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Simulating photoacoustic waves from individual nanoparticle of various shapes using k-Wave

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Abstract. Photoacoustic imaging technique has been widely discussed for their potential applications in biomedical field. Current attempts in understanding the photoacoustic signal characteristic of various shapes of nanoparticles is mostly performed through numerical simulations. They require complex mathematical formulations prior to the simulation. Moreover, computationally they are expensive. In this work, k-wave simulation toolbox was used to simulate the photoacoustic signal generated from various shapes of nanoparticles. Seven shapes of nanoparticles are simulated here: sphere, cylinder, hollow cylinder, cube, hollow cube, triangle, and nano star. A point sensor (ultrasound detector) is used to detect the photoacoustic signal. The simulated photoacoustic signal is presented both in time and frequency domain and used for understanding the impact of the various shapes on the photoacoustic signal characteristics. **The detector was placed at various locations to see how the photoacoustic signal characteristics changes with transducer positions. There is a distinguishable signature of the nanoparticle shape on the frequency spectrum of the photoacoustic waves. The simulation time for each nano particle is as short as 40 sec, which is significant improvement over previously reported simulation time of few hours using analytical methods.**

Keywords: Photoacoustics, acousto-optics, simulations.

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1. Introduction

Photoacoustic imaging is an emerging hybrid medical imaging modality combining both optics and ultrasound into a single modality [1-3]. Photoacoustic imaging has found various biomedical applications [4-12] including but not limited to brain imaging, vasculature imaging, tumor imaging, breast cancer imaging etc. A pulsed laser light source illuminates the target object. Light is absorbed by the target object, resulting in local temperature rises within the target object. Subsequently a series of pressure waves are emitted [which are also known as photoacoustic (PA) waves] due to thermoelastic expansion. These waves will be then acquired by ultrasound transducer (detector) to form the optical absorption map of the target object [3].

Human body has many intrinsic optical absorbers (blood, melanin, even water); however, the optical absorption is rather weak in the near-infrared (NIR) wavelength region. NIR window is a well-known optical window for deep tissue imaging [13]. Thus one needs to choose between the imaging depth and high optical contrast. To improve the contrast a popular mechanism is to use contrast agents. The contrast agents used in photoacoustic imaging not only enhances the contrast but also serve as targeted molecular imaging agents [14-29].

Gold has been a very popular metals used for photoacoustic contrast agent [14, 16, 20-22, 25, 27-29]. The shape, size and functionality of these metallic nanoparticles can be tuned to maximize the light absorption to enhance the photoacoustic signal amplitude [30]. Some of these studies suggested that various shape and functionality of gold nanoparticles can be used

as contrast agent for tumor or cancer diagnosis. Gold based spherical nanoparticles have been reported as potential contrast agent in tumour diagnosis [29]. Another study showed gold based cylindrical nanoparticles as potential contrast agent in prostate cancer diagnosis [28]. Silica coated triangular shape nanoparticles were reported to be an effective contrast agent in lymphatic imaging [16]. Carbon nanotubes (having cylindrical structure) were shown to have very strong photoacoustic and thermoacoustic signals [26]. Aside from solid shapes, hollow shape nanoparticles were also studied for their potential as contrast agent in photoacoustic imaging. Hollow shape nanoparticles such as hollow gold nanospheres were reported as potential contrast agent with ability of longer circulation time [22]. Current attempts in studying the effectiveness of different shape and size of nanoparticles were performed intensively through experimental synthesis of nanoparticles followed with a photoacoustic study [31]. This type of experimental method is very challenging and requires high precision measurements. Nanoparticles synthesis plays an important role in defining the shape of nanoparticles, which is usually time consuming and complex.

Fig. 1 Photoacoustic signal generation using k-wave toolbox in MATLAB. Simulation geometry with 200x200x200 voxels (10 nm/voxel) were used for all the three dimensional photoacoustic signal generation simulations. Various shapes of nanoparticles are placed at the center of the simulation geometry. The ultrasound transducer (an ideal point detector) is placed at a distance from the center. The location of the detector was varied for various simulations.

