectively. Specifically, the diameters of these tumors are given by 10 and 17mm. In the analysis carried out in Section 6.7, the metabolic heat generation of the eye tumor has been assumed to have a value that lies between 15,000 and $80,000\text{Wm}^{-3}$. The range of metabolic heat generation is obtained using Equation (6.6), where values of Λ between 1×10^6 and $5 \times 10^6\text{W.day.m}^{-3}$ and an eye tumor doubling time of 63 days have been considered. According to Eskelin et al. [182], the doubling time of a typical eye tumor ranges from 34 to 220 days. Using a value of Λ of $3 \times 10^6\text{W.day.m}^{-3}$, the range of metabolic heat generation corresponding to the range of eye tumor doubling time of 34 to 220 days is calculated to be approximately 13,000-90,000 Wm^{-3} . The lower and upper values of this range are thus, taken to be the low and high values of the eye tumor metabolic heat generation respectively.

Table 6.5 summarizes the low and high values of each of the five factors considered in the ANOVA.

Conventionally, the upper cases (A, B, ..., E) denote the factors while the lower cases (a, b, ..., e) denote the runs. The following 32 runs are carried out: run 1, a, b, c, ..., ab, abc, ..., bcde, abcde. Run 1 corresponds to the case when all factors are at low levels. The lower case(s) appearing in each run indicates that its corresponding factor(s) in the upper case is at high level. For instance, run 'ab' implies that the simulation is

Table 6.5: Low and high values of the five factors considered in the ANOVA

Factor	Description	Low	High
A	Ambient convection coefficient ($\text{Wm}^{-2}\text{K}^{-1}$)	8	12
B	Blood convection coefficient ($\text{Wm}^{-2}\text{K}^{-1}$)	65	300
C	Heat loss due to tears evaporation (Wm^{-2})	20	100
D	Tumor size (mm)	10	17
E	Tumor metabolic heat generation (Wm^{-3})	13,000	90,000

carried out for factors A and B at high level while factors C, D and E and are at low. Likewise, run ‘de’ represents the simulation that is executed when factors A, B and C are low while factors D and E are high. In all the 32 runs carried out, values of the other variables such as thermal conductivity, ambient temperature and body temperature are taken to be at the control level such as given in Chapter 2. Thermal conductivity and blood perfusion rate of the eye tumor at the control level are taken to be $0.5\text{Wm}^{-1}\text{K}^{-1}$ and $0.0063\text{m}^3\text{s}^{-1}\text{m}^{-3}$ respectively. Observations are made at the superior of the corneal surface (see Figure 6-1) where temperature rise is expected to be the largest.

Results obtained from ANOVA are summarized in Table 6.6. Interactions of factors beyond the 10th rank are collectively treated as the errors due to their very small effects when combined. From the results presented in Table 6.6, tears evaporation rate (C) appears to be the most dominant factor. This is followed by blood convection coefficient (B), metabolic heat generation of eye tumor (E) and ambient convection coefficient (A). Combination of factors D and E (DE) ranks 5th, while size of eye tumor (D) ranks 6th. The effects of both tears evaporation rate and ambient convection coefficient are negative; implying that larger values of A and C yield a cooler corneal surface.

The fact that combination DE ranks higher than factor D is not surprising given that the size and metabolic heat generation of the eye tumor are mathematically related. In the case when two tumors have the same volumetric metabolic heat generation, Q_m , a larger-sized tumor generally produces a greater amount of metabolic heat than a smaller-sized tumor.

To determine the significance of the effect of each factor and interaction in Table 6.6,

Table 6.6: Results obtained from the ANOVA

Rank	Factor	^a SS	^b DOF	^c MS = $\frac{SS}{DOF}$	$F_o = \frac{MS}{MSE}$
1	C	1.365	1	1.365	2089.17
2	B	1.099	1	1.099	1681.26
3	E	0.479	1	0.479	733.25
4	A	0.352	1	0.352	538.63
5	DE	0.177	1	0.177	271.20
6	D	0.162	1	0.162	247.12
7	BE	0.128	1	0.128	195.59
8	BD	0.103	1	0.103	157.29
9	BC	0.059	1	0.059	90.32
10	BDE	0.037	1	0.037	55.79
	Errors	0.014	21	^d MSE = 0.0065	
Total DOF = 31 (32-1)					

^aSS: sum of squares; ^bDOF: degree of freedom^cMS: Mean square; ^dMSE: Mean square of error

the control limit F_{α, ν_1, ν_2} is calculated, where α , ν_1 and ν_2 are the significance level, the numerator DOF and the denominator DOF respectively. Values of ν_1 and ν_2 are given by 1 and 21 respectively. For a significance level, α of 1%, the value of $F_{\alpha, \nu_1, \nu_2} = F_{0.01, 1, 21}$ obtained from the F distribution chart is found to be 8.017. Since the values of F_o for all the factors and interactions shown in Table 6.6 are greater than 8.017, it may be concluded that these factors and interactions have significant effects on the corneal surface temperature.

6.8.2 Taguchi method

From the results of ANOVA carried out in Section 6.8.1, all the five factors, namely ambient convection coefficient, blood convection coefficient, tears evaporation rate, tumor size and tumor metabolic heat generation have been found to contribute significantly to the temperature changes at the superior of the corneal surface. Since our objective is to detect the eye tumor based on the warmer corneal surface temperature, it is essential

that the thermal signal captured using the IR camera comes only from the eye tumor and is not affected by the other factors that are classified as noise.

In this section, an optimization procedure based on the Taguchi method [172] is carried out to determine the optimal setting of factors that maximizes the thermal signal from the factor of interest, while minimizing effects from noise factors. The Taguchi method is a statistical tool developed by Genichi Taguchi [172]. It is used primarily in the manufacturing sector but has recently been applied to various other fields such as in biomedical engineering [33]. The Taguchi method discriminates between signal and noise and estimates the positive or negative effect of each factor in each alternative level.

Analysis based on the Taguchi method is carried out for all the five factors, namely factors A, B, C, D and E, which have been shown in the ANOVA, to be significant factors. Each factor is again assumed to have two levels, namely low and high, where their respective values are such as presented in Table 6.5. The signal of interest is defined by the effects from the factors pertaining to the eye tumor, namely the size (D) and the metabolic heat generation (E), while effects from the ambient convection coefficient (A), blood convection coefficient (B) and tears evaporation rate (C) are categorized as noise.

One of the more important variables in the Taguchi method is the signal to noise ratio (SNR), which reflects the variability in the response of a system caused by noise factors [172]. Three types of SNR are available, namely ‘larger the better’, ‘nominal the best’ and ‘smaller the better’. Since the signal of interest is defined by the increase in corneal surface temperature, it is decided that the ‘larger the better’ SNR shall be used here. This is mathematically given by

$$\text{SNR} = -10 \log \left(\frac{1}{n} \sum_{i=1}^{i=n} \frac{1}{y_i^2} \right), \quad (6.21)$$

where n is the number of occurrences and y_i is the i^{th} response of the system defined by the temperature at the superior of the corneal surface.

Table 6.7 summarizes the results obtained from the Taguchi analysis. Values of T_{ave}

represent the mean response of a particular factor at a given level. From Table 6.7, the response of the system is found to increase as size and metabolic heat generation of the eye tumor increase. The values of SNR in Table 6.7 suggest that the signal from the eye tumor is maximized when the size of the tumor becomes larger or when the metabolic heat generation of the tumor increases. This conclusion is however, not definite as the combination of factors A, B and C that causes the effects from the eye tumor to be insignificant has not been considered.

Table 6.7: Results of the Taguchi analysis

D	E	C	low	high	low	high	low	high	low	high	T _{ave}	SNR
		B	low	low	high	high	low	low	high	high		
		A	low	low	low	low	high	high	high	high		
low	low		35.85	35.34	36.26	35.94	35.97	35.11	36.09	35.78	35.75	31.06
low	high		36.01	35.50	36.30	35.98	35.75	35.26	36.13	35.82	35.54	31.09
high	low		35.89	35.38	36.22	35.88	35.89	35.14	36.04	35.71	35.77	31.07
high	high		36.49	35.98	36.42	36.08	36.22	35.73	36.24	35.91	36.13	31.46
T _{ave}			36.06	35.55	36.30	35.97	35.86	35.31	36.13	35.80		
SNR			31.14	31.02	31.20	31.12	31.09	30.96	31.16	31.08		

For a more conclusive analysis, the effects and the average values of SNR ($\overline{\text{SNR}}$) of the various factors at both the low and high levels are calculated. These are presented in Table 6.8. The values of $\overline{\text{SNR}}$ of a particular factor are obtained by calculating the mean of the SNR values in Table 6.7 at the desired level. Similarly, the values of effects in Table 6.8 are obtained by averaging the values of T_{ave} in Table 6.7 for a particular factor at a given level. For instance, the value of $\overline{\text{SNR}}$ and the effect of factor A at low level are calculated using

$$\overline{\text{SNR}}_{A,\text{low}} = \frac{31.14 + 31.02 + 31.2 + 31.12}{4},$$

and

$$\text{Effect}_{A,\text{low}} = \frac{36.06 + 35.55 + 36.3 + 35.97}{4},$$

respectively.

Table 6.8: Effects and average SNR of various factors

Factor	SNR		Effect	
	low	high	low	high
A	31.12	31.07	35.97	35.78
B	31.05	31.34	35.70	36.05
C	31.15	31.04	36.09	35.66
D	31.08	31.11	35.79	35.95
E	31.07	31.12	35.76	35.99

From Table 6.8, it is found that the combination of factors A, B and C at low, high and low respectively produces effects that are stronger than the effects of factors D and E. This combination is undesirable since the signal that is captured comes primarily from factors A, B and C, which have been classified as noise. The opposite combination is thus preferred where factors A, B and C are at high, low and high respectively. At this combination, the effects are found to be smaller than the effects of factors D and E (see bold numbers). As a result, contributions of the noise factors on the signal are minimized. A similar conclusion may also be derived from the values of $\overline{\text{SNR}}$ in Table 6.8.

