

Title: Understanding the role of fast and slow dopamine signaling in vivo at Harvard medical school

Location: Bernardo Sabatini Lab, Harvard Medical School, Boston, USA

Dear master student:

We would like to let you know about a new internship opportunity in our lab that involves investigating dopamine dynamics in vivo. Dopamine plays an important role in behavior (learning, movement, motivation etc.) and several neurological diseases/disorders (Parkinson's disease, addiction and others). Fast (phasic) dopamine signals play an important role in learning and can modulate movements on a fast timescale. Slow (tonic) dopamine has been thought of as a set-point, which can determine the impact of the fast dopamine response. However, our understanding of how dopamine works in the brain and how it causes neurological disease remains limited. Part of the problem is that we are lacking techniques that allow for the capture of the simultaneous two modes of dopamine signaling. In the last three years we have developed a new system that allows for the measurement of absolute dopamine concentration in vivo at high speed, which has given us for the first time the capability to measure fast and slow dopamine simultaneously in freely moving mice. This project involves answering the following longstanding questions in the field:

- 1. Does tonic dopamine change during learning, motivation and animal state?
- 2. What is the impact of tonic dopamine change on behavior?
- 3. What is the effect of tonic dopamine on phasic dopamine and downstream circuit signaling?

This internship involves answering the questions stated above and learning essential and cuttingedge techniques for the field of systems neuroscience. Techniques taught in this internship include Fluorescence lifetime photometry and absolute dopamine measurement, in vivo optogenetics and/or DREADDs manipulation, drugs testing, mouse behavioral analysis, brain extraction and histological analysis. In addition, depending on the interest of the student, we can teach programming/data analysis, mouse brain surgery, two-photon fluorescence lifetime microscopy and other techniques. Besides teaching specific techniques, we are dedicated to mentoring students and encourage development of various skills essential for a starting scientist, such as critical thinking, discussing science, independence and experimental planning. Finally, our lab environment and wider neuroscience Harvard medical school community allow many opportunities for students, such as attendance of journal clubs, excellent talks and conferences.

We are looking for a biology/neuroscience master student that can tackle this project with us for a period of 8-12 months, starting between mid-January-March 2025. No previous mouse experience is required to apply for this internship, enthusiasm and motivation is enough!

Please don't hesitate to reach out to us (email: bart_lodder@hms.harvard.edu) if you have any questions and/or if you are interested in the internship.

Thanks,

Tarun Kamath and Bart Lodder PhD students in the Bernardo Sabatini lab