

Proposed Summer 2012 HHMI Undergraduate Research Projects

Detection of glucose in Exhaled Breath Condensate

The objective of this research is to develop a new, noninvasive, portable glucose measuring device based upon exhaled breath condensates. Controlling the blood glucose level is critical to diabetic patients, and the current method of measuring the blood glucose level is to prick a finger and collect a drop of blood. This process is not patient-friendly. We hypothesize that the lung lining fluid is in equilibrium with that in the blood. If this is the case, this may provide a method to non-invasively accurately approximate the glucose concentration blood. The glucose in the respiratory fluid can be collected by condensing the Exhaled Breath Condensates (EBCs). The objectives of this protocol are to 1. Determine a predictive functional relationship between the glucose levels in the exhaled breath condensate and that in the blood and 2. Estimate the uncertainty and confidence in the predictions.

Comparative analysis of the genomes of Enterobacteriaceae

Use bioinformatics to look for rules in the conservation of gene order in Salmonella, E. coli, and related bacteria

Computational modeling of 3D structures and network of protein interactions

Student will be involved in developing computational modeling of 3 dimensional structures of protein protein docking complexes. The project includes development of scoring functions which combines, for example, by regression, many different features of protein interaction. We also plan to integrate protein protein network information to protein complex modeling. Please see our website <http://kiharalab.org>

Gene regulation on eye development and disease

In this project, student will participate in a genetic and/or chemical perturbation of zebra fish eye development which is designed to understand related fundamental processes disturbed human eye diseases; He will analyze the morphological changes as well as conducted immunohistochemical analysis and in situ hybridization analysis with various marker to determine the cellular and genetic problems after the perturbation. Our established pipeline includes descriptive analysis, parametric and non-parametric data analyses for the appropriate sample types, which are implemented in R. Thus the student will be exposed to the basic skills for data analysis with R. / / Another possible project would be more bioinformatic in nature. We have established a draft gene network by biotapestry (<http://www.biotapestry.org/>) and will collect more data in the coming months. We would also like to have a student to add new information. I do hope to see if modeling work can be done using this network.

Systems Biological Analysis of Protein Kinase Specificity

Protein-protein interaction experiments have given considerable information on how protein kinases, which are key regulators of cell development and response, interact with other cellular proteins. Since these interactions are primarily with the proteins that are regulated, via phosphorylation, by the kinases, it opens the door to using bioinformatic approaches to determine the target sites that the protein kinases recognize. This in turn will lead to much better understanding of the integration of different regulatory processes in the cell, as well as to the potential construction of computational models of signal transduction. / This is a bioinformatics/computation project and does not involve wet-laboratory research. While experience with programming may be helpful, it is not at all required as the project will use existing software and not focus on developing new algorithms or programs.

Optogenetic neuromodulation of epilepsy

The intent of this project is to develop a toolbox of implantable devices with accompanying base station (BS) for wireless powering and a graphical user interface (GUI) for wireless communication. The devices will have the capacity for multi-channel neural recording, optical and electrical stimulation, wireless telemetry, wireless powering, and embedded algorithms for closed-loop feedback and stimulation. Development will occur through three overlapping phases: 1) prototyping with commercial off-the-shelf (COTS) components 2) designing application specific integrated circuits (ASICs) and 3) validation with in vivo behavioral experiments. / Aim1: To develop novel, implantable devices for closed-loop electrical and optical stimulation. / Aim2: To test and validate the devices in vivo with transgenic mice. /

Agent-based simulation and modeling for sexually transmitted diseases

As the novel 2009 H1N1 strain of influenza rapidly spread around the globe, public health agencies scrambled to understand and control its spread. In order to make informed decisions on school closures, travel restrictions, and uses of limited resources such as antiviral medications, public health authorities needed to know the rate of spread and severity of the new strain, as well as whether prior flu vaccines or exposure to existing strains provided any immunity to H1N1/09. / / Agent-based modeling is a class of computational models for simulating actions and interactions of autonomous agents with a view to assessing their effects on the system as a whole. In predicting the spread of infectious disease, high-fidelity agent-based simulations have become a noticeable contributor. They can track individual movements and interactions in a complex social network. / / the student will help refine a developed agent-based simulation and conduct sensitivity analyses on key model parameters.

Hydrogen Peroxide in Growth Cone Guidance Signaling

Reactive Oxygen Species (ROS) are well known for their harmful effects causing cellular damage, potentially leading to chronic and degenerative diseases. However, ROS also have major signaling functions in various cell types, suggesting that the redox potential of the cell has to be tightly regulated for normal cell functioning. Our lab has recently discovered that the organization and dynamics of the growth cone actin cytoskeleton as well as neurite outgrowth depend on ROS. The goal of this project is to test the hypothesis whether well-established axon guidance molecules such as Nerve Growth Factor (NGF) use hydrogen peroxide, a major ROS, as signaling molecule in growth cone responses. This project

involves neuronal cell culture (chick and/or Aplysia neurons), fluorescent ROS probes, live cell imaging and quantitative and statistical analysis of digital images.

