Caltech
Student-Faculty Programs

Session B Abstracts

The neuro-immune axis in the dural meninges and its role in migraine
Amina Tajammal
Mentors: Diane Mathis, William M. Clemons, Jr., and Miguel Marin Rodero

Migraines affect over 12% of the global population and are the most common neurological disorder in humans. Most existing therapies target the symptoms of migraines and focus on prevention; however, the exact mechanism by which they occur and progress is not well-understood. Migraines are strongly linked to the meninges, specifically the dura mater, which hosts diverse immune populations. Mouse models have established that regulatory T (Treg) cells play a crucial role in maintaining meningeal homeostasis; ablating them has been shown to cause neurodegenerative-like effects, including impaired neurogenesis and memory impairment. In terms of treatment, research and subsequent clinical trials have demonstrated that CGRP (calcitonin gene-related peptide) inhibitors are highly effective at treating the immediate symptoms of migraines. CGRP is a neuropeptide released by TRPV1+ (transient receptor potential vanilloid 1) neurons in the meninges and plays a critical role in the progression of migraines. This project will use immunohistochemistry (IHC) to study the neuro-immune axis by staining Tregs, CGRP, and nerves in the meninges. Subsequent quantitative analyses have been performed to investigate possible cross-talk between Tregs and CGRP+ and CGRP- nerves by analyzing the microscopic proximity of Tregs to these nerves. Analyses thus far have revealed greater proximity between Tregs and CGRP+ nerves, as opposed to CGRP- nerves. Further experiments and data analysis are required to verify this, which will be conducted by staining mouse meninges that have been ablated for Tregs. These will subsequently be compared for differences in innervation, branching, and nerve density. This will provide conclusive evidence on how the neuron-immune axis in the meninges is involved in migraines and help elucidate its mechanism.

Investigating the mechanisms of *Arabidopsis thaliana* root hydrotropism in the context of osmotic stress
Andrew N. Oldag
Mentors: Trevor M. Nolan and Irene Liao

Increased interest in the dynamics of root growth under drought stress flowed from the general trends of an increase in global drought and uncertainty over agricultural crop production. The process of hydrotropism involves a detection of a difference in surrounding water potentials and a growth of the root towards areas of increased water abundance, thus it represents an interesting issue of root development in both a spatial and temporal context. We are investigating the dynamics of *Arabidopsis* growth in both water limited and hydrotropism inducing conditions to understand the mechanisms of water presence detection by roots and growth under these conditions. In order to identify dynamics of cellular morphology, we use confocal timelapse live imaging. Whereas to develop a broader understanding of root growth dynamics and the rate at which specific parts of the root grow, also known as root growth velocity, we use kinematic imaging and computer vision techniques. Decreased root growth velocity as well as shifts in the primary zones of cellular division and elongation were observed under increasingly severe drought conditions. Additionally, the root bending angle, the main methodology of differential root growth, increased under more severe hydrotropic conditions.

Identifying differential methylation of distinct T cell intra-lineage sub-populations
Joe K. Afful
Mentor: Ellen Rothenberg

In the T-Cell lineage commitment program, there are three phases of differential transcriptional expression that corresponds to major shifts in cellular identity. This research aims to use Enzymatic Methyl-seq to build epigenetics landscape across these three phases. This could reveal novel potential regulatory regions in the genome required for change in cellular identity. Furthermore, the expression levels of PU.1 a non-T-lineage (myeloid) transcription factor would be perturbed to distinguish its role in diverting lineage fate epigenetically.

Quasi-periodic pattern detection in patients with brain lesions
Aamina Dhar
Mentors: Haris I. Sair and Henry A. Lester

The intrinsic activity of the brain can be explored using resting state functional magnetic resonance imaging (rs-fMRI). Analysis of time-varying activity of rs-fMRI connectivity discovered the existence of quasi-periodic patterns (QPP) in humans, rats and mice. The most prominent QPP reflects a recurring pattern of large-scale anti-correlation between the Default Mode Network and the Task-Positive Network. Studying these QPPs provides a new approach to investigating bold-oxygen level dynamics and their disruptions, since changes in functional connectivity have been reported in neurological and psychiatric diseases, which could subsequently be used as clinical biomarkers. As such, our project aims to investigate the relationship between QPPs and tumor severity in human patients with varying diagnoses. We will extract QPPs from patients with brain lesions and use QPP-derived features to predict the tumor severity of patients to characterize the deviations in intrinsic brain activity.

