
BIOGRAPHICAL SKETCH

NAME: Dario Tommasini

POSITION TITLE: Ph.D. candidate

EDUCATION/TRAINING

INSTITUTION AND LOCATION	Start Date	Completion Date	FIELD OF STUDY
Diablo Valley College, Pleasant Hill	08/2018	07/2020	Biology
University of California, Los Angeles	09/2020	06/2022	B.S. in Neuroscience; B.S. in Molecular, cell, and developmental biology
University of California, Berkeley	08/2022	05/2027	Ph.D. Neuroscience

A. Personal Statement

I am pursuing a Ph.D. in Neuroscience at UC Berkeley to obtain the fundamental academic training required to establish and run my own research group. As an independent scientist, I plan to investigate the molecular basis of neuron evolution and establish the first rigorous model for how neurons evolve. My long-term research goal is to connect the emergence of novel neuronal properties to specific nucleotide substitutions in the DNA that occurred during vertebrate evolution.

My fascination with cell type evolution and gene regulation dates back to my previous research experiences studying viruses and neural gene expression. As a community college student, I studied bacterial viruses as an intern at Sandia National Labs and became mesmerized by the regulatory logic involved in their precisely timed life cycles. To my astonishment, this logic was inscribed in their DNA. I also came to appreciate the power of high-throughput sequencing to study the molecular processes within cells, and became determined to apply these methods to study of the nervous system. When I transferred to UCLA, I explored the regional differences between oligodendrocyte (myelin-forming cells) populations and their association with neurological diseases. Through hands-on experience with bioinformatic analyses, I became proficient in designing rigorous computational experiments and interpreting complex biological signals. This skillset allowed me to be productive during my lab rotations as a 1st year graduate student, where I studied enhancer evolution (Prof. Karthik Shekhar), validated human brain organoids using single-cell RNA-sequencing (Prof. Helen Bateup), and studied the statistical properties of spontaneous activity in the retina (Prof. Marla Feller). Ultimately, my previous research background has provided me with a strong foundations to study the nervous system using genomics, bioinformatics, and statistics.

As a PhD student in the lab of Prof. Shekhar, I am investigating the evolutionary conservation of amacrine cells in the retina. To gain insights into the evolution of amacrine cell structure and function, I initiated a collaboration with Prof. Teresa Puthussery, who is a leading expert in dissecting retinal circuits in various species. The proposed project will enable me to expand my computational biology skillset while receiving hands-on training in immunolabeling, morphological analysis, and functional imaging from Prof. Puthussery's group.

B. Positions, Scientific Appointments and Honors

Research positions

05/2023 – Present	Graduate student researcher, Prof. Karthik Shekhar – UC Berkeley
08/2022 – 05/2023	Neuroscience rotation student (Prof. Karthik Shekhar, Prof. Helen Bateup, Prof. Marla Feller) – UC Berkeley
08/2020 – 10/2022	Undergraduate researcher, Prof. Brent Fogel – UCLA
04/2019 – 09/2022	Biological research and development intern, Dr. Kelly Williams – Sandia National Labs

Teaching appointments

12/2024 – 05/2025	Graduate student instructor, Molecular and Cell Biology – UC Berkeley
12/2023 – 05/2024	Graduate student instructor, Molecular and Cell Biology – UC Berkeley

Honors and Awards

- 2025 F31 – National Institute of Health
- 2024 Award for best 15-minute platform talk, Vision Science Retreat – UC Berkeley
- 2022 1st place for abstract, Schiebel Scholars Meeting – University of California, Los Angeles
- 2022 Dean's Honor List – University of California, Los Angeles
- 2021 Schiebel Scholarship for Neuroscience – University of California, Los Angeles
- 2020 Transfer Alumni Gold Shield Scholarship, Alumni Scholars Club – University of California, Los Angeles
- 2020 Academic Honors – Diablo Valley College

C. Contributions to Science

I. Development and evolution of the vertebrate visual system

As a rotation student in Prof. Marla Feller's lab, I investigated the cellular mechanism behind retinal wave propagation bias – a tendency for spontaneous activity in the developing retina (retinal waves) to propagate in the nasal direction. My contribution to this project was to develop a statistical framework to test hypotheses about the nature of this bias. I proposed various probabilistic models of retinal wave propagation, which we tested by fitting to whole-retina calcium imaging data. This work has the potential to reveal novel properties of the neural circuits that drive spontaneous activity in the developing visual system.

