Personal, Relevant Background, and Future Goals Statement
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My path into neuroscience began with a simple observation: that people can inhabit the same room and not be living in the same world. In *[redacted]*, I worked as a teaching assistant in a first-grade classroom supporting *[redacted]* the autism spectrum. During lessons, he would point to shapes he perceived in ceiling tiles and ask whether I could see the same doors or track lines he saw. The patterns were stable and meaningful to him, yet invisible to me. Later, I lived next door to *[redacted]* schizophrenia. He would murmur in response to voices that only he heard, and one night I found him scrubbing spilled milk into the floor because he believed it would protect us from harm. These experiences made clear to me that perception is not a passive recording of the world. The brain selects, weights, and interprets experience in ways that can diverge profoundly across individuals. I wanted to understand how those interpretations are formed, and how they change across development, aging, and disease.

Intellectual Merit: To begin studying how different minds extract and update meaning from the same environment, I joined Dr. Bernardo Sabatini's laboratory at Harvard Medical School, where I examined how learning strategies change as cortical circuits mature in mice. Working with postdoctoral fellow Dr. Kevin Mastro and in collaboration with Dr. Beth Stevens, I learned viral targeting, histology, acute slice preparation, and whole-cell patch-clamp physiology, which allowed me to measure changes in inhibitory microcircuit function directly. I then learned to run and modify the two-armed bandit task (2ABT), writing behavioral control logic in Arduino and adapting MATLAB pipelines to quantify trial-history dependence and reinforcement learning parameters. As I trained animals daily, I observed that mice differed not only in how quickly they learned, but in the balance they struck between relying on recent outcomes versus longer reward histories. These differences were stable across days within the same animal, suggesting a trait-like learning strategy rather than trial-to-trial variability.

We focused on the maturation of parvalbumin-positive (PV) interneurons in medial prefrontal cortex (mPFC), which strengthen inhibitory control over pyramidal neurons during adolescence. Whole-cell recordings confirmed developmental increases in PV-interneuron firing capacity and inhibitory synaptic transmission. Behaviorally, we adapted a Recursively Formulated Regression Model (RFLR)[1] and confirmed that adolescent animals weighted recent outcomes more heavily, while mature animals integrated evidence over longer timescales. When PV-interneuron activity was both chemogenetically and optogenetically reduced in adult mice, their learning behavior shifted toward the adolescent pattern. This work forms the basis of **a manuscript in preparation, on which I am a co-author**, and provided my first clear indication that learning strategy can be mechanistically grounded in circuit development.

In the course of modeling the behavior, I noticed a second pattern distinct from the change in evidence-integration timescale. Older mice not only integrated over longer histories; they also updated less from each reward. The magnitude of reward-based updating declined with age, even when the integration window was held constant. This indicated a shift in outcome valuation, not just in how evidence was accumulated. Because valuation of reward history is governed by dopaminergic signaling in the nucleus accumbens (NaC), this pointed to a neuromodulatory mechanism that changes over lifespan.

To test this directly, I designed and led an independent longitudinal study examining how learning strategy changes within the same individuals across aging. I collected over three million trials across three years from mice performing the two-armed bandit task from early adulthood (P90) through late aging (P750). Using the same adapted RFLR framework, I found that reward-based updating declined past 24 months of age. As reward influence weakened, choice policies became increasingly rigid over time, indicating a progressive loss of behavioral flexibility that could not be explained by cortical maturation alone.

To investigate the potential role of dopaminergic signalling, I implemented fluorescence-lifetime fiber photometry in the NaC. Unlike standard intensity-based photometry, fluorescence lifetime reports the

time a fluorophore remains in the excited state before photon emission. Because this biophysical property changes when dopamine binds the sensor but does not depend on sensor expression level, excitation power, or fiber coupling, lifetime provides a stable baseline reference that enables simultaneous measurement of tonic dopamine levels and phasic dopamine transients in freely-moving animals. This system was recently developed in the Sabatini group and, to our knowledge, provides the first longitudinal lifetime-resolved dopamine recordings during behavior.[2] Using this approach, preliminary analyses show that tonic dopamine levels decline across adulthood, while phasic reward-evoked responses remain largely intact. This dissociation indicates that outcomes continue to be represented, but the baseline neuromodulatory environment required for dopamine-dependent plasticity shifts with age. As tonic dopamine falls, the threshold for updating policy increases; older animals are not failing to encode rewards, but are less able to translate those encoded outcomes into changes in behavior. My next step is to use FLIM-AKAR (fluorescence-lifetime based optical reporter of PKA activity) to directly measure the intracellular signaling threshold at which dopamine drives plasticity, and to manipulate this threshold to test causality. This remains an ongoing project that **I have been fortunate to lead, and preliminary results will be presented at a nanosymposium session at the 2025 Society for Neuroscience (SfN) Meeting.**

However, extending this work made a methodological limitation clear. In systems neuroscience, we often interrogate one cell population at a time, but the computations that shape learning arise from interactions across inhibitory, excitatory, neuromodulatory, and glial networks. For example, whether a reward leads to a change in strategy depends not only on dopaminergic signaling in D1- and D2-spiny projection neurons, but also on how cholinergic interneurons tune synaptic responsiveness and how astrocytes regulate dopamine availability. Standard optogenetic and chemogenetic approaches can reveal whether a population is involved in behavior, but they cannot explain how learning is computed through these coordinated interactions. To truly understand how learning strategies arise and change, we need tools that allow simultaneous measurement and manipulation across multiple interacting cell types in the same behaving animal.