6.8.3 Discussion

Based on the results obtained from the ANOVA and the Taguchi method, the best setting to capture the thermal signal from the eye tumor is when both the ambient convection coefficient and the tears evaporation rate are high, while the blood convection coefficient is low. To increase the value of the ambient convection coefficient simply means to increase the convective heat loss from the corneal surface. In practice, this can be realized by keeping the ambient temperature low. To increase the evaporation rate of tears, the eyelids of the patient can be kept open for a substantial period of time before measurement is taken. This allows a continuous evaporation of tears and prevents blinking that refreshes the layer of tears on the corneal surface. However, steps should be taken to ensure that the eyelids are not refrained from blinking for too long as this

would induce tearing, which may cause severe changes in the temperature of the corneal surface. It is also possible to increase the tears evaporation rate by reducing the humidity of the surroundings [188].

The blood convection coefficient depends on the blood flow inside the choroid [63]. In the human body, a physically inactive individual helps to maintain the blood flow at its basal level. Consequently, any major fluctuation in the blood flow rate is avoided. Blood flow inside the human eye however, has been shown to be autoregulated [20]. This means that the human eye is able to maintain an almost constant level of blood flow despite changes in the perfusion pressure that are usually associated with physical activities. According to Lovasik et al. [189], the choroidal blood flow increases by only 10% when an individual undergoes physical activity such as cycling. Kiss et al. [190] discovered that significant changes in the choroidal blood flow is only possible during heavy physical activity that increases the ocular perfusion pressure by nearly 70%. Although it may seem that the autoregulation of the ocular blood flow helps to maintain the blood convection coefficient at an almost constant level regardless of whether the patient is physically active or otherwise, it should be noted that the blood convection coefficient is the second most dominant factor that affects the corneal surface temperature (see Table 6.6). This factor should therefore, be kept at its lowest (basal) level possible so that the interference on the signal is minimal.

It is also found that the thermal signal from the eye tumor becomes stronger when the size of the eye tumor increases. Likewise, a larger metabolic heat generation produces greater warming effects, thus leading to a stronger thermal signal. From a clinical point of view, this means that the detection of the eye tumor is more efficient when the growth of eye tumor is at the later stages. This may not be feasible since an early detection is crucial in the treatment of the eye tumor. This aspect requires further investigations before a definite conclusion can be drawn. One of the factors that has been excluded from this study is the location of the eye tumor. As pointed out in Section 6.7, when an eye tumor grows at the back of the human eye, changes in the corneal surface temperature

becomes very small and may not be effectively detected using an IR camera. For such cases, it may be possible to amplify the thermal signal from the eye tumor by using the combination of factors in Table 6.8 that minimizes the effect of noise.

Owing to the lack of similar studies, neither qualitative nor quantitative comparisons of the numerical results obtained in the present statistical analysis is possible. Nevertheless, if the results from the present study are compared to those obtained from the analysis carried out on breast tumor [33], similarities in the setting of factors that minimizes the effects of noise can be found. In breast tumor detection [33], the signal from the tumor can be measured effectively by setting the noise factors to levels such that heat loss from the surface of the breast is maximized (cold-stress test), while heat sources that originates from inside the breast that are not caused by the tumor are minimized. From our analysis, a similar pattern is observed where the best setting for detecting the eye tumor involves an increase heat loss from the corneal surface while heat from the ocular blood flow is kept as low as possible.

6.9 Concluding Remarks

A three-dimensional model of the human eye has been successfully developed to investigate the effects of an eye tumor on the ocular temperature distribution. To account for the unknown thermal properties of the eye tumor, simulations have been performed for a range of values of the eye tumor thermal conductivity, blood perfusion rate and metabolic heat generation. These values have been derived from the thermal properties of tumors that grow at various parts of the human body. Despite the possible differences in the cellular structure between each type of tumor, the actual thermal properties of the eye tumor are not expected to be significantly different from the range of values used in this study.

From the numerical results presented in this study, the presence of an eye tumor inside the human eye has been found to cause an increase in the ocular temperature

distribution. This has been attributed to the metabolic heat generation of the tumor tissues. An increase in the corneal surface temperature and an asymmetrical thermal profile on the corneal surface have also been observed. The magnitude of temperature rise and the degree of thermal asymmetry have been suggested as potential indicators of eye tumor inside the human eye.

When carrying out the parametric optimization in Section 6.8, it has been assumed that the use of IR thermography for detecting eye tumors is a feasible choice. This hypothesis remains to be fully verified although earlier experimental and numerical investigations appear to support it [183–185]. The most common method in diagnosing eye tumor is through visual inspection using an ophthalmoscope and this is usually performed by an ophthalmologist. The use of IR thermography as an alternative technique for detecting eye tumor is certainly promising since it offers a quick and intelligent diagnostic tool. It may be used as a preliminary screening tool in mass screenings and any identification of tumor can be verified by the ophthalmologists using the ophthalmoscope. This issue requires more investigations to be carried out in the future however.

One of the major setbacks that may impede any future investigations is perhaps, the rare occurrences of eye tumor within a given population. The American Cancer Society estimates that about 2,390 new cases of all primary intraocular cancers are diagnosed in the year 2008 [191]. This figure is relatively smaller than the 180,000 cases of breast cancer diagnosed annually [33]. Nevertheless, eye tumor should not be taken lightly since vision loss from cancer is the next most important health related concern after death [192].

Chapter 7

Critical Discussion of the Numerical Models Developed

7.1 Introduction

Various techniques of the boundary element method have been used in Chapters 2 to 6 to investigate different mathematical problems involving heat transfer inside the human eye. The numerical schemes developed for solving each specific problem are discussed in this chapter. Advantages and limitations of the numerical techniques used for solving these problems are explored.

7.2 The Human Eye Model

The model of the human eye developed in this thesis is divided into six components, namely the cornea, anterior chamber, lens, posterior chamber, vitreous and sclera. The iris, choroid and retina are modeled together with the sclera as one homogeneous region. The optic nerve is assumed to have no significant effect on the heat transfer inside the human eye such that it can be ignored from the solution domain. This assumption is critical as it allows the human eye to be modeled in the Oxz coordinate system. Us-

ing an axisymmetrical model, it is possible to replicate the three-dimensional heat flow inside the actual human eye using a two-dimensional geometry. This is of great computational advantage. Applications of the axisymmetrical models however, are limited to problems where the governing equations and boundary conditions also exhibit axisymmetrical characteristics. The effects of gravity on the natural convection flow inside the anterior chamber and the presence of tumor inside the human eye in the problems investigated in Chapters 4 and 6 respectively, eliminate the axisymmetrical features of the model. Consequently, the axisymmetrical boundary element model is not used in these chapters.

The human eye model developed in this thesis offers a more detailed anatomical description when compared to the models developed by other researchers. In the models developed by Scott [22, 48] and Ridouane and Campo [24], only four ocular components were considered, namely the cornea, anterior chamber, lens and vitreous. Although Amara [23] divided the human eye into regions occupied by the cornea, anterior chamber, lens, ciliary body, vitreous and retina, the thermal properties specified for the anterior chamber, iris and ciliary body are the same. Essentially, these regions are mathematically homogeneous. In the present model, the iris is distinguished from the anterior chamber by the different thermal properties used [71].

7.3 The Boundary Element Method

One of the first steps involved in the development of a numerical scheme based on the boundary element method is the derivation of the integral representations from the governing equations to be solved. The expression of the integral equations derived depends on the type of fundamental solution used. In this thesis, derivations of the integral equations have been carried out using the fundamental solution of the Laplace equation. When the governing partial differential equation is elliptic and homogeneous, such as given by the steady state heat diffusion equation in Chapters 2 and 3, the integral

equation obtained consists only of boundary integrals. Other types of partial differential equations give rise to domain integrals, which may be dealt with using various numerical techniques.

7.3.1 Advantages of the boundary element method

One of the main advantages of the boundary element method, as pointed out in Chapter 1, is that it requires only the boundaries of the solution domain to be discretized. Consequently, the level of discretization used in the boundary element method is smaller than those used in domain methods. In the models presented in Chapters 2 and 3, a total of 290 boundary elements have been used to obtain mesh-independent numerical solutions. This is relatively smaller than the number of domain elements used in models employing a full domain discretization. For instance, Amara [23] and Cvetković et al. [50] employed 887 and 10,441 finite elements respectively to simulate the heat transfer inside the eye. In the finite volume model developed by Ridouane and Campo [24], a total of 2,250 cells were used.

Differences in the number of elements used between the boundary element method and the finite element method are more critical in the three-dimensional models. In the three-dimensional model developed in Chapter 6, approximately 2,300 boundary elements have been found to be sufficient to produce mesh-independent numerical solutions. This is very small when compared to the number of finite elements used by Ng and Ooi [193], which approaches 55,000. With lesser number of elements used, the system of linear algebraic equations assembled also becomes smaller. Eventually, this reduces the computational cost (memory and execution time) needed to obtain a numerical solution.

The requirement for only the boundaries of the solution domain to be discretized also leads to simplicity in data preparation. Since no domain discretization is involved, meshing in the boundary element method can be done more efficiently than the finite element method. This is particularly favourable when modeling complex multi-layered geometries such as the human eye.

In carrying out the boundary element method in each chapter of this thesis, discontinuous linear elements have been used to approximate the variation of physical variables across each boundary element. Accuracy of the approximation may be further improved by using higher order elements such as quadratic and cubic elements. The use of higher order elements may increase the complexity of the problem formulation however. One of the advantages of using discontinuous boundary elements is that it does not require the variation of the physical variables between two neighbouring elements to be continuous [84]. As a result, problems involving corners where discontinuities usually exist, can be modeled without much difficulty. This is shown in Figure 7-1.

Figure 7-1: Discontinuities at a corner point between neighbouring elements

7.3.2 Limitations of the boundary element method

Advantages of the boundary element method have been described in the preceding section. One of the more apparent benefits of the boundary element method is the assembly of a smaller system of linear algebraic equations. In theory, a smaller system of equations requires less computational effort in order to obtain a numerical solution. Nonetheless, it has to be pointed out that the system of equations generated using the boundary element method is not as sparse as those obtained using domain methods, such as finite element and finite difference methods. For problems involving a single homogeneous domain, the system of linear algebraic equations generated becomes fully populated. This presents no difficulty when the size of the system of equations is small. However, when the size of

the system of equations becomes larger, problems associated with ill-condition matrices and increased computational cost are encountered. In this case, problems associated with stability and computational inefficiency are experienced.

