A biomechanical model for prediction of brain consciousness state under hyper-gravity condition

Swandito

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**A BIOMECHANICAL MODEL FOR PREDICTION
OF BRAIN CONSCIOUSNESS STATE UNDER
HYPER-GRAVITY CONDITION**

SWANDITO

SCHOOL OF MECHANICAL AND AEROSPACE ENGINEERING

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ABSTRACT

When an individual is subjected to high gravitational force in the upward direction (approximately $+4G_z$ and beyond), an ischemic insult to the brain due to the large drop in the cerebral perfusion pressure will occur. During the period of the insult the brain will debar some its neural activities as part of its survival mechanism, a process that may lead to the Loss of Consciousness (LOC). Once the LOC has occurred, even if the blood flow is returned immediately, an incapacitation period is unavoidable. Gravitational-force induced Loss of Consciousness (G-LOC) has always been a problem in the aviation field, especially for the pilots of the high performance aircrafts. Given that the G-LOC poses real potential danger to the safety of the pilot and the aircraft, it is desirable if some premonitory indicator can be developed to alert the pilots if he/she is going to reach the G-LOC state.

A biomechanical model utilizing both real time measurements and computations based on an integrated cerebral blood flow modelling was proposed to be developed in order to achieve the aforementioned objective. Significant amount of modelling was attempted on quantifying the cerebral perfusion volume since this factor is largely accepted as the main somatic reason contributing towards the LOC episode. Spatiotemporal quantification of the blood flow in the human vasculature was complemented by the non-invasive method offered by Doppler ultrasound.

The research work was divided into a few stages. The first stage was the development of the experimental rig to test the current state-of-the-art Doppler ultrasound sensing technology. *In vitro* assessment of the Doppler technique was carried out with a custom made phantom and probe positioning mechatronics system. Obtained experimental data were found to be consistent with the theoretical results found in the literature. Based on the results analysis, it was envisioned that appropriate use of the technique together with the blood flow modelling can greatly improve the flow volume quantification.

The second stage comprised the derivation of the blood flow modelling by utilizing Computational Fluid Dynamics (CFD) method. The derivation was intended to improve the accuracy of the input from the Doppler. Subsequently, it was combined with the fully integrated biomechanical model, derived based on the human population data, to provide reliable quantification for the modelled major arteries responsible for the cerebral blood flow. Simulations were carried out under a number of flow parameters while exploring a set of possibilities, e.g. physiological variation, acceleration pattern, which may occur in real application. This resulted in an encouraging outcome which was corroborated by an analytic solution derived to validate the said model.

In the third stage, a modified Windkessel model, as a lumped-model representing the cardiovascular system, was developed to monitor the cerebral blood flow volume that goes to the brain during different hyper-gravity conditions by incorporating various relevant parameters while accounting for other parts of systemic circulation. Validation of the simulation results was

done by comparing them with the available G-LOC experimental data. Generally, the model was able to faithfully reproduce the mean G-LOC data obtained from the available centrifuge experimental data. However, a discrepancy still existed, especially in the standard deviation of the G-LOC range. This may be attributed to the variation of the physiological properties of each individual subject, e.g. dimension of the arteries, blood oxygenation rate, etc., which was only partially accounted for in the simulation.

Finally, following the successful development of the modified Windkessel model, all the models and the inputs from sensor measurement were integrated and simulated. From a few hundreds of simulations performed based on extensive scenarios, analysis of the result were deemed to be satisfactory and with this the efficacy of the model was concluded very positively. Major contributions are especially noted in the arguably pioneer hybridization of the Doppler and CFD for flow measurement, and the development of the customizable integrated G-LOC predictive model which attempted to tackle the crucial problem in the aviation industry.

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NOMENCLATURE

Abbreviations

2D	2-Dimensional
2WM	2-element Windkessel Model
3D	3-Dimensional
3WM	3-element Windkessel Model
4WM	4-element Windkessel Model
A-LOC	Almost Loss of Consciousness
AGSM	Anti-Gravity Straining Maneuver
ANN	Artificial Neural Network
BMF	Blood Mimicking Fluid
CAD	Computer Aided Design
CBF	Cerebral Blood Flow
CCA	Common Carotid Artery
CFD	Computational Fluid Dynamics
CMRO ₂	Cerebral Oxygen Metabolic Rate
CO	Cardiac Output
CT	Computed Tomography
CW	Continuous Wave
D-H	Denavit-Hartenberg
DTM	Decay Time Method
DUS	Doppler Ultrasound
ECA	External Carotid Artery

EEG	Electroencephalogram
EJ	Ejection Time
G-force/G	Gravitational force
G-LOC	Gravity Induced Loss of Consciousness
GOR	Gradual Onset Rate
HR	Heart Rate
ICA	Internal Carotid Artery
ID	Internal Diameter
IEC	International Electrochemical Commission
LOC	Loss of Consciousness
MRI	Magnetic Resonance Imaging
NS	Navier-Stokes
PPM	Pulse Pressure Method
PW	Pulsed Wave
RAS	Reticular Activating System
RBC	Red Blood Cell
ROR	Rapid Onset Rate
RPM	Rotations Per Minute
SRS-NIRS	Spatially Resolved Spectroscopy-Near Infrared Spectroscopy
SV	Stroke Volume
SVPP	Stroke Volume over Pulse Pressure (method)
TMP	Tissue Mimicking Phantom
TOI	Tissue Oxygenation Index
USAFSAM	United States Air Force School of Aviation Medicine
VA	Vertebral Artery

WM	Windkessel Model
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Symbols

$ $	Absolute value
$\int_a^b c$	Integration
$\frac{\partial}{\partial}$	Partial differentiation
∇	<i>Del</i> operator
$+G_z$	Gravitational force in the upward direction
t	Time

General Doppler Ultrasound

θ	Angle between the ultrasound beam and the blood vessel axis
ρ_0	Density
A	Time averaged cross sectional area of the vessel
c	Speed of sound
D	Diameter of the vessel
$f_d, \bar{f}_d(t), f_t$	Doppler shift frequency, instantaneous mean Doppler shift frequency, transmitted zero crossing frequency
K	Bulk modulus
$\bar{Q}$	Time averaged volumetric flow
T	Total time period
$v, \bar{v}(t)$	Velocity of the blood, mean velocity of the blood

General Kinematics

α	Angle between vector p and z with respect to z
β	Angle between projection of vector p on xy plane with respect to x
$p(a,b,c)$	Point in space described using Cartesian coordinate system
R	Length of vector p from the origin
w	Rotational axis
x, y, z	Axes in Cartesian coordinate system

General Statistics

α	Level of significance
σ	Standard Deviation
μ	Mean
$f_x(x)$	Probability density
F - ratio	Ratio between estimate of common variance from individual observations and estimate of common variance using population mean
$F_{Critical}$	Critical value of the F -distribution for accepting or rejecting the null hypothesis at certain level of significance
p -value	A function of the observed sample results that is used for testing a statistical hypothesis
X	Sample's mean
z	Normal deviate

Fluid Dynamics

δ	Boundary layer thickness
ρ	Density of the fluid
μ	Dynamic viscosity
A, A_p, A_d	Luminal cross-sectional area, luminal cross-sectional area of parent vessel, luminal cross-sectional area of daughter vessel
D	Diameter of the vessel
g	Body accelerations
h	Position with respect to the radius
k	The tapering factor
L	Length of the vessel
L_v	Distance needed to reach within 1% of the fully developed velocity at the centerline or mid-plane
P	Pressure
Q, Q_p, Q_d	Volumetric flow volume, volumetric flow volume in parent vessel, volumetric flow volume in daughter vessel
Re	Reynold's number
$r(x)$	Radius of the vessel at x
r_{dis}, r_{pr}	Mean distal radius, mean proximal radius
R, R_z, R_o	Radius, radius at z , original radius
u, u_p, u_d	Velocity of blood flow, velocity of blood flow in parent vessel, velocity of blood flow in daughter vessel
u_{max}	Maximum velocity

U, U_0	Mean velocity, original mean velocity
ν	Kinematic viscosity
v_r, v_θ, v_z	Velocity in radial direction, velocity in θ direction, velocity in axial direction
x	The location along the artery
X	The required inlet length
z	Position with respect to axial direction
<i>Windkessel Model</i>	
$\gamma, \gamma_{App}, \gamma_W$	Shear rate, apparent shear rate, wall shear rate
η	Non-Newtonian viscosity
τ	Delay time
ρ	Density of the blood
A_0	Original cross-sectional area
C	Capacitance/ aortic compliance
C_a	Total arterial O_2 concentration
ε	Efficiency of the O_2 metabolism
E	Young's modulus
E_n, E_f, E_0	Net O_2 extraction fraction, unidirectional extraction fraction of O_2 , unidirectional extraction fraction of O_2 at resting condition
f, f_0	Local perfusion rate, local perfusion rate at resting condition

$F_C(t), F_C^{(i)}$	Neurological spike frequency, lower value of neurological spikes frequency
$F_C^{(s)}, F_C^{(0)}$	Upper value of neurological spikes frequency, central point of the afferent neurological spikes frequency
$F_S(t), F_S^{(i)}, F_S^{(s)}$	<i>sympathetic</i> neurological spikes frequency, lower value of <i>sympathetic</i> neurological spikes frequency, upper value of <i>sympathetic</i> neurological spikes frequency
$F_V(t), F_V^{(i)}, F_V^{(s)}$	<i>vagal</i> neurological spikes frequency, lower value of <i>vagal</i> neurological spikes frequency, upper value of <i>vagal</i> neurological spikes frequency
G_{T_S}, G_{T_V}, G_R	Gain associated with the <i>sympathetic</i> contribution, gain associated with the <i>vagal</i> contribution, gain associated with <i>sympathetic</i> contribution on arterial resistance
g	Gravitational force
h	Vertical distance between heart and specified location at the brain
h_t	Wall thickness
Hb	Hemoglobin
i	Current/ blood flow
k, n	Constant
$k_{F_C}, k_{F_S}, k_{F_V}$	Shape parameter of the afferent spikes sigmoidal curve, shape parameter of the <i>sympathetic</i> exponential curve, shape parameters of the <i>vagal</i> spikes sigmoidal curve
k_T, k_R	Time constant

K_1	Max. rate parameter which governs delivery of O_2 to tissue
L	Length of the artery
n	Number of the applied G-force
O_2	Oxygen
p_m	Measured pressure
P_H	Hydrostatic pressure
P_H^1	Hydrostatic pressure at 1G
$P_a^{(0)}, P_a(t)$	Central point of the arterial pressure, arterial pressure
$P_{Ao,Mean}$	Mean aortic pressure
$P_{Ven,Mean}$	Mean venous pressure
$P_a O_2$	Partial pressure of O_2
$P, \Delta P$	Pressure, pressure difference
q_m	Measured flow
r_0, r	Original radius of the artery, radius of the artery
R_C, R_U, R_L	Cerebral resistance, upper body resistance, lower body resistance
$R, R^{(0)}$	Peripheral resistance of arterial network, value of arterial resistance in the case of heart denervation
$S_a O_2$	Percentage saturation of Hb in O_2
$T, T^{(0)}$	Time period of one heartbeat, value of heart period in the case of cardiac denervation
u_C	Voltage/ blood pressure

V	Volume of the given segment
$\overline{W}$	Mean power entering the arterial system
$\overline{W}_P$	Mean squared values of measured arterial pressure
$\overline{W}_Q$	Mean squared values of measured arterial flow
Z_c	Aortic impedance
Z	Total arterial resistance

Chapter 1 Introduction

1.1 Background

The research on Gravity Induced Loss of Consciousness (G-LOC) has been conducted for more than 80 years [1, 2, 3]. During this long span of research activity some hypotheses and some proofs with regard to the psychosomatic cause of the episode and methods to increase the G tolerance have been engendered. Earlier it was believed that the LOC was caused by the lack of energy supply to the brain due to insufficient cerebral blood flow to meet the brain's metabolic demand or otherwise known as the brain ischemia. However, this hypothesis was subsequently debunked, at least to a certain degree, as other research has shown that the cause is not as passive as it was originally believed. LOC is a product of the active 'survival mechanism' acted by the brain during the reduced supply period [1].

In an upright posture, the distance between the brain stem and the heart is about 30 cm [3]. Hence, assuming a rigid-tube like arterial system, there is a 22 mmHg drop of blood pressure for every +1 G_z of force acting on human [1]. It is clear that the higher the G-force the lower the blood pressure in the brain will be. When the cerebral blood pressure drops, the brain will give a 'signal' to the heart to increase the blood pressure through various vascular sensory systems for example the baroreceptor which is located at the carotid sinus. However, there is a limit to which the heart can increase the blood pressure and once the limit is exceeded, brain ischemia will occur. When the duration of the insult has

exceeded a certain threshold, the LOC will occur even if the cerebral blood flow is returned to normal immediately [1]. This ‘interval’ happens because when the blood pressure drops ischemia does not occur everywhere in the brain at the same time but it happens gradually starting from the cerebral cortex down to the mid brain and finally when it reaches the brain stem, where the Reticular Activating System (RAS) exists, LOC occurs as its sequela.

Considering the corollary following a period of incapacity could be devastating [3, 4, 5], it is imperative that the ischemic could be detected before it reaches the threshold. Once it is detected, the G-force can immediately be lowered in order to prevent the G-LOC episode within the hypothesized interval or in the case that the LOC episode is inevitable, auto-pilot could be automatically engaged based on the prediction to help preventing damage and casualty. In order to do this, a reliable and effective G-LOC predictive model is needed. The predictive model is intended to rely much on the input from the Cerebral Blood Flow (CBF) measurement and quantification. Therefore, a sensor which is able to provide fast and precise measurement of the CBF is required.

In terms of the sensing system, there are a few systems that are generally used to quantify the arterial blood flow. Magnetic Resonance Imaging (MRI), Computed Tomography (CT) and Doppler Ultrasound (DUS) are some of the examples. Every method has its own strength and weaknesses. For example the MRI has a very good resolution. However, its application is rather restricted due to its compatibility issue. In this project, Doppler ultrasound was chosen as the main candidate for the cerebral blood flow measurement. Compared to the

rest of the measurement techniques, perhaps ultrasound is the most suitable candidate for the purpose of the application expounded earlier. Ultrasound is non-invasive, which is the primary reason for its selection. It is also compact and generally requires non-specific environment to work with. The Doppler ultrasound itself is an established imaging and profiling modality. By utilizing the Doppler's law, it is able to evaluate the targeted moving object in term of the direction and velocity [6, 7].

Despite its advantages, there are a few constraints in using the ultrasound [6]. It needs a medium that has acoustic impedance constant close to that of the ultrasound material's in order to transfer the ultrasound beam effectively. In its due course the beam will experience attenuation such as scattering, refraction, etc. thus limiting its depth of penetration or spatial resolution. Careful preparation is required to fully maximize its functionality. But the main concern for the use of the Doppler ultrasound, in this case, is to what extent its accuracy can be relied upon. All of the DUS systems suffer from similar problems in measuring the velocity (profile) of the flow. Those problems are the measurement of the component of the velocity which is parallel to the axis of the Doppler transducer, measurement of the angle between the axis of the flow and the transducer's axis and last but not least the measurement of the cross-sectional area of the blood vessel.

Considering these drawbacks that a DUS has, another way to quantify the CBF which is by modelling the blood flow through the arterial vasculature network based on fluid dynamics equation was considered. The modelling based on the

governing equations would complement the measurements conducted by DUS. With regard to the blood flow modelling, plenty of researchers have attempted it and most of them are using the Navier-Stokes (NS) equation and its derivation in modelling the blood flow [8, 9, 10, 11, 12]. During its course of derivation several suppositions were introduced mainly to the mechanics of the arterial wall. While the result's accuracy still leaves large room for improvement, the outcome so far, to the author's knowledge, is encouraging. This, in particular, applies to specific flow with limited conditions.

Aside from using the formulation from fluid mechanics, arterial blood flow modelling can also be approached from a slightly different perspective, which is by forming them as a lumped model. Among them, the notable one is the Windkessel model [4, 13, 14]. In this model the blood flow and pressure in the arterial system are derived from electrical analogies represented by a number of elements. The necessity to have more elements or higher degree lumped model is depending on the purpose of the study. The Windkessel models are widely used and have a long history of development. It is believed that these models along with the other similar lumped models (e.g. viscoelasticity, inertia, back pressure, etc.) could closely represent the arterial blood flow and the cardiac system albeit with the existence of discernible disparity between the measured blood flow and the theoretical models. However, this trait of being able to represent the systemic flow as a whole is particularly attractive since the flow to certain parts of the body will directly and indirectly influenced by the flow to the rest of the parts. Based on this, many inferences could also be made especially with some well-defined modification (e.g. by adding more elements

such as resistances, the blood flow to certain area can be divided into more regions, etc.) to the basic model [4, 15].

To be able to accurately measure the CBF will not give a direct inference as to when a person will undergo a G-LOC period. There is also a need to develop a model to predict the G-LOC with CBF as its main defining rule. So far there is no definite model that can confidently predict the occurrence of G-LOC. These models employ different strategies and approaches such as by using a Spatially Resolved Spectroscopy-Near Infrared Spectroscopy (SRS-NIRS) to measure the Tissue Oxygenation Index (TOI) or by using analysis from the Electroencephalogram (EEG) signals generated by the brain [16, 17]. Each has their own strength and limitation. There is also a predictive model which was derived from a percolation theorem which states that “The global behavior of a system can be construed by making a reasonable assumption about the dynamic of the local systems” [1, 18]. Hence, by defining the possible cause of the underlying mechanism of the G-LOC such as the physiologic mechanism of the ‘arousal’, neural response to the metabolic threats, and oxygen utilization in neural tissue and defining the interaction rule between them, one can predict when the G-LOC will occur. The model derived reportedly is able to give satisfactory result which agrees to the statistical data developed from myriads of GLOC experimental data. However, although the outcome is good, it is only fitting the general population data. Since every person’s G-force tolerance is different, and the range of the differences is relatively large, that model might not be suitable for individual use.

Here in this project, a model which is able to reduce if not eliminate the weaknesses found from other studies for example the ability to account to the variability of the individual response towards the G-LOC based on his/her physiological parameters is proposed. These functionalities together with the utilization of ultrasound as the main sensing modality, which has not been attempted yet in this kind of application, set it apart from the other models found in the literature.

1.2 Objective

The final objective of the research work was to develop a biomechanical model for G-LOC prediction with real-time input. In order to reach this there were several sub-objectives which had to be satisfied. The sub-objectives are enumerated below:

1. To propose and verify the feasibility of a sensor mechanism for the intended application,
2. To produce an improved arterial blood flow model which includes, but not limited to, compensatory mechanism and tissue oxygenation model,
3. To generate customizable G-LOC predictive model based on several physiological quantifications.

1.3 Scope

The focus in this study was to develop a biomechanical model for G-LOC prediction with real-time input. The proposed study was limited to: *in vitro* experimentation, simulation modelling performed by using selected commercial software available in the university and output analysis by utilizing data available in literature. Centrifuge experiment with human test subjects was not attempted in this study.

1.4 Overview of the Report

This report is divided into several major chapters as follows,

- Chapter 1 elaborates on the background and motivation of the research. Here, the objectives of the research are also stated.
- Chapter 2 presents the literature review on the G-LOC related bioengineering topics especially the progress that has been achieved in the G-LOC research.
- Chapter 3 gives a brief review on the ultrasound sensing technology in particular the Doppler ultrasound and discusses the testing of the acquired Doppler system in an *in-vitro* setup. Procedure, objectives of the tests, test outcome and its analysis are given in appropriate sequence.

- Chapter 4 deals with the blood flow modelling based on CFD and Navier-Stokes equation. The effect of parameters' variation are examined and presented. Comparison of the numerical and analytic results is also shown.
- Chapter 5 shows the development of Windkessel model, a lumped-model representing the cardiovascular system as well as the foundation of the G-LOC predictive model. The integration of the CFD model together with the input from Doppler ultrasound during the predictive model development is also elaborated. To complete the chapter, detailed scenarios generated for the model simulations and the analyses of the results which validate the efficacy of the developed model are also showcased.
- Chapter 6 elucidates the conclusion and states the future work plan of this research work.

Chapter 2 Literature Review

In this section, detailed account on the nature of the G-LOC is propounded utilizing the published latest insight. Some aspects of the G-LOC can be properly perceived while the rest may require more comprehensive thinking or perhaps imagination. A historical review on available G-LOC studies is also briefly presented to give insight to the advancement that has been made in dealing with G-LOC related matters.

2.1 G-LOC: The Property, Dynamic and Effect on Human Physiology

During a flight, the pilot is continuously under the influence of gravitational (G)-force. The effect of the G-force is three dimensional (3D) and is measured in G unit in which 1G is equal to the earth gravitational force ($9.81ms^{-2}$). Figure 2.1 shows the components of the G-force in 3D (denoted by G_x , G_y and G_z). Each of these components is further divided into negative and positive to indicate the direction of the G-force component with respect to the reference frame or object.

Humans are able to withstand higher G level in the x and y directions (longitudinal and lateral plane) but have lower resistance against G-force in the z direction or transverse plane (the $+G_z$ is the main concern in this research, for the sake of brevity from here forward whenever the G is mentioned it is

referred to $+G_z$ unless stated otherwise). Fundamentally every human is used to withstand 1G which is the normal ‘Earth gravitational pull’. Under normal circumstances, the average human is able to withstand up to 3-3.5G without any noticeable changes physiologically. Higher than this level of G-force people may experience; grey out, black out and finally loss of consciousness or commonly referred as the G-LOC.

Figure 2.1 Three-dimensional components of G-force (G_x , G_y and G_z) acting on human body with positive and negative signs indicating the direction of the force (adopted with modification from [19])

G-LOC technically refers to a cognitive state wherein a person’s awareness to the world with which he is interacting is lost due to acceleration induced cerebral hypoxic [2, 3, 20]. Underneath this seemingly simple statement lies deep philosophical and biological science which requires understanding of a number of different scions of knowledge. Over time, various hypotheses have

been made in order to explain the G-LOC. For example, G-LOC was conjectured as the after-effect of the mechanical impact of acceleration on the brain. Under hyper-gravity condition, the brain is compressed against the base of skull and some of the brain functions are hypothesized to be altered in due process, e.g. black out happens due to the compression of the optical chiasm by the frontal cortex [1]. However, this hypothesis was later proven to be not entirely true. The compression effect is there, however it is not significant enough to create damage to the brain or alter the brain function for the G level below 20G as has been proven by an experiment with traverse G [21, 22].

A model known as hydrostatic (haemostatic) model attempted to quantify the relationship between the blood pressure and the visual symptoms observed during the exposure to the acceleration stress and it managed to do so quite successfully [23]. Based on this model, it was concluded that the LOC is caused by reduced supply of blood flow to the upper part of the body, in this particular case when the level of the blood flow that goes to the brain is lower than a certain threshold value. Once the blood volume level is below this threshold value, LOC will definitely occur even if the blood supply to the brain is restored instantly. Up until now, this model is largely used to provide basic general understanding with regard to the cause of the LOC.

