Undergraduate Summer Internship in Systems Biology

Internship Project Description: Summer 2018

Project Title: Various Projects in the Gunawardena Lab
Supervisor Name: Jeremy Gunawardena
Lab PI Name: Jeremy Gunawardena

Project Description:
The Gunawardena Lab studies cellular information processing using a combination of experimental, mathematical and computational techniques. We have a tradition of mentoring undergraduate students into scientific research and welcome students from groups who are underrepresented in science. Several of our students have been first authors on papers arising from their undergraduate work (details can be found on our website at http://vcp.med.harvard.edu/people). Our students come from a range of backgrounds and countries and usually work on theoretical projects, as it is difficult to make progress on an experimental project in a short internship.

Projects arise from the main research directions in our lab. At present, we are interested in the following kinds of question. **How is information encoded through post-translational modification (PTM) of proteins**? The concept of "PTM code" is often mentioned in the literature but it has been hard to explain how this works in biochemical terms, to assess how much information is being "encoded" and how that information is accessed by other cellular processes. We are working on this partly in collaboration with Galit Lahav's lab, with the heavily modified tumour suppressor protein, p53, as our example. For an overview, see PMID 22899623 (available on our website, along with other papers below). **A second question is, how does energy expenditure contribute to molecular information processing**? An important insight came from John Hopfield's classical results on kinetic proofreading. Hopfield's work can be interpreted as saying that, if a biochemical mechanism is trying to accomplish some information processing task and the mechanism operates without expending energy at thermodynamic equilibrium, then physics sets an upper bound to how well it can perform that task. We call this the "Hopfield barrier". What are the Hopfield barriers for different kinds of information processing? How can these barriers be broken by expending energy? What trade-offs arise in expending energy to achieve desirable properties, such as speed and accuracy? These kinds of ideas are particularly significant in trying to understand how eukaryotic genes are regulated, which has become an important focus in our lab, partly in collaboration with Angela DePace's group (PMID 25475875, 27368104). **Finally, a third direction concerns learning, a particularly complex form of information processing that is widespread in both biological and computational systems**. We are developing machine learning algorithms to analyse complex datasets that come from clinical sources, such as cytokine profiles (PMID 26553024), but we are also interested in how learning is accomplished within the organism. Are there analogies between learning by neuronal networks and information processing by biochemical networks?

Our lab offers a halfway house between the biological and the mathematical sciences. If you are not scared of mathematics, have a strong interest in modern biology and are willing to work really hard for a couple of months, you could have a lot of fun.