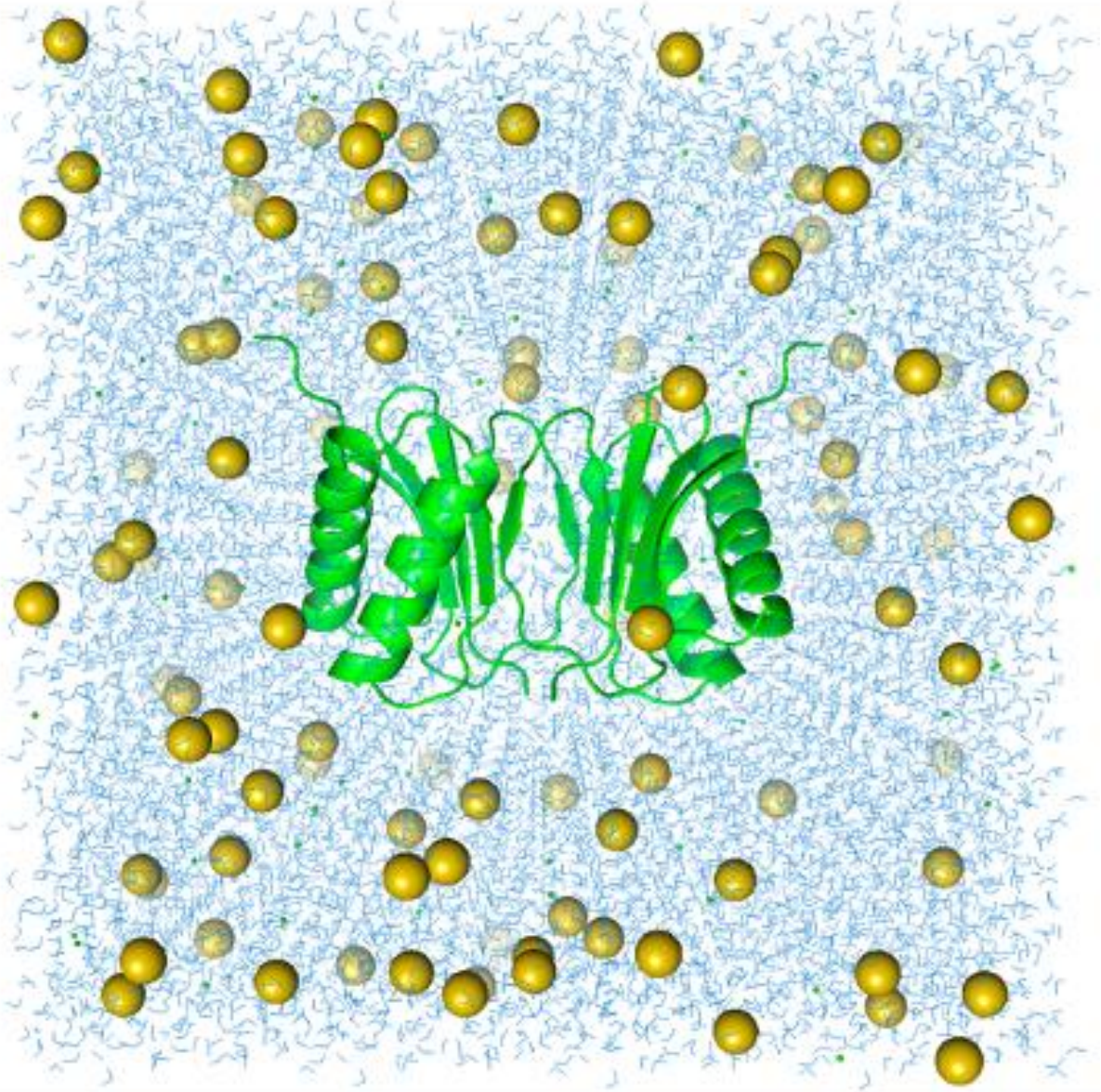
Introduction and Graduate Studies using Molecular Dynamics Simulations

