Eric Kenji Lee
Boston University BBC Ph.D. Statement of Purpose

As a hopeful future neuroscientist, I am interested in elucidating cognitive mechanisms of the cortex that help link sensation to behavior. Specifically, I am interested in exploring population dynamics during behavior and decision-making and applying computational methods to the parsing of electrophysiological and/or calcium-imaging data. Using an experimentally informed approach, I also hope to apply dimensionality reductive and machine learning techniques to the data to expose latent spaces salient to the observation of learning and decision-making; central to these approaches is my belief in both theory grounded in biological priors and in using theory to drive new experimentation; a virtuous loop. As a Ph.D. student at Boston University in the BBC Program, and later as a professor of neuroscience, I hope to investigate, elucidate, and probably complicate our understanding of how the brain makes sense of the world.

The summer after my freshman year, I joined the University of Hawaii's MRI Lab under Dr. Linda Chang investigating the deficits in working memory among HIV/AIDS patients. I learned MATLAB and presented my results showing a decrease in frontal lobe activation with a corresponding increase in task performance during a cognitive intervention – a sign of improved working memory. The PI showed me that the default parameters I used in my analysis were incorrect because the smoothing was too small to make the variability of atrophied brains comparable to controls. In my excitement at a positive result, I neglected to critically evaluate my priors. In that summer, I learned it is not enough to know how to write code, a scientist must understand that selecting an algorithm (and corresponding parameters) is to assume priors regarding the data. I returned to campus convinced that a math major alone was insufficient and declared a double-major with biochemistry. I struggled with this increased workload and after consulting with academic advisors, I was referred to a physician where I was diagnosed with delayed sleep phase disorder (a circadian rhythm disorder) which significantly hampered my academics. After treatment, I did much better academically; I later went on to do well in a master's degree in applied mathematics at the UW while working full-time as a research assistant.

In the master's program, I worked on non-parametric techniques – these methods can expose latent phenomena and are relatively conservative in their priors. I explored these methods especially in the context of model-building and have begun to apply these techniques to data problems. In an independent study, I used multichannel singular spectrum analysis to show evidence for the differential modulation of Pacific salmon subpopulations by oscillatory climatological phenomena. These results have important implications for fisheries management and is currently being written up as a first-authored manuscript. I hope to continue to apply these approaches to functional data in the brain.

In 2015, I joined the Allen Institute under Dr. Jérôme Lecoq investigating the functional properties of neurons in mouse visual cortex during behavior. I conducted retinotopic mapping using intrinsic signal imaging and wrote automated analyses in Python. I also utilized 2-photon calcium-imaging to record single neurons across cell types, layers, and areas in mice transgenically modified to express GCaMP6f (a fluorescent indicator of neuronal activity). We showed that, even in putatively lower-order areas like V1, neurons are highly-selective for abstract features. These neurons are more specific than previously supposed by "simple" models and gives evidence against

the canonical model of hierarchical computation. Our manuscript is currently under review at *Nature*. From this experience, I gained a more circumspect understanding of the data I was collecting, and this was crucial towards my success on one project in which I helped to develop a solution for murine eye tracking.

An essential component of our imaging set-up was an eye tracker composed of a camera trained on the eye and an illuminator. Unfortunately, we were seeing an untenable artifact: the pupil would transiently switch from gray to white during the experiment which was not amenable to our eye tracking software. I was entrusted to work with Dr. Michael Buice to find a solution to this problem which was jeopardizing a key deliverable for our project. In the literature, I found separate phenomena known as the bright and dark pupil effects and reasoned there was not enough angular distance between the camera and the illuminator thus producing an intermediate effect. I conducted pilot experiments with different geometries and processed the data with original code. This suggested adjustments to the set-up and algorithm parameters. I presented a geometry robust to this effect (along with a parameter set) that properly processed the associated data in time for our data release. I presented this work as a first-authored poster at the Society for Neuroscience conference in 2017. This success would not have been possible if I had not had so much daily hands-on knowledge of our 2-photon imaging rig and the ability to understand the eye tracking algorithm.

At the Program in Brains, Behavior, and Cognition, I hope to work with Professor Chandramouli Chandrasekaran in using probe electrophysiology to explore goal-directed behavior in dorsal premotor (PMd) and dorsolateral prefrontal cortex (DLPFC) of the macaque. I've been aware of Professor Chandrasekaran's work during his tenure as a postdoc in the Shenoy lab and have had several opportunities to chat with him including speaking about me joining his new lab at BU. I bring a strong quantitative background in exactly the sorts of approaches that have received much traction in this subfield (dimensionality reduction and machine learning) which I hope to leverage to develop into models of cognition in this context. I also have previous animal experience in a visual discrimination paradigm so I understand some of the difficulties regarding behavioral training and *in vivo* recording especially in 2-photon imaging.

After six years of neuroscience research, I feel I am passing through a liminal stage: I'm beginning to understand neuroscience not as a monolithic construct contained in the *Principles of Neural Science*, but rather as an active community of teams of physiologists, behaviorists, and theorists each contributing complementary – often competing – voices to the conversation. I have deeply enjoyed being both privy to and a participant in this research community and hope to continue this while at Boston University training to be a future professor.

Thank you for reading and I hope you will take my application into consideration.

Sincerely,
Eric Kenji Lee