In recent years, several computer simulations studies were demonstrated for studying photoacoustic signal generation and their characteristics from biological cells and nanoparticles [32-35]. A numerical study of spheroidal wave function was demonstrated for characterizing the PA wave produced by RBCs and MCF7 cell nuclei [32]. Another simulation study on PA signals from cells with endocytosed gold nanoparticles demonstrated that the gold nanoparticle enhances cellular optical absorption without altering their thermophysical parameters [35]. A theoretical modeling of PA signals from mixtures of melanoma and RBCs was also discussed [34]. Analysis of photoacoustic response from Gold-Silver alloy nanoparticles has been done using finite element (FE) model [33]. These simulations help in understanding the photoacoustic signal generation without physically doing the experiments. However, these simulations require complex mathematical modelling prior to the simulation process depending on the simulation geometry and the target objects. Moreover, these simulations are computationally expensive, thus may take longer

computation time. Therefore, there is a need for an easy and fast simulation process to understand the photoacoustic signal generated from various shapes of nanoparticles.

The aim of this work is to demonstrate a fast and easy computational simulation approach to simulate photoacoustic signal generation from various shapes of nanoparticles. The shapes of nanoparticles are studied here rather than their composition or other properties. The simulated photoacoustic signal is presented in both time and frequency domain to understand the impact of the shapes of nanoparticles on the generated photoacoustic signal.

2. Method

k-Wave simulation toolbox [36] was used for this study. k-Wave is a free open source MATLAB based simulation toolbox. It allows creation of geometric shapes, various simulation geometry, pulsed light excitation, and detector parameters. The simulated output is a time domain photoacoustic signal generated from the target object. Desktop computer running windows operating systems with 64 bit Intel Core7 i7-4770 processor [@ 3.40 GHz], 8 Gb RAM was used in this work.

Fig. 2 Various shapes of nanoparticles used for this simulation study. a) nano sphere (120 nm diameter), b) nano cylinder (300 nm diameter and 610 nm length), c) hollow nano cylinder (300 nm outer diameter, 150 nm inner diameter, and 610 nm length), d) nano cube (170 nm side), e) hollow nano cube (170 nm side, hollow center is of 70 nm side), f) nano triangle (127 nm equilateral triangle with 110 nm height), and g) nano star (consists of two 127 nm equilateral triangle with 250 nm height).

Figure 1 shows the simulation setup. A three-dimensional computational grid of 200x200x200 voxels (10 nm/voxel) with a perfectly matched boundary layer to satisfy the boundary condition was used for all the simulations. A 1500 m/s medium sound speed was used. For simplicity an acoustically homogeneous medium was considered with no absorption or dispersion of sound. A total of 994 time steps each of 3 pico-seconds were used in the simulations. Only one nanoparticle was used as a target object at the center of the simulation geometry. The pulsed light excitation was assumed to be homogeneous on the nanoparticle and thus the initial pressure rise inside the nanoparticle is also assumed to be homogeneous. The excitation laser light is considered to be an ideal delta pulse. However, more realistic finite pulse width (typical laser excitation is around 5-10 ns) can also be implemented in k-wave [37]. An ideal point sensor (Ultrasound detector) was created to acquire the photoacoustic signal. **Most conventional photoacoustic imaging is done with comparatively lower bandwidth ultrasound detectors (100 MHz center frequency and 75% nominal bandwidth). However, there are studies with much higher ultrasound frequencies have been used. For example, up to 1.2 GHz center frequency ultrasound detectors has been used for photoacoustic imaging of single cell [38]. Hence, in this simulation study we haven't**

limited the ultrasound frequencies to low bandwidth, instead, for simplicity ideal point detector with infinite bandwidth is considered here. However, more practical ultrasound detector (single element or array ultrasound transducers) with finite bandwidth and sizes can also be considered. The point sensor was located 750 nm away from the center of the objects. The location of the sensor was also changed at different axis direction to check how the PA signal varies with the various location of the sensor. Only one point sensor at a particular axis direction was simulated in each simulation sets. Seven different shapes of nanoparticle were used. These seven shapes were sphere, cylinder, hollow cylinder, cube, hollow cube, triangle and star as illustrated in Fig. 2. These are the shapes which are normally used in photoacoustic contrast agent development using metallic nanoparticles. Sphere shaped nanoparticle was built with a diameter of 120 nm. Cylinder and hollow cylinder were built with a diameter of 300 nm and height of 610 nm. The diameter of hollow center was 150 nm with same height. Cube and hollow cube were built with same length of 170 nm. The width of hollow center was 70 nm and length of 170 nm. Triangle shaped nanoparticle was built with 127 nm equilateral sides and 110 nm height. Star shaped nanoparticle was built by combining two equilateral triangles of 127 nm length and 250 nm heights. The wide range of dimension is unavoidable due to the restriction of voxel size in forming the different shape of nanoparticles. The hollow shaped nanoparticles were created with same dimension as their corresponding solid shaped nanoparticles. For instance, a hollow cylinder nanoparticle was created with the same diameter and length of solid cylinder nanoparticle.

