Photoacoustic NeuroImaging

Computer Integrated Surgery II

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Timothy Mullen & Darian Hadjiabadi

Mentors: *Dr Emad Boctor, Dr Behnoosh Tavakoli, & Dr Daniel Thorek*

Introduction

As part of preliminary research into photoacoustic imaging of neuronal firing:

- Designed and constructed gelatin phantom
- Performed photoacoustic characterization of commercially available fluorescent dyes
- Tested photoacoustically responsive dyes for ability to be used as pH indicators across the pH range seen in neuron action potential
- Tested a Phthalocyanine dye with skull phantom

Current brain imaging modalities do not provide sufficient spatial and temporal resolution to fully understand the signal flow between neurons in the brain in response to stimuli. JHU's NIH BRAIN Initiative grant project seeks to overcome this barrier using voltage or pH sensitive dyes that can precisely indicate the firing of very small numbers of neurons with good time resolution. To be effective, the signal output by these dyes must be observable through a non-invasive method. The advantages of photoacoustic imaging, namely its rapid, sub-millimeter accurate, non-invasive acquisition, make it a promising candidate for this project.

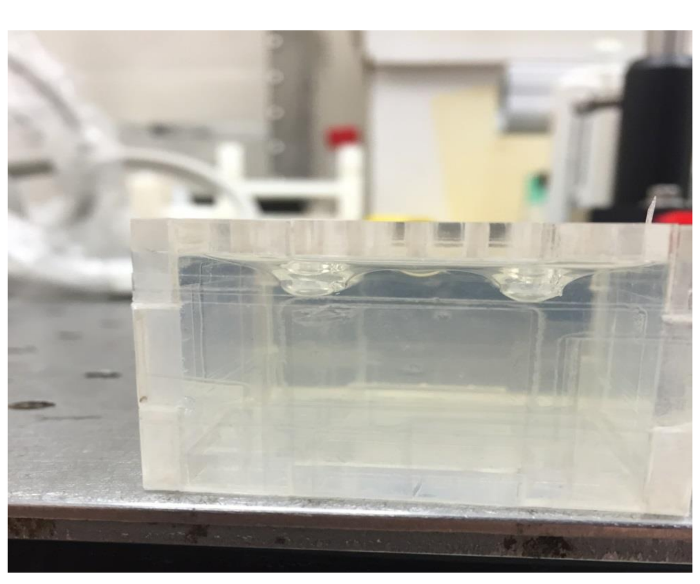
The Problem

Current neuro-imaging technologies cannot capture the precise details of neuron signaling cascades.

- fMRI has poor spatial resolution, and has a temporal resolution in the seconds range.
- EEG has excellent temporal resolution but signals can only be monitored from the scalp.

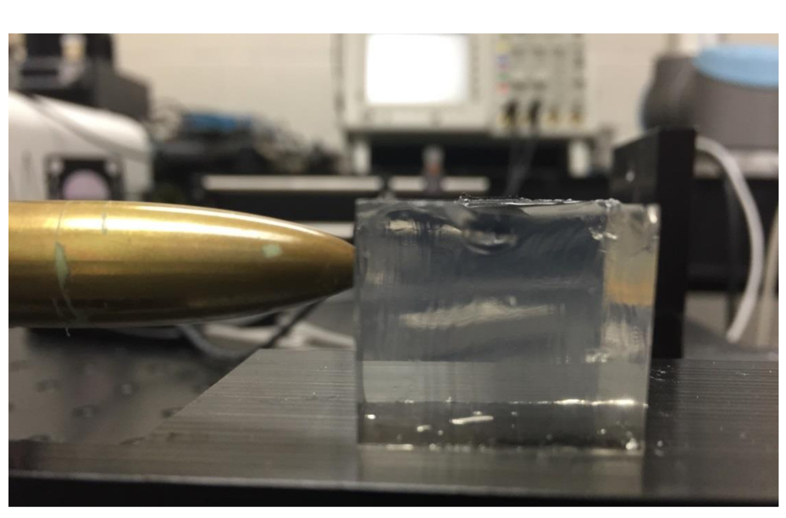
The NIH grant is currently for exploratory purposes, and photoacoustics is a potential but unproven solution. Over the course of the semester, our aim has been to produce preliminary photoacoustic response spectra. While the absorbance spectrums of many of these dyes are known, photoacoustic response is not completely predicted by absorbance. The influence of other variables necessitates quantitative testing.