2.2 Human Tolerance Level to G-LOC

Any part of the body requires constant supply of sugar and oxygen. The brain requires about 15% of total cardiac output despite its relatively small size (about 2% of total body weight). In such, 50-54 ml of blood/ minute is required for every 100 grams of brain tissue [24, 25]. In order to furnish the demand, blood is constantly pumped into the brain. When the G-force is increased, the heart will increase the blood pressure in order to overcome the external pressure so as to keep the supply constant. However, there is a limit to which the heart could increase the blood pressure and once it exceeds the limit then it leads to Brain Ischemia. This ischemic insult is believed to cause the brain to lose most of its cognitive function and finally end up in an unconscious state. However it was later found that the unconscious state is not as passive as it has been early deduced. The fact that some brain functions are shut down is not just because of the reduced supply from the blood flow but it is the active survival mechanism of the brain in order to preserve the most important functions of the brain.

Some of the most notable symptoms that can occur during the high-G are the grey out and black out. Grey out (greying vision due to diminished blood supply to the eyes) typically occurs the earliest and thus can serve a natural warning system for the next symptom to appear should the G-force continue to be increased. Black out (the complete loss of vision) happens subsequent to the grey out and a sign that the retinal has lost its blood supply. Brain ischemia is the last thing that happens, the low oxygen supply causes the neural function to

shut down and if the period of the ischemic insult is longer than a certain duration, irreparable brain tissue damage may occur (Figure 2.2).

Figure 2.2 CBF thresholds for brain tissue preservation (adopted from [26])

Every individual has different level of tolerance against G-force due to a number of contributing factors in which differences in physiological conditions have significant contributions. However, it is still possible to statistically outline the general population tolerance toward the G-force. Figure 2.3 perhaps gives the most accurate illustration on the human G tolerance curve. It shows the diagram of the mean G tolerance for a set of onset rate obtained from a number of experiments [21].

Figure 2.3 is quite useful when it comes to give a fair prediction of what would be expected for a certain G-force level. As can be seen from figure, the Gradual Onset Rate (GOR) produces lower *G* tolerance level. Due to the longer period of increment, the cardiovascular reserves and reflex is able to play a role in it thus the visual symptoms are experienced more distinctively. On the other hand, on the Rapid Onset Rate (ROR) the pilot is able to generally have higher *G* tolerance level. However, they will reach the LOC state in very short amount of time with little or almost no visual symptoms. The reason that the subject who experiences the ROR does not directly go into the LOC is because of the functional buffer period. This period refer to the oxygen reserve in the brain tissue which enables the brain to properly function for a few seconds (4-7 seconds) without any blood supply at all [25]. It is also understood that during ROR there is almost no time for the cardiovascular system to respond to the reduced blood supply to the brain. There is no noticeable effect for the *G* level below 3.5G as the cardiovascular system is still able to keep up with the increasing *G* level.

The weakness of the diagram in Figure 2.3 is that it is not dynamic. The *G* level experienced by the pilot is changing over time. Similarly, the physiological response of the human body in particular the cardiovascular system is also changing over the time. Hence the figure offers little help when it comes to the actual acceleration profile.

Figure 2.3 Tolerance curve (adopted with modification from [21])

In terms of the G-LOC verification during experiments, it is generally difficult to accurately verify as to what point an individual is experiencing the G-LOC. This is mostly because the subject most of the time doesn't realize they have experienced the G-LOC. Visual symptoms are not really helping in determining the G-LOC especially when the rapid onset rate is applied. The change in the subject's behaviour in the subsequent experiments also contributes to the variation in his/her G tolerance level. Objective measurements of tolerance are implemented such as by using the blood pressure, EEG, blood content of the ear, blood volume in the brain [1, 27]. However none of these methods are very successful in determining the G-tolerance let alone predicting the G-LOC. It is imperative to be noted that aside from the visual symptoms the subject also experiences psychological effects such as confusion, disorientation, altered judgment and suppression of G-LOC recognition [1, 3, 22]. The variability

among individuals, as has been stated earlier, is the thing that prompts the large discrepancy between individuals in terms of their G tolerance level. Table 2.1 gives a brief overview of the variation in human tolerance level toward G-force.

Table 2.1 G Tolerance based on 1000 experimental subjects (adopted from [3])

Criterion	Mean Threshold (G)	Standard Deviation (G)	Range (G)
Grey out or Loss Of Peripheral Vision	4.1	+0.7	2.2-7.1
Blackout	4.8	+0.8	2.7-7.8
Unconsciousness	5.4	+0.9	3.0-8.4

Another important thing with regard to the G-LOC episode is the incapacitation period. The person who experiences the G-LOC will remain incapacitated for a period of time which is proportional to the length of the ischemic insult. This period of incapacitation is divided into two categories, namely the absolute incapacitation period and relative incapacitation period. The absolute incapacitation period refers to the length of time where the subject loses his consciousness while the relative incapacitation is that the subject has regained his consciousness but is still unable to perform active movement. This also includes a period of disorientation and confusion. Little study has been done in order to understand more about the time needed for regaining total capacitation. However it is generally understood that the subjects do not suffer from deleterious effects physiologically following the LOC. The episode itself is not described as harrowing instead some felt quite a pleasant feeling. The psychological effect after regaining consciousness varies which includes feeling

anxiety, embarrassment, euphoria, frustration, denial and depression [1, 2, 3]. Again the long term psychological effect on the subject is little understood. Table 2.2 lists the mean incapacitation period of a centrifuge study by Houghton [28].

Table 2.2 G-LOC Recovery time (adopted from [28])

Criterion	Mean G level (SD)	Absolute incapacitation (sec)	Total incapacitation (sec)
GOR	7.2 (0.8)	16.6	32.3
ROR (2 sec)	6.1 (0.7)	12.1	23.7
ROR (4 sec)	6.3 (0.8)	Combined with the ROR (2 sec)	

2.3 G-LOC: History and Related Studies

The earliest case of G-LOC was documented in 1919 in “The Medical problems of flying” [29]. In one of its articles, occurrence of what was dubbed as ‘fainting in the air’ was presented. Experiments had been conducted to explore more about this phenomenon. However, aside from the (relatively crude) establishment of the range at which G-LOC occurred and the G-LOC’s duration, there was no attempt on providing medical basis to explain the phenomenon [29, 30].

Afterwards, for almost a decade there was not much study done pertinent to G-LOC until Von Diringshofen in his attempt to explain the nature behind G-LOC proposed haemostatic theory of acceleration tolerance in early 1930 [30]. The theory explained that the human acceleration tolerance was related to the cardiovascular ability to provide the required quantity of blood flow to the brain. In order for the blood to reach the cortical area, it had to overcome the hydrostatic barrier caused by vertical distance between the heart and the brain [31] (Figure 2.4). By representing the distance between the heart and the brain as a rigid column, the pressure change given a certain G level was calculated based on the hydrostatic pressure difference [1] and the blood pressure at the brain was then determined.

Figure 2.4 Hydrostatic barrier: Distance between heart and brain (adopted from [31])

Based on this calculation of the pressure gradient, human tolerance to G was estimated to be within 4.5 to 5.5 G. This tolerance range was engendered from the data of the blood pressure which were monitored continuously during the experiments conducted in a medically instrumented aircraft. Until now the haemostatic theory is still largely used to give brief prediction on the human response toward the acceleration stress albeit relatively unreliable actual measurement method and some flaws with regard to its theoretical base (e.g. assumption of the rigid column, etc.). This is because the prediction produced by this theory, even though it is not very accurate, is still within a certain range of the actual measurement of the acceleration stress tolerance. However, while it is useful to give preliminary insight to the G tolerance level, a more reliable method is needed when an accurate measurement is important.

A number of experiments to explore more about the G-LOC were conducted in the following decade. During this period, researchers were able to statistically quantify the duration and level of G needed to cause the G-LOC episode. It was also found that longer duration of relatively lower G-force was more likely to produce G-LOC compared to the short burst of high G-level. Even though there was no definite quantification was recorded but the incapacitation period following the G-LOC was also gauged [32]. With this, the danger of the G-LOC was thus further recognized especially in the military context due to the large presence of the military high performance aircrafts.

Although the etiology of the G-LOC was not clearly established, techniques to improve G tolerance had been developed since 1920's [33]. The techniques

collectively were called AGSM (Anti-Gravity Straining Maneuver). Among the AGSM were special breathing technique to improve the intra thoracic pressure, muscular tensing and G-suit to reduce the blood pooling in the lower part of the body (e.g. legs, feet). As the time went by, the AGSM was further refined. Different breathing techniques were conceived and applied. One of the more recent one was the L1 manoeuvre which was derived by the USAFSAM (United States Air Force School of Aviation Medicine) [34]. The L1 manoeuvre was developed based on the previous manoeuvre technique and was supposedly able to reduce throat irritation during tints application. The AGSM were reported to be able to give (additional) 3.5 to 4G tolerance on average when it was done correctly.

The importance of the G-LOC study was becoming more prominent during and after the World War II [30]. The main reason for this was due to the many class-A aircraft mishaps that happened in which a proportion of those mishaps couldn't be attributed to the pilot error or machine malfunction. Numerous centrifuge (Figure 2.5) studies were conducted all around the world to further study the phenomenon. Progress was made especially in classifying the symptoms that precede G-LOC episode. It was noted that sometimes no symptoms appear preceding the G-LOC and this further exacerbated the potential danger of the G-LOC. The physiological condition following a G-LOC episode was also observed and the incapacitation period was divided into absolute and total incapacitation period which substantially described the mental and physical capacity of the pilot during the G-LOC period and the period following the G-LOC episode [1, 30, 35].

Figure 2.5 Human centrifuge for high-G training available in Singapore

Aeromedical Research Centre (adopted from [36])

In 1950s, US Navy conducted a G-LOC study and gave report on the G-tolerance end point [30]. 1000 subjects were participating in the trial and the study became one of the largest G-LOC experiments ever conducted. In this experiment the G-LOC mean tolerance range for different G level was established statistically. Due to the number of the participants, the tolerance range was deemed to be the most reliable and used by numerous other studies as the reference in their related research. In the following study, the rapid G-LOC was found to have a constant time of occurrence regardless of the G-Level. As explained from the earlier graph (Figure 2.3) this could be attributed to the functional buffer period due to the oxygen reserve in the brain tissue. In ROR, usually there is not enough time for AGSM or the body compensatory

mechanism to take effect. Because of this, it can be said that nothing can be done to increase the G-LOC tolerance in ROR cases. AGSM and G-LOC prediction are more concentrated in the GOR cases.

The research on G-LOC subsequently died down for more than a decade. The interest resurfaced after a retrospective study on G-LOC was published in early 1970's [37]. The article was focusing on the sudden incapacitation during flights. In its conclusion, G-LOC was pointed as the cause of some of the unexplained crashes. During this period G-LOC was thought to be affecting the most advanced aircraft only. However this was later debunked by a number of studies. One of them was the study conducted by the Australian air defence in 1988 [38]. In its report, the G-LOC was found to also occur in light aircraft. However, the occurrence was largely attributed to the physiological condition of the pilot. It was understood that pilots who had undergone G-LOC training and had more prior exposure to the G-LOC had the tendency to have higher G tolerance level compared to the pilots who had not. In the gist, G-LOC is a deleterious occurrence that can happen in a lot of settings and has to be taken seriously.

The demand for pilots to have higher G-tolerance level had been increasing especially with the advancement of the fighter planes. However, there is a limit to which human body and technology can help, at least for the time being, to increase the G-tolerance level. Due to this, studies to find a way to predict the occurrence of G-LOC was considered. There are many factors contributing to the tolerance level of the pilots such as pilots' mental and physiological

condition (e.g. fatigue, experience and exposure toward G-LOC, fitness, inherent body condition, etc.) [38]. These factors may lower or improve the pilot's G-LOC tolerance level significantly. Due to these copious contributing factors, predicting the occurrence of G-LOC becomes an uphill task. It is recognized that some symptoms like grey out and black out can be a tell-tale sign that G-LOC episode is imminent. However, there are cases in which G-LOC episodes come without any preceding symptoms [35]. In the last two decades, several studies had attempted to predict the occurrence of G-LOC by utilizing a number of ways.

In early 1990, G-LOC topic was studied to another new level by Cammarota [1]. In his research, he attempted to develop a model that emulates the global dynamics of the G-LOC. The model developed incorporated a number of theories from a series of interrelated disciplines such as neuroscience, medicine and bio-physics. LOC due to the linear acceleration stress, in this case gravity, was hypothesized to be more than just a cardiovascular failure as it had always been inferred. LOC which happens as a sequela to the ischemic insult to the brain was believed to occur partly because of a certain protective mechanism maneuvered by the brain to ebb the effect of reduced metabolic supply.

In developing the G-LOC predictive model, Cammarota adopted the percolation network from the complexity theory. Complexity theory deals with a complex system which is spatially protracted with copious degrees of freedom and a bevy of interacting local dynamics systems [1, 39]. This theory hypothesizes that the global dynamic behavior of a system could be constructed by making a

proper assumption about the interaction between its local dynamics. The interaction is characterized by a set of rule and it is usually simple. The system's dynamics is highly non-linear and there also exists self-organization within which the global order emerges without any interference from anything resembles that of a global controller.

The percolation model which is created by using simple regular framework and by establishing simple interaction rules among the elements in the network is developed in order to describe the behavior of the connected clusters in the random network of the complex system (Figure 2.6). Such interaction rules are derived from the scaling concepts such as fractal and power law. In conjunction with this, the consciousness and unconsciousness was loosely analogized as a phase transition. Example of phase transition in life such as when solid becomes liquid, or when a ferrous material becomes ferromagnetic once its temperature passes below the Curie temperature.

In deriving the complete model, several hypotheses and reasonable assumptions were developed by Cammarota. This is because the determination of consciousness, operation of both peripheral and central nervous system are considered not really distinctive. Some global symptoms can be quite distinct in G-LOC state, e.g. the loss of postural motor control, loss of facial muscle tone, eye fixation or closing of the eyes, while others may not be that clear-cut. The information on global behavior at the phase transition are also difficult to be obtained because in most of the experiments conducted the acceleration was halted before the G-LOC could occur since G-LOC (previously) was considered

dangerous to the test subject, there was also the lack of external stimuli to determine whether the person was still conscious or not and the use of rapid onset rate (ROR) at most cases in order to minimize the presumable danger.

Figure 2.6 Percolation model with randomly connected clusters of nodes (left) [39] and nodal placement representation of different parts of the cerebral tissue (right) [40]

The model was reported to be able to duplicate the induction of LOC in humans. However, the duplication was only for a general population data (mean value). It could not give the prediction for individual data. This was expected since there is quite a wide range of G-tolerance variation from one person to another person because of a number of physiological condition and external stimuli. These conditions and stimuli are difficult to be enumerated let alone to be standardized. Another reason for this weakness is perhaps the parameters considered for the LOC induction were too few. It only included the oxygen metabolism rate and eye level blood pressure drop.

The models for these two main parameters were also static and derived from another model of similar nature. It was also noted that a number of assumptions were set for the models. While those assumptions were justifiable, they might not represent the true nature of the system's behavior or mechanism. For example, it was hypothesized that RAS was the main party responsible for the phenomenon called consciousness. However, in other research it was stated that in order to be conscious, human needs to utilize different part of the brain simultaneously [5].

In order to improve the model, the number of parameters considered significant to G-LOC could be increased and while retaining the already used parameters, improvement to those parameters might be necessary. To have a dynamic model is also another way to go and perhaps to add a weighted value to these parameters to determine their significance to the global behaviors can also be done in order to acquire a more sophisticated predictive model.

Based on the argument that the LOC was caused by the loss of oxygen supply to the brain due to the diminishing cerebral blood flow, G-LOC prediction based on the cerebral tissue oxygenation level was attempted in the Japan Air Self Defence Force Aeromedical Laboratory [16]. A Spatially Resolved Spectroscopy-Near Infrared Spectroscopy (SRS-NIRS) was employed to measure the Tissue Oxygenation Index (TOI). Basically, NIRS is a system that detects the changes in absorption and transmission rate of NIR light in human tissue by using optical technique. The changes in turn give information of the

tissue haemoglobin saturation level. SRS-NIRS is a modification of the normal NIRS to overcome the extra-cranial contamination [16].

The study was able to establish the critical oxygenation level for the G-LOC episode. However, it could not account for the wide differences between individuals and further study to improve on that was suggested. It was also noted that there was error in the TOI measurement. The error was believed to be due to the contamination caused by the limitation of the technique and the effect of the G-force on the human physiology (e.g. skin movement, transudation fluid, etc.) which affected the accuracy of the measurement. In a nutshell the relation between cerebral oxygenation level and G-LOC was proved to exist by TOI. However, there were many other inherent variables that were not accounted yet. Hence, TOI while it could be used to evaluate the effect of AGSM (for example), it might not be very useful in the prediction of G-LOC.

One of the hardest parts in the G-LOC study is to determine the exact time at which the G-LOC occurs. Failure in determining the timing has significant deleterious effect in establishing the correct G-LOC range. Observed physical symptoms had been used to help in determining the G-LOC period. However, this method was subjective and inaccurate because sometimes not even the person experiencing the G-LOC realized that he/she had been experiencing G-LOC let alone the observer. In order to rectify this problem, a G-LOC study which uses Electroencephalography (EEG) had been attempted [17]. EEG is

basically a recording of the brain electrical activity, which resulted from the firing of ionic current by the brain's neurons [4].

The study hypothesized that the consciousness could be monitored by detecting and analysing the EEG signals from the brain. In its study, the signals were quantitatively characterized and analysed using Discrete Wavelet Transform. It was anticipated that based on the analysis, the various states of incapacitation could be determined. The result showed that A-LOC (Almost-LOC) phenomena could be distinctly detected. However, since there was no specific condition (brain's 'state') that could be accurately defined with regard to each of the symptoms; the determination could only be done qualitatively. It was also noted that standardization might not be probable because the variation of the EEG state between individuals varied largely.

Chapter 3 Doppler Ultrasound Testing

Spatio-temporal quantification of the blood flow in human vasculature has been greatly aided with a number of imaging techniques available. One of them is the Doppler ultrasound. Due to its non-invasive property, the number of Doppler applications in clinical practice has significantly increased during the last decade [41]. However, like any other imaging technique, there are a number of factors that may affect the accurate measurement of the Doppler ultrasound. Doppler ultrasound's efficacy in measuring the volumetric blood flow in human body was thus re-verified by performing an *in vitro* assessment of the approach. It is understood that the accuracy of the Doppler system depends mainly on the precise positioning of the system with respect to the target, measurement niceties of the vessel size, and the presence of interfering noise. Hence, when performing the experiment, these factors which may cause the inaccuracies were minimized so that the optimized Doppler measurement could be carried out and its results could subsequently be analyzed.

The research work performed in relation to the Doppler testing is consolidated in this chapter. It represents the first stage in the series of stages undertaken to achieve the objectives stated in the Chapter 1. The following subsections give elaborate explanations with regard to the experiment fixture, testing procedure and testing results. In depth discussion pertinent to the obtained results are also presented.

3.1 The Objectives of the Test

The objectives of the experiments were as follows:

- To measure the similarity of the volumetric fluid flow calculation between Doppler system and the actual flow in the study,
- To find out the applicability of Doppler ultrasound system in measuring the arterial blood flow for the stated application of G-LOC,
- To propose necessary measurement protocols and improvements to be implemented,
- Act as a platform for determining the next step/direction to be carried out in this project.

3.2 Doppler Ultrasound

A brief review of the Doppler ultrasound technology which is the basis of the sensor application of this project is presented in this subsection. It is intended to highlight some of the important characteristics of this sensing modality especially its application value for the purpose of this research.

3.2.1 Doppler Ultrasound System

Doppler ultrasound is a technique to measure the velocity of moving objects inside the human body. It is derived from the ‘Doppler effect’ phenomenon in which the frequency of the sound observed by the observer moving relative to

the wave source is changing in accordance to the velocity of the relative motion [6, 7, 42]. In its typical application, the ultrasound beams are transmitted by the ultrasound transducer into the body. The echoes from the beam will then be analysed by the receiving transducer. One transducer can both transmit and receive ultrasound beam although they can also be separate transducers. From the echoes, the system is able to pinpoint the coordinate from where the echo has originated and by calculating its amplitude it is also able to construct the plane image of the object.

The ultrasound waves itself are produced mechanically from push-pull action of a propagating medium e.g. piezoelectric ceramic. The action is controlled by a predetermined electrical signal. The range of the ultrasound frequency is determined by its purpose. Lower frequency such as that within 2-10 MHz is typically used for Doppler and higher frequency such as 20 MHz is used for imaging purpose. Lower frequency will have lower spatial resolution while having higher frequency causes aliasing problem [42]. Therefore, compromise is needed to achieve optimum use.

There are two types of waves generated by the Doppler system namely continuous wave (CW) and pulsed wave (PW). Usually both waves are used in order to maximize their strength. In Doppler application the amplitude, frequency and phase of the ultrasound wave are of the utmost importance. The shift in the frequency and phase of the scattered waves are used to determine the velocity of the moving object. Mathematically, the Doppler shift is given by [6],

$$f_d = \frac{2f_t v \cos \theta}{c} \quad (3.1)$$

where f_t is the transmitted zero crossing frequency, θ is the angle between the ultrasound beam and the blood vessel axis, v is the velocity calculated from the Doppler shift frequency and c is the speed of sound in soft tissue (which is around 1540m/s and in blood is within 1540-1600 m/s range). c depends on its bulk modulus (K) and density (ρ_0) and can be written as,

$$c \cong (K/\rho_0)^{0.5} \quad (3.2)$$

There are many types of Doppler ultrasound available in the market for different kinds of purposes such as for vascular imaging, blood flow motion detection, harmonic movement tracking of vascular organ etc. The majority of Doppler ultrasounds (DUS) can typically be divided into several broad categories based on its functionality, namely velocity detecting DUS, Duplex DUS, profile detecting DUS, and velocity imaging DUS. In terms of the ultrasound wave it is either Pulsed Wave (PW) Doppler or Continuous Wave (CW) Doppler [6]. While the CW will give better accuracy, it cannot tell the direction of the flow and the provenance of the echo like PW does. Hence, to have both PW and CW combined in a single DUS system is common. Sometimes the Doppler is combined with the B-scan echo and thus we have the duplex system. This is very useful in order to extracting the information pertaining to a particular flow's velocity in a predefined point.

3.2.2 Volumetric Blood Flow Measurement

One of the most important applications of the Doppler ultrasound is the measurement of volumetric blood flow. For this purpose, a duplex Doppler system is commonly utilized. The pulse-echo system is devised to insonate the target area, most commonly a vessel, where sample volumes are then collected, modulated and subsequently displayed. The system is non-invasive, relatively very accurate if required measurement conditions are met and it doesn't create interference to the flow dynamics of the measurement target.