3D micron-resolution brain tractography via scattered light imaging
Derek W. Days
Mentors: Michael M. Zeineh and Ellen Rothenberg

This project aims to generate the first complete 3D tractography of a human brain specimen at micrometer resolution through Computational Scattered Light Imaging (ComSLI). While existing methods like diffusion magnetic resonance imaging (dMRI) and 3D-Polarized Light Imaging (3D-PLI) are limited by resolution or the inability to resolve crossing fibers, ComSLI can map multiple crossing nerve fiber orientations in 2D sections with resolutions down to a single micrometer.

First, ComSLI was applied to histology slides to determine nerve fiber orientations. These 2D sections were then coregistered to high-resolution photographs of the tissue block surface with MRI data. Key computational tools, including the Scattered Light Imaging ToolboX (SLIX), Advanced Normalization Tools (ANTs), and Tensor Image Registration Library (TIRL), were used for data analysis and 3D reconstruction.

This novel approach will allow for the detailed visualization of key hippocampal pathways, offering critical insights into the brain's connectivity and the microstructural changes associated with neurodegenerative diseases like Alzheimer's.

Investigating the effects of sex variations on trophectoderm function and embryo fitness using stem cell-based models
Manasvi Pinnaka
Mentors: Magdalena D. Zernicka-Goetz and Sergi Junyent

In vitro fertilization (IVF) has long been associated with a higher male-to-female birth ratio when compared to natural conception, but the mechanisms underlying this phenomenon are still poorly understood. During early development, both mouse and human embryos form the same fundamental structure, the blastocyst, which consists of three main lineages: the epiblast (EPI), the primitive endoderm (PrE), and the trophectoderm (TE). Mouse embryos, therefore, serve as an ideal model to

study the developmental means by which these sex-specific differences arise. Meglicki et al. (unpublished) found that in late preimplantation development, the TE of male mouse embryos develops faster than that of females in high glucose cultures. To further evaluate this connection between sex and TE function, this study utilized blastoids, stem-cell based embryo models developed by the Żernicka-Goetz lab that highly resemble the natural blastocyst. Male and female TSC lines were generated to model the TE and cultured with pre-established male and female ESC lines (to mimic the EPI) and inducible Gata4-expressing cell lines (to mimic the PrE) in low and high glucose environments. To assess the impact of sex variations on early embryo fitness, the composition/proportion of each cell lineage and overall blastoid formation efficiency were compared across conditions.

Modeling oscillating and rotating locomotion of active nematic droplets
Rohan Mehta
Mentors: Matthew W. Thomson and Fan Yang

Active nematic droplets offer a minimal platform for programmable microscale locomotion, yet existing hydrodynamic models fail to capture the full range of experimentally observed behaviors. We revisit the continuum framework of Giomi *et al.* and systematically vary boundary conditions (homeotropic versus planar anchoring) and initial nematic alignment (uniform versus isotropic). High-resolution pseudo-spectral simulations uncover previously undiscovered modes of locomotion under planar anchoring and isotropic alignment, which qualitatively resemble oscillating and rotating modes seen in experiment. By exploring the dynamics of these modes, we take an important step towards building a more accurate theory of active nematodynamics, which can eventually be applied towards general programming of active droplet locomotion.

Building a brain cellular microscopy data portal for accelerating AI-driven segmentation and analysis in neurodegenerative diseases
Noelle Y. Wilkinson
Mentors: David A. Van Valen and Joud Mari

Understanding how neuronal morphology contributes to cognition and disease requires large-scale, standardized datasets of neuronal images. Traditional tracing methods capture only simplified skeletonized representations of neurons and lack volumetric details that are crucial for advanced analysis. Recent advances in neuronal segmentation have enabled more comprehensive representations, known as volumized masks, which preserve fine structural details of dendrites and axons, as well as their spatial organization and connectivity. These annotations are better suited for AI and machine learning based approaches to studying morphology in neurodegenerative disease contexts. However, current public data repositories remain limited in diversity, annotation type, and imaging modality, restricting reproducibility and scalability in the field. To address this gap, we are developing an open-source, cloud-based data portal of 2D and 3D neuronal microscopy images curated and annotated for segmentation applications. The portal currently includes 9 datasets with approximately 35,000 raw images and 250,000 cells. It will feature metadata-driven search, filtering, visualization, and download capabilities through a user-friendly web application. By releasing this resource to the neuroscience community, we aim to accelerate AI-driven morphological analysis, establish new benchmarks for segmentation tasks, and promote reproducible, large-scale research at the intersection of neuroscience and machine learning.