

April 6, 2017

National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

To Whom It May Concern,

I am a PhD student working in the computational biophysics lab of Dr. Grace Brannigan at Rutgers University Camden. Enclosed is my application to the NIH F31 Ruth L. Kirschstein Predoctoral Individual National Research Service Award. Dr. Brannigan's Lab specializes in computational biophysics, specifically proteins, membranes, and small molecules through molecular dynamics simulation.

In my proposal: **Computational Analysis of Nicotinic Acetylcholine Receptors in model *Xenopus* Oocyte and Neuronal Membranes Using Coarse Grained Approaches**, I present three aims I hope will benefit the biomedical community. First, I will simulate a series of model *Xenopus* oocyte membranes with various ratios of lipids containing the polyunsaturated fatty acid DHA and characterize the nicotinic acetylcholine receptor (nAChR) boundary lipids, to determine if oocyte membranes supply nAChR with lipids that promote functionality, and if not, what may be suitable alternatives. This will benefit experimentalists supplying preferential lipids to incorporate into experimental membranes.

Secondly, I want to understand what determines the membrane domain that nAChR (and other pentameric ligand-gated ion channels (pLGICs)) partition to. Are domain preferences determined by protein sequence, so that, for instance, excitatory and inhibitory pLGICs would be organized into different domains? Or is it determined by which lipid domain is most flexible and can deform most easily around the general conical shape of the pLGIC transmembrane domain, regardless of the pLGIC sequence?

Finally, I propose using the skills I develop to construct a package for an open source, widely-used molecular visualization and analysis software (VMD). This package will allow users to quantify elastic moduli of arbitrarily complex lipid bilayers, in order to allow other researchers to bridge elastic and molecular perspectives of cell membranes.

Please assign this application to the following: Institutes/Centers: NIGMS (General Medicine) and NIDA (Drug Addiction).

Please assign this application to the following: Irena Levitan, James Kindt, José Lasalde-Dominicci, Pei Tang, Ryan Hibbs

These individuals all specialize in pentameric ligand gated ion channels and/or membranes. As our proposal focuses on the effects that nAChR and its membrane have on each other, we feel these individuals would be the best matches.

Please do not assign this application to the following:

Please expect letters of recommendation will be sent from: Dr. Joesph Martin, Dr. Sean O'Malley, Dr. Jérôme Hínen.

This research is multidisciplinary in nature; using both physics and computer science to better visualize and analyze biological phenomena at the nano-scale.

If accepted, I look forward to preforming this research to better the tools of our scientific community. Thank you for your time and energy evaluating my proposal.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

A handwritten signature in black ink, appearing to read 'Liam Sharp', with a stylized, cursive script.

Liam Sharp