The velocity is estimated from the echo analysis. In general the mean velocity is reported unless it is the velocity profile detecting system. The mean velocity can be further calibrated using the angle correction factor. Hence, the more reliable the knowledge about the velocity vector, the better is the velocity flow that can be estimated. The time average volumetric flow through a vessel is given by the following equation [42],

$$\bar{Q} = \frac{1}{T} \int_{t=0}^T A(t) \bar{v}(t) dt \quad (3.3)$$

where $A(t)$ is the time averaged cross sectional area of the vessel, T is the time period and $\bar{v}(t)$ is the mean velocity calculated from the mean Doppler shift frequency. The calculation for $\bar{v}(t)$ is depicted by,

$$\bar{v}(t) = \frac{\bar{f}_d(t)c}{2f_i \cos \theta} \quad (3.4)$$

where $\bar{f}_d(t)$ is the instantaneous (instantly measured) mean Doppler frequency shift, f_i is the transmitted zero crossing frequency, θ is the angle between the

ultrasound beam and the blood vessel axis, c is the velocity of ultrasound in soft tissue,

The accuracy of the Doppler ultrasound is affected by a number of factors such as non-uniform insonation of the blood vessel, differential attenuation between soft tissue and blood, frequency dependent attenuation and scattering, high pass filter designed to reject high amplitude low frequency Doppler shift, poor signal to noise ratio. Following are some of the factors that are the most significant in its effect to the measurement outcome [6, 7].

- *Measurement of vessel area*

The measurement of the vessel diameter is usually done from the image generated by the Brightness-mode, also known as B-mode/B-scan, where a linear array of transducers simultaneously scans a plane and display the scanning output as a two dimensional image on screen. The cross sectional area is calculated by assuming that the cross-sectional area of the vessel is circular, elliptic or other calculable area. It is also possible to rotate the image plane in order to obtain the full display of the cross sectional area. However, a single measurement can lead to serious error since the vessel diameter change dynamically depends on the cardiac blood pressure and other factors. Possible causes for vessel area measurement errors are listed as follows: 1) it is not possible to totally eliminate the error due to the changing vessel diameter. The error can instead be reduced by taking the average vessel diameter over a series of measurements. One study found that peak-to-peak diameter

variation was 2.8% in femoral arteries and 6.7% in the common carotid arteries. The error in flow measurement due to using the average arterial diameter rather than true instantaneous diameter were 2.2% (1.5-3.8%) and 1.3 % (0.4-3.6%). 2) in normal human body, the shape of the vessel cross sectional area is hardly perfect circle or ellipse. 3) The axial resolution of the pulse-echo system is determined by the length of the pulse. On the other hand, lateral resolution is determined by the beam's width. Although the length and the width is considerably very small but when they are compared to the diameter of blood vessels, their size can still be quite significant and this will affect the measurement's accuracy. Furthermore, the placement of the beam will also affect the accurate measurement of the vessel diameter.

- *Measurement of angle*

The angle between the ultrasound beam and the blood vessel can be measured by rotating a dedicated cursor on the B-scan image to align with the axis of the vessel. Since it is the cosine of theta that determines the components of velocity measured by the Doppler probe, the accuracy of this measurement becomes more critical at angles approaching 90 degrees.

Several solutions to the problem of inaccurate determination of vessel area and measurement angle have been presented. These include: the use of multiple transducers to give 2-Dimensional (2D) or even 3-Dimensional (3D) velocity vectors which is done in the effort to avoid making assumption on certain flow

characteristics ; garnering multiple samples in a 2D plane instead of relying on uniform insonation in order to measure the shape of the instantaneous velocity profile; development of an Attenuation Compensation method by producing two ultrasound beams with one beam used to calibrate the other; and the development of the assumed velocity profile method which is the variation of Duplex method, where the mean velocity is determined from the time-averaged maximum Doppler shift [6, 43, 44, 45, 46]. While these methods reduce the error, they require substantial amount of computational power and having multiple transducers creates complications in system arrangement and calibration.

3.3 Doppler Experiments: Accuracy of the Doppler Measurement

The experimentation performed could generally be separated into two parts, the first one was the experimentation with the focus on the accuracy of the Doppler measurement and the second one was the experimentation with the focus on the reliability of the Doppler measurement. This was done to gauge the competency of the Doppler in the pre-stated application. This subsection elaborates in detail on the experimentation with the focus on finding the accuracy of the Doppler.

3.3.1 Experimental Setup

The accuracy of the Doppler technique depends mainly on the precise positioning of the ultrasound source with respect to the target blood vessel, measurement details of the vessel size, and the presence of interfering noises

(e.g. artefact, bubbles) [6, 47]. When performing the experiments, these factors were minimized to optimize Doppler measurement. In order to achieve the objectives, a custom designed experimental fixture was being utilized. The experimental setup (Figure 3.1 and Figure 3.2) mainly consisted of tissue mimicking phantom, blood mimicking fluid (BMF), BMF reservoir, pumping system which includes the tubing, Doppler ultrasound system, and the probe holder which was attached to a positioning system with four degrees of freedom.

Figure 3.1 Experimental rig for Doppler ultrasound testing

Figure 3.2 Schematic diagram of the experimental setup

Following is the brief explanation of each of the involved components,

Positioning jig

A mechanical arm was configured for positioning of the Doppler probe. The diagram of the mechanical interface is given in Figure 3.3. The Doppler probe was attached to the end-effector of the arm. The mechanical arm consisted of four degrees of freedom (DOF) for precise positioning of the ultrasound probe with respect to the predefined target. A commercially available linear guide [48] was utilized for better alignment and accuracy. The movement precision was expected to be within 0.1mm for translational axis and 0.1° for rotational axis. Available travel distance for each axis was ensured to have enough leverage for small distance transducer movement.

Figure 3.3 Schematic diagram of the mechanical arm

Pumping System and Silicone Tubing

A peristaltic pumping system (P100L-100 [49]) was used to pump the BMF through the phantom vessel. With the pump, the flow speed of the liquid could be varied from 0 to 99 rotations per minute (RPM). The volumetric fluid flow was calculated from the reference formula given by the manufacturer (Calculation 3.1: Equation 3.5) with respect to the internal diameter of the silicone tubing that was used. Given the tubing diameter, the maximum flow output that could be achieved was 1000 ml/min which was more than the CBF volumetric flow (750-800 ml/min).

There were two tubing diameters that were used, 2.7mm diameter and 8mm internal diameter tubing. For each of the tubing, the pump roller needed to be adjusted and the flow output calibrated for accuracy. The adjustment and calibration was done manually by matching the actual flow output and the theoretical flow output. The diameter of the silicone tubes used did not precisely match the internal diameter of the Common Carotid Artery (CCA) and Internal Carotid Artery (ICA) due to the difficulty of obtaining the suitable tube dimension. However, this did not pose as a problem since the phantom was used to gauge the applicability and efficacy of the Doppler ultrasound and the aberration in internal tube diameter was not expected to alter the outcome of the experiment. Furthermore, it was possible to interpolate/extrapolate the result to determine the output of a certain tube diameter based on these two tubes that were used.

Doppler Ultrasound System

The Doppler system manufactured by *Aloka. Inc* was selected (Figure 3.4) was used in this project. This Doppler system has all the features necessary for the accurate measurement of the blood flow. It also comes with an imaging system that will enhance the sampling calculation of the velocity measurement.

Following are some of its extolled features [50]:

- Five frequencies range for greyscale imaging and Doppler.
- Tissue harmonic echo imaging for reduced artefact and optimal resolution
- Integrated data management subsystem
- Multi display capability for concurrent analysis of the blood flow region and its morphological information
- Multi beam processing that enables dynamic imaging and real time tracking
- Real time free angular M-mode for real time tracking

Generally, the first two features enable users to obtain good resolution images in different depth level. The next two features facilitate users in doing the analysis by giving multi-inputs concurrently. The last two features give users the ability to track changes online.

Figure 3.4 Picture of *Aloka Prosound SSD-3500 SX* Doppler ultrasound system taken from [50], inset (top-right corner) is a picture of the same system used in this project

Tissue Mimicking Phantom (TMP)

For the tissue mimicking phantom, *Agar* was utilized. It was chosen due to its similarities to the human tissue in term of the substantial mechanical properties. Furthermore, it is readily available, it is easy to be made and shaped into particular shape according to the requirements. Table 3.1 shows *agar* properties compared to the International Electrochemical Commission (IEC) guideline. IEC is the international standards and conformity assessments body for all fields of electrical, electronic and related technologies (electrotechnology) [51] .

Table 3.1 Properties of a standard TMP and some of the published TMPs [52, 53]

Physical Quantity	IEC Standard for tissue mimics	Gelatin	Agar
Density (kg m^{-3})	1040 ± 100	980	1050 ± 10
Velocity (m s^{-1})	1540 ± 15	1539	1540 ± 10
Attenuation ($\text{dB cm}^{-1} \text{ MHz}^{-1}$)	0.5 ± 0.05	0.51	0.5-0.85

Blood Mimicking Fluid

In case of blood, the Doppler echo is collected from the scattered signal by the Red Blood Cell (RBC). Hence, the blood mimic for the Doppler ultrasound application should closely match the physical properties of the blood. It has to contain particulates which can represent the RBC. In this project, the BMF solution was made from the mixture of glycerol, sodium iodide (table salt) and water. The composition of the mixture was, 37%, 16% and 47% respectively which was based on the specification given in [54]. It had been proven that the physical properties of this composition were able to mimic the physical properties of the blood (and inherently the effect of RBC in the blood). In the application, this solution was able to give a clear Doppler flow image and the solution itself was relatively easy to be made. Prior to this, only water-salt solution was tried. However, the result was not encouraging. Table 3.2 shows the comparison of the properties of this BMF with the properties of the BMF standard according to International Electrochemical Commission (IEC) guideline and the human blood.

Table 3.2 Properties of a standard BMF and one of the published BMF [6, 54]

Properties	IEC Standard for blood mimics	Human Blood @37°C	BMF at room temperature
Scattering Particle	-	Red Blood cell	Glycerol
Particle size	-	7	-
Hematocrit (% Volume)	-	45	53
Density (kg m ⁻³)	1050±40	1053	1244
Viscosity (mPa s)	4±0.4	(3 ~ 4)*	4.31±0.03
Velocity (ms ⁻¹)	1570±30	1583	-
Attenuation (dB/cm MHz)	<0.1	0.15	-
Backscatter (f ⁴ m ⁻¹ sr ⁻¹)	1-10 x 10 ⁻³¹	4 x 10 ⁻³¹	-

**Normal value at major arteries, blood is a Non-Newtonian fluid so the actual range of the viscosity can be very large*

3.3.2 Experimental Procedure

Measurement of the Vessel Cross-sectional Area

In order to calculate the volumetric blood flow, the cross sectional area of the blood vessel has to be determined. There are a few methods to measure the cross sectional area and one of those methods is by using the B-scan image from the ultrasound system (Figure 3.5). This method which was also applied

in this project was considered to be the most effective especially when the resolution of the system was high and the positioning of the probe with respect to the blood vessel was known quite well.

Using the same imaging technique it was possible to see the vessel from different plane of view and thereby facilitating the determination of the vessel diameter. By placing the probe orthogonal to the vessel, the cross sectional area could be viewed, and in order to verify that the probe was indeed placed 90 degrees with respect to the vessel longitudinal axis, the probe was rotated in small angle to obtain the smallest diameter. It is imperative that the value of the diameter be taken as accurately as possible since a small deviation from the 'actual' diameter will have significant effect in calculating the volumetric blood flow due to the exponential function of vessel diameter in the calculation of the total vessel area (Calculation 3.1: Equation 3.6). An example of such error which leads to a large percentage of deviation in calculating the actual output is also given in section 3.5.

The area of the blood flow was considered to be a perfect circle. However, this is not in the case of the actual blood vessel. The circumference of the circle is not smooth and the diameter is changing dynamically due to the varying blood pressure. In fact it is found that the variation in the common carotid artery is up to 6.7% [55] . Other sources of errors can be ascribed to the limitation of the ultrasound axial resolution and uniformity of the ultrasound insonation. However, the effects of these factors were relatively insignificant in this project. This is because the size of the vessel was known and the Doppler

ultrasound system used was able to uniformly insonate the vessel's cross-section with good resolution.

Figure 3.5 Cross-sectional area of the blood vessel which is not a perfect circle

The angle of the ultrasound beam with respect to the blood vessel axis was found by aligning a dedicated cursor on the B-scan image with the vessel axis. It was found that the optimum angle is about 60 degrees where the compromise between the B-scan and Doppler scan can be achieved [56, 57]. Accurate aligning poses a problem especially since the flow was not totally parallel to the vessel axis and alignment of the probe with respect to the jig was not perfect as well. This matters because the flow was assumed to be parallel to the vessel axis and any correction in angle measurement was referenced to the vessel axis. It also has to be noted that at around 60 degrees angle, the error of the angle measurement can lead to a high error in the flow estimation. This is because, around that angle, slight change in the angle may rapidly change the cosine function.

Measurement of the Volumetric Blood Flow

The volumetric BMF flow was measured by using Doppler probe. A typical image of the Doppler imaging system is shown by Figure 3.6. The left side shows the sagittal plane of the BMF vessel and the right side shows the mean velocity of the flow over time. The trough happened due to the rotation of the motor roller. The pump utilized two rollers to achieve pressure gradient at the two sides of the tubes in order make the fluid flow from one point to another. Hence in one rotation of the pump, two crests and two troughs are expected as can be seen from Figure 3.6

Figure 3.6 Doppler flow image: velocity profile

Simulating the pulsatile flow is understandably more difficult than the constant flow reenactment. The waveform flow is produced by using the pump through its flow cycle. It is theoretically possible to emulate the systole and diastole

flow; however, in this preliminary experiment the pump was utilized to produce constant flow instead of waveform flow. The reflected pressure waveform at the distal end was due to the change in impedance. The change creates bipolar BMF flow due to the discordance between Doppler waveform and the flow waveform. Doppler flow measured outside of the tube boundary as seen in the B-scan was due to the movement of the tube inside the agar.

Calibrating the Pump

Due to the changing of the tubes and roller adjustment, the output from the pump was expected to be slightly different from the theoretical calculation (Calculation 3.1: Equation 3.5). In order to compare the theoretical output and the actual output from the pump, a number of tests were done. The tests done for the bigger tube diameter involved motor speed up to 60 RPM only, due to the limitation of the measuring reservoir used. However, this did not affect the conclusion that can be inferred from the tests because the projected errors demonstrated a known pattern and therefore the error from other motor speeds could be interpolated or extrapolated.

The errors could be attributed to the measurement errors during the flow output calculation and the precision of the pumping timing. Nevertheless, the percentage of the error was less than 5% for almost all of the tests, except for one which was considered an outlier, and this error seemed to be lesser when the volume of the output was higher (Figure 3.7). One probable reason for the outlier was due to the human error in recording the measurement details.

However, this should be an isolated case as the rest of the points are relatively close to each other. Hence, it could safely be assumed that the actual output matched the theoretical output and therefore the theoretical calculation can be used for subsequent calculation where nominal flow output is required.

Calculation 3.1: Flow Volume

Internal Diameter (ID) of the tubing = 2.7 mm and 8 mm. and from [49]

$$\text{motor(RPM)} = \frac{\text{Flow Volume (ml / min)}}{\text{Flow Rate (ml / rev)}} \quad (3.5)$$

$$\text{Vessel area (cm}^2\text{)} = \frac{1}{4} \pi D^2 \quad (3.6)$$

$$\bar{v}(\text{cm / s}) = \frac{\text{Flow Volume (ml / min)}}{60 \frac{1}{4} \pi D^2} \quad (3.7)$$

where $\bar{v}$ is the average velocity of the flow across the vessel and D is the diameter of the vessel.

- The flow rate for ID 2.7 and ID 8 were 1.5 and 10, respectively.
- Motor speed was set to be in the range of 40 to 90 RPM for ID2.7 and 40 to 60 RPM for ID8.
- Flow volume was in the range of 60 to 135 ml/min for ID2.7 and between 400 to 600 ml/min for ID8
- The mean velocity ($\bar{v}$) was in the range of 17.47 to 39.3 cm/s for ID2.7 and 13.26 to 19.89 cm/s for ID8.

Figure 3.7 Error in actual pump flow output

3.3.3 Preliminary Results of the Volumetric Flow Measurements

In this subsection the result of the preliminary results of the Doppler ultrasound volumetric flow volume is presented. Figure 3.8 shows the experimental result for variable beam steering angle with constant flow rate (diamond-shaped points) and constant beam steering angle with variable flow rate (rectangular-shaped points).

Figure 3.8 Comparison between the flow volume measured by Doppler ultrasound and the actual output (ID: 2.7mm, Flow correction angle=60°)

As can be seen from the figure, calculated errors between theoretical and actual output are high especially for the one with constant beam steering angle. This might be due to the error in the beam steering angle because in the series 1, some of the results are better (point no 2 and 3). Meanwhile the variation in the flow rate does not seem to be significantly affecting the overall error considering that series two has relatively similar error values (15-25%). These results show the importance of the relative beam insonation position. Detailed

explanations are postulated pertinent to the results and are elaborated in the following.

Beam Steering Angle and Correction Angle

In the Doppler ultrasound system used here, the beam steering angle and the correction angle were the two variables that define the measurement angle. The beam steering angle and correction angle play important roles in the accuracy of the output. From the results obtained earlier, with small beam steering angle the error was much smaller (first three points). However, this doesn't mean that the smaller the steering angle the smaller the error, it is just that in this case the low steering angle (and the correction angle set) happened to correct the misalignment between the velocity flow and Doppler waveform.

As illustrated in Figure 3.9 the correction angle cursor could help in estimating the correction angle by comparing its position (orientation) with the actual position (orientation) of the probe and the target. It was also understood that the position of the probe with respect to the BMF vessel changed with each experiment (at least by a few degrees). This was caused by moving the probe in order to get a better image and also by changing the *Agar* (*Agar* shrinks and is decaying over time) which made fixed reference hard to be achieved.

To assist in establishing the relative position of the probe and the target, kinematics modeling was employed (Calculation 3.2; Figure 3.10). Kinematics modeling of a manipulator structure is a way to describe a manipulator position

with respect to a fixed Cartesian frame without concerning itself with the force and the moments that cause the motion [58]. The formulation of the kinematics model can be divided into two parts which are **forward kinematics** and **inverse kinematics**. The former is used to determine a general and systemic way to describe the motion of the end-effector as a function of the joint motion. Meanwhile, the latter concerns the transformation of the desired motion prescribed to the end-effector in the workspace into the corresponding joint motion [58].

Figure 3.9 Doppler system angle correction to align the orientation of the ultrasound beam and the fluid flow

It is axiomatic that the inverse kinematics was needed in the case presented here. Let a, b , and c represent an arbitrary point in space, p , where the target is located. The distance from the end-effector to the point p can then be calculated as per Equation 3.8. From here, based on the arithmetic and geometry function, the travel distance and rotational angle of each of the joint can be calculated (Equation 3.9 – 3.15). For some positions in the joint space, due to the redundancy of the DOF, more than one solution can be obtained. In

order to simplify this, two scenarios were generated, one without horizontal axis-2 movement and one with a predefined rotational axis position.

The coordinate system developed for the positioning jig, which placement in the test rig is shown in Figure 3.1, can be seen in Figure 3.10. The coordinate system was derived using the modified Denavit-Hartenberg (D-H) method [59]. D-H is a standard robot kinematics model due to its value in physical interpretation, strict definition and applicability in multiplicative structure. On the other hand, the modified D-H refers to a D-H method with a slight alteration in its derivation in order to eliminate the weakness of the original D-H method in the case of tree and closed-loop structure robots. The employment of kinematics model helped in choosing the beam steering and correction angle as well as position verification. Ultimately, the objective of the exercise was to have accurate measurement angle.

Calculation 3.2: Inverse Kinematics

Point in space, $p=(a,b,c)$

$$\text{Length } (R) = \sqrt{a^2 + b^2 + c^2} \quad (3.8)$$

$$\text{Vertical Axis } (z) = c = R \sin \alpha \quad (3.9)$$

$$\text{For: Horizontal Axis2 } (y) = 0 \quad (3.10)$$

$$\text{Rotational Axis } (w) = \beta = \tan^{-1}(b/a) \quad (3.11)$$

$$\text{Horizontal Axis1 } (x) = a/\cos \beta \quad (3.12)$$

$$\text{For: Rotational Axis } (w) = \text{Constant} \quad (3.13)$$

$$\beta = \tan^{-1}(b/a) \quad (3.14)$$

$$\text{Horizontal Axis1 } (x) = R \cos \alpha \cos \beta \quad (3.15)$$

$$\text{Horizontal Axis2 } (y) = R \cos \alpha \sin \beta \quad (3.16)$$

Figure 3.10 Coordinate system of the positioning jig

Steady Laminar Flow

The blood flow in arteries is predominantly laminar especially during rapid forward flow [41]. This is because, in large arteries such as the aortic arch, the compliance of the aortic wall contributes in limiting the turbulence, while in small arteries such as capillaries, the flow velocity is relatively low and the small diameter size makes the viscosity effect dominant. Note that the term laminar and turbulence used here are based on the fluid dynamic definition, because for medical researchers and practitioners, unsteady flow, even if it is laminar, is often called turbulent.

In this experiment, the flow was considered to be a steady flow even though waveforms were produced due to the pumping action. Due to the relatively flat waveform, a constant mean flow rate was also used. From Calculation 3.3, it was theoretically verified that the flow inside both tubes were laminar. This verification is important since the type of the flow (i.e. laminar or turbulence) will affect the Doppler measurement. It was also found that the tube length was sufficiently long for the fluid to reach steady-state flow profile. Theoretically the entrance length effect was totally nullified by sufficient length of the tube where the measurement point was set [60]. However, unsteady flow could be seen qualitatively during the tests. This unsteady flow contributed to the inaccuracy in the velocity flow measurement due to the non-uniformity of the flow profile which was the basis of the Doppler volumetric flow calculation.

One of the possible reasons for the unsteadiness is that even though the length was sufficiently long, the path was not totally straight, especially when the fluid was moving. There was no force applied to hold the tube in fixed position and hence unsteady flow was produced during the experiment (this can also be seen from the Doppler color flow image especially near the vessel's wall). The tube was slightly bent or contorted in some places and this created non-uniform cross-sectional area along the tube. The kind of change in the dimension which causes unsteady flow is well documented in many cases [61, 62, 63]. The flexibility of the silicone tube might have responsibility for this as well. Another possible source for unsteadiness was from the pumping action. However, to minimize this, sufficient tube length was used so that the flow can reach steady state condition as explained in the previous paragraph. The extent

of the unsteady flow's effect on volumetric flow calculation is difficult to estimate except with a few well developed models under limited conditions.

Calculation 3.3: Entrance Effect and Laminar Flow

Laminar flow in circular uniform tube: $2000 \leq \text{Re}_{crit} \leq 2500$ [62]

$$\text{Re} = \bar{v}D/\nu \quad (3.17)$$

$$\nu = \frac{\mu(\text{kg} / \text{ms})}{\rho(\text{kg} / \text{m}^3)} \quad (3.18)$$

$$X = 0.03D(\text{Re}) \quad (3.19)$$

where ν is the kinematic viscosity, μ is the dynamic viscosity (4.31e-3), ρ (1244) is the density of the fluid, X is the required inlet length.