The accuracy of the numerical solution obtained using the boundary element method depends partly on how well the boundary integrals of the fundamental solution and its normal derivative are evaluated (see Equations (2.12), (4.38) and (6.16)). Ideally, it is preferable for these integrals to be evaluated analytically in order to reduce the errors that may be introduced from performing these integrals numerically. In practice, this preference is limited by the complexity of the fundamental solution. In Chapter 4, the simplicity of the Laplace fundamental solution expressed in the Oxy coordinate system allows the boundary integrals described in Equation (4.38) to be evaluated analytically. In the Orz coordinate system, the fundamental solution of the Laplace equation and its normal derivative are expressed in terms of the elliptic integrals of the first and second kind. This make analytical evaluation of the boundary integrals described in Equation (4.38) difficult. In this case, these integrals have to be computed numerically, which may introduce some numerical errors. Furthermore, the additional numerical computation increases the total computational time of the numerical scheme.

The boundary integrals in the $Oxyz$ coordinate system are defined by double integrals (see Equation (6.16)). As a result, analytical evaluation of these integrals is extremely difficult, if not impossible. In an effort to minimize the errors that may be produced from calculating the double integrals numerically, these integrals have been evaluated semi-analytically. In the semi-analytical evaluation, the inner integral is computed analytically. Integration of the resulting mathematical expression is then performed numerically using the Gaussian quadrature. This approach not only minimizes the errors that may be introduced into the numerical result, but also reduces the total computational time of the numerical scheme.

The boundary element method is complicated by the need to obtain the fundamental solution of the governing partial differential equations. This can be mathematically

very challenging, especially when the partial differential equation has coefficients that vary from point to point in space. In non-linear problems, it may be mathematically impossible to obtain fundamental solution of the governing partial differential equation. This makes the application of the boundary element method restricted to only a few problems. Nevertheless, this may no longer be an issue with the development of the dual reciprocity method [156].

7.4 The Dual Reciprocity Method

Integral equations derived from elliptic partial differential equations with constant coefficients (such as the Laplace equation) consist of boundary only integrals. The presence of non-homogeneous terms in non-homogeneous partial differential equations give rise to domain integrals in the integral equations derived [83]. Various techniques such as the cell integration technique [55], the particular solution method [194], the Monte Carlo method [195] and the dual reciprocity method [156] have been developed to treat the domain integrals in the boundary element method.

Out of the four methods mentioned, the cell integration technique is by far, the most straightforward. In this technique, the domain integral is evaluated by dividing the original domain into a series of smaller cells. Integration is then numerically performed in each cell using integration formulae such as the Gaussian quadrature. This approach is less preferred by researchers since discretization of the original domain into smaller cells destroys the boundary only characteristics of the boundary element method. Furthermore, numerical integration carried out over the entire domain can be computationally very expensive. This becomes more critical in three-dimensional problems.

The dual reciprocity method has been regarded by many as one of the most noticeable and effective techniques for dealing with domain integrals in the boundary element method [135]. In the dual reciprocity method, the domain integral is converted into equivalent boundary integrals using an approximation based on a series of radial basis

functions that are centered about a set of selected points and the reciprocal theorem. When implementing the dual reciprocity method, the collocation points are usually selected on both the boundary and interior of the solution domain. Although points are selected at the interior, this step does not present the same level of computational difficulty as experienced in the full domain discretization. Moreover, the number of points needed in the dual reciprocity method to obtain accurate numerical results for most linear problems is generally, not large [196].

The choice of radial basis functions plays an important role in determining the accuracy of the dual reciprocity method. Wrobel et al. [197] proposed the radial basis function of the form

$$\phi_{\text{axis}}(r, z; \xi, \eta) = \mathcal{R}(r, z; \xi, \eta) \left(1 - \frac{\xi}{4r}\right), \quad (7.1)$$

for solving problems in the Orz coordinate system. One of the limitations of the radial basis function in Equation (7.1), is the presence of singularity at $r = 0$. Furthermore, the particular solution, $\varkappa_{\text{axis}}$ corresponding to the aforementioned radial basis function, which is given by [197]

$$\varkappa_{\text{axis}} = \frac{\mathcal{R}(r, z; \xi, \eta)}{12},$$

is an arbitrary choice and lacks mathematical foundation [158]. More recently, Wang et al. [158] presented a radial basis function that is derived using an approach that is mathematically more sound. The proposed radial basis function, which is given by Equation (5.25), has been used in the implementation of the dual reciprocity method in Chapter 5.

When solving the three-dimensional problem in Chapter 6, the radial basis function of the form

$$\phi_{3D}(x, y, z; \xi, \eta, \zeta) = 1 + \left(\frac{\mathcal{R}(x, y, z; \xi, \eta, \zeta)}{\mathcal{R}_{\text{max}}}\right)^3, \quad (7.2)$$

has been used for carrying out the dual reciprocity method. The parameter $\mathcal{R}_{\text{max}}$ in the expression above operates as a scaling parameter that scales the radial basis function

according to the dimension of the problem. One of the main purposes of introducing the scaling parameter, $\mathcal{R}_{\max}$ is to improve the condition number of the system of equations generated from the collocation of Equation (7.2) at the collocation points selected across the solution domain. Without the scaling parameter, the system of linear algebraic equations set up may become poorly conditioned, which ultimately affects the accuracy and performance of the dual reciprocity method.

7.4.1 Advantages of the dual reciprocity method

Advantages of the dual reciprocity method are generally emphasized by the technique used when dealing with the domain integrals. The dual reciprocity method, which does not require a full domain discretization, helps to maintain the boundary only characteristics of the boundary element method. Consequently, benefits associated with the requirement of boundary only discretization, such as a lesser demand of computational memory and ease in data preparation, are retained in the dual reciprocity method. The simplicity of implementation highlights another advantage of the dual reciprocity method.

The dual reciprocity method has also proven to be a versatile numerical tool for solving different types of partial differential equations [196]. Originally developed in 1983 for solving elastodynamics problems [156], the dual reciprocity method has since undergone numerous development, where problems governed by various partial differential equations such as time-dependent and non-linear partial differential equations have been successfully solved [196]. More importantly, the ability of the dual reciprocity method to produce results that are accurate is perhaps, one of the features that makes it a popular and reliable numerical technique for treating domain integrals in the boundary element method.

7.4.2 Disadvantages of the dual reciprocity method

Some of the disadvantages encountered in the boundary element method are prevalent in the dual reciprocity method. Problems associated with fully populated matrices are

aggravated in the dual reciprocity method due to the additional points collocated at the interior of the solution domain. When solving large-scale problems, a large number of interior collocation points has to be selected to accurately describe the variation of physical variables inside the domain [198]. Consequently, a system of linear algebraic equations that is dense and large is generated. This results in matrices that are ill-conditioned; leading to both computational inefficiency and stability issues.

Problems associated with fully populated matrices may be avoided using the CS-PD-RBF (see Equation (4.68)). The CS-PD-RBF was first used by Chen et al. [135] as an interpolation function in the dual reciprocity method in 1999. The compactly supported characteristic of the CS-PD-RBF yield matrices that are more sparse than those produced using radial basis functions that are not compactly supported [135]. The sparsity of the system of linear algebraic equations reduces the computational cost and improves the efficiency of the numerical scheme developed. Although the CS-PD-RBFs have been found to produce numerical results that are more accurate than the ATPS and the multiquadrics [135,136], accuracy of the results essentially depends on the selection of a free parameter, s (see Equation (4.68)). Since the optimum value of the free parameter is problem-dependent, and no guidelines are yet available for selecting the free parameter, application of the CS-PD-RBFs in the dual reciprocity method has been restricted to purely theoretical problems.

7.4.3 Solving natural convection flow using the dual reciprocity method

Prior to the development of the numerical scheme presented in Chapter 4, attempts have been made to solve the problem involving natural convection inside the anterior chamber using the dual reciprocity method (not reported in this thesis). Results from the numerical investigations carried out revealed that the dual reciprocity method performs very poorly when used to solve the thermally driven flow problem. For the purpose of illustration, let us consider the domain integral that exists in the integro-differential

equation described in Equation (4.22), which is given by

$$I = \iint_R \Phi_{2D}(x, y; \xi, \eta) \left\{ u(x, y) \frac{\partial}{\partial x} [T(x, y)] + v(x, y) \frac{\partial}{\partial y} [T(x, y)] \right\} dA(x, y). \quad (7.3)$$

To carry out the dual reciprocity method, the terms inside the curly brackets ‘{ }’ in Equation (7.3) are approximated using a series of radial basis functions that are centered about M points, $(a^{(1)}, b^{(1)})$, $(a^{(2)}, b^{(2)})$, ..., $(a^{(M-1)}, b^{(M-1)})$, $(a^{(M)}, b^{(M)})$, such that

$$\begin{aligned} u(x, y) \frac{\partial}{\partial x} [T(x, y)] &\approx \sum_{m=1}^M \gamma_1^{(m)} \phi_{2D}(x, y; a^{(m)}, b^{(m)}), \\ v(x, y) \frac{\partial}{\partial y} [T(x, y)] &\approx \sum_{m=1}^M \gamma_2^{(m)} \phi_{2D}(x, y; a^{(m)}, b^{(m)}), \end{aligned} \quad (7.4)$$

where $\gamma_1^{(m)}$ and $\gamma_2^{(m)}$ are unknown coefficients that can be determined by letting point (x, y) in Equation (7.4) be given by $(a^{(m)}, b^{(m)})$, for $m = 1, 2, \dots, M-1, M$, to generate a system of linear algebraic equations that can be inverted to give

$$\begin{aligned} \gamma_1^{(j)} &= \sum_{j=1}^M W^{(mj)} \left[u^{(j)} \frac{\partial T^{(j)}}{\partial x} \right], \quad \text{for } m = 1, 2, \dots, M-1, M, \\ \gamma_2^{(j)} &= \sum_{j=1}^M W^{(mj)} \left[v^{(j)} \frac{\partial T^{(j)}}{\partial y} \right], \quad \text{for } m = 1, 2, \dots, M-1, M, \end{aligned} \quad (7.5)$$

where $u^{(j)}$, $v^{(j)}$, $\partial T^{(j)}/\partial x$ and $\partial T^{(j)}/\partial y$ are values of $u(x, y)$, $v(x, y)$, $\partial T(x, y)/\partial x$ and $\partial T(x, y)/\partial y$ at point $(a^{(j)}, b^{(j)})$ respectively and the coefficients $W^{(mj)}$ are given by

$$\begin{aligned} \sum_{j=1}^M W^{(kj)} \phi_{2D}(a^{(j)}, b^{(j)}; a^{(m)}, b^{(m)}) &= \begin{cases} 1, & \text{if } k = m, \\ 0, & \text{if } k \neq m, \end{cases} \\ \text{for } m &= 1, 2, \dots, M-1, M. \end{aligned}$$