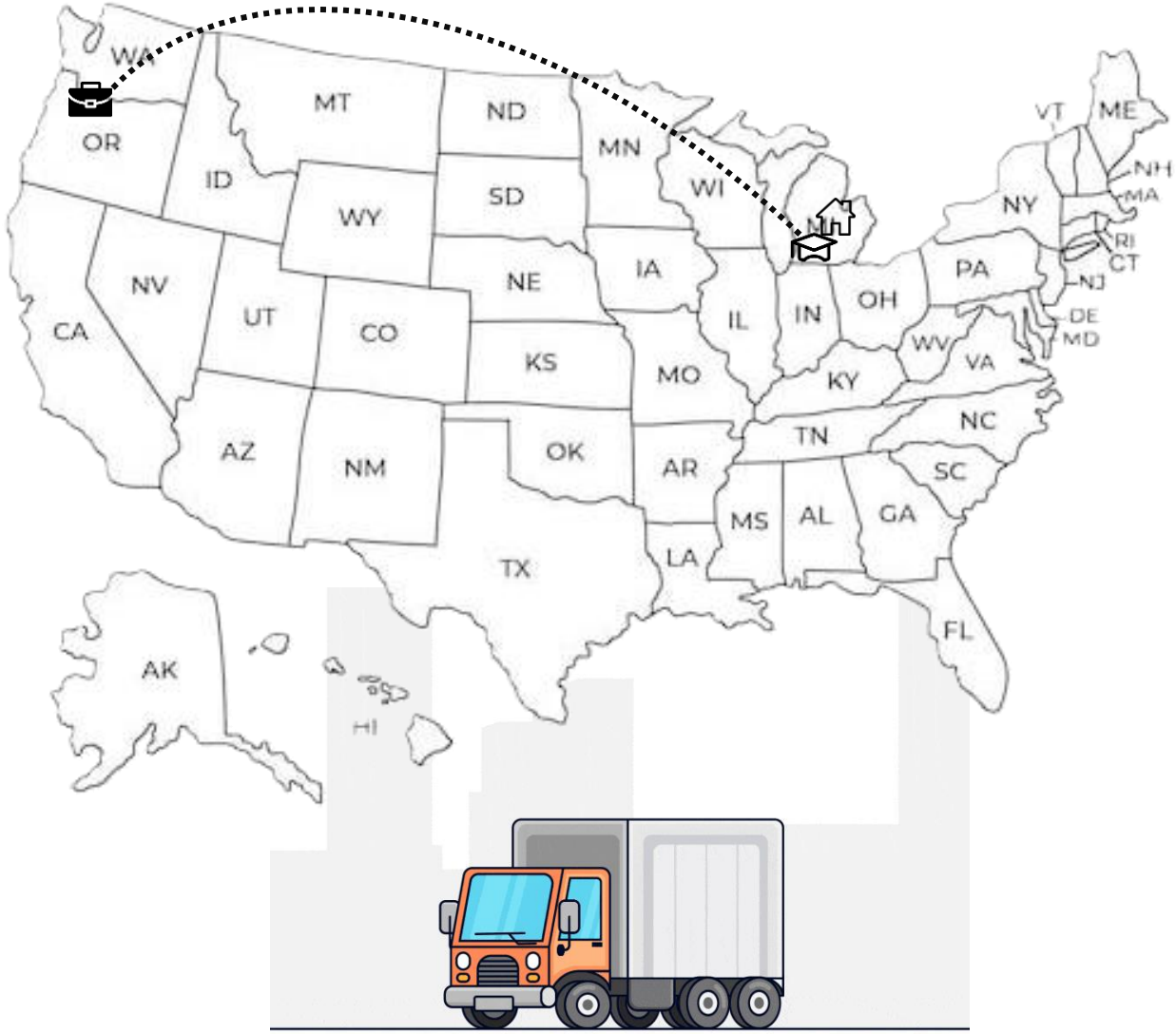


Shelby Santos

Oregon Health and Science University,
Biomedical Engineering, Zuckerman Lab

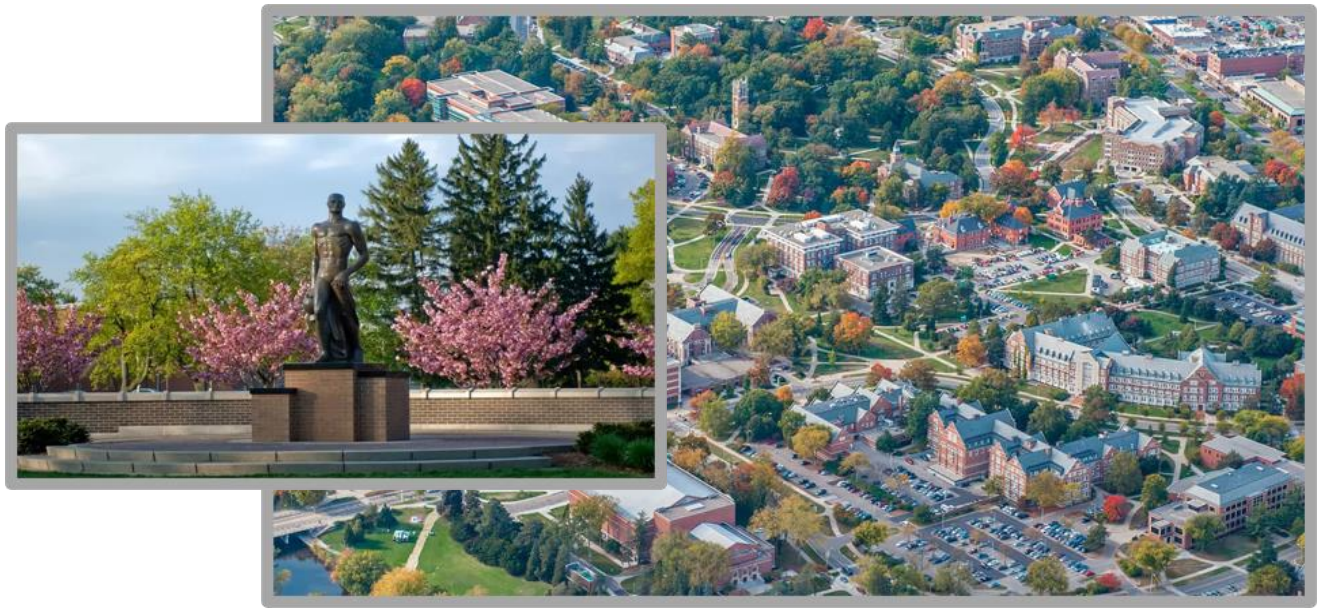
Background

- Grew up in **Saginaw**, Michigan
- Earned my Bachelors in Science at Michigan State University in **Spring 2021**
- After graduation, moved to Portland, Oregon to explore graduate school opportunities
- Began as a **research assistant** in the Zuckerman Lab
- Began the **PhD program** in Biomedical Engineering at Oregon Health and Science University in **Spring 2023**