- The calculated ν is $3.46 \times 10^{-6} (\text{m}^2 / \text{s})$
- The calculated Re is in the range of 136.3 to 306.7 for ID2.7 and 306.6 to 459.88 for ID8
- Minimum entrance length X is 24.84(mm) for ID2.7 and 110.03(mm)

3.3.4 Results of the Volumetric Flow Measurements

In order to reduce the error due to the inaccuracy in determining the relative position of the probe and the target, in the future, a positioning jig with automated system could be a viable solution. The envisaged automated positioning system will have a number of sensors and actuators to automatically move the probe in accordance to the movement of the target based on the feedback from the sensors. For the system's control, common control approach which is widely available (commercially) such as PID [64] can be adopted. The automated system will be able to give a good control of the position and orientation of the probe with respect to the target (i.e. blood vessel). However,

even though the position reference is accurate, the flow waveform did not really conform to the axis of the flow vessel. Hence, aside from having sensor based automated system, model estimate of the flow waveform is also needed for correct angle correction and beam steering.

Based on the inference from the previous tests that the unsteadiness was mainly caused by the tube, the tube was then manually clamped and the position of the probe with respect to the predefined target was measured more vigorously in order to improve the results. However, before that, the error in flow output measurement was estimated for different motor speeds in different correction angles. This was done in order to verify the severity of the effect of the angle measurement inaccuracy toward the flow calculation. From the result, useful information could also be extracted for analysis purpose. Figure 3.11 shows the plotted graphs of the measurement error for different set of conditions.

From the graphs it can be seen that the flow measurement error (ε) increases in both direction deviating from the correct measurement angle (α). Fortunately, ε is relatively small (<5%) as long as the error in α is less than $\sim 3^\circ$. Hence, for small error in α , it can be said that flow output measurement is within tolerable accuracy. It is also found that it is good to have smaller α (less than 60°) in order to minimize the ε caused by the error in α . However, it has to be noted that the B-scan image needs the probe to be orthogonal to the target. Therefore, compromise is needed and 60° measurement angle is considered to be optimum.

Figure 3.11 Measurement errors for different measurement angle

In this experiment, linear caliper which has resolution of 0.1 mm is used to measure the position of the probe with respect to the target. The measurement method used is triangulation method in which three points are determined and the distance for the third point is found from the correlation of the known distance of the other two points and the third point. This is done in order to improve the measurement accuracy. It is determined that there are three sources for inaccurate measurement of the α : 1) Probe placement within the holder, 2) Tissue mimicking phantom placement, 3) Vessel placement within the tissue mimicking phantom. Each of these three factors contributes 0 to 2° (absolute value) error in position measurement. The cumulative error can be as big as $\pm 6^\circ$ which in turn will give extremely high error in the volume flow calculation

since the flow calculation depends on the cosine of the angle between probe beam and the flow vector (Equation 3.3-3.4) [6]. Fortunately the occurrence of ‘extreme’ error is very small. Using Gaussian distribution (Calculation 3.4) [65], the most-likely-to-occur error is predicted. The standard deviation is calculated to be $\sigma=2$ based on the obtained experimental results. This estimation of the σ can be further improved by taking more samples. However, in our case the samples taken were sufficient to be the representative of the general sample population.

Calculation 3.4: Normal (Gaussian) Distribution

- Assuming normal distribution
- Probability density function of a normal distribution

$$f_x(x) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-\mu)^2}{2\sigma^2}} \quad -\infty < x < \infty \quad (3.20)$$

$$z = \frac{X - \mu}{\sigma} \quad (3.21)$$

- Mean (μ) is defined at 60° for -15° beam steering angle
- Standard Deviation (σ) is 2
- For 95% confidence interval, $-1.96 < z < 1.96$

Using the calculation elaborated above with beam angle of 15° , a range of error in α was determined. Subsequently, the corresponding ε with respect to a range of α for different motor speeds were experimented and plotted in Figure 3.12. From Figure 3.12 it can be inferred that the flow output error will likely be under 12%. The $\sigma = 2$ used is considered large if automatic positioning system is employed since such mechatronics system has even better accuracy. Hence, it is expected that the result can be further refined.

Figure 3.12 Errors obtained for different pump's motor speeds and flow velocities

3.4 Doppler Experiments: Reliability of the Doppler Measurement

The previous subsection has elaborated on the Doppler testing with the focus on the accuracy of the Doppler. In this subsection the testing which was focusing on the consistency of the Doppler measurement is elaborated in detail.

3.4.1 Experimental Setup

The setup was very similar to the one described in the earlier section, with the exception of the pump and the shape of the tubing used. In this experiment, the pulsatile pump from Harvard apparatus [66] was utilized (Figure 3.13). The pump was reportedly able to give pulsatile output that closely simulated the ventricular action of the heart. The ratio of the systole to diastole can be adjusted by the options provided by the pump. This also applies to the volume of ejection per-stroke. By utilizing these functions, a range of output pattern can

be produced. In this experiment, an arterial network resembling the aortic arch and its branches (brachiocephalic, left common carotid artery and left subclavian artery) were built. The Doppler sensor was positioned to measure the flow through the left common carotid artery. In the proposed application, Doppler will also be measuring the blood flow at the common carotid arteries.

Figure 3.13 Pulsatile blood pump and tubing setup

3.4.2 Methodology

The procedure in doing the experiment was also very similar to the one explained in section 3.3. In this experiment, the output of the pump was determined by varying the stroke volume and rate and by varying the output phase ratio (systole-diastole ratio). The phase ratio used was 30/70, 35/65 and 45/55. On the other hand, the flow volume was within the range of 4.2-5.6 L/min by adjusting the stroke volume and rate. In this experiment, the focus

was on the consistency on the Doppler measurement accuracy. Hence, during the sample-taking the position of the setup was unchanged, only the pump outputs were varied.

3.4.3 Results

The result obtained from the Doppler measurement and the actual flow output was recorded for each of the experiment. The discrepancy between the two outputs was calculated and the resultant error was tabulated. Figure 3.14 shows the deviation of the error from the mean error calculated.

Figure 3.14 Deviation value from the mean error

As can be seen from the figure, the Doppler measurement was relatively consistent. The maximum deviation is recorded to be within 3 percent in absolute value (standard deviation of 1.48%), even when there was a relatively wide variation in the flow output. It can be concluded that the Doppler measurement is consistent and reliable. Furthermore, the pulsatility of the flow

could also be inferred to have little or no effect on the accuracy and reliability of the Doppler measurement.

3.5 Conclusions

The Doppler ultrasound experiment shows compelling result with regard to its efficacy in blood flow measurement. The accuracy and reliability of the Doppler to produce the desired output has been verified even though it is still not perfect. It is also concluded that there is a possibility to improve the results by employing an automatic positioning system. By using the automated system, theoretically, much lower measurement error could be generated and thus it will result in lower flow quantification error.

With regard to the use of the Doppler system in the proposed application, there are a couple of issues that may give potential challenge in its implementation. The first one is the difference between the condition inside the plane/centrifuge and the condition prescribed in the *in-vitro* setting; inside the plane/centrifuge, the system will be subjected to the High-G environment. However, considering that there is plenty of mechatronic equipment inside the plane and they all are working fine in high-G condition, Doppler system is expected to be a non-exception because component-wise (mechanical-electrical system), they are essentially very similar. The second one is the movement of the pilot during the piloting (e.g. breathing, looking at the side), and this poses a problem in maintaining the contact between the probe and tissue. The problem can be minimized by using smaller ultrasound probe but this will also compromise the

ultrasound insonation of the targeted area (e.g. in case uniform insonation for flow measurement) since the scanned area will be smaller for the same processing speed. On the other hand, studies pertaining to the application of ultrasound on moving target (e.g. organs) and methods to compensate for the movement have also been conducted [67]. These studies may also be applicable in this application. However, this is outside the scope of this research and no further detail will be provided here.

Aside from the two issues explained in the previous paragraph, in using the ultrasound, the formation of the bubble inside the medium (e.g. ultrasound gel, water, etc.) has to be cautioned. Bubble in the medium may significantly affect the ultrasound measurement. However, this problem can be effectively eliminated by carefully choosing the gel with no air bubble present or by eliminating the trapped air bubble inside the gel (or other mediums) prior to the application [6, 68]. Furthermore, using an appropriate handling method bubble formation can be avoided during the application [69]. In this study, an air tight flexible case was envisioned to house the gel without any bubble. Since there is no contact between the gel and the air and there is no air trapped inside the gel from the beginning, it is hypothesized that high G will not cause any bubble formation inside the gel.

A complementary method in providing the spatio-temporal blood flow quantification during the actual application was also proposed to further improve the Doppler results. Blood flow modeling based on fluid dynamics principle was chosen and its modeling is elaborated in detail in the next chapter.

Chapter 4 Cerebral Perfusion Modelling

In Chapter 3, the results obtained from a series of tests involving a number of parameters in the Doppler ultrasound experimentation were elaborated. It was found that when the beam angle and the relative position of the probe and the target were defined with sufficient accuracy, the measurement of the blood mimicking fluid volumetric flow could be obtained with little error. The result can be further improved by introducing automated system, which will reduce the inaccuracy that may result from the manual adjustment and measurement, and flow reference model.

As previously elaborated, the brain stem which is the main part of the brain that decides the state of consciousness is critically dependent on the supply of blood to its region. Its location, which is testament to its importance, is at the centre of the brain. This is one part of the brain that is highly inaccessible by sensory system such as ultrasound. The use of other sensory systems, such as MRI, is impractical in our application. Due to this the CBF modelling is deemed as necessary. The input from the ultrasound sensor is complementing the flow modelling. It can be used as feedback parameter to fine tune the model and input parameters for the online model. More than one input from the sensor system is preferable since it gives higher accuracy with more data given.

Based on the aforementioned inference that the measurement output's accuracy can be improved by using flow modelling, blood flow modelling was subsequently attempted specifically for the cerebral vascular network. The

Doppler flow velocity was one of the input parameters along with other physiological parameters such as the dimension of the arteries, blood velocity etc. Because of the vastness of the network and the diversified conditions of each of the arteries, arterial groups were identified and a number of conditions for the model were laid out. It was also important that the model was not overly complicated to facilitate a fast simulation while maintaining the desired accuracy. Furthermore, the flow modelling was also extended to improve the accuracy of the Doppler measurement itself.

This chapter is divided into a few sections. Section 4.1 states the objective of the blood flow modelling, section 4.2 and 4.3 give a brief review on the cardiovascular system and cerebral vasculature network. Section 4.4 to section 4.8 cover the development of the blood flow model and elaborate on the simulation outcome. Finally, section 4.9 gives the conclusion to the work shown in this chapter.

4.1 The Objectives of the Modeling

Following were the objectives of the cerebral blood flow modeling,

- To define the vasculature network to be modeled and its physiological properties,
- To determine the suitable flow model which may include developing the mathematical model and defining the relation between each parameters,
- To apply appropriate simulation technique and analyze the result,

- To extend the flow model to improve Doppler measurement and analyze its efficacy,
- From the results of the relatively advanced flow modeling techniques, a less complex model to be developed for online application purposes.

4.2 Review of the Cardiovascular System

In this chapter the modelling of the blood flow is shown. It is imperative that some knowledge with regard to the cardiovascular system and properties of the blood flow to be elucidated prior to the elaboration of the modelling for proper initiation. In this subsection the aforementioned issues are broached briefly.

The cardiovascular system basically consists of heart, blood vessels and blood [24]. Heart pumps the blood to and from the whole body through a complex network of blood vessels and from the circulated blood the body gets its supply of oxygen and food and also get rid of unwanted substances. With regard to the blood circulation, there are two pathways involved which are pulmonary circulation and systemic circulation (Figure 4.1). The pulmonary circulation sends and receives blood from the lungs where the exchange between oxygen and carbon dioxide takes place. On the other hand systemic circulation supplies the oxygenated blood to whole body.

The brain requires about 15% of total cardiac output despite of its relatively small size (about 2% of total body weight). In other words, 50-54 ml of blood/minute is required for every 100 grams of brain tissue [25]. There are mainly

two paths in which the blood is delivered to the brain; these two paths are the Common Carotid Artery (CCA) and the Vertebral Artery (VA). CCA is responsible for about $\frac{2}{3}$ of the total blood flow to the brain while VA takes account for the rest of the required CBF [10]. The CCA itself is bifurcated into Internal Carotid Artery (ICA) and External Carotid Artery (ECA). The ICA provides blood flow to the brain and the ECA to the face.

Figure 4.1 Systemic and pulmonary circulations (adopted from [70])

Blood supply to the whole body is discharged by the heart's left ventricle periodically. The amount of the blood discharged for each contraction (heart beat) is referred as *Stroke Volume* [24]. Human heart beat and stroke volume are not constant over time. They are affected by numerous factors. Similarly the blood pressure also varies over the time due to a number of parameters such as blood viscosity, change in the stroke volume (e.g. due to exercise), etc.

In order to accommodate the changes in the blood pressure, blood supply demand, etc. the body has its own compensatory mechanism (homeostasis) [25]. Through such mechanism the body (heart) may beats faster or slower, may increase the stroke volume, may dilate or constrict the arteries in order to stabilize the pressure and to satisfy the blood supply demand.

Blood vessels can be divided into arteries, capillaries and veins and depending on their diameter, they can be further classified into several groups as shown by Figure 4.2. The size of the vessel has good influence to the flow of the blood and is extremely important parameter in modelling of the blood flow. In order to simplify the classification, the arterial groups can be arranged into a few networks. The elastic arteries and muscular arteries belong to the Macrovascular Network. It is patient specific and it is possible to reconstruct them from the clinical image taken. Smaller muscular arteries and arterioles (typically in the range of 10 to 500 μm) belong to the Mesovascular Network and lastly capillary bed which belongs to the Microvascular Network [71].

Figure 4.2 Grouping of blood vessel based on their diameters (adopted from [24])

Last but not least, blood is ‘A mixture of cellular components suspended in a fluid called plasma [24]’. The major cellular components in the blood make up are erythrocytes, leukocytes and platelets. These components determine the viscosity of the blood, a major parameter that significantly affects the flow.

When the coefficient of viscosity of a fluid is constant for all shear rates, the fluid is a Newtonian fluid. Blood viscosity is not constant over time. This is especially true in microcirculation where the mechanical behavior of the blood is dominated by the viscosity. However, in major arteries where the size of the cell components are small compared to the vessel diameter and the shear rates are high, blood can be considered as a Newtonian fluid [61]. Thus, in general blood is a non-Newtonian fluid. However, if only major arteries are modeled, blood can be taken as a Newtonian fluid. This will also simplify the calculation because blood is one of the fluids whose flow is highly difficult to be modeled if its Non-Newtonian property is taken into account [8, 10, 11, 60, 61, 72].

4.3 Physiological Properties of the Cerebral Vasculature Network

There are thousands of arteries in human body with different geometry and mechanical properties. Hence, it is imperative to divide them into groups so as to facilitate the modeling. Fortunately, arteries with similar size and geometry typically have similar properties as well, therefore expediting the process of categorizing them [24, 52]. Here in this project, only the major arteries (with diameter of 0.5 mm and above) were modeled using the CFD while the arterioles and capillaries were modeled as a lumped system.

Figure 4.3 shows the major cerebral arteries which will be the main components in the blood flow modeling. The figure depicts the aortic arch and major arteries bifurcated from it, where the blood is pumped by the heart to the whole body. The Doppler will measure the flow property, in this case the velocity, at one discrete point in the common carotid artery. The model built in this research was catering for the normal arterial network as shown in the figure with parameters which account for the majority of the population. However, it is possible to alter some parts of the model in order to cater for a slightly more diversified arterial network.

Figure 4.3 Major arteries of cerebral vasculature [73]

The physical properties of the major arteries in the cerebral arterial system are enumerated in Table 4.1. Some longer arteries are segmented, and the length of each segment is defined based on the ratio developed by [61]. This was done to facilitate the mathematical computation of the model. The ratio is given by,

$$\frac{L}{d} \approx 25 \pm 5 \quad (4.1)$$

where L is the length of the vessel and d is the vessel diameter. For the geometry, the length, radius, and the thickness of the arterial wall are the main concern.

Table 4.1 Physiological properties of the Macro-vascular Network of the cerebral arterial system (reproduced with some averaging from) [61, 71, 74]

No	Arterial segment	Length (mm),	Initial radius (mm)	Thickness (mm)	Elastic modulus
1	Ascending Aortic	40	14.0	1.65	0.4
	Aortic Arch I	20	12.2	1.25	0.4
	Brachio-cephalic	35	5.5	0.8	0.4
	Aortic Arch II	40	11.7	1.15	0.4
2	Right Common Carotid Artery	180	2.5	0.65	0.4
3	Right Subclavian	35	4.2	0.7	0.4
4	Left Common Carotid Artery	210	2.5	0.65	0.4
5	Left Subclavian	35	4.2	0.7	0.4
6	Right Internal Carotid	200	3.5	0.5	0.8
7	Left Internal Carotid	200	3.5	0.5	0.8
8	Right Vertebral	150	1.35	0.35	0.8
9	Left Vertebral	150	1.35	0.35	0.8
10	Right External Carotid Artery	180* (50)	1.5	0.4	0.8
11	Left External Carotid Artery	180* (50)	1.5	0.4	0.8

**Partially modeled. The partial length used is shown in the brackets.*

Each person has slightly different arterial properties. Hence, the data tabulated in Table 4.1 are only showing the mean value representative of the general population obtained from a few sources. These data were used to model the arterial network in this study. Table 4.2 lists the blood parameters which are used in this model. The parameters are obtained from a few of sources [9, 10, 11]. In case the parameter is in a certain range, an average value or a most commonly used value within that range was chosen.

Table 4.2 Blood modeling parameters

Parameters	Value	Remark
Blood density	1030-1070 (kg/m^3)	1060 was used
Coefficient of thermal conductivity	0.492 (W/mK)	
Hematocrit	45 %	Considered as constant
Blood viscosity	0.003-0.004 ($Pa.s$)	0.0035 was used. In major arteries blood behaves as a Newtonian fluid
Plasma viscosity	0.00135 ($Pa.s$)	
Temperature	298 (K)	Room temperature (25°C)
Gravity	1G = 9.81 (m/s^2)	

4.4 Cerebral Blood Flow (CBF) Modeling

Blood flow modelling has been studied in details for many years [10, 11, 12, 13, 14, 71, 72, 75]. Various modelling parameters either standing alone or in combination with each other have been presented in numerous publications.

Most of them are intended to be used in specific parts of the vasculature under specific conditions or assumptions. It is undeniably difficult to have a model that can cater for a wide range of predefined conditions. Even so, some have tried to find a general model that can be used as a representative for a good range of vasculature and its parameters variation, although slight modification is still needed. Arguably, it is close to impossible to find a universal model that can account for the multitude of parameters variation of a complex system of human physiology within the limit of the online calculation efficiency that is normally required. One may find oneself in continuous quest to find the optimum model within limited resources given the certain objectives that need to be satisfied.

The challenge in this research was to have a sufficiently accurate model that is able to quantify the blood volume that goes to the cerebral vasculature network while keeping the model less complex. As has been elaborated in the preceding chapter (Chapter 2), brain stem is responsible for deciding the conscious/unconscious state of the brain. Hence, it was desired that the flow volume in the brain and especially those flowing into the brain stem could be calculated well.

In terms of the model used, there are two types of blood flow modelling. The first one is the lumped system modelling and the second one is the detailed modelling of each part of the vasculature network. While the latter has the advantage in terms of the accuracy due to its rigorous modelling, the former one is more applicable due to its reduced complexity and thus lower computational power required [61, 76]. For the purpose as per the objectives stated in the

chapter one, it is imperative to have a model which is able to spatio-temporally quantifying the blood volume that goes into brain with high accuracy. However, monitoring or deducing the volume online with complex model put strain on the system. In order to ensure reliability, system with better computational power has to be used and this may mean that the system's compactness has to be compromised which poses a problem due to the space constraint of the application. Hence, to ensure its efficiency, it is of paramount importance that the model developed can optimize the output while maintaining relatively simple constitution.

4.5 Computational Fluid Dynamics (CFD) Modeling

The model developed in this project was required to be able to give flow rates and possibly pressure in the major arteries and predict values in some discrete points in the smaller arteries in the cerebral neural system. The model should also be extended to be coupled with a short-term blood flow regulation mechanism. In doing the modelling, CFD software, which in this case was *ANSYS-Fluent*, was utilized. *ANSYS-Fluent* [77] was chosen because of its broad physical modeling capabilities that come with the flexibility to implement extensive customization based on user-defined function and its Finite Volume Method basis which has advantages especially together with an unstructured mesh. The shape of the human vasculature network is non-conformal and therefore an unstructured mesh is the most suitable mesh to be applied. The shape and dimension of the human artery differs from person to person. Abnormalities are commonly found with some arteries are occluded or jointed

in unusual manner [75]. These anomalies account for about 5% of the population and for the purpose of this project were treated as non-existent.

There were a few stages in which the simulation was done. The first was the modelling of the artery to be simulated. The model's specifications were based on the specifications listed in table 4.1 and table 4.2. The modelling was done in either *ANSYS Design Modeler* or by utilizing other CAD software after which the model was imported into the *ANSYS Design Modeler* (Figure 4.4). In this case *Creo Parametric* CAD software was utilized because compared to the *ANSYS-design modeler*, *Creo Parametric* is more versatile in creating complex shape and has many enhanced feature that is superior compared to other CAD software. Once the model was generated by the *Creo Parametric*, it was then imported to the *ANSYS* domain. It has to be noted that since two of them are different modeling software, some incongruity may appear afterwards due to the import. For example, the overlapping portion of the model which may not be a problem in *Creo Parametric* will be the cause of inaccuracy in the *ANSYS*. Extreme caution has to be taken in developing the model to also account for these kinds of differences in the software used.

In the developed 3D model, arteries were taken to have tubular shape and to be axisymmetric. The vessels that exist in both sides of the body were also assumed to have similar geometrical shape, albeit some variations still existed and they were in mirror image of each other.

The major arteries such as the aorta, brachial and the subclavian were assumed to have continuous taper with a constant exponential rate which was governed by the following equation [61],

$$r(x) = r_{pr} \exp(kx) \quad (4.2)$$

where r_{pr} is the mean proximal radius, $k = \log(r_{dis} / r_{pr}) / L$ is the tapering factor, r_{dis} is the mean distal radius, L is the length of the vessel, and x is the location along the artery.

Figure 4.4 *Creo Parametric* model of cerebral vasculature (left) and *ANSYS Design Modeler* model of cerebral vasculature (right) which were developed for the blood flow modeling and simulation

For the carotid arteries, linear tapering was adopted based to the assumed little difference between exponential tapering and linear due to the much smaller size of their diameter. As explained earlier, every individual has slightly different arterial size and shape, hence a slight different in the model from the assumed mean value was tolerable and the model was assumed to be still within the accurate range.

The following stage was the meshing of the model. Unstructured mesh was generated for the model. It was based on the computer controlled parameters. Considering the shape of the model, unstructured mesh was the most suitable type of the mesh. However, note that in terms of the grid size, it is imperative to apply different grid sizes (Figure 4.5) in order to eliminate the incorrect outcome that may be resulted from choosing a certain grid size. The final grid size was chosen once the difference in the outcomes resulting from using different grid size is no longer apparent, which is usually achieved when the grid size is sufficiently small (the number of nodes and elements are large).