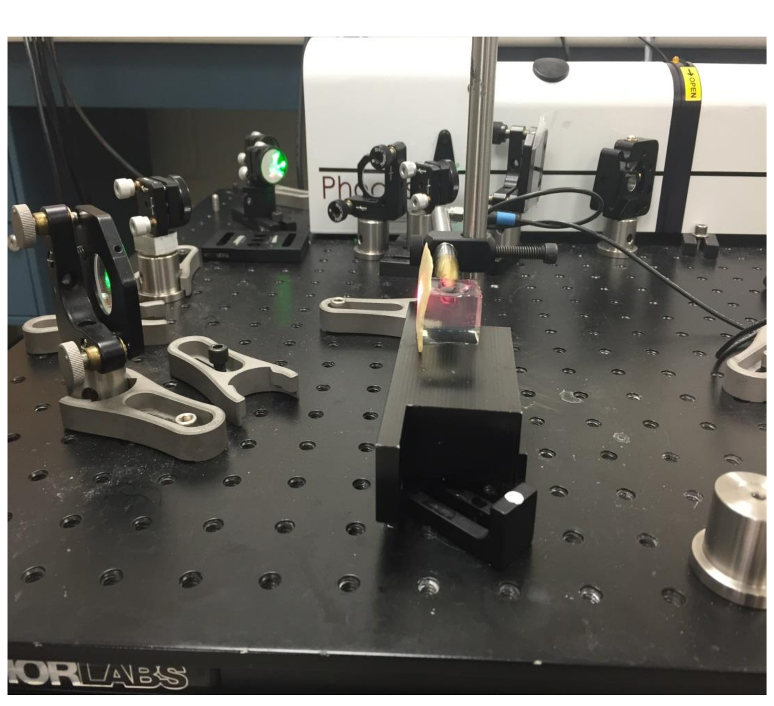
The Solution



(Left) We designed and iteratively improved a phantom mold, to be cast with porcine gelatin. The phantom contains four separate wells to hold different candidate dyes. The use of cast wells in the aqueous gel creates a nearly homogeneous path for light and acoustic signal transmission, avoiding material transitions common in other phantoms.

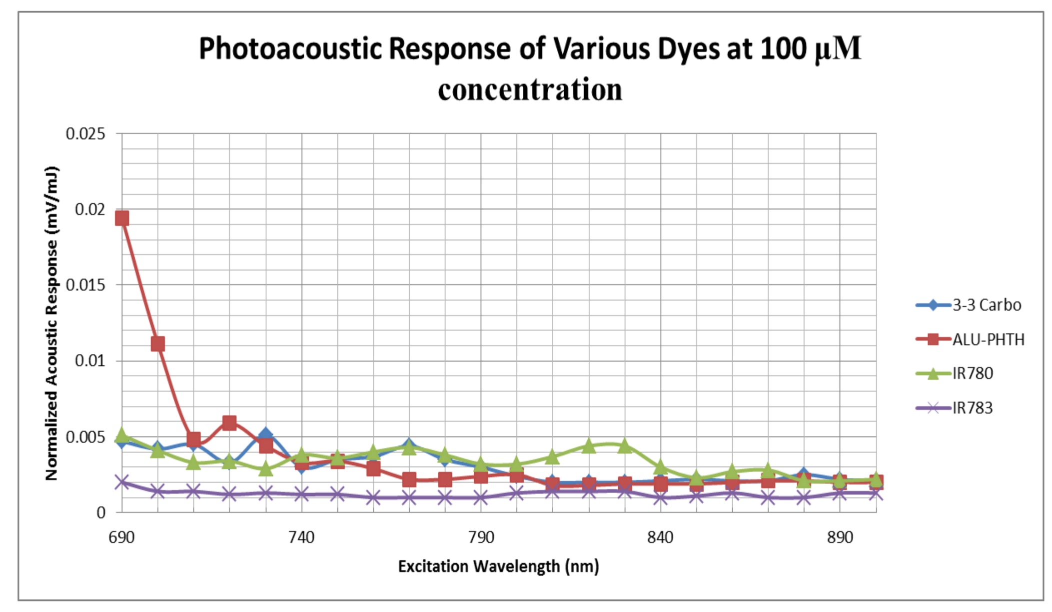
(Right) A hydrophone was pushed up against the gel phantom in order to acquire the photoacoustic signal. At a distance of approximately 10 mm from the well, it will take 6-8 microseconds to receive the photoacoustic output.