Education

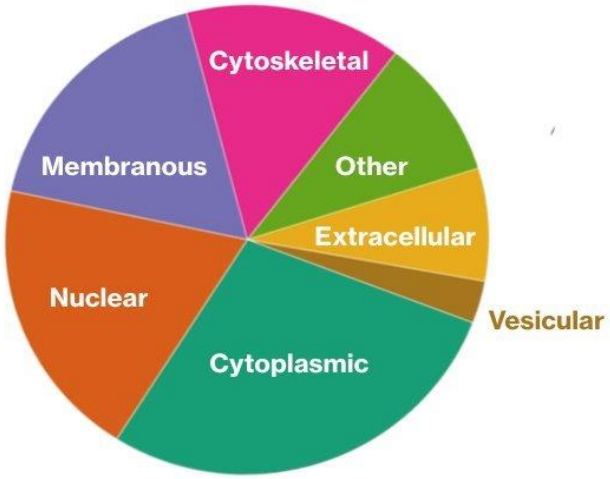
- During my undergraduate, I **majored** in Biochemistry and Molecular Biology and Biotechnology and **minored** in Computational Mathematics, Science, and Engineering
- As a PhD student, I have taken courses on Probability and **Statistics**, Scientific Writing, Data Visualization, Software **Engineering**, and Product **Development**
- There are plenty of opportunities outside of school (as you know…) to learn new things