Fig. 3 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticle. The point detector is located on the positive x axis.

3. Results and Discussion

The simulated results are shown as photoacoustic waves and their corresponding frequency spectrum (Fig. 3 to Fig. 12). Photoacoustic signal is presented in blue and the frequency spectrum is shown in black. As mentioned earlier, the point detector is adjusted to detect the photoacoustic signal at different positions around the nanoparticle. Each figure represents the photoacoustic signal and their frequency spectrum for all the seven shapes of nanoparticles for a particular location of the receiving detector. The simulation results of each shape are plotted in the following sequence across Fig. 3 to Fig. 12: sphere (a-b), cylinder (c-d), hollow cylinder (e-f), cube (g-h), hollow cube (i-j), triangle (k-l), and star shape (m-n).

Fig. 4 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticle. The point detector is located on the negative x axis.

Figures 3 and 4 show the results when the detector is placed along the positive and negative side of the x axis, respectively. Different photoacoustic signal characteristics are observed across the seven shapes. The photoacoustic signals generated by hollow shape nanoparticles are different from that of solid shapes as shown in Fig. 3 to Fig. 12 [Figs. (c, e) and (g, i)]. Differences are also observed in the frequency spectrum of the photoacoustic signal from hollow shape nanoparticle as compared to their respective solid shape counterpart. One can easily verify the simulated photoacoustic waveforms with analytically derived waveforms for regular geometry such as spherical shape. However, when the shape becomes complicated for example star shaped, analytical derivation becomes difficult. Therefore, this simulation toolbox offers an easy alternative for irregular shapes of the target objects.

Next, the point detector location is changed to the positive and negative side of the y-axis, and corresponding simulated results are shown in Figs. 5 and 6, respectively. Similar photoacoustic signals and frequency spectrums are observed on sphere, cylinder, hollow cylinder, cube and hollow cube, as compared to the simulated results when the detector was located at the x-axis. Differences in results are observed for the triangular and star shaped nanoparticles. This is due to the non-symmetric structure of these two shapes with respect to the z-axis. With irregular geometry, the photoacoustic signal detected by the detector at different location will behave differently. This characteristic was also observed clearly on triangular nanoparticle [Fig. 5 (k) and Fig. 6 (k)], even when the detector is shifted to the opposite side along y-axis.

Fig. 5 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticle. The point detector is located on the positive y axis.

Figures 7 and 8 are the simulated results when the detector was placed on the z-axis, on top of the object and bottom of the object with same distance from the center of the object, respectively. In general, the photoacoustic signal and frequency spectrum are different as compared to the results obtained with the detector located on the x-axis [Figs. 3 and 4] and y-axis [Figs. 5 and 6]. One exception being the spherical nanoparticle, as it is symmetric with respect to all the 3 axes, the photoacoustic signal generated by it will have same profile irrespective of the detector position. Even though, cube nanoparticles can also be considered as regular shape over the 3 dimensional spaces, however the edge of the cube could affect the propagation pattern of simulated photoacoustic signal. With the location of the detector on the z-axis, the simulated results from hollow shape nanoparticles are similar to their respective solid shape as per Fig. 7 (e-j) and Fig. 8 (e-j). The only difference observed are the signal intensities, solid shape nanoparticle produces stronger photoacoustic signals compared to their respective hollow shape nanoparticle.

Next the detector was placed at four different locations on the x-y plane (45 degree, 135 degree, -45 degree, and -135 degree). Figures 9 to 12 show the corresponding simulated results. The location of detector is purposely placed diagonally to the object in order to see any new possible signal characteristics. With the changes in the detector location, the distance of point detector to the center of the object is slightly increases. This resulted change in the time of arrival of the photoacoustic signal to the detector. The photoacoustic signals simulated from the shapes with edges are different as compared to the photoacoustic signals when the detector location was on the x, y, or z axis. Generally, similar photoacoustic signals and frequency spectrums are observed on each shape of nanoparticles as seen in Fig. 9 to Fig. 12. Only the photoacoustic signal from triangular nanoparticle behaves differently.

Fig. 6 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticle. The point detector is located on the negative y axis.

Fig. 7 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticle. The point detector is located on the positive z axis.