The third stage was to input the relevant parameters and also user-defined function into the system before the simulation to be carried out. In this stage, parameters were varied for the analysis. The type of the flow, the energy equation, boundary conditions and a number of other things were available to be chosen for the purpose of the analysis. It is important that several assumptions with regard to the flow to be properly defined before inputting these parameters as it has enormous effect on the outcome of the simulation. Of course one may choose to change the assumptions and simulate them for

subsequent comparison. In all of the simulations, the arterial wall was assumed to be impermeable. Hence the conservation of mass was valid. The flow of the blood toward the cells in the arterial wall was neglected because the amount is insignificant compared to the total flow of the blood inside the vessel [10, 61]. An example of the parameters chosen during this stage such as: no heat exchange energy, the flow was laminar, the gravity is 9.81 m/s^2 , grid size – ‘fine’ with min size of $8\text{e-}4$, pulsatile flow, and the convergence criteria for the continuity equation is $1\text{e-}05$. Finer grid and better convergence criteria can be used. However, based on the earlier simulation results (Chapter 3) and the experiment, it was shown that the parameters used in the simulation were sufficient to achieve the desired objective.

Figure 4.5 Model mesh generated by ANSYS

The fourth or the last stage was analysing the simulation result. In this stage, the velocity profile, pressure, density could be visualized and plotted. An example of the velocity pattern at a particular flow outlet generated by the CFD simulation is shown by Figure 4.6. The simulated simple flow had a uniform and constant inlet flow velocity perpendicular to the inlet surface, incompressible, laminar and without any thermal exchange. The color code shown in Figure 4.6 represents the magnitude of the outlet velocity with blue color represents the lowest velocity and the red color represents the highest velocity. Depending on the objectives, different parameters would be examined. This part is further expounded in section 4.7.

Figure 4.6 An example of the flow profile pattern at a partial arterial outlet generated by the CFD simulation. Different flow velocities generated across the cross-sectional area of the artery

4.5.1 Sensitivity Analysis of the CFD Model

In this part of the study, the sensitivity of the CFD model was assessed by varying partially the dimension and the shape of the artery/arterial network and varying the dynamic properties of the fluid (especially blood density and viscosity). The objective of this exercise was to re-affirm the capability of the CFD to give the hypothesized outcome when certain parameters are changed. In its final objective, the CFD model was also expected to be able to be customized for individuals; hence, this variation of the physiological parameters study would further bolster the confidence in using CFD model to improve the cerebral blood flow quantification.

The simulations were done in sets. In each set only one parameter was varied while keeping the other parameters unchanged. This was done in order to be able to analyse the effect of one particular parameter at a time. To vary more than one parameter at the same time will have the potential to delude the observation although there is also a possibility that combination of a number of parameters will give rise to certain effect. However, in this case, it was assumed that supposition principle applies and therefore the combined effect of certain parameters deemed to be insignificant compared to the accrual effects of the individual parameters.

In terms of the variation in the arterial size, the dimensions were varied within 10% of its mean average value. It was found that the changes in the dimension changed the total output of the flow. The change was proportional to the change

in size which was in line with the Poiseuille's Law [10]. As for the shape, its variation was not clearly quantifiable. However, qualitatively it was a slight change in the delineation such as the angle of curve and the bending. In term of the volume, it was done so that it is safe to enunciate that the changes due to the outline have miniscule effect to the changes in the total volume of the arterial portion. It was still unclear whether the effect of the change in shape also affected the total flow volume since the change in shape inadvertently also created a slight change in the cross sectional area or arterial volume even if discretion had been put in place to ensure that the changes in the volume was miniscule. Hitherto, the change in the output due to the change in shape was not totally conclusive yet as the relationship between the interacting parameters was not established clearly or in this case quantified rigorously.

For the viscosity, there were small changes (less than 3%) in the end result. It can be concluded that the change in viscosity (within 10% of the average value) was too small to have a large effect to the whole flow. This may be explained by the radius of the artery being simulated. Only major arteries were attempted in the simulation. In major arteries inertia dominates the blood flow, unlike in smaller arteries where blood flow is dominated by the viscosity. If the flow is described by the Navier-Stokes equation (for incompressible flow: Equation 4.3), the second term on the right side of the equation (which represents the viscosity term) is negligible.

In a nutshell, this study had served its purpose. The simulated model generated different flow profiles for a slight change in the parameters such as model

dimension, shape, the dynamics of the flow, governing equations, physiological parameters. The variation of the outcome was influenced by the variation of the parameters in the hypothesized manner which concludes the reliability of the model. The exercise also shows that the model can be well customized for individual physiological parameters.

Before the analysis of the simulation result, it was considered necessary to validate the model and CFD. Hence, an analytic solution was developed to assess one example of the simulation result, which is elaborated in the following section.

4.6 Analytic Solution to CBF Modelling

The use of the CFD simulation package greatly aids the calculation of the flow properties of interest. It is of paramount importance that the nature of the simulation to be properly understood and an amount of verification to be attempted in order to substantiate the result of the CFD analysis. In this subsection an analytic solution based on the NS equation for one case of the simulation is presented for this purpose.

4.6.1 Governing Equations

CFD software that was used to develop the computational model was built based upon the principle of the fluid dynamics. Substantiating the results given by the software requires an analytical model to be built upon the same principle.

A nearly unidirectional flow derived from the Navier-Stokes (NS) equation (Equation 4.3) for the cylindrical coordinates system was adopted as the basic model for the analytical approach. This model was chosen due to its relative simplicity compared to the other models with more directions and/or dimensions (e.g. 3D model) which is necessary in order to obtain the result analytically. A simplified model such as the one which is elaborated in this section has also been used extensively and been proven to be able to give highly accurate flow properties in its application. It can also be further developed to a more complex model to suit other objectives [10, 61, 62]. Following are the governing equations used for the derivation of the model. They consist of the NS equation for the cylindrical system (equation 4.4-4.6) and the equation for the conservation of mass (equation 4.7). Equations 4.4-4.6 are the elaborated forms of equation 4.3 for cylindrical coordinate system.

- NS Equation

$$\rho \left[\frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \bullet \nabla \mathbf{v} \right] = -\nabla p + \mu \nabla^2 \mathbf{v} + \mathbf{f} \quad (4.3)$$

- NS Equation for cylindrical coordinate system

r component:

$$\rho \left[\frac{\partial v_r}{\partial t} + v_r \frac{\partial v_r}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_r}{\partial \theta} - \frac{v_\theta^2}{r} + v_z \frac{\partial v_r}{\partial z} \right] = \rho g_r - \frac{\partial P}{\partial r} + \mu \left[\frac{\partial}{\partial r} \left(\frac{1}{r} \frac{\partial}{\partial r} (r v_r) \right) + \frac{1}{r^2} \frac{\partial^2 v_r}{\partial \theta^2} - \frac{2}{r^2} \frac{\partial v_\theta}{\partial \theta} + \frac{\partial^2 v_r}{\partial z^2} \right] \quad (4.4)$$

θ component:

$$\rho \left[\frac{\partial v_\theta}{\partial t} + v_r \frac{\partial v_\theta}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_\theta}{\partial \theta} + \frac{v_r v_\theta}{r} + v_z \frac{\partial v_\theta}{\partial z} \right] = \rho g_\theta - \frac{1}{r} \frac{\partial P}{\partial \theta} + \mu \left[\frac{\partial}{\partial r} \left(\frac{1}{r} \frac{\partial}{\partial r} (r v_\theta) \right) + \frac{1}{r^2} \frac{\partial^2 v_\theta}{\partial \theta^2} + \frac{2}{r^2} \frac{\partial v_r}{\partial \theta} + \frac{\partial^2 v_\theta}{\partial z^2} \right] \quad (4.5)$$

z component:

$$\rho \left[\frac{\partial v_z}{\partial t} + v_r \frac{\partial v_z}{\partial r} + \frac{v_\theta}{r} \frac{\partial v_z}{\partial \theta} + v_z \frac{\partial v_z}{\partial z} \right] = \rho g_z - \frac{\partial P}{\partial z} + \mu \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v_z}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2 v_z}{\partial \theta^2} + \frac{\partial^2 v_z}{\partial z^2} \right] \quad (4.6)$$

- Conservation of Mass Equation

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{V}) = 0 \quad (4.7)$$

Nomenclature 4.1

$[A(z, t) = \pi r(z, t)^2](m^2)$	Luminal cross-sectional area
$[v(z, r, \theta, t)](m/s)$	Velocity vector in cylindrical coordinate where z is the longitudinal coordinates and r and θ are the polar coordinates
$\rho(kg/m^3)$	Density of the fluid (blood)
$[P(z, r, \theta, t)](N/m^2)$	Pressure in the fluid
$[r(z, t)](m)$	Radius distance in the vessel
$[g(z, t)](N/m^2)$	Body accelerations
$t(s)$	Time component

In order to develop the model based on the NS equation for the flow mentioned above, several assumptions were established and enumerated in the following (some have been listed in section 4.4. However, for the sake of completeness, they are again mentioned in the following list),

- The major arteries such as the aorta, brachial and the subclavian have an approximated continuous taper with a constant exponential rate which is governed by the equation 4.2,
- Incompressible (density of the blood is taken as a constant),

- c) The artery wall is impermeable. Hence the conservation of the mass is valid.
The flow of the blood toward the cells in the arterial wall is neglected because the amount is insignificant compared to the total flow of the blood inside the vessel [10],
- d) Tubular system and axisymmetric. Furthermore, the vessels that exist in both sides of the body also have the same geometrical shape and dimension albeit in mirror image of each other,
- e) No thermochemical, no heat transfer and no electromagnetic effect,
- f) For major arteries, the blood has the characteristics of the Newtonian fluid.

4.6.2 Derivation of the Constitutive Equation for the Blood Flow

The constitutive equations derivation elaborated in this subsection was done for the blood flow in the brachiocephalic artery. This artery is the result of the bifurcation from the ascending aorta and it is the closest bifurcation to the left ventricle where the blood is ejected from the heart to the whole body. In average the heart pumps 5L of blood every minute [61]. Considering that the average heartbeats of human is 70-80 beats per minute, this roughly translates to about 60 to 70 ml/beat or 80ml/s (flow volume = Q). From Table 4.1, the cross sectional area (A) of the ascending aorta can be calculated. Dividing the Q with A , the mean flow velocity is estimated to be 0.13m/s. This result is corroborated by [57] in which the mean flow velocity was recorded to be 0.11 m/s (at rest) and arguably higher during maximum exercise. For the sake of simplicity, a value of 0.15m/s was used to represent the mean flow velocity in the ascending aorta in this exercise. Similarly, this value was also used as the input parameters in the CFD simulation.

The flow from the ascending aorta is then bifurcated into the aortic arch and the brachiocephalic artery. In order to estimate the mean inlet velocity to the brachiocephalic artery, conservation of mass equation was used. Based on the equation, the relationship between the parent vessel and daughter vessels at the bifurcation can be represented as,

$$\rho_p Q_p = \rho_{d1} Q_{d1} + \rho_{d2} Q_{d2} \quad (4.8)$$

Figure 4.7 shows the representative figure of a typical bifurcation where the subscript p denotes ‘parent’ and d_1 and d_2 denote ‘daughter 1’ and ‘daughter 2’ respectively. Based on the measurement value obtained in [57], the flow volume that goes to the brachiocephalic artery is about 17-20% from the total flow volume of the ascending aorta and this value may have larger range depending on each individual. Alternatively, if the velocity is assumed to be uniform for both daughter vessels, based on the area calculation (using the parameters described in Table 4.1) the percentage of blood flow that goes toward the brachiocephalic is about 16.9%, which is not much different to the measured value. Henceforth, a mean value of 18% was chosen to be used, and coupled with the assumption that blood is incompressible, equation 4.8 can be simplified to,

$$0.18(u_p A_p) = u_{d1} A_{d1} \quad (4.9)$$

The cross sectional area of the parent and daughter vessel was known (Table 4.1). By inserting the value of the flow velocity of the parent vessel calculated in the beginning of this subsection, the mean flow velocity at the inlet of the brachiocephalic artery was calculated to be $\approx 17.5\text{cm/s}$.

Figure 4.7 Geometry of an arterial bifurcation showing the parent vessel and the two daughter vessels

In order to determine whether the flow could be modelled as a fully developed flow or not, entrance effect had to be calculated. In the relation to the entrance effect, the distance needed for the flow to reach a fully developed state is called entrance length (for cylindrical system) and can be estimated from the following formula [62]:

$$\frac{L_v}{R} = 1.18 + 0.112 \text{ Re}, \quad \text{Re} = \frac{2UR}{\nu} \quad (4.10)$$

where L_v Is the distance needed to reach within 1% of the fully developed velocity at the centreline or mid-plane U is the mean velocity, R is the radius of the artery and ν is the kinematic viscosity. From equation 4.10, it was found that $\text{Re} \approx 432.5$ and $L_v \approx 274.6 \text{ mm}$.

From the above calculation, it could be inferred that the length of the brachiocephalic artery is not long enough to have a fully developed flow and the $\text{Re} \gg 1$ indicates that the inertia effect is dominant in the flow. The Re obtained was also less than 2.1×10^3 , a value which is commonly used to

estimate as to when the flow transition from the laminar to turbulent occurs in pipe flow setting. Henceforth, it was arguably safe to assume that the flow inside the brachiocephalic artery is laminar. It has to be noted though that geometric non-idealities, and flow instabilities also have effect on the flow property. However, at the point of time, these factors were taken as relatively insignificant.

Figure 4.8 shows an approximate flow profile at $z < L_v$ (the outline is an illustrative of an arterial wall with an exaggerated taper). No-slip condition at the wall has started to be imposed and causes high shear rates at the flow near the wall resulting in $\frac{\partial v_z}{\partial r} \neq 0$. However this does not happen across the entire cross-sectional area of the tube but confined in small region of thickness $\delta(z)$ close to the wall or otherwise known as *wall boundary layer* [78]. In the central part of the tube, the velocity profile is relatively flat and can be represented by $v_z = u(z)$. The flow inside the arterial network is time dependent due to the pulsatile nature of the heartbeat. The effect of the pulsatile flow is especially prominent in the major arterial network. Fortunately, the viscoelastic properties of the arterial wall reduce the pulsatile effect and in this derivation the flow is assumed to be time independent and therefore all terms in the equation is independent of t .

Figure 4.8 Developing flow in a channel

Due to the high Re , the viscous effect is considered negligible especially for the flow in the core region. However this is not the case in the flow near the wall. Here, the effect of the viscous force is still apparent and cannot be totally neglected. Another important property arises from the small region $\delta(z)$ is that the v_r is much smaller than v_z . In the core region, the v_r is negligible. Hence it can be concluded that the terms in the z components are much more dominant compared to the terms in r components of the equation. Due to this, it is also safe to assume that the pressure gradient P is a function of z only.

$$\left| \frac{\partial P}{\partial z} \right| \gg \left| \frac{\partial P}{\partial r} \right| \approx P = P(z) \quad (4.11)$$

The NS equation given in (equation 4.4-4.6) can then be rewritten as:

Core region:

$$v_z \frac{\partial v_z}{\partial z} = -\frac{1}{\rho} \frac{\partial P}{\partial z} + g_z \quad (4.12)$$

Since $v_z = u(z)$,

$$u(z) \frac{\partial u(z)}{\partial z} = -\frac{1}{\rho} \frac{\partial P}{\partial z} + g_z \quad (4.13)$$

Near wall region:

The flow in the near wall region can be represented by,

$$v_r \frac{\partial v_z}{\partial r} + v_z \frac{\partial v_z}{\partial z} = g_z - \frac{1}{\rho} \frac{\partial P}{\partial z} + \frac{\mu}{\rho r} \frac{\partial}{\partial r} \left(r \frac{\partial v_z}{\partial r} \right) \quad (4.14)$$

Using the continuity equation (equation 4.7), which for cylindrical coordinates can be represented by,

$$\frac{\partial \rho}{\partial t} + \frac{1}{r} \frac{\partial (r \rho v_r)}{\partial r} + \frac{1}{r} \frac{\partial \rho v_\theta}{\partial \theta} + \frac{\partial \rho v_z}{\partial z} = 0 \quad (4.15)$$

Equation 4.15 can be further simplified based on the no-slip condition and equation 4.11 to,

$$v_r(r, z) = -\frac{1}{r} \int_0^R r \frac{\partial v_z}{\partial z} dr \quad (4.16)$$

Substituting equation 4.13 and 4.16 into equation 4.14 and multiplying both sides with r yields,

$$\left(-\int_0^R r \frac{\partial v_z}{\partial r} dr \right) \frac{\partial v_z}{\partial r} + r v_z \frac{\partial v_z}{\partial z} = r u(z) \frac{\partial u(z)}{\partial z} + \frac{\mu}{\rho} \frac{\partial}{\partial r} \left(r \frac{\partial v_z}{\partial r} \right) \quad (4.17)$$

4.6.3 Solving the Derived Equation

In order to use equation 4.17, appropriate form of the velocity profile has to be assumed. It is known that the fully developed velocity profile for laminar flow in pipe is (full derivation of the equation can be found in books such as [61, 62]):

$$v_z(r) = u_{\max} \left[1 - \left(\frac{r}{R} \right)^2 \right] \quad (4.18)$$

Using equation 4.18, a velocity profile function can be approximated and one of the possible velocity equations that can evolve into it is:

$$v_z(h, z) = u(z) \left[1 - \left(\frac{h}{\delta(z)} \right)^2 \right] \quad (4.19)$$

Given the boundary condition of,

$$\begin{aligned} v_z(r_0, z) &= u(z), & \delta(0) &= 0, & v_z(r_0, L_v) &= u_{\max}, \\ \delta(L_v) &= R, & 0 \leq h &\leq \delta(z) \end{aligned}$$

Based on the conservation of the mass, the flow influx is constant throughout the channel. In relation to the channel radius and mean flow velocity, their constitutive relation can be depicted by,

$$Q(z) = \pi r^2 U(z) \quad (4.20)$$

where $U(z)$ denotes the local mean velocity, which can be calculated from the following equation,

$$U(z) = \frac{2}{R^2} \int_0^R v_z r dr \quad (4.21)$$

At the entrance the thickness of the boundary layer is equal to 0 and as the flow evolves at the end of the entrance length, the thickness of the boundary layer is practically the radius of the channel. Assuming the elliptical shape, the thickness of the boundary layer can be approximated by the following expression [78],

$$\frac{\delta}{R} \sim \left(\frac{vz}{R^2 U} \right)^{0.5} = \left(\frac{z}{R \text{Re}} \right)^{0.5} \quad (4.22)$$

As the length of the channel $L \ll L_v$, the resulting boundary layer thickness is $\delta(z) \ll 1$ (based on the estimated layer thickness through eq. 4.22). As shown by Figure 4.9, the total flow volume can be computed from the flow volume in the core region and the flow volume near the wall. The $R-r$ is a general term used here to describe the thickness of the boundary layer. As the channel is tapered the R and r are different depending on the z . Therefore, for the sake of clarity R_z and r_z are used to represent the R and r respectively at a specified location z .

Figure 4.9 Total flow volume at distance z

Utilizing linearized approximation for the velocity near the wall and the near wall flow area, $u(z)$ can be calculated by,

$$Q(z) = Q \quad \Rightarrow \quad Q_0 = Q_{core} + Q_{wall} \quad (4.23)$$

Inserting the appropriate function,

$$\pi R_0^2 U_0 = \pi r_z^2 u(z) + 2\pi \left(\frac{R_z + r_z}{2} \right) \delta(z) \frac{1}{2} u(z) \quad (4.24)$$

Eliminating π and substituting $\delta(z)$ results in,

$$R_0^2 U_0 = r_z^2 u(z) + \frac{1}{2} u(z) (R_z + r_z) (R_z - r_z) \quad (4.25)$$

After simplification equation 4.25 can be written as,

$$2U_0 \frac{R_0^2}{(R_z^2 + r_z^2)} = u(z) \quad (4.26)$$

Substituting in equation 4.26 to equation 4.19 for the velocity profile function gives,

$$v_z(h, z) = 2U_0 \frac{R_0^2}{(R_z^2 + r_z^2)} \left[1 - \left(\frac{h}{(R_z - r_z)} \right)^2 \right] \quad (4.27)$$

4.6.4 Comparison of Analytic and Numerical Solution

The analytical and numerical solutions were compared by arbitrarily taking a sample, at $z = 10$ mm from the brachiocephalic artery inlet, in x-y plane that cut across the centerline of the artery. Figure 4.10 shows the comparison between the two outputs at the said predefined location. As can be seen from the figure, both solutions resemble each other in terms of the quantitative and qualitative measures. Admittedly, there are disparities between the two of them especially in the near wall boundary layer which can be attributed mainly to a number of generalizations and assumptions made in the development of the analytical solution. However, it can be concluded that the analytic solution was able to verify the numerical solution and to provide the sought after substantiation to proceed with the numerical solution, for this particular study.

Figure 4.10 Analytic and Numerical solution comparison at $z = 10$

4.7 CFD Model of Arterial Network under G-Loading

The major arterial network that is responsible for the cerebral perfusion was developed and was subsequently simulated under different G-Loading, which is shown in this subsection. Subsequently, the work expounded here was also integrated with the G-LOC predictive model, the development of which will be explained in Chapter 5. The integration created a hybrid model which is the fruition of one of the research objectives: to build a model able to predict G-LOC based on the cerebral perfusion rate.

4.7.1 Objective and Methodology

The main objective in this exercise was to find out the correlation between the cardiac output (CO) and the blood flow volume that goes through the carotid artery (left and right) which the Doppler will measure or in other words, to

determine the CO based on the Doppler input through the CFD modeling. The main reason for this is that the CO is the drive input to the G-LOC predictive model. By knowing the real time CO (based on the Doppler and CFD), the G-LOC predictive model is getting a real time feedback and can be tuned (this will be explained further in Chapter 5).

As has been stated earlier in the previous subsection, each individual has slightly different size and shape of the arterial network. A model representative of the general population based on the mean data presented in Table 4.1 was used here. The corresponding model was built in *Creo Parametric* and subsequently exported to the *ANSYS* where the CFD simulation was performed. The steps done was similar to the one explained in section 4.5.

From different input parameters and boundary conditions for particular simulation, different flow output and distribution are generated. Figure 4.11 shows an example of pressure variation along the arterial network generated by the CFD and Figure 4.12 shows the velocity vector at particular pressure outlets. In these two figures, the color code red represents the highest value obtained and the color code blue represents the lowest value obtained.

The velocity distribution at each outlet of interest can be obtained from the graphs generated by the CFD. These quantifications were subsequently exported to *Matlab*, in which a surface fitting can be generated. Polynomial surface fitting were chosen for the set of data obtained from CFD with regard to the output distribution for certain input parameters. Hence, there will be a series

of polynomial function generated for different set of input parameters. Due to the limited numbers of the original data collected from the CFD simulations, interpolation based on the available polynomial fitting was also integrated in the formulation.