Social cognition in territorial vs. social bird species

The general goal of the project is to assess the sensory mechanisms involved in visual social perception in species with different levels of sociality in order to understand the basic mechanisms of social information use. We will compare the behavior of a highly territorial species with that of a highly social species. We have already run a series of experiments to assess the occurrence of gaze following behavior and the degree to which these two species respond to head and body postures in a hierarchical fashion. A large portion of the videos of these experiments have been coded. The plan for the undergraduate student is to first code the remaining videos. Second, the student will be trained in some relevant aspects of experimental design and statistical analyses to analyze the data. The PI will mentor the student following the conceptual framework of the class he teaches (Ecological Statistics) to ensure the successful completion of the project.

Age-related changes in auditory brain regions

This project will investigate age-related changes in neuronal structure and protein levels within auditory brain nuclei. Using a rat model of aging, brain tissue from young and aged rats will be processed using immunohistochemistry to investigate protein levels and distribution. The power of this study is that the tissue will be from animals that have been extensively screened with auditory function tests to evaluate their hearing abilities. As such, any changes seen in the immunohistochemical analysis can be correlated with hearing ability. Students who participate in this project will gain hands-on experience in the following areas: tissue sectioning, immunohistochemistry, light microscopy, confocal microscopy, image analysis, and qualitative and quantitative data analysis.

Origins of Locomotion and Synovial Joint Lubrication

Bio tribology is the science of biological surfaces in sliding contact encompassing the concepts of friction, wear, and lubrication of interacting surfaces. This bioscience field has emerged from the classical field of tribology and is of paramount importance to the normal function of numerous tissues, including articular cartilage, blood vessels, heart, tendons, ligaments, and skin. Interestingly, critical lubricant molecules in the articulating (e.g. knee and hip) joints of our bodies have enabled terrestrial walking of animals. Here, we will compare molecular sequences of lubricants across a broad range of species, to determine the extent that mechanical force and stress influence body mass and low surface friction through protein glycosylation.

Quantitative and molecular analysis of zebra fish embryonic heart defects

The vertebrate heart is one of the earliest organs to develop during embryogenesis and about 1 in 100 live births exhibit congenital heart disease. More children die from congenital heart disease than all forms of pediatric cancer combined. The formation of a functional heart involves multiple steps including specification of cardiac progenitor cells, linear cardiac tube formation, cardiac looping and

cardiac chamber formation. These distinct steps are spatially and temporally regulated by a complex interplay of multiple families of transcription factors and signaling molecules. / / Zebra fish is an excellent model for studying cardiac development due to the unique optical clarity of embryos, rapid development and high fecundity. We have generated two zebra fish lines with severe cardiac phenotypes by combining two different genetic mutations and the induction of high glucose (sugar) uptake. Our goal is to characterize the cardiac defects in these zebra fish during embryonic development by

Recording and analysis of neural signals in the central auditory pathway

Students will learn to record the neural responses of rats evoked by sounds. The projects are aimed at determining how sound features are encoded by neurons under normal conditions, during age-related hearing loss, and in the developing auditory system where neural organization and signaling are changing rapidly.

Quantitative Evaluation of Electrode-Tissue Interfaces

Chronically implanted micro devices in brain tissue can serve as bidirectional communication channels for neuroprostheses. Unfortunately, these interfaces are susceptible to rejection from the inflammatory processes in the brain. Several experimental treatments exist to characterize the interfaces as a function of time post-implant; however, these data have not been completely quantified in a computational framework to fully characterize their usefulness. / / This project will focus on the statistical evaluation and quantitative modeling of data relating to failure of microelectrode devices implanted into the brain tissue of behaving rats. The data will include, but not be limited to: neurophysiological data, bioelectrical data (impedance spectroscopy and cyclic voltammetry), and behavioral data evoked by electrical micro stimulation.

Isotope-assisted metabolic profiling in Arabidopsis

Compound identification is a key factor limiting progress in metabolomics research. We are using stable isotope labeling to simplify metabolic profiling results and to provide information on the metabolic source of compounds identified within such experiments. Briefly, unlabeled, deuterium or ¹³C labeled amino acids are fed to Arabidopsis seedlings. After several days of growth, total metabolites are extracted and profiled using LCMS. By identifying metabolites whose m/z values shift when a specific amino acid is fed, we can determine the metabolic precursor of the identified metabolite and by cross-referencing these data with metabolic profiles of natural accessions of Arabidopsis, we can gain access to the genes and enzymes required for its synthesis.

Analysis of domain deletions of CHD3 protein in Arabidopsis

The goal of this project is to elucidate how CHD3 proteins contribute to repression of gene expression and determination of developmental identity in the model plant Arabidopsis thaliana. CHD3 proteins are ATP-dependent chromatin remodeling factors that dynamically alter chromatin structure. To understand how PKL-mediated remodeling contributes to gene repression, we are generating alleles of PKL that lack

conserved sequence domains and characterizing the activity of the resulting mutants with regards to in planta function. / / Based on our experience with undergraduates in our lab, the generation and phenotypic analysis of transgenic wild-type and pkl plants that are expressing domain deletion alleles of PKL will be an ideal summer project for an undergraduate. Transgenic plants that express a void vector or that express a wild-type allele of PKL will serve as controls. / / The student will meet with the PI individually at least once a week and will work with a graduate student in the lab.

Analysis of data related to calcium metabolism and childhood obesity

Data from several nutrition studies will be analyzed using SAS. The studies are focused on calcium metabolism and childhood obesity.