Simulating controllable acoustic waves via photoacoustic with COMSOL Multiphysics 5.3a

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Background:
Deep brain diseases therapy holds promise for a growing number of neurologic disorders, but suffers from a lack of effective drug delivery approach for blood brain barrier penetration. Among traditional treatments, direct intracerebroventricular injection, which enables high local drug concentrations, induces infection, inflammation, and is not readily repeatable. Currently, ultrasound modulation is an emerging treatment approach, as ultrasounds have been shown to modulate neural activities. Many hypotheses have been made to explain the mechanism of ultrasound-mediated neuromodulation, including production of heat and tissue cavitation. Recently, multiple pieces of evidence have indicated that intramembrane sonoporation and activation of mechanosensitive channels are the two main contributing factors underlies ultrasonic neuromodulation. Several simulation and modeling studies have shown that the positive and negative pressures exerted by ultrasound on cells change membrane fluidity and lead to expansions and contraction of the lipid bilayer. This can cause membrane pore formation and ion exchange, which can lead to the accumulation of charge over the course of tens of milliseconds until an action potential threshold is reached. Furthermore, the propagation of the mechanical waves can also cause the activation of mechanosensitive channels, which leads to membrane depolarization and, subsequently, neuron activation.

Clinical testing still requires a craniotomy to allow for ultrasound propagation into the brain because of ultrasonic heating of the skull, and beam aberration caused by the skull's irregular shape and large acoustic impedance. With the lack of an efficient delivery approach, there is a clear need for a method of ultrasound generation in the deep brain. We address this unmet need via development of fiber-based photoacoustic technology for the nasal pathway, which enables localized ultrasound generation in the deep brain.

Idea: photoacoustic technique to enable controllable acoustic wave generation
A fiber-based photoacoustic generator will be built by using pulsed laser for external light excitation; the fiber tip generates acoustic waves through the optoacoustic effect by a specially designed Nano-polymer composite layer at its coating layer. Compared with the electronic transducer, the fiber based photoacoustic generator has much smaller size, making it fit for deep brain implementation.

Objective:
In a pilot study, we have demonstrated that the frequency of photoacoustics (PA) can be modulated via the geometry of fiber coating, which is the key to ultimately realize desirable frequency generation.

Now we want to clearly illustrate the relationship between the PA geometry and the ultrasound it generates. Being able to find this relationship is key in being able to generate specific ultrasounds that can potentially modulate neural activity. Simulations are the best way to find this relationship, as we are able to effectively control the parameters and quickly test different conditions within the system.

The steps:
We used Comsol Multiphysics 5.3a as the tool for our simulation. Here, the project is separated to the following steps:

1. Master the basic operation of the software
2. Repeat the results in a related simulation paper, "Finite element modeling of an optical fiber photoacoustic generator performance". This allows us to confirm that our simulation methods are correct.
3. Match the simulation results with our experimental results
4. Find the parameters for desired ultrasound generation

Work Summary:
We focused specifically on repeating the results of the associated simulation paper (steps 1-2). The first few days were spent getting familiar with the software via tutorial builds (e.g. Laser Heating of a Silicon Wafer) and mastering the basic workflow in Comsol. From there, we worked on repeating the results of the related simulation paper. Upon creating a simulation that produces results that closely matches those in the paper, we created another simulation using identical parameters, but one that has a spherical absorption film rather than a rectangular one. This allows us to begin comparing simulation results with experimental onces.

Modeling Setup:
We constructed a 2D-axisymmetric geometry of our photoacoustic generator setup built up in 4 dimensions (3 space dimensions and 1 time dimension). In it, a thin absorption film with radius 62.5um was placed on top of the optical fiber tip with the same radius, which was then pointed towards a semi sphere of water with radius 1mm. A domain point probe "P" was defined in order to monitor acoustic pressure and was placed at (1e-4, 14e-4) meters. The absorption film was created using graphite foil and the optical fiber was made with glass fiber. Meshing elements inside the model had maximum size 30um in the fiber tip and 1um in the absorption film. Three physics were applied to the model: solid mechanics, heat transfer in solids, and pressure acoustics. Additionally, the temperature coupling, thermal expansion, and acoustic-structure boundary multiphysics were selected. Computations were done from 0 to 3000 nanoseconds, with a step size of 30 nanoseconds.

The heat source was applied to only the absorption film domain, and was defined by the equations G(y,t) and I(t), which represpresent heat flux and laser power density, respectively.

$$G(y,t) = I(t)\frac{(1-R)}{\delta}\exp(-\frac{y}{\delta}) \qquad I(t) = \frac{E_p}{A\cdot\tau_p}\exp(-\frac{4\cdot(t-\tau_p)^2}{\tau_p{}^2})$$

Here, R is reflectivity, y is the axial direction, and A is the area of the absorption film surface. Then, keeping all parameters the same, we created a separate simulation in which we had a spherical absorption film rather than a rectangular one. In this simulation, the spherical film had radius 200um and had a max meshing element size of 6um.

Results:

In the simulation with the rectangular absorption film, we were able to match the original paper's graph of ultrasound pressure. Our simulation's graph had the same general shape, as well as similar extrema compared to the original. Additionally, the acoustic pressure animation displayed one singular propagation of acoustic pressure, indicating that our heat source equation is correct. The temperature visual was similar to the one in the original paper, and our stress model showed no outstanding data points.

However, in the simulation with the spherical absorption film, we were unable to match the simulation results with our experimental results. As of now, there are many unaccounted for oscillations in the acoustic pressure graph, which isn't seen at all in the experimental results. In the acoustic pressure visual, we can see the initial propagation of pressure, followed by many weaker propagations.

Future Directions:

Currently, the first order of business is adjusting the spherical film simulation to match our experimental results. Until we are able to do this, we cannot experiment to try to find the relationship between the PA setup and the produced ultrasound. Currently, we believe that there needs to be adjustments made in the heat source expression and/or the materials list. Our heat source needs to have a more exponential growth curve; the growth needs to be more drastic.

Once that is complete, we will begin looking for ways to identify the relationship between the PA generator setup and the produced ultrasound. One particular experiment we wish to try is adjusting the radius of the absorption film and seeing how that impacts the produced ultrasound. This would be the beginning of our finding a method of producing desired ultrasounds. Changing one parameter at a time, we will monitor how the produced ultrasound is affected, and develop a potential relationship between the PA geometry and the ultrasound.

Besides creating a concrete relationship between these two items, we also want to experiment with a simulation that utilizes a concave absorption film which focuses the laser shot through the optical fiber. We want to observe what type of ultrasound a focused laser would create, and that can be accomplished by having a concave absorption film.