Substituting Equations (7.4) and (7.5) into (7.3) yields

$$I = \sum_{j=1}^M \left[u^{(j)} \frac{\partial T^{(j)}}{\partial x} + v^{(j)} \frac{\partial T^{(j)}}{\partial y} \right] \sum_{m=1}^M W^{(mj)} \times \iint_R \Phi_{2D}(x, y; \xi, \eta) \phi_{2D}(a^{(j)}, b^{(j)}; a^{(m)}, b^{(m)}) dA(x, y). \quad (7.6)$$

The first order derivatives, $\partial T^{(j)} / \partial x$ and $\partial T^{(j)} / \partial y$ in Equation (7.6) may be expressed in terms of $T^{(j)}$ by approximating the unknown variable $T(x, y)$ using an approach that is similar to Equation (7.4), such that [196]

$$T(x, y) \approx \sum_{m=1}^M \gamma_3^{(m)} \phi_{2D}(x, y; a^{(m)}, b^{(m)}), \quad (7.7)$$

where $\gamma_3^{(m)}$ are unknown coefficients that may be expressed as

$$\gamma_3^{(j)} = \sum_{j=1}^M W^{(mj)} T^{(j)}, \quad \text{for } m = 1, 2, \dots, M-1, M, \quad (7.8)$$

where $T^{(j)} = T(a^{(j)}, b^{(j)})$.

Differentiating Equation (7.7) with respect to x and y and substituting Equation (7.8) into the resulting expressions, yield

$$\begin{aligned} \frac{\partial}{\partial x} [T(x, y)] &\approx \sum_{j=1}^M T^{(j)} \sum_{m=1}^M W^{(mj)} \frac{\partial}{\partial x} [\phi_{2D}(x, y; a^{(m)}, b^{(m)})], \\ \frac{\partial}{\partial y} [T(x, y)] &\approx \sum_{j=1}^M T^{(j)} \sum_{m=1}^M W^{(mj)} \frac{\partial}{\partial y} [\phi_{2D}(x, y; a^{(m)}, b^{(m)})], \end{aligned} \quad (7.9)$$

Letting point (x, y) in Equation (7.9) be given by $(a^{(n)}, b^{(n)})$, for $n = 1, 2, \dots, M-1, M$,

one arrives at

$$\begin{aligned}\frac{\partial T^{(n)}}{\partial x} &\approx \sum_{j=1}^M T^{(j)} \sum_{m=1}^M W^{(mj)} \frac{\partial}{\partial x} [\phi_{2D}(a^{(n)}, b^{(n)}; a^{(m)}, b^{(m)})], \\ &\quad \text{for } n = 1, 2, \dots, M-1, M, \\ \frac{\partial T^{(n)}}{\partial y} &\approx \sum_{j=1}^M T^{(j)} \sum_{m=1}^M W^{(mj)} \frac{\partial}{\partial y} [\phi_{2D}(a^{(n)}, b^{(n)}; a^{(m)}, b^{(m)})], \\ &\quad \text{for } n = 1, 2, \dots, M-1, M,\end{aligned}\tag{7.10}$$

where the unknown first order derivatives of temperatures, $\partial T(x, y)/\partial x$ and $\partial T(x, y)/\partial y$ are now expressed in terms of unknown nodal temperatures and known first order derivatives of the radial basis functions.

Equation (7.10) may be substituted into Equation (7.6) to give

$$\begin{aligned}I &= \left\{ \sum_{j=1}^M u^{(j)} T^{(j)} \sum_{n=1}^M W^{(nj)} \frac{\partial}{\partial x} [\phi_{2D}(a^{(n)}, b^{(n)}; a^{(j)}, b^{(j)})] \right. \\ &\quad \left. + \sum_{j=1}^M v^{(j)} T^{(j)} \sum_{n=1}^M W^{(nj)} \frac{\partial}{\partial y} [\phi_{2D}(a^{(n)}, b^{(n)}; a^{(j)}, b^{(j)})] \right\} \\ &\quad \times \sum_{m=1}^M W^{(mj)} \iint_R \Phi_{2D}(x, y; \xi, \eta) \phi_{2D}(a^{(j)}, b^{(j)}; a^{(m)}, b^{(m)}) dA(x, y).\end{aligned}\tag{7.11}$$

Following the steps of the dual reciprocity method highlighted in Chapter 6, the domain integral in Equation (7.11) may be converted into equivalent boundary integrals. The steps outlined in Equations (7.3) to (7.11) may be repeated for the other domain integrals in Equations (4.19) to (4.21). Upon converting the domain integrals into boundary integrals, the numerical procedure where the boundaries of the solution domain are discretized, can be carried out as usual to obtain a numerical solution.

The steps highlighted in Equations (7.3) to (7.11) are plagued by two shortcomings that make them less preferable when dealing with natural convection problems. Firstly, a large number of interior points is required in order to model accurately the non-linear

terms in the governing equations. Since the numerical procedure involves multiplication of a series of fully-populated matrices (see Equation (7.11)), one may run into problems such as increase in demand of computer memory and computational inefficiency and instability. Recent development of the dual reciprocity method have discovered that these problems may be alleviated by coupling the dual reciprocity method with the domain decomposition technique [136, 198].

Secondly, differentiation of the radial basis functions carried out in Equation (7.9) to approximate the first order derivatives of the unknown variables can lead to significant numerical errors. In the attempt to solve the natural convection problem using the dual reciprocity method, problems with convergence are encountered when Ra reaches 15,000. This may be attributed to the errors produced when differentiating the approximation in Equation (7.10). As the number of iterations of the numerical scheme increases, the errors accumulated from each step increase as well. Eventually, the numerical scheme breaks down.

Such problems have been avoided in Chapter 4 by transferring the partial derivatives of the unknown variables to the fundamental solution. However, this may not apply in the dual reciprocity method since the numerical procedure requires the fundamental solution in the domain integral to be expressed in its original form.

7.5 Non-linear Problems

7.5.1 Non-linear boundary condition

Although the governing equation describing the heat flow inside the human eye in Chapters 2, 3, 5 and 6 are linear, the presence of heat radiation on the boundary condition specified on the corneal surface gives rise to a non-linear boundary condition. The non-linearity has been treated using an iterative scheme that solves for the system of linear algebraic equations sequentially, until the temperature on the corneal surface, where the non-linearity is defined, satisfy a predefined convergence criterion.

7.5.2 Natural convection

Natural convection inside the anterior chamber is described using the Navier-Stokes equations, which presents a non-linear problem to be solved. To avoid problems associated with large fully populated matrices, the domain decomposition technique has been employed together with the boundary element method. The domain decomposition technique generally divides the solution domain into a series of smaller subdomains. Consequently, the system of linear algebraic equations assembled is block banded, where each block corresponds to one subdomain. By increasing the number of subdomains, the system of linear algebraic equations becomes more sparse. This enables the system of equations to be solved at a much reduced computational cost.

Perhaps, the only limitation of the domain decomposition technique when used together with the boundary element method is the requirement of a full domain discretization. This eliminates the advantages associated with the boundary only characteristics of the boundary element method. However, since it is computationally very difficult to solve natural convection problems without using the domain decomposition technique [127], the benefits of the boundary only characteristics of the boundary element method may have to be compromised. The task of carrying out a full domain discretization is made easier with the availability of commercialized mesh generator software.

Many aspects of the numerical scheme developed for solving the natural convection problem in Chapter 4, such as the transfer of first order derivatives from the unknown variables to the fundamental solution and the use of cell integration technique to calculate the domain integrals are similar to the boundary-domain integral method [124]. However, one of the main differences between the numerical scheme in Chapter 4 and the boundary-domain integral method lies in the approximation of the unknown variables in the domain integrals. In Chapter 4, the unknown variables are approximated using a series of radial basis functions. In the boundary-domain integral method, approximation based on quadratic interpolation functions, which are similar to the shape functions used in the finite element method, have been used.

By approximating the unknown variables using the radial basis functions, existing nodes on the boundary can be used as part of the collocation points. This maintains discontinuity between neighbouring boundary elements. According to Škerget et al. [128], a stable and accurate numerical scheme based on polynomial interpolation functions requires continuity to be stated at the corner nodes of each subdomain. One of the consequences of specifying continuity between boundary elements is the setting up of an overdetermined system of linear algebraic equations. Special numerical schemes would have to be employed in order to these overdetermined system of equations.

7.6 Time-dependent Problems

7.6.1 Time-stepping dual reciprocity method

Investigations on the temperature changes inside the human eye during treatment of LTKP gives rise to a time-dependent problem. The presence of time derivative and heat generation terms in the transient heat diffusion equation lead to domain integrals in the integro-differential equation. The dual reciprocity method has been used to approximate these domain integrals into equivalent boundary integrals. Unknown temperatures that are functions of time are assumed to vary linearly within each time step, while the first order time derivative of temperature is approximated using an accurate finite difference formula [84] (see Equations (5.21) and (5.22)). To further improve the accuracy of the transient approximation, higher order approximations such as polynomial interpolation function may be used [199].