Figure 4.11 An example of pressure variation along the arterial network

Figure 4.13 shows an example of the polynomial surface fitting generated by *Matlab*. In this particular instance, there are two parameters in the horizontal plane, namely b and c , which represent the gravity loading and the normalized cardiac output respectively. Meanwhile, on the vertical axis, the parameter v represents the percentage of cerebral blood flow that goes through the arteries of interest. The profile generated here was obtained based on CFD data for a particular percentage of vasoconstriction/dilation.

Figure 4.12 Velocity vector at different outlets. Inset shows the velocity vector in the arterial branching

Figure 4.13 Polynomial surface fitting of three interdependent parameters: percentage of cerebral blood flow (v), gravity loading (b) and normalized cardiac output (c), generated in *Matlab* based on the CFD simulation data

These series of the formulations obtained from the CFD and subsequent curve-fitting were integrated into the G-LOC predictive model developed (which is explained in Chapter 5). The resulting hybrid model is then used to predict the G-LOC occurrence for various scenarios presented. The CFD simulation is not only essential for the aforementioned purpose, it was also found that combining CFD with Doppler measurement can improve the accuracy of the blood flow quantification as presented in the following section.

4.8 CFD Model for Improving the Doppler Measurement

As was explained in Chapter 3, the accuracy of the Doppler technique depends mainly on the precise positioning of the ultrasound source with respect to the target blood vessel, measurement details of the vessel size, and the presence of interfering noises (e.g. artefact, bubbles). When performing the experiments, the inaccuracies from these factors were minimized to optimize the Doppler measurement. However, as shown by the output given in the chapter, the error was still present and it was desired that the error could be reduced further. The research work expounded here, shows the attempt to improve the accuracy of the Doppler measurement due to the imprecise positioning of the probe by combining it with the CFD modelling based on Navier-Stokes equation.

4.8.1 Development of the CFD Model for the Experimental Setup

During the experiment, the insonation area might not be known exactly despite efforts to make the accurate placement. The deviation of this insonation/measurement plane from the precise measurement plane creates

inaccuracies in the Doppler output. With the utilization of the CFD, it was expected that the deviation in the measurement plane could be corrected.

In order to perform a detailed analysis, the CFD model had to be developed for the particular flow network in which Doppler measurement were performed and subjected for improvement. Using the parameters obtained from the components in the experimental setup (Chapter 3), the model was developed in *ANSYSs Fluent* following the same stages given in section 4.5 (Figure 4.14). Similar conditions were prescribed such as by using unstructured mesh, computer controlled parameters for determining the size of the mesh near the wall. The assumptions made with regard to the flow such as, the permeability of the vessel's wall, the flow pulsatility, were properly defined following the condition of the set-p.

A number of measurement sets generated by the Doppler system from the experimental setup (Chapter 3) were taken. Each of these sets was associated with certain input parameters (i.e. motor speed, beam angle, correction angle) and was subsequently embedded into the CFD simulation. From the CFD simulation, a new flow profile was generated for each set.

In the first experimental setup, an averaged constant flow rate was assumed despite the waveform flow profile generated by the pump. This assumption was also used for the CFD analysis. In order to find out whether there will be significant discrepancy arises due to this linearization; the effect of using constant flow versus pulsatile flow for the same flow volume in the CFD was

studied. In the study, a number of variables were defined which include the shape of the vessel (complex shape with branching and tapering vs simple uniform tubular shape), flow velocity and pulsatility pattern, external force (gravitational force) and type of fluid (e.g. blood, water).

Figure 4.14 *Ansys Fluent* model of the fluid flow in the experimental setup with a velocity profile shown at the outlet

Figure 4.15 shows the comparison of the flow output generated by CFD with constant flow input versus pulsatile flow input. The ‘cross’ and ‘dot’ are showing the flow volume for a particular flow outlet at a particular setting, for constant and pulsatile flow input respectively. The difference between the two is shown by the green bar below.

As can be seen from the figure, there is only a slight difference (mean =1.08%) between the flow volume of the constant and pulsatile flow. This small difference was deemed to be insubstantial. Hence, it was inferred that using constant or pulsatile flow in the CFD for the purpose elaborated in this study will generate the same result. In the case of blood flow in the cardiovascular system, the further the flow from the heart, the less pulsatile the flow is [76]. The reason for this is mainly due to the aortic arch compliance. The elasticity of the arteries, in particular aortic arch, reduces significantly the pulsatility of the blood flow. As such, in order to reduce the simulation time, a constant flow input can be safely assumed, at least for the study shown here. However, when the computational power is adequate to produce an output in a much shorter time than the time that was needed for the simulation explained here, pulsatile flow should be used for the input.

Figure 4.15 CFD flow output comparison for constant and pulsatile flow

4.8.2 Integration of the CFD Result into the Doppler Measurement

The simulated model generated different flow profiles for different values of the parameters. Figure 4.16(a) shows the typical flow velocity profile generated at a partial arterial outlet. From the figure, it can be seen that different flow velocity, as represented by different colour codes (blue color represents the lowest velocity while the red color represents the highest velocity), are generated at different points across the cross-sectional area of the tube creating a parabolic shape with the highest velocity is at the axis of the flow. In order to give a clearer representation of the said velocity flow profile, a 2D flow profile taken from the centre of the 3D profile in Figure 4.16(a) (line A-A) is re-illustrated by Figure 4.16(b). In the diagram shown by Figure 4.16(b), the horizontal axis denotes the (radial) position and the vertical axis shows the corresponding velocity.

The new flow profiles were then analysed and based on the analyses, the average flow velocity across the experimental outlet could be obtained for different sets. These CFD flow velocities were then compared with their respective Doppler measurements to establish the correlation between the Doppler sample and the flow profile (e.g. the difference between the average velocity measured by Doppler compared to the average velocity generated by the CFD). By comparing the two results, the correction factor could be calculated. (It is also possible for deviation of the Doppler measurement plane from the central measurement plane to be established). Using the correction factor from the Doppler-CFD correlation analysis, the BMF flow quantification

obtained from the Doppler ultrasound measurement (as elaborated in Chapter 3) was re-calculated.

(a)

(b)

Figure 4.16 *Ansys Fluent* flow velocity profile. (a) Flow velocity profile at a partial outlet. (b) Illustrative diagram of the 2D flow velocity profile taken from line A-A

Figure 4.17 shows the change in the flow quantification error from the stand alone Doppler measurements compared to the combined Doppler and CFD approach for different test sets. Clearly, the error percentage of the simulated flow output with respect to the theoretical flow output was improved for majority of the cases. Meanwhile, some experimental results did not experience any changes in the accuracy and a few suffer from worsening accuracy. The reason for the latter group could be attributed to the high accuracy obtained previously from the Doppler ultrasound measurement. When such accuracy has been obtained from the Doppler, the CFD appears to have limited ability to ameliorating it further. Hence, no changes in the error percentage and in one or two cases resulted in worse errors. However, it is noted that the improvement obtained far outweighed the undesirable output and even for the worsening errors, they are still within the error range shown in Figure 3.12. It is thus inferred that the combined Doppler and CFD approach is able to give better accuracy than standalone Doppler measurement.

A statistical comparison method namely non-parametric test was done [65] to support the conclusion that the improvement was made after the Doppler measurement had been combined with the CFD. Using binomial distribution, it was computed that $p\text{-value} < 0.05$ with $D=17$ (number of improvements). This means that it is safe to say that the median skewed in the favour of the improvement.

Figure 4.17 Errors obtained after combining the Doppler measurement and CFD

4.9 Conclusions

In this chapter, the arterial model for the CBF quantification has been expounded. The modelling framework had been established and studies with numerous variations in the modelling parameters had been performed. The result from the simulation showed that these variations affect the output and therefore has to be estimated properly. It is admitted that there are still a number of improvements that can be made. For example, the model developed in this study was using the mean values, and the variation around the mean values, obtained from human population data for its geometry and boundary conditions. In the future, the model will be constructed based on each individual's specific arteries' geometry and boundary conditions obtained from a number of imaging/measurement techniques (e.g. Magnetic Resonance Imaging, Computed Tomography-scan, etc.). However, it can be concluded that the model, so far, has given the desired outcome. The mapping of the cerebral

blood flow distribution during G-Loading which was one of the main objectives had been established under rigorous modelling and simulation exercise. This work piece is an integral part to the integrated G-LOC predictive model developed which is shown in chapter 5.

An extension of the CFD modelling to further improve the output obtained from the Doppler measurement had also been developed. The CFD model recalculated the BMF flow output based on the input from the Doppler measurement. This combined approach was shown to be able to yield improvement for the majority of cases and collectively able to increase the Doppler accuracy. However, there is a need to have intimate knowledge of the detail of the flow network for the method to be reliable and accurate; but fortunately, this can be achieved by rigorous offline modelling. In conclusion, the approach showed good outcome.

A version of the studies shown here, that reports on the combined ultrasound and CFD modelling in arterial blood flow quantification, has been published in Flow Measurement and Instrumentation journal [41].

Chapter 5 Cerebral Perfusion Modelling Based on Extended Windkessel Model

In Chapter 3, it has been discussed that Doppler ultrasound had been chosen as the main candidate for the cerebral blood flow measurement. The results obtained from a series of tests involving a number of parameters in the Doppler ultrasound experimentation was found to be sufficiently accurate when the beam angle and the relative position of the probe and the target were defined properly. The input from the Doppler measurement is intended to be supplied to a G-LOC predictive model as an integral parameter to determine the cerebral volumetric flow rate which in turn will determine the consciousness state of the subject during hyper-gravity condition. In this chapter, the development of the said predictive model is discussed. It is arranged into a few subsections. Subsection 5.1 summarizes the objective of the study presented in this chapter. Subsection 5.2 explains briefly the basic Windkessel model and its variations. This Windkessel model was chosen as the basic model for the CBF monitoring system. Subsection 5.3 and 5.4 explore the development of the model's parameters in detail. Subsection 5.5 propounds the model simulation result accompanied by its analysis. Subsection 5.6 shows the development of the fully integrated G-LOC predictive model and finally, subsection 5.5 gives the conclusion of the study.

5.1 Objectives and Scope of the Model Development

The objective of the study presented here is to develop a model which is able to give a relatively accurate quantification of cerebral perfusion rate. A modified Windkessel model, as a lumped-model representing the cardiovascular system, is chosen to be further developed to quantify the cerebral blood flow volume that goes to the brain during different $+G_z$ conditions.

Lumped model was chosen due to its ability to account for global circulation while requiring a relatively lower computational power as compared to higher order model such as 2D or 3D blood flow model. This is important since the proposed application of the G-LOC predictive model shown in this thesis was to be used in planes where a relatively standard computing system with real time calculation capability was envisaged. This is not something that can be achieved by having a complex model which requires high computational power and longer computation time. With regard to the lumped model for blood flow, such models are extensively used in blood flow modelling. In addition, they are actually of great interest in the context of multiscale model. In many cases, they are also coupled with a 3D model in order to have detailed information in some areas and to also account for the global circulation [15, 61, 74, 79, 80, 81].

The model is required to integrate a number of parameters which are paramount to quantify the CBF such as the peripheral resistance, arterial compliance, oxygen delivery rate, compensatory mechanism, arterial wall dynamics, and blood hemodynamic for the quantification and G-LOC prediction purpose.

Simulation and testing of the model is subsequently performed in *Matlab* [82] environment with different $+G_z$ loading patterns. Validation of the simulation results is done by comparing them with available G-LOC experimental data.

5.2 Review of the Windkessel Model

In this study, a model which is able to monitor the cerebral perfusion rate under acceleration stress was required. Based on the perfusion rate, the determination of the consciousness state will subsequently be performed. The model developed was based on the Windkessel model which is one of the most trusted models in the context of cardiovascular application due to its relatively simple nature and ability to give good accuracy in general prediction. Essentially, it is a model that simulates the cardiovascular system by using an electrical circuit analogy. Depending on the number of elements used, the Windkessel model (WM) can be divided to 2-element, 3-element and 4-element WM [83, 84, 85] as shown in Figure 5.1.

Figure 5.1 Basic Windkessel model

The 2-element Windkessel model (2WM) is the simplest among the three. It was first developed by Otto [23]. The model consists of peripheral resistance, R , and total arterial compliance, C . Although, it is able to provide the basic

exponential blood pressure based on the values of systolic and diastolic pressure, it fails to accurately predict the relation between pressure and flow [86].

With further developments in the computing capabilities, the computation of the aortic flow became possible and this led to the introduction of aortic input impedance, Z_c to the 2WM which essentially evolved it to a 3-element Windkessel model (3WM). This additional element improves on the shortcoming of the 2WM and basically acts as a link between the model and the pressure and velocity wave travel aspects of the arterial system [87]. The necessity of this addition to better describe the pressure and flow throughout the entire cardiac cycle is corroborated by [88]. Thus, the 3WM performs much better than the 2WM and is able to give accurate prediction of cardiovascular output in many applications under general conditions. However, it is also found that the 3WM is rather inaccurate in the low frequency range. A fourth element, inertance (L), is then introduced in order to improve this weakness creating the so called 4-element Windkessel model (4WM). This inertance is the summation of all compliances and inertance from the entire arterial system [89]. Note that it is highly difficult to determine an accurate inertance term and this term only improves the 3WM in the low frequency range [90] .

5.3 Development of the Basic 3-element Windkessel Model (3WM)

To determine which model should be adopted, it is imperative to consider various criteria such as the required output, complexity of the model, etc. Amongst the three Windkessel models mentioned earlier, 3WM is the most widely adopted model since it gives good accuracy while having less complexity [84, 85, 91]. Therefore, 3WM was chosen as the basic model to be developed for the aforementioned purpose. The 3WM can be represented by the following mathematical equation:

$$i(t) = \frac{u_c(t)}{R} + C \frac{d(u_c(t))}{dt} \quad (5.1)$$

$$\text{or} \quad \left(1 + \frac{Z_c}{R}\right)i(t) + Z_c C \frac{di(t)}{dt} = \frac{u(t)}{R} + C \frac{d(u(t))}{dt} \quad (5.2)$$

where i is current or blood flow, u is the voltage or blood pressure, u_c is the capacitor voltage, R is the peripheral resistance of arterial network, Z_c is the aortic impedance, C is capacitance or aortic compliance and t is time.

As shown in Figure 5.1 the 3WM consists of total arterial resistance (input impedance and peripheral resistance) and aortic compliance. The accuracy of the model depends on the value of these elements. Therefore, their values have to be determined carefully and validated using available experimental data to render their accuracy. The voltage and current in the model are used to represent the blood pressure and flow rate in ascending aorta and can be directly obtained by digitizing the experimental data of human blood flow and pressure.

5.3.1 Threshold Benchmark from Literature

Some parameters values that are integral to the model developed in this research can be gathered from the available literatures and are listed in Table 5.1 and 5.2. Table 5.1 shows the critical threshold of cerebral blood flow and oxygen consumption rate before a certain condition will occur. The values were obtained from theoretical calculation based on human physiological properties [92]. Table 5.2 gives the overview of the variation in average human tolerance level towards G-force as obtained from a centrifuge experiment with 1000 subjects seated upright with a 13° seatback angle without anti-G suit [3].

Table 5.1 Cerebral blood flow and brain oxygen consumption rate [92]

	Cerebral blood flow (ml/s)	Oxygen consumption (ml/s)
Resting	13.33	0.88
Vision problem	7.53	-
Critical value	5.07	0.35
Cell infarction	2.67	-

Table 5.2 Mean G tolerance range [3]

Symptom	Mean G tolerance (+Gz)	Range	Standard deviation
Resting	4.1	2.2-7.1	0.7
Vision problem	4.7	2.7-7.8	0.8
Critical value	5.4	3.0-8.4	0.9

5.3.2 Total Arterial Resistance

Figure 5.2 shows the ascending aorta flow waveform. The dotted line is the digitized data from Raymond et al. [79] and the solid line represents a Fourier series with 6 harmonic functions generated by *Matlab* to fit the data. The curve fitting Fourier series is given by:

$$\begin{aligned}
 f(t) = & a_0 + a_1 \cos(\omega t) + b_1 \sin(\omega t) + a_2 \cos(2\omega t) + b_2 \sin(2\omega t) + a_3 \cos(3\omega t) \\
 & + b_3 \sin(3\omega t) + a_4 \cos(4\omega t) + b_4 \sin(4\omega t) + a_5 \cos(5\omega t) + b_5 \sin(5\omega t) \\
 & + a_6 \cos(6\omega t) + b_6 \sin(6\omega t)
 \end{aligned}
 \tag{5.3}$$

where

$a_0 = 103.1$	$a_4 = -6.847$	$b_1 = 152.2$	$b_5 = -15.56$
$a_1 = 26.69$	$a_5 = 18.95$	$b_2 = 48.86$	$b_6 = 6.014$
$a_2 = -105.2$	$a_6 = 0.9624$	$b_3 = -44.96$	$\omega = 7.56$
$a_3 = -34.39$		$b_4 = -20.78$

Figure 5.2 Ascending aorta blood flow waveform

Figure 5.3 shows the ascending aorta flow pressure waveform. The dotted lines show the digitized data of the measured human blood flow pressure from two different studies (top is from Kroeker et al. [93] and bottom is from Murgo et al. [94]). There might be a slight variation in the measured data between individuals for both the blood pressure and flow waveforms, however the curve-fit (solid line) generated here is assumed to be able to represent the general population data. In addition, the waveform period is averaged to be 0.8s which translates to 75 heartbeats per minute. The Fourier series for the flow pressure waveform is in the form of equation (5.3), with the parameters as follows:

$a_0 = 96.62$	$a_4 = 1.173$	$b_1 = 4.236$	$b_5 = 0.7252$
$a_1 = -13.81$	$a_5 = 1.563$	$b_2 = -4.843$	$b_6 = 0.8433$
$a_2 = -2.729$	$a_6 = -0.7732$	$b_3 = -1.752$	$\omega = 8.061$
$a_3 = 1.298$		$b_4 = -1.106$	

Using the blood flow (Figure 5.2) and pressure functions (Figure 5.3), input impedance, peripheral resistance and aortic compliance can be systematically determined as explained in the following steps. The total arterial resistance can be directly calculated as [85],

$$Z = \frac{(P_{Ao,Mean} - P_{Ven,Mean})}{CO} \approx \frac{P_{Ao,Mean}}{CO} \quad (5.4)$$

where Z is the total arterial resistance (Ohm), $P_{Ao,Mean}$ is the mean aortic pressure (mmHg), $P_{Ven,Mean} \approx 0$ is the mean venous pressure (mmHg), and CO is the cardiac output (ml/s).

Figure 5.3 Ascending aorta blood pressure waveform

5.3.3 Input Impedance and Peripheral Resistance

The input impedance is calculated using the energy balance method which is able to give results comparable to other optimized methods and it remains valid even when the compliant element is changing [95]. The input impedance, Z_C , can be obtained as follows,

$$Z_C = \frac{\overline{W}_P - Z\overline{W}}{\overline{W} - Z\overline{W}_Q} \quad (5.5)$$

where, $\overline{W}_P$ is the mean squared values of measured arterial pressure, $\overline{W}_Q$ is the mean squared values of measured arterial flow, and $\overline{W}$ is the mean power entering the arterial system. These three parameters can be calculated using the following equations.

$$\overline{W} = \frac{1}{T} \int_0^T p_m(t) q_m(t) dt \quad (5.6)$$

$$\overline{W}_p = \frac{1}{T} \int_0^T p_m^2(t) dt \quad (5.7)$$

$$\overline{W}_q = \frac{1}{T} \int_0^T q_m^2(t) dt \quad (5.8)$$

where T is time period of one heartbeat, p_m is measured pressure and q_m is measured flow. Once the total resistance and input impedance has been calculated, the peripheral resistance (R) can be easily obtained from:

$$R = Z - Z_c \quad (5.9)$$

5.3.4 Aortic Compliance

There are many methods available to estimate the total arterial compliance (C) for the WM such as *The Stroke Volume over Pulse Pressure Method* (SVPP), *The Decay Time Method* (DTM), *The Pulse Pressure Method* (PPM), *The area method*, *The parameters estimation method* and a few others [85]. SVPP is among the earliest and is arguably the most commonly used one, due to its simplicity. The compliance is determined by adding the compliances of all vessels which is the ratio of the change in volume (ΔV) over the change in pressure (ΔP). It is difficult to estimate the volume changes accurately as some of the blood volume are lost through the peripheral and this lost blood volume is hard to be quantified. Thus, compliance value based on the change in volume over pressure method may result in an over-estimation of the compliance [96]. In DTM, the exponential decay of pressure is related to the characteristics decay time (RC) by using an exponential fit. DTM shows good result provided that the interject pressure is accurate [97]. However, obtaining the said pressure

accurately is difficult and thus it is usually estimated simultaneously with the decay time using non-linear least square method which in turn adds more complexity to the model.

The method adopted in this study is the PPM which is based on the fitting of the systolic and diastolic pressures [98]. Segers et al. [99] found that PPM gives better estimation compared to the *area method* and SVPP. Also, based on Stergiopoulos et al. [97] work, it is concluded that PPM and DTM give comparatively similar result, especially in the hemodynamic condition where the coefficient of wave reflection is in the range of normal to high. Segers et al. [99] further commented that PPM is the most appropriate method for total arterial compliance estimation applicable to a wide range of hemodynamic conditions. PPM bases its parameters calculation using 2WM. It has to be noted that while the 2WM model gives relatively inaccurate result, its impedance in the low frequency range matches closely the actual impedance.

Figure 5.4 shows the schematic diagram to determine the compliance based on PPM [97]. As has been shown in equation 4, the peripheral resistance is calculated as the ratio of mean aortic pressure ($P_{Ao,Mean} = P_M$) to cardiac output ($CO = Q_M$). Note that for 2WM the total arterial resistance (Z) is equal to peripheral resistance (R). However, in 3WM, Z is equal to input impedance (Z_C) plus peripheral resistance (R) [100]. Subsequently, the compliance is computed iteratively by trial and error approach by modifying equation (5.1) to:

$$C \frac{d}{dt} P_M(t) + \frac{P_M(t)}{R} = Q_M(t) \quad (5.10)$$

Once the ratio of the difference between measured peak pulse pressure (PP_a) and computed peak pulse pressure (PP_d) over PP_a is lower than a certain threshold (ε), the best estimate of the compliance is considered to have been obtained.

Figure 5.4 Schematic diagram of *Pulse Pressure Method*

Using the steps elaborated above and illustrated in Figure 5.4, we can obtain the compliance which in this instance is a constant value. However, in actuality compliance is not constant. Arterial compliance is a non-linear function of blood pressure. Mathematically, it can be described as follows [61],

$$C = \frac{dV}{dP} \approx \frac{3A_0L}{2} \frac{r_0}{Eh_t} \quad (5.11)$$

where V is the volume of the given segment, P is the pressure, r_0 is the original radius of the artery, $A_0 = \pi r_0^2$ is the original cross-sectional area of the artery, L is the length of the artery, E is the Young's modulus and h_t is the

wall thickness. As can be seen from equation (5.11), the compliance can also be found from properties of the vessel and the Young's modulus. However, the radius of the vessel is directly influenced by the pressure inside the vessel (as elaborated further in the subsequent section).