In my first project as a graduate student in Prof. Karthik Shekhar's lab, I pursued the evolutionary origin of the tetrapod double cone, an unorthodox photoreceptor found only in certain tetrapods. These cells are called "double cones" because they are composed of two different cones – a principal and an accessory member. I led this project by developing and applying comparative transcriptomic methods like those described in **Aim 1**. Notably, I was able to i) isolate double cones in single-cell data, ii) pinpoint novel markers for the principal and accessory members, and iii) align photoreceptors across five vertebrates that span the emergence and loss of double cones. Based on this computational analysis, we concluded that both members of the double cone likely evolved from red cones, and provided a potential mechanism for their origin. I highlighted this work at the *2024 Berkeley Neuroscience Conference* as a 5 minute lightning talk and at the *2024 Berkeley Vision Science Retreat* as a 15 minute platform talk.

Since the conclusion of this project, I have diverted my efforts to studying amacrine cells, for which I have designed the Research Strategy proposed here. The preliminary data discussed in **Aim 1** and **Aim 2** were presented at the *2023 Berkeley Neuroscience Conference*, *2024 Berkeley Neuroscience Conference*, and the *2024 Gordon Research Conference on Visual System Development*.

1. Pitcher M, Oosterboer S, **Tommasini D**, Wei W, Feller M. The synaptic basis of retinal wave propagation bias. In preparation. 2024.
2. **Tommasini D**, Yoshimatsu T, Baden T, and Shekhar K. Comparative transcriptomic insights into the evolutionary origin of the tetrapod double cone. *Current Biology*. 2025.
 - a. **Oral:** *Berkeley Neuroscience Conference* (2024). Tahoe City, CA.
 - b. **Oral:** *Berkeley Vision Science Conference* (2024). Oakland, CA.
3. **Tommasini D**, Monavarfeshani A, Dinesh V, Hahn J, Marre O, Tangeman J, Blackshaw S, Puthussery T, Sanes JR, and Shekhar K. The extreme diversity of amacrine cell types has deep evolutionary roots. *bioRxiv*. 2026
 - a. **Poster:** *Gordon Research Conference on Visual System Development*. (2024) Lucca, Italy.
 - b. **Poster:** *Berkeley Neuroscience Conference* (2023). Tahoe City, CA.
 - c. **Poster:** *Berkeley Neuroscience Conference* (2024). Tahoe City, CA.
 - d. **Nanosymposium:** *Society for Neuroscience* (2025). San Diego, CA.

II. Identification of a novel class of mobile genetic elements in bacteria

As a Biological Research and Development intern at Sandia National Laboratories, I studied prophages – bacterial viruses that can insert their genomes within bacterial chromosomes. My advisors, Dr. Kelly Williams (PI) and Dr. Catherine Mageeney (postdoc), discovered a small "satellite" prophage inserted within a larger "helper" prophage in the chromosome of a pathogenic *E. coli* strain. I used CRISPR-cas9 editing to remove the two prophages from the bacterial strain, a control for downstream experiments. I then designed and carried out an extensive time course experiment to profile the copy number and genomic arrangement of the two

prophages after inducing excision with a DNA damaging agent. My experiments revealed that the helper excises first from the bacterial chromosome, carrying the satellite with it. Then, the satellite excises from the helper after taking advantage of its replication machinery. I analyzed the genomic arrangement of these prophages and noticed that the satellite had inserted itself in the late operon of the helper, providing an explanation for the delayed excision. Using bioinformatics, we discovered that the satellite is just one member of a novel clade of phylogenetically-related prophages that insert themselves within the late operon of other prophages. These experiments led us to propose that this is a novel parasitic relationship between bacterial viruses.

1. **Tommasini, D**, Mageeney, CM, Williams, KP (2023). Helper-embedded satellites from an integrase clade that repeatedly targets prophage late genes. *NAR Genom Bioinform*, 5, 2:lqad036.