Unlike the time-marching scheme proposed by Wrobel [83], the time-stepping scheme developed in Chapter 5 does not require the variation of heat flux with time to be approximated. Consequently, the solution of heat flux is always half a time step ($\frac{1}{2}\Delta t$) ahead of temperature at the previous time step and $\frac{1}{2}\Delta t$ behind the solution of temperature at the present time step. One of the advantages of maintaining the solution of heat flux to be $\frac{1}{2}\Delta t$ ahead of the previous time step is that knowledge of heat flux at the initial condition

($t = 0$) is not required for the numerical scheme to work. On the other hand, if heat flux is approximated using an expression that is similar to Equation (5.21), knowledge of the values of heat flux at the initial condition becomes a necessity, which in most practical problems, are unknowns.

The time-stepping scheme developed in Chapter 5 is plagued by several drawbacks. Firstly, the approach requires repeated evaluation of the system of linear algebraic equations in each time step. This may be time consuming, particularly when the size of the system is large. Secondly, the consecutive increment in time steps from the initial condition to the final time level can lead to a tedious task, particularly when the desired solution is at a high time level. For instance, 83 and 188 steps are required to reach the final time level during pulsed and continuous-wave (minute coagulation) laser radiation respectively. Thirdly, the time-stepping scheme becomes less efficient when the problem is highly transient. In highly transient problems, values of Δt have to be selected to be sufficiently small to accurately simulate the large changes in temperature over a very short period. As a result, the number of steps needed to reach the final solution increases, which ultimately prolongs the computational time of the numerical scheme. Problems with stability of the numerical scheme arise if Δt is selected to be too small however [83].

Various mathematical techniques such as the Laplace transformation technique and the use of time-dependent fundamental solution may be employed together with the boundary element method to solve time-dependent problems. These techniques, which are discussed briefly in the subsequent sections, may be explored in future studies.

7.6.2 Laplace transformation technique

With reference to the Orz coordinate system, the Laplace transformation of the temperature, $T(r, z, t)$ may be expressed as

$$\mathcal{L}[T(r, z, t)] = U(r, z, p) = \int_0^{\infty} T(r, z, t) \exp(-pt) dt, \quad (7.12)$$

where U is temperature in the transformed space and p is the Laplace transform parameter. Applying the transformation in Equation (7.12) into the governing equation describing the transient temperature changes inside the eye during LTKP (Equation (5.1)) yields

$$\nabla_{\text{axis}} (\kappa_i \nabla_{\text{axis}} U_i(r, z, p)) = \rho_i c_i [pU_i(r, z, p) - T_{i,o}(r, z)] + \frac{\mathbb{S}_i(r, z, p)}{p}, \quad (7.13)$$

where $T_{i,o}(r, z)$ is temperature at $t = 0$ at point (r, z) and $\mathbb{S}_i(r, z, p)$ is the heat generated inside the eye in the transformed space. Note that the original governing equation in physical space and time has been transformed into one that is defined in the transformed space, p .

The integral equation derived from Equation (7.13) is given by [83, 84]

$$\begin{aligned} \lambda(\xi, \eta) U_i(r, z, p) = & \int_{\Gamma_i} U_i(r, z, p) \frac{\partial}{\partial n} [\Phi_{\text{axis}}(r, z; \xi, \eta)] \cdot r \cdot ds(r, z) \\ & - \int_{\Gamma_i} \Phi_{\text{axis}}(r, z; \xi, \eta) \frac{\partial}{\partial n} [U_i(r, z, p)] \cdot r \cdot ds(r, z) \\ & + \iint_{R_i} \Phi_{\text{axis}}(r, z; \xi, \eta) \left\{ \frac{1}{\alpha_i} [pU_i(r, z, p) - T_{i,o}(r, z)] \right. \\ & \left. - \frac{1}{\kappa_i} \frac{\mathbb{S}_i(r, z, p)}{p} \right\} \cdot r \cdot dA(r, z). \end{aligned} \quad (7.14)$$

The domain integral in Equation (7.14) may be approximated into an equivalent boundary integral using the dual reciprocity method. Following the execution of the dual reciprocity method, the boundary discretization procedure can be implemented as usual. Solutions of Equation (7.14) are numerically obtained for a sequence of arbitrarily selected values of p .

One of the disadvantages of the Laplace transformation in the boundary element method lies in the inversion of the calculated solution from the transformed space to the physical space. This is usually carried out numerically using various algorithms such as

the algorithms of Stehfest [201] and Schapery [202]. These algorithms generally require the selection of an inversion parameter. While the solution obtained from the boundary element method may be accurate, a poor selection of the inversion parameter may severely affect the accuracy of the inverted solution. This problem is worsened by the lack of proper guidelines for choosing the optimal value of transform parameter.

7.6.3 Time-dependent fundamental solution

In the time-stepping dual reciprocity method presented in Chapter 5, the integro-differential representation of the governing equation has been derived based on the fundamental solution of the Laplace equation. Alternatively, one may choose to adopt the time-dependent fundamental solution, which is expressed in the Orz coordinate system as [203]

$$\begin{aligned} \Phi_{\text{axis-time}}(r, z, t; \xi, \eta, t') &= \frac{1}{[4\pi\alpha(\tau - t')]^{\frac{3}{2}}} \exp \left[-\frac{r^2 + \xi^2 + (z - \eta)^2}{4\alpha(t' - t)} \right] \\ &\times \int_0^{2\pi} \exp \left[\frac{r\xi \cos(\theta - \theta_o)}{2\alpha(t' - t)} \right] d\theta. \end{aligned} \quad (7.15)$$

Using the time-dependent fundamental solution in Equation (7.15) to derive the integral representation of Equation (5.1), one obtains [83]

$$\begin{aligned} \lambda(\xi, \eta)T_i(\xi, \eta, t) &= \int_{t_o}^{t_f} \int_{\Gamma_i} T_i(r, z, t) \frac{\partial}{\partial n} [\Phi_{\text{axis-time}}(r, z, t; \xi, \eta, t')] \cdot r \cdot ds(r, z) dt \\ &- \int_{t_o}^{t_f} \int_{\Gamma_i} \Phi_{\text{axis-time}}(r, z, t; \xi, \eta, t') \frac{\partial}{\partial n} [T_i(r, z, t)] \cdot r \cdot ds(r, z) dt \\ &- \frac{1}{\kappa_i} \int_{t_o}^{t_f} \iint_{R_i} \Phi_{\text{axis-time}}(r, z, t; \xi, \eta, t') S_i(r, z, t) \cdot r \cdot dA(r, z) dt \\ &+ \iint_{R_i} \Phi_{\text{axis-time}}(r, z, t; \xi, \eta, t') T_{i,o}(r, z) \cdot r \cdot dA(r, z), \end{aligned} \quad (7.16)$$

where t_o is the initial time, t_f is the final time at which the desired solution is evaluated and $t' = t_f - t_o$. The use of the time-dependent fundamental solution yields integral equation that consists of integrations in both space and time. Hence, both spatial and temporal discretization are required in order to solve Equation (7.16).

One of the shortcomings of the numerical scheme based on the time-dependent fundamental solution is the presence of time integration. The additional numerical integration performed for time integrals may increase the overall computational demand of the numerical scheme. To reduce the number of time integration performed, Brebbia et al. [55] proposed that the initial condition for each time step is taken at the solution obtained from the previous time step. Although effective, this approach involves repeated evaluation of domain integrals which may not be computationally feasible. As an alternative, Brebbia et al. [55] also suggested for the initial condition in each time step to be reset to the initial condition. By doing so, the domain integral is evaluated only once. Nevertheless, this approach increases the computational effort needed for the time integration since the level of time discretization is refined.

7.7 Summary

Various numerical techniques of the boundary element method developed for solving the mathematical problems described in each chapter of this thesis have been critically discussed. Discussion is primarily focused on the advantages and disadvantages of the boundary element method when solving each specific problem of the human eye. Additionally, discussion is carried out on the performance of the various numerical techniques that have been employed to improve the numerical scheme of the boundary element method, such as the dual reciprocity method, the time-stepping scheme and the domain decomposition technique.

In general, the boundary element method has been found to perform very well when solving elliptic partial differential equations with constant coefficients. Other types of

partial differential equations that describe some of the problems investigated in this thesis, such as time-dependent partial differential equation and the Pennes bioheat equation, can be efficiently dealt with using different variation of the dual reciprocity method. When the governing partial differential equation is non-linear, the domain decomposition technique has to be adopted in order to improve the performance of the numerical scheme. In the case of the natural convection flow, the numerical scheme developed using the dual reciprocity method along with the domain decomposition technique fails due to the accumulation of numerical errors. To avoid this problem, a numerical scheme based on the cell integration technique has to be used.

Methods for overcoming the limitations of the numerical techniques employed have been recommended. Alternative techniques for dealing with some of the mathematical problems in this thesis have also been suggested. These are open for future studies.

Chapter 8

Conclusion and Directions of Future Research

8.1 Overview of Thesis

The human eye is acknowledged to be a unique biological structure that presents a host of engineering related problems to be solved [9]. In this thesis, four mathematical problems involving heat transfer inside the human eye have been successfully solved. These problems are specifically given by

1. sensitivity analysis, which investigates how various parameters such as environmental conditions and physiological variations affect ocular heat transfer,
2. effects of natural convection induced by the flow of aqueous humor on the heat transfer inside the anterior chamber,
3. transient temperature changes inside the eye during treatment of LTKP and
4. effects of eye tumor on the temperature distribution inside the human eye.

The problems mentioned above have been investigated with the objective of improving our understanding of the thermal behavior of the human eye in the different ocular

conditions considered. Furthermore, it is hoped that the results obtained from each chapter of this thesis may contribute to the expansion of literature on the mathematical models of the human eye.

Each specific problem has been solved numerically using the boundary element method. The choice of using the boundary element method is motivated by the lack of boundary element models of the human eye in literature. Despite being relatively new, the boundary element method has established itself as a leading alternative in numerical analysis [60]. The studies carried out in this thesis are thus, aimed at demonstrating the feasibility of the boundary element method in modeling ocular heat transfer.

8.2 Major Conclusions

The models presented in this thesis have been developed based on the dimensions of the actual human eye that may be found in literature [13, 15, 70]. Two types of models have been developed, namely the axisymmetrical model and the three-dimensional model. The three-dimensional model is obtained by rotating the axisymmetrical model, 360° about the pupillary axis. Additionally, a two-dimensional model of the anterior chamber that is sampled at the mid-sagittal plane is developed for the purpose of investigating the thermally driven flow of aqueous humor.