The relationship between E , h_t and r_0 is described by Ottesen et al. [61] as a function of r_0 (i.e. $\frac{Eh_t}{r_0}$). When the radius is larger than a certain threshold, this ratio becomes a constant. Thus, it can be inferred that for larger arteries, the change in compliance is mainly determined by the change in the radius of the artery. On the other hand, for smaller arteries, the change in compliance is less significantly affected by the change in the diameter as concluded in a study by [13].

These studies reinforce the dynamic characteristic notion of the compliance. Ideally, it is better to have a nonlinear model of the compliance in order to emulate its real characteristics. However, the additional accuracy gained may not outweigh the extra complexity. A comparative study on the effect of using constant and nonlinear compliance in 3WM was done by Fogliardi et al. [101]. From this study it was inferred that although the nonlinear 3WM is able to match the real blood flow volume curvature more accurately, the linear version is comparable to the nonlinear 3WM in terms of the total output. Thus, “the nonlinear 3WM cannot be preferred over the traditional linear version of this model [101]”. Considering this point, the compliance value used in this study is a constant compliance obtained using the PPM.

5.3.5 3WM Computation

Comparisons of the computed values of the elements with their counterpart found in three earlier investigations are tabulated in table 3 to gauge the accuracy and reliability of the computed values. As can be seen from the table, the value of R and Z_c found here are quite similar with their counterparts. However, the C value computed is quite different from the values found in the literature. It is worth noticing that the computed C value is, on the other hand, quite close to the calculated C value from 4WM given by Hlavac [83] which is 1.22. As summarized by Westerhof et al. [85], the compliance value computed by 3WM tends to be an overestimation; meanwhile, the 4WM can give an accurate prediction. Based upon this, the value of C computed as described earlier was deemed to be accurate and continued to be used in this study.

Table 5.3 Computed values of the 3WM and the comparison with their counterparts

	R	C	Z_c
Present investigation	0.88	1.25	0.02
Li (2009) [84]	0.86	2.7	0.02
Wang [4]	0.87	2.8	0.031
Hlavac [83] – for 3WM	0.79	1.75	0.033
Hlavac [83] – for 4WM	0.79	1.22	0.056

5.4 Windkessel Model for G-LOC

In order to use the WM model for the purpose of this study, a number of modifications were required which are presented in this section.

5.4.1 Modification to the Peripheral Resistance

The peripheral resistance includes all arterial resistances except for the aortic resistance or input impedance. Due to hydrostatics height differences, the blood flow to different areas of body during acceleration could be starkly different; those located above the heart level will have significant decrease of the blood flow and vice versa. In light of this, Wang [4] divided the peripheral resistances into three major groups, namely cerebral resistance, upper body resistance and lower body resistance. These divisions carry significant importance in the estimation of the cerebral perfusion rate during high G condition.

The values of each of the resistances are determined using Ohm's law based on the proportion of blood volume that flows to specific regions under normal condition (Figure 5.5). Kety [102] states that blood flow proportion for cerebral, upper body and lower body region is 13%, 74% and 13% respectively. Using these values in Ohm's law (equation 5.12), the resistance for each of the regions can be established accordingly.

$$\frac{1}{R} = \frac{1}{R_c} + \frac{1}{R_u} + \frac{1}{R_L} \quad (5.12)$$

$$R_c = R_u = 7.962R \quad (5.13)$$

$$R_L = 1.35R \quad (5.14)$$

where R_C is the cerebral resistance, R_U is the upper body resistance and R_L is the lower body resistance. R_C and R_U share the same resistance value since the proportion of blood flow that goes to these regions is identical. With the modification to the total peripheral resistance, the basic 3WM for the G-LOC is shown in Figure 5.5.

Figure 5.5 Modification to the total peripheral resistance

5.4.2 Dynamics of Arterial Resistance

In standard fluid dynamics notation, Hagen-Poiseuille's law can be expressed by:

$$\frac{\Delta P}{Q} = \frac{8\mu L}{\pi r^4} \quad (5.15)$$

The term on the left describes the change in pressure over volumetric flow rate, which is essentially is the resistance in the WM model. Hence, based on equation (5.15), it can be inferred that the arterial resistance (R_i) depends on the radius of the vessel (r) and the viscosity (μ) of the blood. The third term which is the length of the vessel (L) is considered to be immutable since the change of length of the vessel is assumed to be negligible [63].

The arterial resistance is most affected by the change in the vessel diameter. And the dynamics of the vessel diameter itself is directly related to the blood

pressure. When the pressure increases, the diameter of the artery also increases and vice versa. This dynamics will be elaborated more in section 5.5 since the change in the arterial diameter is also directly related to the compensatory mechanism.

As mentioned above, the other parameter that influences the arterial resistance based on the equation (5.15) is the viscosity of the blood. The viscosity changes over time based on factors such as hematocrit, temperature and shear stress [103]. Haematocrit is basically the volume percentage of the red blood cells in blood. For the purpose of our study, it is assumed to be constant since no discernible change is expected during the relatively short period of the G episode. With regard to the temperature, this parameter is also assumed to be constant. Aside from the relatively short period of the G episode, the assumption was also based on the condition of the environment where the subject and the system will be placed. In the said environment, the temperature will be controlled to stay at a certain level. Thus, in this study the dynamic of the viscosity is solely defined by the shear rate. Additionally, with constant temperature attribute, the thermoregulatory mechanism of the body will not come into effect and therefore will not be considered in this study as well.

Figure 5.6 shows the relationship between blood viscosity and the shear rate for different haematocrit reproduced from the work done by Fung [103] based on a study by Chien et al. [104]. Figure 5.7 shows the relationship between blood viscosity and shear rate for different temperature reproduced from the work done by Fung [103] based on a study by Merrill et al [105]. From Figure 5.6, it

can be seen that for shear rate smaller than 1 s^{-1} , the change of the viscosity with respect to the change in shear rate is very large. On the other hand, for shear rate larger than 100 s^{-1} , blood viscosity is close to a constant. Hence, depending on the shear rate, blood can also be considered as a Newtonian fluid or Non-Newtonian fluid. In case of the Newtonian fluid, the viscosity is a constant [10, 41].

Figure 5.6 Relationship between blood viscosity and shear rate for different haematocrit level at 37°C (reproduced from [103])

The divisions of shear rate elaborated above can also be correlated to the size of the arteries. Based on its size, arterial vessel can be divided into a number of categories such as elastic arteries, muscular arteries, arterioles, and capillaries [24]. In major arteries such as elastic arteries, it is safe to consider the blood as a Newtonian fluid. However, for the smaller muscular arteries and arterioles, a Non-Newtonian model should be assumed. The viscosity of the blood in capillaries needs to be modelled differently such as by using the Fahraeus-Lindqvist effect [76, 106]. However, this will complicate the WM model

developed here. Thus, for calculation of the peripheral resistance, the relationship between blood viscosity and shear rate within shear rate range of 1 s^{-1} to 100 s^{-1} is the only one considered to represent the general population of the peripheral arteries.

Figure 5.7 Relationship between blood viscosity and shear rate for different temperature at haematocrit level of 44.8 (reproduced from [103])

Since the haematocrit and temperature is assumed to be constant here, the relationship between blood viscosity and shear rate at particular temperature and particular haematocrit level can be extrapolated from both figures within assumed tolerable accuracy range. The mathematical model that depicts the shear rate-viscosity relationship based on power-law fluid is given by [107],

$$\eta = k\gamma^{n-1} \quad (5.16)$$

where η is the non-Newtonian viscosity, γ is the shear rate and k ($=27.2$) and n ($=0.48$) are the constants found from curve-fitting the graphs (Figure 5.6 and Figure 5.7). The shear rate is computed by,

$$\gamma_{App} = \frac{4Q}{\pi r^3} \quad (5.17)$$

where γ_{App} is the apparent shear rate, Q is the volumetric flow rate, and r is the radius of the vessel. This depiction is further improved by introducing the Rabinowitsch correction [108] to obtain the true shear rate, γ . The simplified version of the γ for power law fluid is given as follows,

$$\gamma = \frac{4Q}{\pi r^3} \left(\frac{3n+1}{4n} \right) \quad (5.18)$$

Assuming steady and quasi-steady laminar flow where equation 5.15 still applies, by substituting equation 5.16 and 5.18 into equation 5.15 and solving for the Rabinowitch correction, a general formula for the arterial resistance can be represented as,

$$R = \frac{\Delta P}{Q} = \frac{7Lk[4Q]^{n-1}}{\pi^n r^{3n+1}} \quad (5.19)$$

5.4.3 Dynamics of Blood Oxygenation Rate

Quantifying the cerebral perfusion rate alone does not directly give inference as to when the G-LOC episode will occur. Fundamentally, G-LOC happens due to the reduced supply of oxygen delivered by the blood required for brain metabolism. The blood flow rate reduction has a linear relationship with the amount of oxygen content [76]. Therefore, the tissue oxygenation (flow-rate and reserves) is another important factor to be considered in order to predict the occurrence of the G-LOC.

Oxygen is predominantly delivered to the whole body through blood circulation. It is a very complex dynamic process that involves a number of parameters such as the blood flow rate, the oxygen absorption and extraction rate (which in turn depends on the transport phenomena) and physiological characteristics of the involved somatic part [76].

In this study, we adopted a model derived by Buxton and Frank [109] due to its relative simplicity and its capability to deliver reliable result. The model hypothesized that there is a tight coupling between the cerebral blood flow (CBF) and the cerebral oxygen metabolic rate ($CMRO_2$) based upon two well-supported assumptions which are: 1) there is no capillary recruitment and 2) the oxygen metabolism is efficient. The quantitative relationship governing the oxygen (O_2) transport can thus be defined by,

$$CMRO_2 = \varepsilon K_1 C_a \quad (5.20)$$

where, $\varepsilon = \frac{E_n}{E_f}$ which is assumed to be ≈ 1 is the efficiency of the O_2 metabolism (calculated as the ratio of the net O_2 extraction fraction (E_n) over the unidirectional extraction fraction of O_2 (E_f)), $K_1 = E_f f$ is the max rate parameter which governs delivery of O_2 to tissue which is computed by multiplying the unidirectional extraction fraction of O_2 with the local perfusion rate (f), and C_a is the total arterial O_2 concentration. The unidirectional extraction fraction can be computed from,

$$E_f = 1 - (1 - E_0)^{\frac{f_0}{f}} \quad (5.21)$$

where, the subscript '0' on some of the variables denote the value of the respective variable at resting condition. The C_a can be computed from [110],

$$C_a = 1.34(Hb)(S_aO_2) + 0.0031(P_aO_2) \quad (5.22)$$

where, 1.34 is the Hüffner's constant, Hb is the hemoglobin concentration in grams per 100 ml of blood, S_aO_2 is the percentage saturation of Hb in O_2 , P_aO_2 is the partial pressure of O_2 (0.0031 ml of O_2 dissolved per 100 ml plasma per mmHg).

The S_aO_2 and P_aO_2 are assumed to be constant since the pilot is generally under good ventilation condition. Normal range of S_aO_2 is about 93-100%, normal range of Hb for adult male is about 13-18 g/dL, and normal range for P_aO_2 is about 80-100 mmHg. Based upon this range, a value of 90% for S_aO_2 , 15 g/dL for Hb and 90 mmHg for P_aO_2 are taken arbitrarily for the computation of the arterial oxygen content.

In actuality, there are many factors involved in the blood oxygenation process which affects the rate such as the transit time, gases exchange area and a few other factors, all of which involve the lungs and respiration process. To model all of these will unduly complicate the 3WM model attempted. And even with the most rigorous oxygenation modelling, some inaccuracies are expected due to the nonlinear nature of the parameters and the difficulty to accurately gauge all of them. Based on this, a simple oxygenation rate depicted by equation (5.20)-(5.22) was adopted and presumed to be sufficient for the purpose of this study.

5.4.4 Compensatory Mechanisms for Blood Pressure Regulation

Human body is conditioned to maintain the stability of its internal parameters through a biological principle known as *homeostasis*. During the period of increased acceleration, blood flow volume that goes to the brain is reduced thus creating internal instability. Given this condition, the body will attempt to restore the balance. There are basically three main sensory mechanisms for this, namely *chemoreceptor*, *mechanoreceptor* and *baroreceptor* reflexes [111].

Among the three, baroreceptor is considered to be the main regulator for short term pressure control and has been extensively modelled [61, 112, 113, 114]. Baroreceptor regulation is known to be short term; however, some studies have shown that it also plays a role in the long-term regulation of the blood pressure. There are two sensor locations for baroreceptor reflex, the aortic arch and the carotid sinus. The reflex is mainly responsive to the stretching dynamics caused by the blood pressure dynamics on the arterial wall.

There are two ways in which the baroreceptor responds to the stimulation: 1) by affecting the contractility of the arterial system and 2) by influencing the heart rate, which in turn affects the cardiac output. For changing the heart beat rate, its response to the stimulation is very rapid which allows adjustment to be performed by heart in beat to beat basis. However, modulation of the vascular resistance is slower with time delay of at least 2 seconds [61].

In this study which addresses acceleration induced gravitational force, the effect of the change in the arterial pressure is considered to be short-term and therefore the baroreceptor reflex is adopted as the sole cardiovascular control mechanism that adjusts the heart rate and arterial resistance. A diagram showing the baroreflex-based cardiovascular control model based on the study by Vielle [114] is presented in Figure 5.8.

Figure 5.8 A diagram of baroreflex-based cardiovascular control model

As can be seen from Figure 5.8, the baroreceptor receives input in terms of the arterial pressure. The change in the arterial pressure causes the baroreceptor to produce respective neurological spike to the central controller which is located at the brain stem. Based on the input from the baroreceptor, the central controller issues command signal to the peripheral effectors. Following is the mathematical model for each of these stages, whereby the quantitative values for certain parameters are adopted from Vielle [114].

- *Baroreceptor.* A Sigmoidal (“S” shape) curve of neurological spike signal is produced upon the change in arterial pressure. The equation for the neurological spike is,

$$F_C(t) = \frac{F_C^{(i)} + F_C^{(s)} e^{\frac{P_a(t) - P_a^{(0)}}{k_{FC}}}}{1 + e^{\frac{P_a(t) - P_a^{(0)}}{k_{FC}}}} \quad (5.23)$$

where $F_C^{(i)}$ (2.52 spikes/s) is the lower value of neurological spikes frequency, $F_C^{(s)}$ (47.78 spikes/s) is the upper value of neurological spikes frequency ($F_C^{(s)} > F_C^{(i)}$), $P_a^{(0)}$ (92 mmHg) is the central point of the arterial pressure and k_{F_C} (11.758 mmHg) is the shape parameter of the afferent spikes sigmoidal curve.

- *Central controller.* Signal from the baroreceptor is received via afferent fibres and the output from the processed signal is sent to peripheral effectors via the *sympathetic* fibres and *vagal* fibres.

For *sympathetic* fibres:

$$F_S(t) = \text{Max} \left\{ F_S^{(i)} + \left(F_S^{(s)} - F_S^{(i)} \right) e^{-k_{F_S} F_C(t)} ; F_S^{(is)} \right\} \quad (5.24)$$

where $F_S^{(i)}$ (2.1 spikes/s) is the lower value of *sympathetic* neurological spikes frequency, $F_S^{(s)}$ (16.11 spikes/s) is the upper value of *sympathetic* neurological spikes frequency, $F_S^{(is)}$ (2.66 spikes/s) is the low threshold value for F_S corresponding to the minimum *sympathetic* activity ($F_S^{(s)} > F_S^{(is)} > F_S^{(i)}$), k_{F_S} (0.0675 s/spikes) is the shape parameter of the exponential curve,

For *vagal* fibres:

$$F_V(t) = \frac{F_V^{(i)} + F_V^{(s)} e^{\frac{F_C(t) - F_C^{(0)}}{k_{F_V}}}}{1 + e^{\frac{F_C(t) - F_C^{(0)}}{k_{F_V}}}} \quad (5.25)$$

where $F_V^{(i)}$ (3.2 spikes/s) is the lower value of *vagal* neurological spikes frequency, $F_V^{(s)}$ (6.3 spikes/s) is the upper value of *vagal* neurological spikes frequency ($F_V^{(s)} > F_V^{(i)}$), $F_C^{(0)}$ (25 spikes/s) is the central point of the afferent neurological spikes frequency and k_{F_V} (7.06 spikes/s) is the shape parameter of the *vagal* spikes sigmoidal curve.

- *Peripheral effectors.* Based upon the signal from the brain, the heart rate and the arterial resistance are modified. The change in the heart period is computed as,

$$\frac{dT(t)}{dt} = \frac{1}{k_T} \left(-T(t) + T^{(0)} - G_{T_S} \ln(F_S(t - \tau) - F_S^{is} + 1) + G_{T_V} F_V(t) \right) \quad (5.26)$$

where T is the heart period, $T^{(0)}$ (0.58 s) is the value of heart period in the case of cardiac denervation, k_T (2 s) is the time constant, G_{T_S} (0.13 s²/spikes) is the gain associated with the *sympathetic* contribution, G_{T_V} (0.09 s²/spikes) is the gain associated with the *vagal* contribution and τ (2 s) is the delay time. Meanwhile, the change in the arterial resistance is computed as,

$$\frac{dR(t)}{dt} = \frac{1}{k_R} \left(-R(t) + R^{(0)} - G_R \ln(F_S(t - \tau) - F_S^{is} + 1) \right) \quad (5.27)$$

where k_R (6s) is the time constant, G_R (0.328 s².mmHg/ml. spikes) is the gain associated with *sympathetic* contribution, and $R^{(0)}$ (0.66 s.mmHg/ml) is the value of arterial resistance in the case of heart denervation.

5.4.5 Dynamics of Cardiac Output

In the previous subsection, it was expounded that in the event when the supply of the blood flow to the cerebral region diminishes, the heart will pump faster to restore the amount of blood flow required. The change of this pumping rate will affect the cardiac output which is the input to the 3WM because cardiac output (CO) is essentially a product of heart rate (HR) and stroke volume (SV). The heart rate and stroke volume are interdependent, as higher heart rate results in shorter ejection time and this in turn reduces the stroke volume. Figure 5.9 shows the relationship between HR and CO from studies done by Weissler et al. [115] and Lu et al. [116]. The relationship between the heart rate and ejection time (EJ) was computed first followed by the determination of the relationship between the EJ and SV. Based on these two relationships, the CO was calculated with respect to the HR.

Figure 5.9 Relationship between heart rate and cardiac output

For the data presented in the Weissler et al. [115] study, the HR range was from 40 to 120 (beats/min). From Figure 5.9, it can also be discerned that although the curves from both studies bear similarities, the curve from Weissler et al. [115] has smaller peak cardiac output compared to the curve from Lu et al. (2004). This may be attributed to the difference in subject pools. Based on its pool of subjects, the curve obtained by Lu et al. (2004) for males was chosen to be used in our study because it was deemed to be more suitable since the majority of the pilots are males. Using a polynomial fitting, the relationship for the said curve can be depicted as,

$$CO = (4.699 \times 10^{-9})(HR)^4 - (2.462 \times 10^{-6})(HR)^3 + 0.0003436(HR)^2 - 0.0057(HR) + 0.3996 \quad (5.28)$$

5.4.6 Effect of the G Force Loading

The physiological nature of G-LOC can be explained by the haemostatic theory of acceleration tolerance [117], which explained that the human acceleration tolerance was related to the cardiovascular ability to provide the required quantity of blood flow to the brain. In order for the blood to reach the cortical area, it had to overcome the hydrostatic barrier caused by vertical distance between the heart and the brain. By representing the distance between the heart and the brain as a rigid column, the pressure change given a certain G level can be estimated based on the hydrostatic pressure difference [1]. This relationship is depicted as follows,

$$P_H = \rho gh \quad (5.29)$$

where P_H is the hydrostatic pressure, ρ is the density of the blood, g is the gravitational force, and h is the vertical distance between heart and specified location at the brain. It was assumed that the distance between the heart and the brain stem is about 30 cm which correlates to P_H of 22 *mmHg* for every 1 G, therefore, equation 5.29 can be simplified to,

$$P_H = nP_H^1 \quad (5.30)$$

where P_H^1 is the hydrostatic pressure at 1G and n is the number of the applied G-force (e.g. 1G, 2.5G etc.).

Equation 5.30 represents the G-loading in term of hydrostatic pressure which is coupled to the 3WM model. During the simulation this hydrostatic pressure is varied dynamically in accordance to the randomly predefined G-force profile.

5.5 Simulation Result and Discussion of the 3WM

Subsequent to the derivation of the model, simulation was performed utilizing the model for a number of different G force loadings. The simulation was run in a few stages with different levels of complexity added gradually. Sensitivity analysis was done by varying the parameters one at a time and the results from these variations were correlated. This was done in an attempt to eliminate the occurrence of possible singularities. In all of the simulations, gradual onset rate was applied which is of interest in this study since rapid onset rate will result in an almost instant LOC without any possible prevention.

5.5.1 3WM with Modified Peripheral Resistance

The modified peripheral resistance model is a straightforward implementation of the 3WM model. A number of Gradual Onset rate (GOR) variations in the range of 0.2G/s – 0.8G/s were performed. This range was deemed to be able to represent the gamut of GOR since onset rate above 1G/s is considered as Rapid Onset rate (ROR). Using this range of GOR, the simulation results showed that the critical G was in the range of 2.79 to 3.01G (mean = 2.9G) based on the critical cerebral blood flow tabulated in Table 5.1.

The critical G was found to be linearly increasing with the increase in the GOR profile. Based on this observation, the variation in the results was subsequently found to be influenced by the occurrence of a delay in averaging the pressure waveform during the simulation process. Although much of the pulsatile nature of the flow has been moderated by the arterial compliance, pulses with varying amplitude can still be observed in the peripheral flow as shown in Figure 5.10. The various curves as shown in the Figure 5.10 are obtained from different parts of blood flow inside the cardiovascular system. The curve with the largest amplitude comes from the flow in aorta and the one that is shown almost flat, comes from the peripheral arteries.

In a real situation, human sensory system performs its own averaging over a specific period of time in order to determine whether the homeostatic condition is imbalanced. If the delay was accounted for in the simulation, the critical G for the same range of input would have been within 2.7-2.83G (mean = 2.75G).

This being said, the delay better reflects the physiological condition of the human body albeit how close the delay time in the simulation is, as compared to the real condition, cannot be accurately quantified yet. Thus, in our study this ‘limitation’ in the simulation pertinent to delay issue was left unadjusted.

Figure 5.10 Pulsatile flow in simulation

We found that the results obtained are in line with the hydrostatic pressure theory of acceleration, which says that there will be no blood flowing into the brain at G force equal to about 4.5G [118], with the calculated critical G of about 2.74G for a given average pressure of 94.5 mmHg going through the R_C . The accuracy acquired by this basic model also validates the assumed reliability of the model for integration of the subsequent parameters for added complexity.