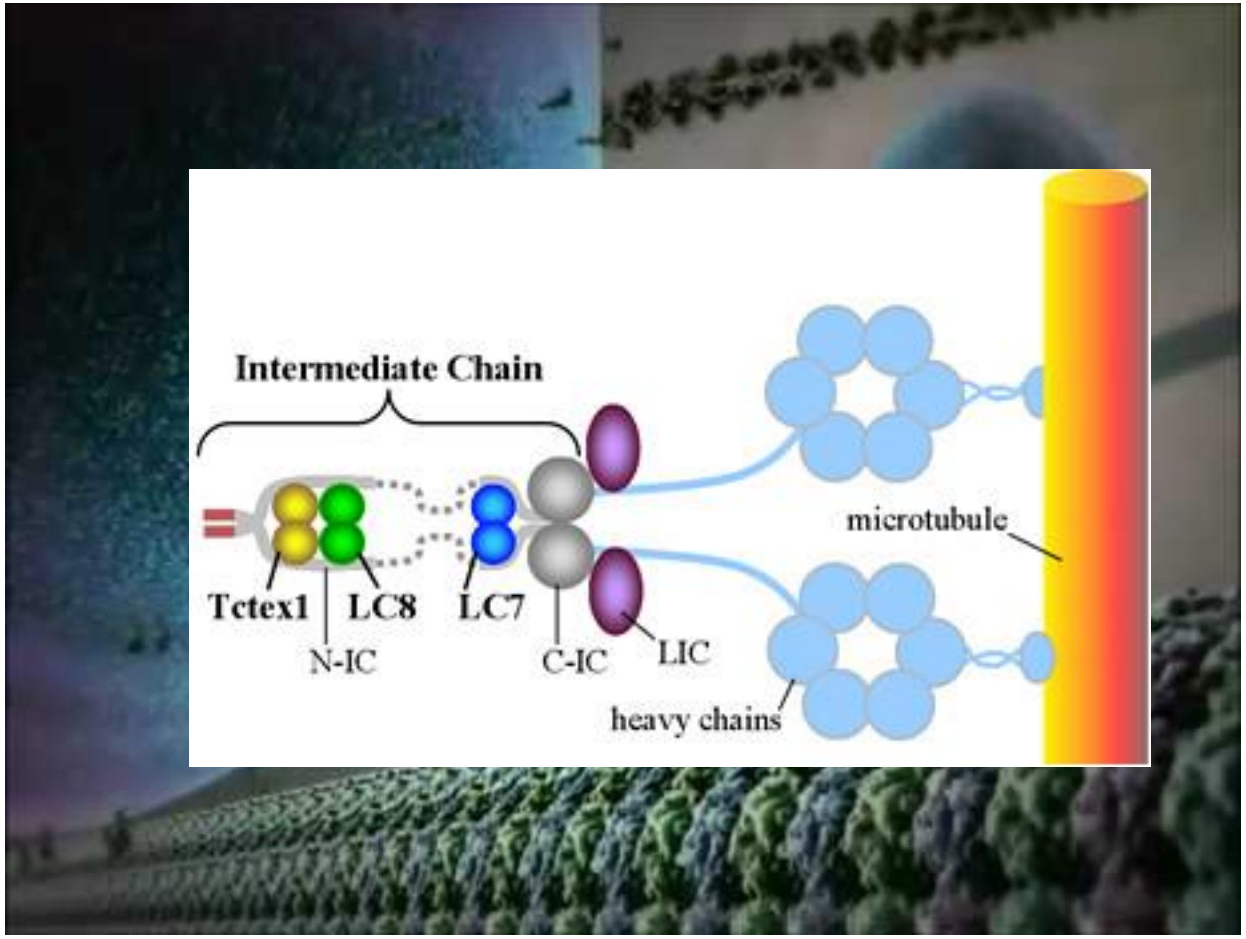


Graduate Research

What is LC8?

- Dynein Light Chain 8 (LC8) is an important protein in the cell, initially characterized as a cargo transport protein
- LC8 is a **molecular hub protein** with **over 100** verified **binding partners**