Prior to the investigations carried out on each of the four specific problems considered, a preliminary study is executed to establish the temperature distribution inside a healthy human eye during normo-thermal condition. This has been presented in Chapter 2. Investigations are performed using the axisymmetrical model. Temperature at the corneal surface predicted using the mathematical model developed showed results that agree with the experimental results obtained using IR thermography. Good agreement between the intraocular temperatures obtained using the present model and the predictions made by other researchers using different numerical methods are also found. For a healthy human eye during normo-thermal condition, the temperature at the center of the corneal surface

is found to be 34.19°C .

A sensitivity analysis is carried out in Chapter 3 using the axisymmetrical model developed in the preliminary investigation in Chapter 2. Effects of six parameters, namely ambient temperature, ambient convection coefficient, body temperature, blood convection coefficient, tears evaporation rate and thermal conductivity of lens are examined. Each parameter has been found to affect the ocular temperature distribution to some extent. Ambient temperature, ambient convection coefficient and blood convection coefficient have been suggested to be important criteria that have to be properly controlled when measuring the temperature of the human eye. This is to ensure that errors and uncertainties are minimized. The potential use of ocular surface temperature in monitoring the health of the human eye and human body is supported by the results obtained from the investigations carried out on the effects of blood convection coefficient, blood temperature and tears evaporation rate.

In Chapter 4, the two-dimensional model of the anterior chamber is used to simulate the flow of aqueous humor inside the anterior chamber. The use of a two-dimensional geometry in this analysis is justified by the numerical observations made by Canning et al. [114]. From a modeling point of view, the use of the boundary element method to simulate the thermally driven flow of aqueous humor inside the anterior chamber is new and it offers an alternative approach to other researchers who may be interested in examining the natural convection inside the anterior chamber. From the numerical investigation carried out in Chapter 4, no significant differences in the heat flux flowing from the inner surface of the cornea are observed between the anterior chambers with and without natural convection. A slight thermal asymmetry in the isotherms inside the anterior chamber is found in the presence of natural convection however. The results obtained from the investigations carried out here suggest that natural convection inside the anterior chamber can be ignored without introducing significant errors to the analysis of ocular heat transfer.

The transient temperature changes inside the human eye during treatment of LTKP

have been investigated in Chapter 5. Unlike previously developed models for the same purpose, investigations in Chapter 5 have been performed using a complete and more realistic human eye model in the *Orz* coordinate system. In order to maintain the axisymmetrical features of the model, some simplifications that are assumed to produce insignificant errors to the analysis, such as simulation of a single laser spot instead of eight, have been made. Different types of laser have been found to produce different thermal responses inside the human eye. Pulsed laser radiation yield highly transient corneal temperature, while a uniform temperature distribution is obtained in the continuous-wave laser radiation. Corneal temperature exceeding 100°C is achieved during pulsed laser radiation, albeit for a very short duration. During continuous wave laser radiation, the cornea is exposed to temperatures that are not greater than 75°C for durations of 10s and 60s in the 10s and minute coagulation respectively.

From the assessment of thermal damage, continuous-wave laser has been found to produce more severe damage than pulsed laser, despite the smaller increase in corneal temperature caused by the continuous-wave laser radiation. This has been attributed to the prolonged heating duration during continuous-wave laser. It is thus deduced that duration of heating plays a more important role than temperature in determining the amount of thermal damage inflicted onto the cornea.

The three-dimensional model of the human eye is used in Chapter 6 to investigate the effects of eye tumor on the temperature distribution inside the human eye. The eye tumor is modeled using established mathematical approaches, whereby metabolic heat generation and blood perfusion rate of tumor tissues are assumed to be larger than the surrounding healthy tissues [32–36]. The growth of tumor inside the human eye is found to produce a warmer ocular temperature distribution. This has been attributed to the superior metabolic heat generation of the tumor. Size and location of eye tumor are among the factors that determine the magnitude of temperature rise inside the human eye. A mean increase in the corneal surface temperature between 0.028 and 0.273°C has been predicted using the mathematical model of the human eye developed.

The magnitudes of temperature increase on the corneal surface have been found to lie within the range of thermal sensitivity of a highly sensitive IR camera. This result offers a new look into the potential use of temperature for detecting eye diseases. Aside from the increase in temperature, asymmetrical isotherms on the corneal surface may also be used to pinpoint the location of tumor growth. In practice, the thermal signal from the tumor may be amplified by reducing the effects of noise factors such as ambient convection coefficient, tears evaporation rate and blood convection coefficient. From the parametric optimization carried out, it has been found that increases in the ambient convection coefficient and tears evaporation rate, and a decrease in blood convection coefficient, are ideal settings that maximizes the thermal signal from the tumor.

The advantages and disadvantages of using the boundary element method in solving the problems considered in this thesis are critically discussed in Chapter 7. One of the major benefits of the boundary element method is the setting up of a smaller system of linear algebraic equations, which helps to reduce the demand of computational memory. The system of linear algebraic equations generated however, is very dense, and in problems involving only a single homogeneous domain, the system of equations becomes fully populated. This may reduce the computational efficiency of the numerical scheme developed. This drawback is not substantial in the investigations carried out in Chapters 2, 3, 5 and 6, where the problems are governed by linear partial differential equations. Problems with stability of the numerical scheme arise in Chapter 4, where the governing partial differential equations are non-linear. In this case, the domain decomposition technique has been used to improve the condition of the matrix generated.

One of the objectives of this thesis is to establish the boundary element method as a feasible numerical alternative for solving mathematical problems involving heat transfer inside the human eye. This has been demonstrated by the successful simulations of the various ocular problems investigated in this thesis. The capability of the numerical models to solve a wide range of problems including those governed by non-linear and time-dependent partial differential equations showcases the versatility and robustness of

the boundary element method.

8.3 Directions of Future Research

8.3.1 Improvements of the models developed

Methods for improving the accuracy of the models developed for solving each specific problem have been recommended in each chapter of this thesis. The following summarizes the recommendations presented in Chapters 2 to 6 for improving the accuracy of the models developed.

1. Effects of eyelids on the ocular temperature distribution may be considered when simulating the heat flow inside the eye. This may be carried out either by treating the eyelids as part of the solution domain or by modeling the thermal effects of eyelids as part of the boundary condition specified on the corneal surface.
2. The boundary condition describing the thermal interaction between the eye and ocular blood flow may be further improved by taking into account the heterogeneous blood flow inside the choroid. This may be accomplished by allowing the blood convection coefficient to vary across the surface of the sclera. Such an approach however, requires an in-depth understanding of the blood flow rate at specific locations inside the choroid.
3. Investigations to determine if errors are introduced in the assumption of negligible blood perfusion inside the iris may be carried out as part of the future studies. Knowledge of the blood perfusion rate inside the iris is required however.
4. In the sensitivity analysis carried out in Chapter 4, the thermal response of the human cornea towards changes in the ambient convection coefficient and tears evaporation rate may be better described based on the cooling rate of the cornea. A time-dependent analysis to model the cooling of the human eye from an initial

temperature can be performed in order to calculate the cooling rate of the cornea for different values of ambient convection coefficient and tears evaporation rate.

5. Investigations of the natural convection inside the anterior chamber may benefit from a better approximation of the boundary condition specified on the surfaces of iris and lens. The studies carried out in Chapter 4 may also be repeated using a complete model of the human eye. This helps to eliminate uncertainties that may be introduced from the assumptions made when specifying boundary conditions on the surfaces of the anterior chamber. Studies involving the anterior chamber of an eye in the supine orientation may be further analyzed using a three-dimensional model.
6. The model developed in Chapter 5 for investigating the transient temperature changes inside the human eye during LTKP may be enhanced by taking into consideration the changes in thermal and optical properties of the cornea when subjected to heat [162, 165]. Effects of the distribution of laser beam as it enters the cornea, such as the intracorneal focusing modeled by Brinkmann et al. [28, 148, 149], may be further explored.
7. A better understanding of the thermal properties of the eye tumor may improve the quality of predictions presented in Chapter 6. The non-homogeneous features of tumor, which are defined by the necrotic center and vascularized periphery, may lead to thermal properties that are non-homogeneous. These attributes may be considered in future studies.
8. The parametric optimization carried out in Chapter 6 may be further improved by taking into account the location of tumor growth as one of the factors investigated. Since eye tumor grows on the irregular surface of the choroid, it is important to obtain a consistent quantification of the distance of tumor to the corneal surface. This may be looked into in future studies.

9. Suggestions for improving the numerical accuracy of the boundary element models have been presented in Chapter 7. In general, higher order boundary elements may be used to obtain more accurate numerical approximations. Likewise, in the transient analysis carried out in Chapter 5, higher order time interpolation may be employed to obtain a more accurate approximation of the time-dependent variables in the integro-differential equation.
10. Various numerical alternatives recommended in Chapter 7, such as the Laplace transformation technique and the time-dependent fundamental solution for solving time-dependent problems, and the use of the dual reciprocity method along with the CS-PD-RBF for solving natural convection problems, may be attempted in future.

8.3.2 Future work

Application of the models developed in this thesis may be extended to investigate various other problems involving heat transfer inside the human eye. The dynamic changes in corneal surface temperature during blinking may be investigated using the axisymmetrical model of the human eye. By understanding how blinking affects the thermal behavior on the corneal surface, investigations in Chapters 2 to 6 may be repeated by including the effects of blinking. This may provide a more accurate description of the thermal behavior on the corneal surface.

The model of the anterior chamber developed in Chapter 5 may be used to estimate the pressure and shear stress exerted on the walls of the anterior chamber during natural convection. The numerical predictions obtained from such a study may help to determine the conditions of flow that cause cells and pigments on the surface of the iris to detach. This may further improve our understanding of the formation of Krukenberg spindle, hyphema, keratic precipitate and hypopyons. Such ocular abnormalities have been attributed to the flow of particulate matter inside the anterior chamber [114,115].

Simulations of particle motion inside the anterior chamber may also be carried out [115]. This may require a three-dimensional model and a time-dependent analysis however.