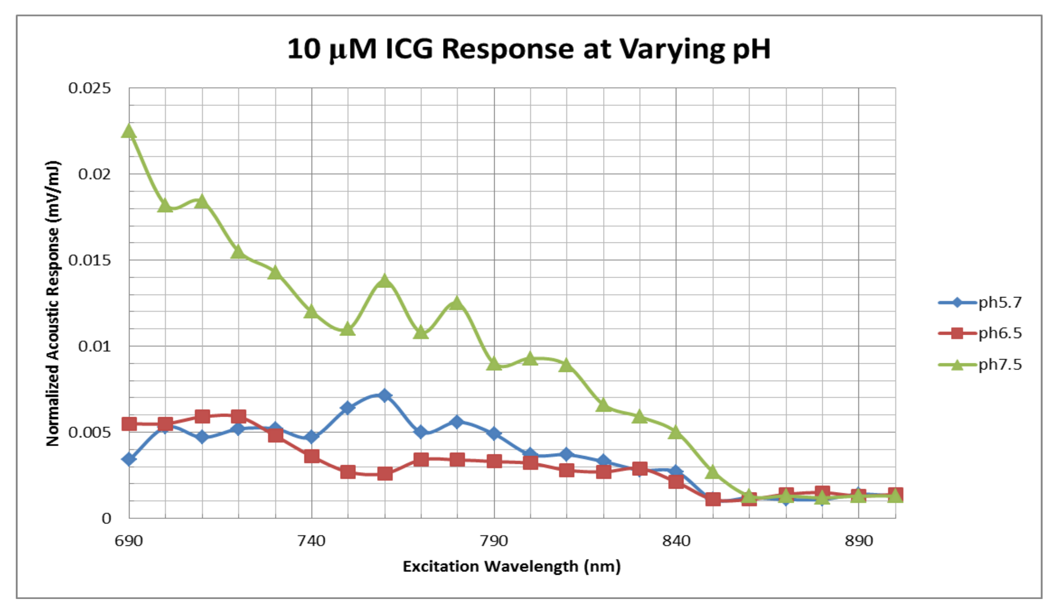


(Left: Full system in use with skull sample) An OPO laser is aimed directly at the well using mirrors. The hydrophone is aimed at the well, at a 90 degree angle to the excitation laser path. The photoacoustic signal is picked up by the hydrophone as the dyes are bombarded by light energy. The hydrophone response is monitored via an oscilloscope (not pictured).