III. Identifying gene expression patterns associated with neurological diseases

It is well-established that neurological diseases differentially target specific brain regions. As an undergraduate researcher in Prof. Brent Fogel's lab at UCLA, I investigated whether this phenomenon had a transcriptional basis. To identify evidence of oligodendrocyte dysfunction in neurological diseases, I mined publically available RNA-sequencing datasets from mouse disease models. Using a systems-level approach to compare gene expression signatures, I discovered that regional populations of oligodendrocytes are more adversely altered in neurological diseases that target their brain region; for instance, cerebellar oligodendrocyte transcription is most altered in ataxia. I then used a statistical approach to identify candidate transcription factors and microRNAs that could be driving these expression patterns. We validated these candidates *in silico* using published data and *in vitro* using a human oligodendrocyte cell line. To demonstrate the utility of these findings, we used one of my regulatory candidates to reverse aberrant gene expression induced by a pathogenic allele associated with ataxia. I also discovered that oligodendrocyte gene expression forms a gradient along the rostrocaudal axis of the mouse forebrain, which is intriguing since gradients of regulatory proteins pattern this axis during embryonic development.

As a graduate student in the Shekhar Lab, I am continuing to investigate gene expression patterns associated with neurological disease. Our collaborator Prof. Milica Margeta at Harvard Medical School and her lab isolated retinal immune populations (microglia, T cells, NKT cells, macrophages, etc.) from mice with and without microbroad-induced glaucoma and performed single-cell RNA-sequencing. My contribution to this project was to i) perform batch correction, dimensionality reduction and clustering of the data, ii) identify and annotate the major cell populations, and iii) perform statistical analyses to find gene expression and cell type proportion differences between experimental conditions. Importantly, we found evidence of immune cell infiltration in glaucoma, and a decrease in the number of homeostatic microglia. This work was highlighted at the *Glaucoma Research Foundation Conference* in August 2024.

1. **Tommasini D**, Fox R, Ngo KJ, Hinman JD, Fogel BL. Alterations in oligodendrocyte transcriptional networks reveal region-specific vulnerabilities to neurological disease. *iScience*. 2023 Mar 8;26(4):106358.
 - a. **Poster:** UCLA Schiebel Scholarship
2. Yin Z, Mukwaya A, Harris J, **Tommasini D**, Baldwin G, Cullen P, Uddin NM, Xue Y, Da Mesquita S, Shekhar K, Margeta M. Single-cell atlas of immune populations in the healthy and glaucomatous retina and optic nerve. In preparation.

IV. Generation of open-source bioinformatic tools for the scientific community

As an undergraduate researcher at UCLA, I realized that we could extract more information from gene expression data by leveraging the multidimensionality of experimental designs. In other words, datasets with multiple time points and tissues present the opportunity to perform multiple sub-level analyses that can then be integrated together to draw more sophisticated conclusions about the underlying transcriptional networks. Since the existing software implementation, WGCNA, was not designed for this sort of analysis, I developed multiWGCNA, an R package for deep mining gene co-expression networks in multi-trait expression data. Having demonstrated that multiWGCNA reveals interesting biological phenomena in mouse models of multiple sclerosis and Alzheimer's disease, we published my software and findings in *BMC Bioinformatics*. To ensure that these methods are more accessible to others, I submitted my package to Bioconductor – the official repository for bioinformatic software in R. These efforts will advance data analysis and benefit the broader neuroscientific community by making bioinformatic tools more accessible to researchers and clinicians. I have

also made a commitment to keeping this software package up-to-date and to provide users with technical support. As of now, I have closed over 20 issues on GitHub, where I have helped various users apply multiWGCNA to their data.

1. **Tommasini D**, Fogel BL. multiWGCNA: an R package for deep mining gene co-expression networks in multi-trait expression data. *BMC Bioinformatics* **24**, 115 (2023).

D. Skills

Computational

- Programming: R, Python, bash, Java, Ruby
- Statistical analysis: maximum likelihood estimation, Bayesian inference, probability theory
- Deep learning: strong theoretical knowledge, experience with implementation
- Single-cell RNA-sequencing analysis: 10x Chromium, Smart-seq
- Spatial transcriptomics: Xenium
- Version control: Git/GitHub
- HPC/cluster computing: SLURM
- Connectomic analysis: serial block-face electron microscopy

Experimental

- Immunohistochemistry
- Confocal microscopy
- Fluorescence microscopy
- Retinal microdissection
- Whole mount retina preparation
- Calcium-imaging using wide-field epifluorescence