Studies of the transient temperature changes and the degree of thermal damage induced onto the cornea are among the first few steps involved in the investigation of LTKP. Results obtained from the present study may be used in future, to estimate the degree of corneal shrinkages based on the second order kinetic model proposed by Manns et al. [151, 152]. Additionally, the amount of stress required for the contraction of the corneal collagen may be calculated using theories of thermoelasticity. These studies are crucial in providing a more complete outlook of LTKP.

One of the main objectives of the investigations carried out in Chapter 6 is to establish the potential of using mathematical models to describe the thermal behavior of ocular diseases. This has been successfully demonstrated from the analysis carried out on eye tumors (choroidal melanoma). Other forms of ocular tumors, such as retinoblastoma, melanoma of the iris and ciliary body and secondary intraocular tumors, may be investigated using the same approach as presented in Chapter 6.

The thermal effects of ocular diseases that are more common, such as glaucoma, cataract and diabetic retinopathy, may be investigated in future studies. Nevertheless, it is important to obtain a proper mathematical description of the thermal behavior of these diseases in order to guarantee accurate and reliable numerical predictions. This may be carried out by observing the symptoms of these diseases and relating them to the thermal characteristics inside the eye. For instance, ocular blood flow in an eye with glaucoma has been found to be smaller than normal eyes [20, 90]. This has been attributed to the increased intraocular pressure, which compresses the blood vessels surrounding the eye [168, 169]. Based on such observation, the thermal behavior of glaucoma inside the eye may be modeled by specifying smaller blood convection coefficient. Similarly, the blurring of the human lens in eyes with cataract may be assumed to change its thermal conductivity such that the temperature distribution inside the human eye is affected. These approaches are mere suggestions and more input, particularly from medical pro-

fessionals are necessary before such the thermal effects of such diseases on the human eye can be mathematically investigated.

8.4 Closing Remarks

Research of the ocular heat transfer shows great potential. An in-depth understanding of the thermal behavior of the human eye provides information that may relate to ocular physiology. Mathematical modeling has proven to be a reliable tool in the studies of ocular heat transfer. This is motivated by the limitations of ocular thermometry (IR thermography), where only temperatures on the corneal surface can be measured. Difficulty in carrying out certain experiments on human subjects such as laser radiation, also make mathematical studies a much preferred choice. Various other mathematical problems involving heat transfer inside the human eye have been suggested for future studies. In solving these problems, the boundary element method provides an attractive alternative to the commonly used finite element method.

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Appendix A

Axisymmetrical linear interpolation functions

Consider Figure A-1 which represents a boundary element, $\Gamma^{(k)}$ defined in the Orz coordinate system. The ‘ $\times$ ’ symbols denote the endpoints of $\Gamma^{(k)}$ and the ‘dots’ denote the boundary collocation nodes selected using Equation (2.8). The boundary element illus-

Figure A-1: Endpoints and boundary collocation nodes of each boundary element in the Orz coordinate system

trated in Figure A-1 may be parameterized using

$$\left. \begin{aligned} r &= r^{(k)} - t\ell^{(k)}n_z^{(k)}, \\ z &= z^{(k)} + t\ell^{(k)}n_r^{(k)}, \end{aligned} \right\} \text{ for } 0 \leq t \leq 1, \quad (\text{A.1})$$

where $\ell^{(k)}$ is the length of element $\Gamma^{(k)}$.

A linear variation of the unknown variable ϕ across the $\Gamma^{(k)}$ may be expressed in the parameterized coordinate as

$$\phi(t) = a + bt, \quad (\text{A.2})$$

where a and b are unknown constants to be determined. Collocating Equation (A.2) at points $(\xi^{(k)}, \eta^{(k)})$ and $(\xi^{(k+N)}, \eta^{(k+N)})$ results in

$$\begin{aligned} \phi_1 &= a + \frac{1}{4}b, \\ \phi_2 &= a + \frac{3}{4}b, \end{aligned} \quad (\text{A.3})$$

where ϕ_1 and ϕ_2 are values of $\phi(t)$ at $(\xi^{(k)}, \eta^{(k)})$ and $(\xi^{(k+N)}, \eta^{(k+N)})$ respectively.

Solving Equation (A.3) leads to

$$\begin{aligned} a &= \frac{1}{2}(3\phi_1 - \phi_2), \\ b &= 2(\phi_2 - \phi_1), \end{aligned} \quad (\text{A.4})$$

which may be substituted into Equation (A.2) to give

$$\phi(t) = \varphi_1(r, z)\phi_1 + \varphi_2(r, z)\phi_2, \quad (\text{A.5})$$

where

$$\begin{aligned} \varphi_1(x, y) &= \frac{3}{2} - 2t, \\ \varphi_2(x, y) &= 2t - \frac{1}{2}. \end{aligned} \quad (\text{A.6})$$

The interpolation functions used in the Oxy coordinate system, $\varphi_1(x, y)$ and $\varphi_2(x, y)$ may also be obtained using the procedure described in Equations (A.1) to (A6).

Appendix B

Selection of nodes in the triangular boundary element

Figure B-1 presents a plane view of the triangular boundary element, $\Gamma^{(k)}$ in the $Oxyz$ coordinate system. The corner points of the triangle are denoted by (x_1, y_1, z_1) , (x_2, y_2, z_2) and (x_3, y_3, z_3) . The boundary nodes denoted by $(\xi_1, \eta_1, \gamma_1)$, $(\xi_2, \eta_2, \gamma_2)$ and $(\xi_3, \eta_3, \gamma_3)$, such as shown in Figure B-1, can be obtained by first, calculating the centroid of the triangular element, (x_c, y_c, z_c) , such that

Figure B-1: Triangular boundary element in the $Oxyz$ coordinate system

$$(x_c, y_c, z_c) = \frac{1}{3}(x_1 + x_2 + x_3, y_1 + y_2 + y_3, z_1 + z_2 + z_3). \quad (\text{B.1})$$

The midpoints between the centroid and each corner of the triangle are then selected to be the $(\xi_1, \eta_1, \gamma_1)$, $(\xi_2, \eta_2, \gamma_2)$ and $(\xi_3, \eta_3, \gamma_3)$, such that

$$\begin{aligned} (\xi_1, \eta_1, \gamma_1) &= \frac{1}{2}(x_c + x_1, y_c + y_1, z_c + z_1), \\ (\xi_2, \eta_2, \gamma_2) &= \frac{1}{2}(x_c + x_2, y_c + y_2, z_c + z_2), \\ (\xi_3, \eta_3, \gamma_3) &= \frac{1}{2}(x_c + x_3, y_c + y_3, z_c + z_3). \end{aligned} \quad (\text{B.2})$$

The approach presented here may be used for selecting the four interior points used in Chapter 4.

Appendix C

Three-dimensional linear interpolation functions

Consider the boundary element in Figure C-1 which may be parameterized into the local coordinates, u and v . For more details on the parameterization of the global coordinates, (x, y, z) into the local coordinates, (u, v) , one may refer to Ang [84]. The boundary collocation nodes in the local coordinates are denoted by (u_1, v_1) , (u_2, v_2) and (u_3, v_3) .

Figure C-1: Collocation nodes in the local coordinates of a three-dimensional boundary element

A linear approximation of the unknown variable ϕ across the element shown in Figure C-1 may be expressed as

$$\phi(u, v) = a + bu + cv, \quad (\text{C.1})$$

where a , b and c are unknowns to be determined. Collocating Equation (C.1) at points (u_1, v_1) , (u_2, v_2) and (u_3, v_3) yields

$$\begin{aligned} \phi_1 &= a + bu_1 + cv_1, \\ \phi_2 &= a + bu_2 + cv_2, \\ \phi_3 &= a + bu_3 + cv_3, \end{aligned} \quad (\text{C.2})$$

where ϕ_1 , ϕ_2 and ϕ_3 are values of $\phi(u, v)$ at (u_1, v_1) , (u_2, v_2) and (u_3, v_3) respectively. Equation (C.2) may be expressed in matrix form as

$$\begin{Bmatrix} \phi_1 \\ \phi_2 \\ \phi_3 \end{Bmatrix} = \begin{bmatrix} 1 & u_1 & v_1 \\ 1 & u_2 & v_2 \\ 1 & u_3 & v_3 \end{bmatrix} \begin{Bmatrix} a \\ b \\ c \end{Bmatrix}$$

or

$$\{\phi\} = [\mathbf{A}] \{\mathbf{b}\}. \quad (\text{C.3})$$

The unknown coefficients, a , b and c can be determined by inverting Equation (C.3) to give

$$\{\mathbf{b}\} = [\mathbf{A}]^{-1} \{\phi\}, \quad (\text{C.4})$$

where

$$[\mathbf{A}]^{-1} = \frac{1}{|\mathbf{A}|} \begin{bmatrix} u_2v_3 - u_3v_2 & u_3v_1 - u_1v_3 & u_1v_2 - u_2v_1 \\ v_2 - v_3 & v_3 - v_1 & v_1 - v_2 \\ u_3 - u_2 & u_1 - u_3 & u_2 - u_1 \end{bmatrix},$$

and $|\mathbf{A}|$ is the determinant of matrix $[\mathbf{A}]$. Substituting Equation (C.4) into (C.1) and

after some rearrangements, one arrives at

$$\phi(u, v) = \bar{\varphi}_1(x, y, z)\phi_1 + \bar{\varphi}_2(x, y, z)\phi_2 + \bar{\varphi}_3(x, y, z)\phi_3, \quad (\text{C.5})$$

where

$$\begin{aligned} \bar{\varphi}_1(x, y, z) &= \frac{1}{|\mathbf{A}|} [(u_2v_3 - u_3v_2) + (v_2 - v_3)u + (u_3 - u_2)], \\ \bar{\varphi}_2(x, y, z) &= \frac{1}{|\mathbf{A}|} [(u_3v_1 - u_1v_3) + (v_3 - v_1)u + (u_1 - u_3)], \\ \bar{\varphi}_3(x, y, z) &= \frac{1}{|\mathbf{A}|} [(u_1v_2 - u_2v_1) + (v_1 - v_2)u + (u_2 - u_1)], \end{aligned} \quad (\text{C.6})$$

are the linear interpolation functions.