5.5.2 3WM with Modified Peripheral Resistance Coupled with Oxygenation Rate

In this simulation, the cerebral blood flow output is coupled with the oxygen metabolic rate of the cerebral tissue. Equations 5.20-5.22 were used to calculate the metabolic rate. The equations were calibrated by using the value given in table 5.1. Similarly, a number of GOR variations were applied (0.2G/s – 0.8G/s) and simulations were performed using the same criterion to decide the critical value as described in section 5.1. The simulation results showed the critical G was in the range of 2.82-3.14G (mean= 2.98G). Compared to the mean value obtained in the section 5.5.1, the mean critical G obtained here is 2.68% higher.

In order to complete equation 5.20-5.22, certain parametric values were tuned, and as a result, a discrepancy in the mean value was obtained. It is possible to further refine the assumed value to obtain close to zero discrepancy. However, this will make the assumption too conservative. Furthermore, the disparity of 2.68 % is considered to be relatively small and therefore the assumed parameter values for the oxygenation model were kept as defined.

Figure 5.11 shows a number of simulation results with different values of the parameters involved (e.g. S_aO_2 , Hb). The variations were determined randomly within the predefined range. As can be seen from Figure 5.11, critical G value changed with the change in the parameter values. When a given parameter value was higher than the mean value, the critical G obtained was

higher than the mean G and vice versa. Subsequently, the new range of the critical G was established within 2.2-3.28G. It can be inferred that the model was able to respond to the changes in the value of the parameters correctly and yielded the expected outcome.

Figure 5.11 Critical G at different value of oxygenation parameters (S_aO_2 , Hb and P_aO_2)

5.5.3 3WM with Modified Peripheral Resistance and Dynamic Heart Rate Coupled with Oxygenation Rate

In this part of the simulation study, the effect of varying the heart rate and thus changing the cardiac output was observed. Under G loading or ischemic condition, the heart pumps faster in an attempt to increase the CO, which in turn increases the cerebral blood flow. Using the HR and CO relationship described in section 5.4.5, simulation with dynamic heart rate was performed. The HR was influenced by the compensatory mechanism; however, in this particular exercise, these HR dynamics were not fully automated. The HR was set in predetermined profile because the main concern at this particular stage was to

analyse the effect of changing the CO toward any improvements in G-LOC tolerance.

From a set of simulation results, increasing the HR to the max value, where the CO was the highest, improves the G-LOC tolerance by an additional 51.7% compared to the base HR which is 75 (Figure 5.12). It can also be seen from Figure 5.12 that an increase in the G-LOC tolerance closely follows the trend of the increase in CO (ref. Figure 5.9). Furthermore, for all the GOR values used (0.2 G/s, 0.4 G/s, 0.6 G/s, 0.8 G/s), the mean critical G obtained was found to be very similar for a given HR.

Figure 5.12 G-LOC tolerance at different Gradual Onset Rate (GOR) at different HR

5.5.4 3WM with Modified Peripheral Resistance, Dynamic Heart Rate and Viscosity Coupled with Oxygenation Rate

In this exercise, computation of the effect of variations in the viscosity on cardiac output was observed. As described in section 3.2, one of the parameters that affects the viscosity is the diameter of the blood vessel. The arteries in peripheral region were assumed to be under muscular arteries and arterioles and therefore their viscosity can be estimated by equation (5.15). When this equation was explored further (equations (5.16)-(5.19)), it was learnt that the viscosity is basically determined by the blood flow and arterial diameter. The vessel diameter was influenced by pressure and also by the baroreflex. However, at this particular stage, the baroreflex was assumed to be non-existent and therefore the arterial diameter was mainly determined by the blood pressure variations. In order to describe the relationship of the blood pressure (P) and arterial radius (r), longitudinal coefficient of 1.6 was used as derived by a study done by Canfield and Dobrin [63]. The relationship can be mathematically formulated as,

$$r = (-1 \times 10^{-10})P^4 + (6.055 \times 10^{-08})P^3 - (1.509 \times 10^{-05})P^2 + (0.002051)P + 0.1356 \quad (5.31)$$

From the simulation results, the effect of viscosity was found to be very small, at least under the particular constraints applied in this exercise. The change in the time to G-LOC was computed to be within 0.1G-0.3G. G-LOC tolerance is reduced when the viscosity is higher and vice versa.

5.5.5 Results from the Integrated 3WM with Compensatory Mechanism

The compensatory mechanism mainly affects two parameters, namely heart rate and the arterial resistance as defined by equation (5.26) and (5.27), which were added so that the model became fully integrated. Some of the parameters were adjusted to reflect the realistic conditions more accurately, for example the central point of the arterial pressure was originally 92 (mmHg) in the study done by Vielle [114], this value was adjusted to 95 (mmHg) which was a more accurate representation based on the blood pressure waveform given in Figure 5.3.

Figure 5.13 shows the layout of our developed model in *Matlab* environment. As can be seen from this figure, all significant parameters that affect the model are networked together. The change in any parameter's value would be feedback according to relevant interdependent parameters and this process is repeated whenever any disturbance in the homeostasis condition is observed. The relevant components will dynamically adjust themselves to restore the stability until such condition can no longer be contained despite their best adjustment.

Similar to the exercises elaborated in the previous subsections, different GOR profiles were generated and simulated in the integrated model as well. However, unlike in the previous exercises, the GOR profile was dynamically changed during the simulation in an attempt to emulate the GOR profile observed in realistic flying situations. Figure 5.14 shows a few representative

examples of the randomly generated dynamic GOR profile used in the simulation (not drawn to scale). As can be seen from the figure, each GOR profile consists of varying degree of GOR in acceleration and deceleration. However, they can be roughly categorized within four major groups, viz. 1) a combination of GOR constant with plateau in between, 2) a combination of positive and negative GOR constants (acceleration and deceleration), 3) a simple combination of a few GOR constants and 4) an acceleration slightly above the critical G followed by a rapid deceleration.

Figure 5.13 G-LOC predictive Windkessel model

Aside from the dynamic GOR profile, variations in the physiological parameters were also accounted for. The procedure was similar to the one expounded in section 5.4. However, at this stage, the variations were not limited to the parameters in the oxygenation model but were applied to the whole integrated model. This would show the possibilities that may happen with different individuals albeit to a limited degree. For this exercise, the variations

were constrained within $\pm 20\%$ from the original values and the variations were randomly generated for each parameter, the results of which are shown in Figure 5.15.

Figure 5.14 A few representative examples of dynamic GOR profile randomly generated

As can be seen from Figure 5.15, a range of critical G was produced (3.94-6.8 G) from variations in individual parameters (mean=1, standard deviation=0.1). The mean critical G obtained was 5.45 G which is very close to the mean G obtained in other representative works (Cochran et al. [3] = 5.4G; Cammarota [1] = 5.392G; Li [84] = 5.92G). In terms of the critical G range, the results shown here form a subset of the critical G range found in other representative works (Cochran et al. [3] = 3.0-8.4G; Cammarota [1] = 3.3-8.8G). This is most likely due to the difference in the range of the parameters' variation assumed or generated. Unfortunately, it is not possible to correlate any specific set of the simulation data in our study to its experimental/published counterpart due to the lack of relevant publicly available information on individual physiological parameters. However, the fundamental response to each parameter on the

critical G, as elaborated in the previous subsections, has been verified to be physiologically sound.

The range of critical G can be larger than shown in the Figure 5.15 since the variation of physiological properties between each individual can be more than the one specified in this simulation. However, this also shows that the simulated model can account for individual variation and one can expect to get a customized integrated model for each individual of interest.

Figure 5.15 Simulation results of the integrated 3WM with compensatory mechanism

Qualitatively, when the value of each of the individual parameters was increased from its predefined mean value, the obtained critical G became higher than the critical G generated when all of the varied parameters were at their mean value (e.g. point 8, 16, 24, 32, 40, and 48 which are shown as ‘green triangle’ in the figure). The reverse happened when each of the varied parameters was reduced (e.g. point 7, 15, 23, 31, 39, and 47 which are shown as ‘red square’ in the figure). Mixed outcomes resulted for intermediate parametric settings. No quantification of these observations were attempted since the effects of variation in parameters are interconnected and influence each other, which makes it difficult to accurately assign a weightage to each parameter. However, if centrifuge data were available for a specific individual the integrated physiological parameters can be tuned in accordance to individual subject’s physiological condition and this customization is envisioned to be able to greatly improve the results.

It was also observed that once the critical G is exceeded, the LOC will happen even though the acceleration was rapidly reversed. This is not surprising given the assumption that once a threshold that separates the consciousness and non-consciousness was crossed, LOC will occur regardless of any change in G profile [1]. The window period that enables a slight overshoot of the critical G was accounted for in the reaction time delay (section 4.1) which was not adjusted.

5.6 Development of the Hybrid Model for G-LOC Prediction

Following the successful development of the extended Windkessel model as elaborated in the preceding subsection, the CFD model were integrated into it to create a hybrid model for the G-LOC prediction. The CFD model was supposed to receive input from the Doppler. However, in this project there was no real centrifuge experiment. Hence, the Doppler input was estimated from the simulation itself. The heart model was pumping blood based on the factors to affect it as elaborated in the previous subsection. The blood flow volume that goes to the brain can be found from the blood pressure and the resistance value that represents the brain. From these values, the blood flow volume that virtually goes to the common carotid artery was estimated using a constant value based on a study Benim et al. [119] and then this value was subsequently inserted to the CFD model to obtain the real time blood flow distribution. The resulting new flow volume based on the CFD model was then used to adjust the cerebral flow volume in the Windkessel domain. The completed hybrid model for G-LOC prediction built in *Matlab* is shown in Figure 5.16. It is generally similar to the one shown in Figure 5.13 except with the additional CFD subsystem and its related parameters.

Figure 5.16 Fully integrated G-LOC predictive model

5.6.1 Simulation Result and Analysis

Simulations were performed to assess the efficacy of the consolidated model. The procedure for the simulation was in uniformity with the one expounded in section 5.5.5. The effects of the different GOR profiles and variations in physiological parameters were explored. The outcome of the simulations with these variations is shown in Figure 5.17. Meanwhile, Figure 5.18 shows the frequency of occurrence for the specific G tolerance range.

As shown in the Figure 5.17, the variations in the input parameters result in the variation of the G tolerance level. In this exercise, the minimum and maximum G tolerances are recorded as 4.077 G and 8.487G respectively. The mean G tolerance obtained is 5.81G which is slightly higher than the one explained in section 5.5.5. This increase in the mean G tolerance is attributed to the additional adjustment by the CFD model.

Figure 5.17 Simulation results of the fully integrated G-LOC predictive model

The mean G tolerance obtained is also slightly higher than the one presented in the Pensacola study (Cochran et al. [3]). The reason for this might be due to the difference in the physiological condition of the subjects considering that the study was done in 1954. On the other hand, the mean G tolerance obtained is considerably lower than the one presented by Whinnery and Forster [120]. In Whinnery and Forster's study, the range of G tolerance for GOR is 3.6-11.7G ($n=236$, n represents the total number of experiments), with the mean G tolerance of 7.31 ± 1.32 Gz ($n = 293$, median = +7.6 Gz). The reason for this is that certain parameters in the simulation were defined based on the Pensacola study, e.g. 13° recline angle, no anti-G suit or combination of other method and device to improve the G tolerance. Meanwhile in the Whinnery and Forster's study, these methods or devices were included in the experiment, although

some of the experiments also excluded the said methods and devices. As explained in chapter 2, the use of special breathing technique and anti-G suit can improve G tolerance significantly (up to 4G if they are done correctly).

Figure 5.18 Frequency of occurrence for specific G tolerance range

In terms of the frequency of the occurrence for specific G tolerance range, the output from the simulation study is comparable to its experimental counterpart. Figure 5.19 shows the comparison of the frequency for the study presented here and the available comparative studies, namely the Pensacola study and the Cammarota study. The Pensacola data have a number of experiments that fell

within the 7-8.4G, however the frequency was not recorded and thus is put as zero in the figure. Meanwhile, the Cammarota simulation grouped together the occurrence above 7.1G and for simplicity sake, they are also grouped in one in 7.1-7.5G. Furthermore, due to the difference in the number of simulations and experiments done, a normalized value is used to represent each datum for comparison purpose.

Figure 5.19 Comparison between the simulation study and its counterparts

As can be seen from Figure 5.189, the simulation output is able to qualitatively and quantitatively give comparable output to the real experimental data. It is worth noticing that the simulation model was built from individual components without being tuned to the experimental data, i.e. the Pensacola study, yet the final outcome was comparable to the experimental data. This corroborates the validity and reliability of the model developed.

The simulation results shown in Figure 5.17 and Figure 5.18 were for the assumed consolidated variation between individual in the general population scheme. The model in Figure 5.20 was primarily developed for the purpose to account for the variation within an individual, and this is achievable by fine tuning each parameter that accounts for the G-LOC prediction for a particular individual following the said individual's physiological condition. In order to validate the model, scenarios where variation of these parameters is within an individual were developed and simulated; for example, a scenario by having an individual with physiological parameters conforming to the population mean value and predefined variance of 0.01 from the mean value. Comparison of the simulation result from one individual to another individual with different predefined physiological parameters was also performed to further assess model. Figure 5.20 Shows the G-LOC range of three individuals with predetermined level of physiological parameters under varied conditions and the frequency of occurrence of their G-LOC is shown by Figure 5.21.

Figure 5.20 Simulation results of the fully integrated model on the G tolerance range based on three distinct models taken from the general population data

As can be seen from Figure 5.20, the three individuals had different G-LOC range and the variation in their G-range was also different. Analysis of variance (ANOVA) [65] performed on the simulation data shown in Figure 5.20 resulted in F - ratio (ratio between estimate of common variance using population mean and estimate of common variance from individual observations) equal to 143.9. For the level of significance (α) = 0.05, the $F_{Critical}(2,117)$ was found to be 3.07. The obtained F - ratio is larger than the $F_{Critical}$, thus it can be concluded that there is a strong evidence that the values between the three groups differ at this level of significance.

Figure 5.21 Simulation results of the fully integrated model on the frequency of the G-LOC occurrence based on the three distinct models taken from the general population data

In the context of the study shown here, it can be inferred that the variation in individual's parameters significantly affect the G tolerance range. This also shows that the fine tuning of the model is able to account for the variation within individual. Since different individuals have different physiological parameters and even for the same individual, variation within their physiological condition is very common. Hence, the feasibility to adjust the model to account for has been demonstrated.

5.7 Conclusions

In this chapter, the development of a hybrid WM to predict the occurrence of G-LOC in the *Matlab* environment has been elaborated. A number of inter-dependent parameters that were perceived to play a significant role in determining the G-LOC were integrated into the model. Simulation studies of the integrated model showed that the model was able to closely reproduce the results obtained from centrifuge experiments in various studies. The model was able to account for the general population data and to be customized to suit the need of particular individual. It can be concluded that the model was able to give the desired outcome and with further improvement by better subject documentation, (e.g. online monitoring of physiological profile of individual pilots), the result could be more accurate.

Chapter 6 Conclusions and Future Works

This chapter gives the conclusion to the whole thesis. The overview of the works pertaining to the research and the accomplishment made are succinctly restated here. In the last section of this chapter, possible future works following the research are briefly explored.

6.1 Review of the Work Done

It is understood that the G-LOC phenomena is a well-known flight hazard especially for the advanced fighter plane. Therefore, the availability of premonitory sensor such as the one proposed here is of great importance. Hitherto, a number of researches have been done pertaining to this research problem. While results have been generated, the outcome is still far from sufficient which result in limited application. One of the weaknesses of those models is that they can only give prediction to fit the general human population data which may not work well for a particular individual since every person's G-force tolerance is different (and by quite a large range).

The objective of this research was to develop a biomechanical model to predict the occurrence of G-LOC in pilots experiencing hyper-gravity condition. By utilizing both real time measurement and computation based on CFD and the Windkessel model, it was envisaged that the developed model can eliminate the aforementioned weakness of the previous predictive models. The use of Doppler ultrasound to provide input in the hybrid model, which to author's

knowledge has not been done previously, is another parameter that set this model apart from the rest.

In the earliest stage of this research, the feasibility of the Doppler Ultrasound system which was proposed as the input measurement modality was verified. The testing of the system involved custom made phantom and mechatronics system under *In vitro* setting. There were two major criteria used to assess the applicability of the Doppler namely, accuracy and reliability. The Doppler experimental results were able to give satisfactory outcome for both criteria. However, it was also noted that, in terms of the accuracy, placement/alignment error of the probe was crucial for achieving the good result.

In order to address the issue with the Doppler accuracy aforementioned earlier, blood flow modelling was also done to measure the cerebral perfusion rate. The premise of cerebral blood flow volume is the main somatic reason for the occurrence of LOC, making the CBF quantification of utmost importance; efforts were made to ensure accurate quantification of the flow volume. Both the Doppler and the blood flow modelling would complement each other. The Doppler provided input that was used to calibrate the blood flow model and the blood flow modeling was then expected to enhance the accuracy of the CBF measurement given by the Doppler system.

The second stage which was the arterial blood flow modeling for CBF attempted in this project consisted of identifying the responsible network and developing the appropriate flow modeling for the network. Simulations were carried out under a number of flow parameters following the development of

the flow model. Numerous variations in the modelling parameters were studied and their effect on the output was carefully determined. It was found that, although a number of improvements can still be made, the model had been able to give the desired outcome. Following this, the hybridization of the CFD and Doppler to further improve the accuracy of the spatiotemporal qualification was done. With rigorous modelling, this combined approach was shown to be able to yield improvement for the majority of cases and collectively able to increase the Doppler accuracy. In conclusion, the approach showed good outcome. In this stage the CFD was also used to map the blood flow distribution among the arterial network responsible for the cerebral blood flow during G-Loading. This mapping was essential for the integrated G-LOC predictive model.

With the Doppler and the developed CFD model, accurate quantification of the blood volume that flows inside the major arteries of the cerebral vasculature is made possible. However, an extremely complex model is required to estimate the blood that flows into the capillary. The blood circulation that goes through the whole body is also important to be accounted for, because they are interdependent and physiological changes such as pooling of the blood when the pilot is subjected to hyper gravity condition affects the blood flow to the other parts of the body. To account for this a lumped model that can simulate the entire blood circulation while the focus is in the CBF was then developed. A modified Windkessel model was chosen to be the lumped-model representing the cardiovascular system.

The developed model incorporated a number of inter-dependent parameters that were perceived to play significant role in determining the G-LOC such as the peripheral resistance, arterial compliance, oxygen delivery rate, compensatory mechanism, arterial wall dynamics, blood hemodynamic, etc. Analysis of the model showed that each of these parameters significantly influences the blood flow volume. The integration of these physiological parameters which are different from person to person was crucial to enable the model to be customized to fit individuals.

Following the successful development of the extended Windkessel model, the CFD model with Doppler input were integrated into it to create a hybrid model for the G-LOC prediction. This fully integrated model was found to be able faithfully reproduce the mean G-LOC data obtained from the available centrifuge experimental data. This was achieved without any fine tuning of the integrated model based on the available data which shows that the individual parameters were well modelled. Finally, it can be concluded that the final model is able to give the desired outcome and the objectives set in the beginning of the study is able to be met.

6.2 Future Works

6.2.1 Centrifuge Experimentation

The model developed in this research had been validated through simulation by comparing them to the available human data. The customizability claim of the model was based on the premise that the model integrated numerous physiological parameters that are unique to each individual. By varying these parameters, different outcomes were generated for the same acceleration pattern which corroborated the hypothesis. For the purpose of the research shown here that was deemed adequate. In the future, however, validation of the model through real centrifuge experimentation with pilots as the test subjects, which is currently outside the scope of this research, has to be done because this is an important step to establishing the model as a serious contender to be used for GLOC prediction.

In order to do the centrifuge experiment, there is a need to have a mechanical interface between the pilot and the probe. This is because there is a need to maintain constant contact between the pilot and the probe for continuous measurement. Thus, the interface will very likely have to be attached close to the neck. The mechanism of the interface is also envisioned to work as a probe automatic positioning system. Recall that in the Chapter 3, this positioning system was also proposed in the effort to further improve the positioning accuracy of the probe and thus the Doppler accuracy. Hence, this interface could be used to serve the two purposes. Due to the space constraint arising

from the attachment place of the interface; there might also be a need to use two or more smaller probes in place of the larger one. Alternatively, it is possible to use ultrasound phased array to replace the conventional probe. The ultrasound phased array has been studied extensively lately and has many attractive qualities [6, 121, 122]. The few points broached here pertinent to the proposed centrifuge experiments are just a few of many things that are required to be done. Even within the one mentioned here, much preparation and work is needed to ensure a fruitful experimentation.

6.2.2 Extension of the Predictive Model

In the context of this research, there are a bevy of parameters that are affecting the level of consciousness of a person such as the external condition (e.g. heat), alcohol, infections, *etc.* [1, 38]. All of these factors are fairly hard to quantify. However, many of them, in one way or another culminate in how their effects on the body affect the cerebral blood supply. Hence, by addressing the problem in the quantifying the CBF, presumably one is also addressing the aforementioned factors. In terms of physiology, it is largely agreed that LOC is caused by diminished cerebral blood flow and hence the oxygen supply. Aside from these two no other significant factors are enumerated in the literature. Therefore, although many physiological factors are stated to affect the LOC, only these two were considered the major/primary factors to be modelled in detail. In terms of psychological-based factor, a few examples could also be found [1, 35]. However, all of them are stated rather superficially and relatively without any concrete substantiation. It is understandable since these psychology

factors are even harder to define and there is no baseline to viably gauge their effect.

The research study shown here was based upon these arguments and even though there were only two major parameters modelled, they were modelled extensively and incorporating a number of relevant interdependent variables. The satisfactory result is a good testament to this. However, in the future, there might be a need to learn about these other factors that may or may not contribute to the process of G-LOC occurrence. As has been stated earlier these other factors are hard to define, therefore a model which was able to handle a highly non-linear system is needed. One of the models that fit into this category is the Artificial Neural Network (ANN) based model. ANN is a computational model that takes its form from the biological neural network [123]. It consists of a group of interconnected network and adaptive in nature based on the flow of the internal and external information during its phases of application.

With the ANN model, the other factors that are hard to be modelled yet contribute to the G-LOC condition, e.g. metabolism rate, effects of the training, can be enumerated to participate in the G-LOC prediction. It has to be noted that not each parameters can and has to be included mainly for achieving relative simplicity while maintaining the accuracy. Each chosen input parameter will need to be carefully justified and will be weighted by a factor which represents the strength of the parameter. The sum of these inputs and their weights represent a certain activity to which predefined simple rules are then applied to these activities to generate the output. ANN requires an extremely

thorough fine tuning in order to have an accurate outcome. If this model is adopted, extensive work is required with numerous experimentation and model training, both online and offline. Figure 6.1 illustrates its working principle in general. Figure 6.1 (a) shows a simple artificial neuron where a number of inputs with their defined weights determine the activity of the neuron. Meanwhile, figure 6.1(b) shows a multi-layered artificial neural network in which the neurons (or nodes) are intricately interconnected in a complex network which enables them to learn and subsequently solve many problems.

Figure 6.1 An illustration of the ANN (Adopted from [123])

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