Differences in the photoacoustic signals (as well as the frequency spectrums) from various shaped nanoparticles reflect their structural differences. Any changes in the location of the detector may result in the change of the simulated frequency spectrum and the photoacoustic signal unless it is geometrically regular over 3 dimensional spaces, for instance a spherical nanoparticle. Irregular shape nanoparticle will generate photoacoustic waves which will be recorded differently depending on the detector position. The signal characteristic reflected in the frequency spectrum or in the photoacoustic pressure signal could be really useful in identifying the structure of a nanoparticle as well.

Fig. 8 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticle. The point detector is located on the negative z axis.

Fig. 9 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticles. The point detector is located on the xy plane ($z = 0$) with an angle of 45 degree with the x-axis.

Moreover, these kinds of simulation required less complicated programming and computationally less demanding. With the stated desktop computer used, it took around **~2 minutes** to complete one set of simulation for one shape of nanoparticles in a simulation environment of 10 nm voxel size. An increase in the voxel size will result faster simulation time. For example, with 15 nm voxel size it takes only **~40 seconds** for one simulation. A decrease in voxel size results in a longer computational time taken. However, more precise photoacoustic signals can be simulated and much finer structure of nanoparticles can be generated with smaller voxel size. **This simulation time is much shorter than previously reported analytical methods, which needs few hours to generate the PA signals [34].** An ideal point detector was used as ultrasound detection system in this work. More complex and realistic ultrasound detectors can also be simulated depending on the need. At present the impact of shape and size are studied here, the properties of the nanoparticles such as density or absorption coefficient can also be altered for more detailed study.

Fig. 10 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticles. The point detector is located on the xy plane ($z = 0$) with an angle of -45 degree with the x-axis.

All these simulations results presented here is with ideal laser pulse excitation. However, in practice typical laser excitation will have 5-10 ns pulse width. Such modifications can easily be incorporated inside the k-wave simulation [37]. One more thing one needs to keep in mind while changing the pulse width is to maintain the thermal confinement condition. Since here the pulse with is infinitely small, so even for nanoscale target size the thermal confinement condition is satisfied. Another assumption in all these simulations is the infinite ultrasound detection bandwidth. In practice the ultrasound detector will have finite bandwidth and therefore, the detected photoacoustic signals will also have lower bandwidth. The combined effect of ideal excitation laser pulse width and infinite ultrasound detection bandwidth leads to very broad frequency spectrum of the detected photoacoustic signals. However, in practice we may not acquire such high bandwidth of photoacoustic signals due to both finite excitation laser pulse width and finite ultrasound detector bandwidth.

Overall, we see there is a distinguishable signature of the shape of the nano particle to the photoacoustic signal generated and its frequency spectrum. However, no quantitative comparison was made between various shapes of the nanoparticle. As the aim of the study was to demonstrate that, it is possible to use a user friendly tool to generate photoacoustic waves from nano particles. Our simulation time is considerably shorter than previously reported analytical methods. Moreover, this tool provides lot of flexibility in terms of object distribution, ultrasound detector characteristics, detector position, medium properties etc. These parameters can be easily modified depending on one's need.

4 Conclusion

Photoacoustic signals generated from single nanoparticle of various sizes can be simulated using k-Wave simulation toolbox in MATLAB. Seven different shapes of nanoparticles are simulated namely sphere, cylinder, hollow cylinder, cube, hollow cube, triangle, and star. Frequency spectrum and photoacoustic pressure signals were used from the simulations. There is a clear variation in the photoacoustic signal depending on the structure of each nanoparticle. From the frequency spectrum also the differences can be observed. These

differences can be useful in identifying the structure of a nanoparticle. This simulation method is simple, cost effective and does not require any prior mathematical modelling. It takes around 3 min to complete one simulation with a normal desktop computer with 15 nm voxel size. When the voxel size used is 10 nm, the simulation time increased to 8-10 min per simulation. More complex and realistic ultrasound detectors can be simulated depending on the need. The properties of nanoparticle in term of absorption coefficient or the surrounding medium can be altered if needed. This simulation method allows a better understanding on which shapes of nanoparticles might be better as contrast agents for photoacoustic imaging.

Fig. 11 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticles. The point detector is located on the xy plane ($z = 0$) with an angle of 135 degree with the x-axis.

Fig. 12 Photoacoustic signals and its frequency spectrums are shown for various shapes of the nanoparticles. (a-b) Sphere, (c-d) Cylinder, (e-f) hollow cylinder, (g-h) cube, (i-j) hollow cube, (k-l) triangle, (m-n) star shaped nanoparticles. The point detector is located on the xy plane ($z = 0$) with an angle of -135 degree with the x-axis.

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