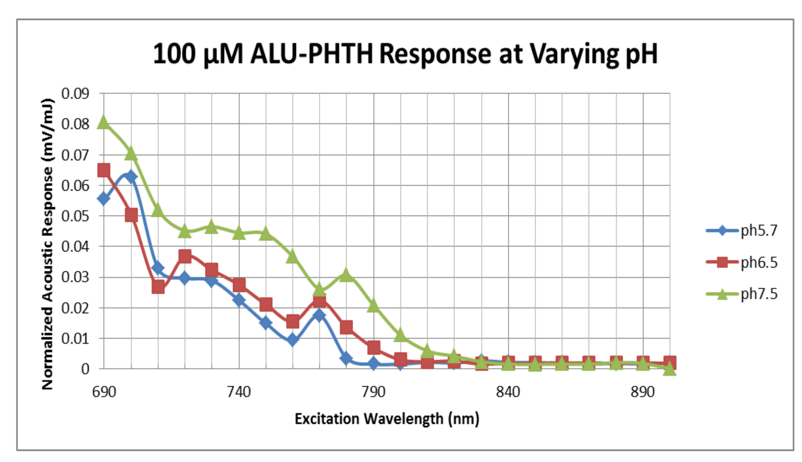
Outcomes and Results

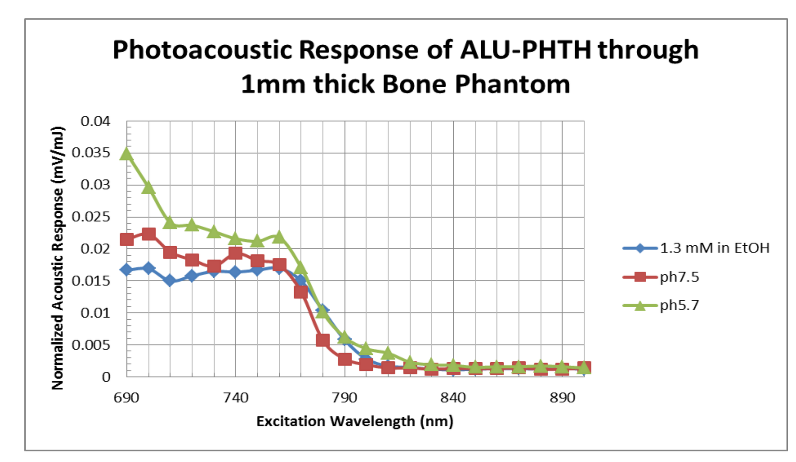


Photoacoustic response spectrums of dyes with absorbance peaks in the near infrared region. For each sample, the output of the hydrophone was divided by the laser's energy at that wavelength to give the normalized response

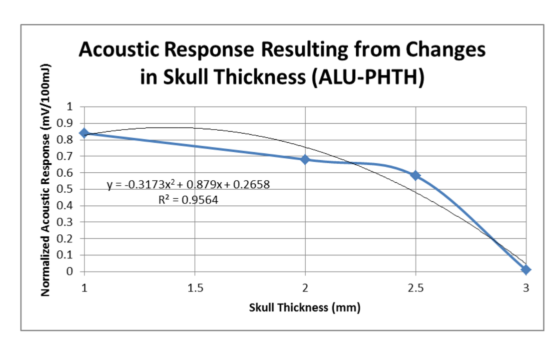


Indocyanine Green (ICG) showed a different early spectrum response at pH 7.5 than at lower pH values. Global maxima also varied with pH





The introduction of a piece of bone between the hydrophone and the phantom seemed to "smooth" the response. The potentially useful local max/min trend at 770 nm disappeared when the bone was introduced



Increasing thicknesses of bone between the hydrophone and gel decreased signal magnitude

Future Work

- Baseline tests on a larger variety of dyes
- More continuous pH variation
- Test more dyes on skull phantoms
- Automate collection

Lessons Learned

- Importance of casting consistency – There was much difficulty in getting a consistent, good quality well. Eventually, casting procedure changes gave a more repeatable product
- Lack of automated data collection mechanism greatly hampered the number of tests we could run and the resolution of our data

Credits

Tim – Phantom design and construction; data collection

Darian – Data processing; data collection

Citations

- Real-Time Imaging of Electrical Signals with an Infrared FDA-Approved Dye. Treger,Jeremy; Priest, Michael.
- Non-Linear Population Firing Rates and Voltage Sensitive Dye Signals in Visual Areas 17 and 18 to Short Duration Stimuli. Roland, Per E; Eriksson, David; Tompa, Tamas
- Photoacoustic imaging of prostate brachytherapy seeds in ex vivo prostate. Boctor, Emad; Kuo, Nathanael
- Biomedical Photoacoustic Imaging. Beard, Paul
- The challenges for quantitative photoacoustic imaging. Cox B.T., Laufer J.G., Bear P.C.

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