Appendix D

Velocity-vorticity formulation of the Navier-Stokes equations

The steady state Navier-Stokes equations in the primitive variables are given in Equations (4.2) to (4.4), which are reproduced here as

$$\begin{aligned} \text{(continuity equation)} \quad \nabla \cdot \vec{v} &= 0, \\ \text{(momentum equation)} \quad \rho (\vec{v} \cdot \nabla \vec{v}) &= -\nabla p + \mu \nabla^2 \vec{v} + \rho g \vec{j}, \\ \text{(energy equation)} \quad \alpha \nabla^2 T &= \vec{v} \cdot \nabla T. \end{aligned} \tag{D.1}$$

Vorticity of a given flow is obtained by taking the curl of the velocity vector, which is mathematically expressed as

$$\vec{\omega} = \nabla \times \vec{v}. \tag{D.2}$$

To obtain the kinetics aspect of flow, i.e. the vorticity transport equation, one may take the curl of the momentum equation such that

$$\rho [\nabla \times (\vec{v} \cdot \nabla \vec{v})] = \nabla \times (-\nabla p) + \mu (\nabla \times \nabla^2 \vec{v}) + \rho g (\nabla \times \vec{j}). \tag{D.3}$$

Equation (D.3) may be simplified using the following vector identities:

$$\nabla \times (\vec{v} \cdot \nabla \vec{v}) = \vec{v} \cdot \nabla (\nabla \times \vec{v}) - (\nabla \times \vec{v}) \cdot \nabla \vec{v} + (\nabla \cdot \vec{v})(\nabla \times \vec{v}),$$

$$(\nabla \times \nabla^2 \vec{v}) = \nabla^2 (\nabla \times \vec{v}),$$

$$\nabla \times (-\nabla p) = 0, \text{ (since } p \text{ is a scalar).}$$

Substituting the aforementioned identities into Equation (D.3) and making use of the continuity equation results in

$$\rho[\vec{v} \cdot \nabla (\nabla \times \vec{v}) - (\nabla \times \vec{v}) \cdot \nabla \vec{v}] = \mu \nabla^2 (\nabla \times \vec{v}) + \rho g (\nabla \times \vec{j}). \quad (\text{D.4})$$

Replacing the definition of vorticity in Equation (D.2) into (D.4) results in the vorticity transport equation

$$\rho[\vec{v} \cdot \nabla \vec{\omega} - \vec{\omega} \cdot \nabla \vec{v}] = \mu \nabla^2 \vec{\omega} + \rho g (\nabla \times \vec{j}). \quad (\text{D.5})$$

In the Oxy coordinate system, only one component of vorticity exist, which is denoted by ω . Consequently, the second term on the left hand side of Equation (D.5) vanishes to give

$$\rho \nabla^2 \omega = \mu (\vec{v} \cdot \nabla \omega) + \rho g (\nabla \times \vec{j}). \quad (\text{D.6})$$

The kinematics aspect of flow is obtained by taking the curl of the vorticity (Equation (D.2)), such that

$$\nabla \times \vec{\omega} = \nabla \times (\nabla \times \vec{v}). \quad (\text{D.7})$$

Using the following vector identity

$$\nabla \times (\nabla \times \vec{v}) = \nabla (\nabla \cdot \vec{v}) - \nabla^2 \vec{v}, \quad (\text{D.8})$$

and employing the continuity equation, Equation (D.7) simplifies to the elliptic Poisson

equation for the velocity vector, i.e.

$$\nabla^2 \vec{v} = -\nabla \times \vec{\omega}. \quad (\text{D.9})$$

In the Oxy coordinate system, Equation (D.9) may be expressed in the individual velocity components as

$$\begin{aligned} \nabla^2 u &= -\frac{\partial \omega}{\partial y}, \\ \nabla^2 v &= -\frac{\partial \omega}{\partial x}. \end{aligned}$$

Appendix E

Transfer of partial derivatives to the fundamental solution

For the purpose of illustration, only the integro-differential equation derived from the vorticity transport equation, which is given by Equation (4.19), shall be considered. For convenience, Equation (4.19) is reproduced here as

$$\begin{aligned}
 \lambda(\xi, \eta)\omega(\xi, \eta) &= \int_C \omega(x, y) \frac{\partial}{\partial n} [\Phi_{2D}(x, y; \xi, \eta)] ds(x, y) \\
 &\quad - \int_C \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial n} [\omega(x, y)] ds(x, y) \\
 &\quad + \frac{1}{Pr} \iint_R \Phi_{2D}(x, y; \xi, \eta) \left\{ u(x, y) \frac{\partial}{\partial x} [\omega(x, y)] \right. \\
 &\quad \left. + v(x, y) \frac{\partial}{\partial y} [\omega(x, y)] \right\} dA(x, y) \\
 &\quad - Ra \iint_R \Phi_{2D}(x, y; \xi, \eta) \frac{\partial}{\partial y} [T(x, y)] dA(x, y). \tag{E.1}
 \end{aligned}$$

The domain integrals in Equation (E.1) may be expressed in vector notation as

$$I = I_1 - I_2 \quad (\text{E.2})$$

where

$$I_1 = \frac{1}{Pr} \iint_R \Phi_{2D} (\vec{v} \cdot \nabla \omega) dA, \quad (\text{E.3})$$

$$I_2 = Ra \iint_R \Phi_{2D} (\nabla \times T \vec{j}) dA. \quad (\text{E.4})$$

The objective here is to transfer the partial derivatives of the unknown variables, in this case, $\nabla \omega$ and $\vec{\nabla} \times T$, to the fundamental solution, Φ_{2D} . Let us first consider I_1 , which from the product rule, gives

$$\vec{v} \cdot \nabla \omega = \nabla \cdot (\vec{v} \omega) - \omega \nabla \cdot \vec{v},$$

where the second term on the right hand side is zero as a consequence of the continuity equation. This leads to

$$\vec{v} \cdot \nabla \omega = \nabla \cdot (\vec{v} \omega),$$

which may be substituted into Equation (E.3) to give

$$I_1 = \frac{1}{Pr} \iint_R \Phi_{2D} \nabla \cdot (\vec{v} \omega) dA. \quad (\text{E.5})$$

Using the produce rule again to describe $[\Phi_{2D} \nabla \cdot (\vec{v} \omega)]$ in Equation (E.5), one obtains

$$\Phi_{2D} \nabla \cdot (\vec{v} \omega) = \nabla \cdot (\Phi_{2D} \vec{v} \omega) - \omega \vec{v} \cdot \nabla \Phi_{2D},$$

which upon substitution into Equation (E.5), leads to

$$I_1 = \frac{1}{Pr} \left[\iint_R \nabla \cdot (\Phi_{2D} \vec{v} \omega) dA - \iint_R \omega \vec{v} \cdot \nabla \Phi_{2D} dA \right]. \quad (E.6)$$

The first integral in Equation (E.6) may be converted into a boundary integral using the divergence theorem, such that

$$I_1 = \frac{1}{Pr} \left[\int_C \Phi_{2D} (\vec{n} \cdot \vec{v}) \omega ds - \iint_R \omega \vec{v} \cdot \nabla \Phi_{2D} dA \right], \quad (E.7)$$

where $\vec{n} = [n_x, n_y]$. Expressing Equation (E.7) in its individual component leads to

$$\begin{aligned} I_1 &= \frac{1}{Pr} \int_C \Phi_{2D}(x, y; \xi, \eta) [n_x u(x, y) + n_y v(x, y)] \omega(x, y) ds(x, y) \\ &\quad - \frac{1}{Pr} \iint_R \omega(x, y) \left\{ u(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] \right. \\ &\quad \left. + v(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi, \eta)] \right\} dA(x, y), \end{aligned} \quad (E.8)$$

where the first order derivatives of the unknown variables have been transferred to the fundamental solution.

Transformation of the second integral, I_2 can be done in a similar manner. Using the product rule, $\Phi_{2D}(\vec{\nabla} \times T \vec{j})$ may be expressed as

$$\Phi_{2D}(\vec{\nabla} \times T \vec{j}) = \vec{\nabla} \times (\Phi_{2D} T \vec{j}) - \nabla \Phi_{2D} \times T \vec{j},$$

which may be substituted into Equation (E.4) to give

$$I_2 = Ra \left[\iint_R \vec{\nabla} \times (\Phi_{2D} T \vec{j}) dA - \iint_R (\nabla \Phi_{2D} \times T \vec{j}) dA \right]. \quad (E.9)$$

The first integral in Equation (E.9) may be converted into a boundary integral using the divergence theorem. This reduces Equation (E.9) to

$$I_2 = Ra \left[\int_C \Phi_{2D}(\vec{n} \times \vec{j}) T ds - \iint_R \nabla \Phi_{2D} \times T \vec{j} dA \right], \quad (E.10)$$

which is expressed in its individual components as

$$\begin{aligned} I_2 = & Ra \int_C n_y \Phi_{2D}(x, y; \xi, \eta) T(x, y) ds(x, y) \\ & + Ra \iint_R T(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] dA(x, y). \end{aligned} \quad (E.11)$$

As in Equation (E.8), the partial derivatives of the unknown variables are now transferred to the fundamental solution.

Substituting Equations (E.8) and (E.11) into (E.2) leads to

$$\begin{aligned} I = & \frac{1}{Pr} \int_C \Phi_{2D}(x, y; \xi, \eta) [n_x u(x, y) + n_y v(x, y)] \omega(x, y) ds(x, y) \\ & - Ra \int_C n_y \Phi_{2D}(x, y; \xi, \eta) T(x, y) ds(x, y) \\ & - \frac{1}{Pr} \iint_R \omega(x, y) \left\{ u(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] \right. \\ & \left. + v(x, y) \frac{\partial}{\partial y} [\Phi_{2D}(x, y; \xi, \eta)] \right\} dA(x, y) \\ & + Ra \iint_R T(x, y) \frac{\partial}{\partial x} [\Phi_{2D}(x, y; \xi, \eta)] dA(x, y). \end{aligned} \quad (E.12)$$

The procedure for transforming the partial derivatives of the unknown variables to the fundamental solution as described in the aforementioned, may be repeated for the other domain integrals in the integro-differential equations defined in Equations (4.20) to (4.22).