To pursue this, I joined George Church's laboratory at the Wyss Institute, where I am *[redacted]*. My current work focuses on *[redacted]*. The long-term aim of this work is to *[redacted]*. This project is ongoing and currently in the platform-development stage, but it is motivated by a clear objective: to build tools capable of measuring and perturbing distributed circuit computation at the scale where learning is actually implemented.

Together, these projects have shaped my scientific arc: development influences how experience is incorporated into circuits, aging alters the neuromodulatory conditions that guide behavior, and learning emerges from distributed interactions across cell types. I am deeply grateful to my mentors who treated my curiosity as something worth cultivating. In graduate school, I hope to continue growing alongside inspiring peers and mentors, and am deeply committed to passing that support forward by mentoring the next generation of passionate students.

Broader Impacts: My broader impact work grows from the same observation that shaped my scientific interests: people learn and interpret the world differently, and those differences are a source of insight worth cultivating. Yet access to scientific training remains uneven. Many students never enter research, not because they lack curiosity, but because they have no environment where their questions are taken seriously and where they are expected to contribute.

Four years ago, there was no undergraduate-run research environment at Harvard where students could independently pursue scientific questions. I helped build and lead what is now the OpenBio Laboratory, a student-run biomakerspace built from the ground up. We negotiated with the university to secure a dedicated BSL-1 laboratory and, with guidance from our faculty mentor Dr. David Mooney, developed

the safety systems, training curriculum, and experimental pipelines required for students to design and execute publishable research. What stood out to me was not only that students were capable of producing meaningful work, but that their ideas were rooted in personal experience, expanding the scientific questions our community considered valuable.

To extend this model beyond Harvard, I co-founded and directed the OpenBio Summer Research Institute (SRI), a free-of-cost program that has matched more than **200 underserved high school students** to-date with PhD mentors across the country. Many students came from **schools without laboratory courses, from U.S. states that are historically under-resourced in STEM, or from international contexts where even consistent internet access was uncertain**. Yet, through SRI, they developed original research projects, each publishing first-author work in collaboration with *The Young Researcher* journal. In many cases, our students have continued into collegiate research positions or conference presentations —undertakings that would likely have been unattainable otherwise. These outcomes reinforced in my mind that curiosity is widely distributed; what is scarce is structure and institutional trust.

Through SRI, I also came to understand a separate truth. When students from different contexts enter research, they bring different problems. A student in Ghana studied heatwave-driven crop instability. A student in rural Arkansas examined fungal resistance in soybean agriculture. A student in Morocco analyzed freshwater supply predictability. These projects emerged not from textbooks, but from personal experiences/environments. And the science was stronger for it. To support exchange across these different research contexts, I helped establish OpenBio's annual conferences, now also entering their fourth year. These events bring together biomakerspaces and student research communities from institutions including MIT, Stanford, Cornell, UBC, Ashesi University, Imperial, RWTH Aachen, and others. With over **1,500 participants across 17 countries,** the conferences are built not simply to present results and hear about leading-edge work from leaders of the field, but to build networks where students can share methods, resources, and scientific framing.

This work began from nothing: no lab, no funding, no precedent. It has since grown into an international network because students were given room to build it. My goal moving forward is to continue expanding environments where students can pursue the scientific questions that arise from their own communities and histories. Those closest to a problem are often those best positioned to solve it. The role of scientific institutions is to equip that agency.

Future Goals: In graduate training, I will study how distributed neural populations implement learning and how neuromodulatory changes alter thresholds for behavioral updating. I plan to develop and apply multi-population measurement and perturbation tools to identify circuit mechanisms that preserve flexibility over time. Long-term, I aim to lead a lab studying how neuromodulatory tone and neuron–glia interactions shape plasticity/decision-making. My research and broader impact work are inseparable. At OpenBio, I have enabled students to generate original work regardless of prior access. I plan to continue this model, creating infrastructure where contribution is encouraged and where students pursue questions rooted in their own lived contexts.

References: [1]Beron CC, Neufeld SQ, Linderman SW, Sabatini BL. PNAS 2022;119:e2113961119. [2] Lodder B et al. Neuron 2025;113:3554–3566. doi:10.1016/j.neuron.2025.08.013.