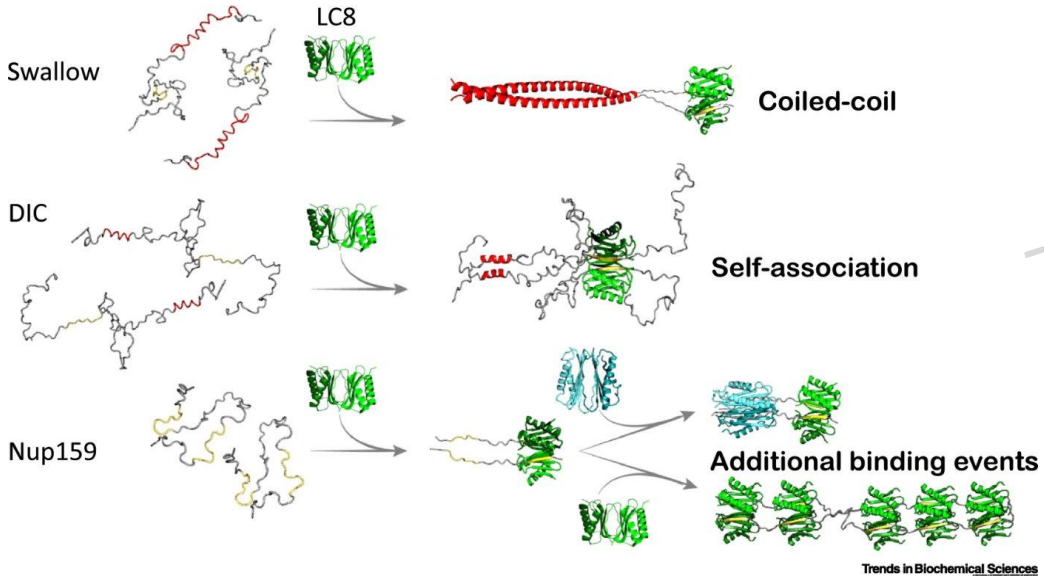


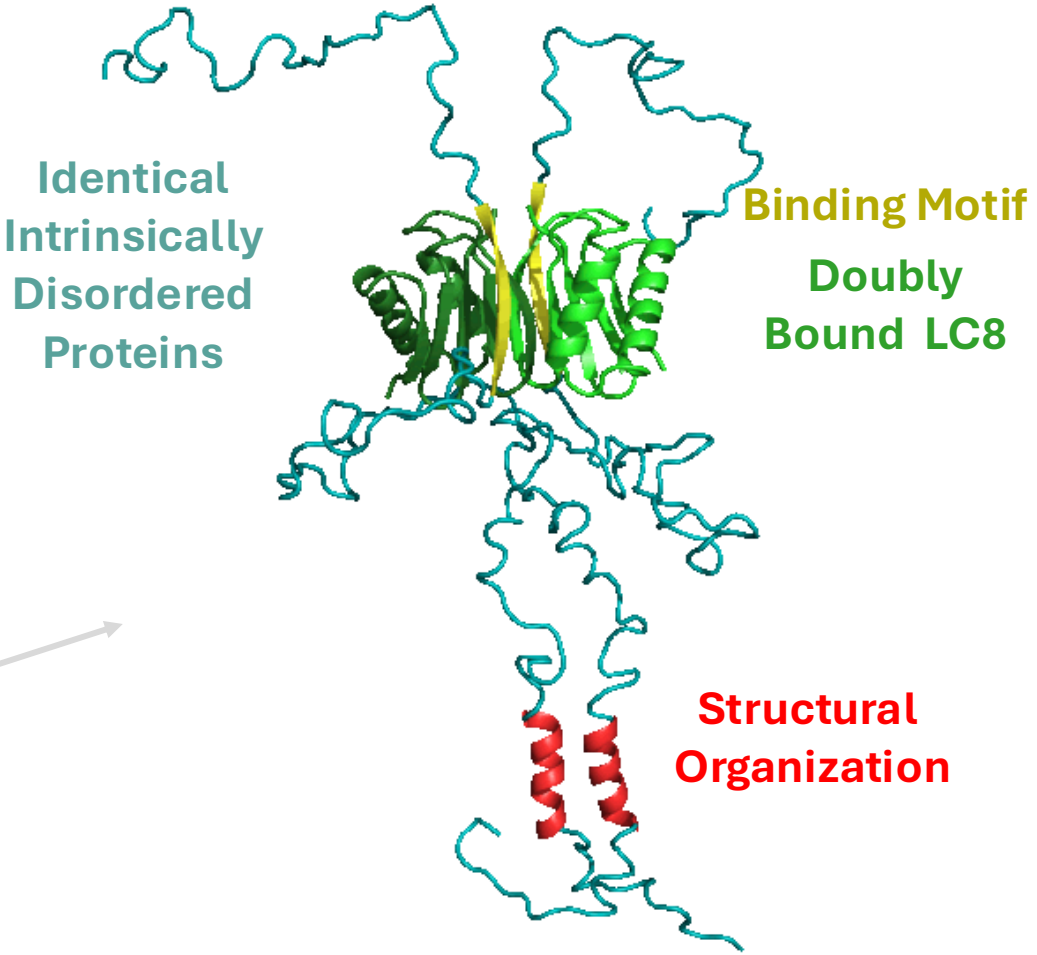


Graduate Research

LC8 is a Dimerization Hub

- LC8 dimerizes intrinsically **disordered** proteins
- Intrinsically disordered proteins lack an ordered (*average*) structure

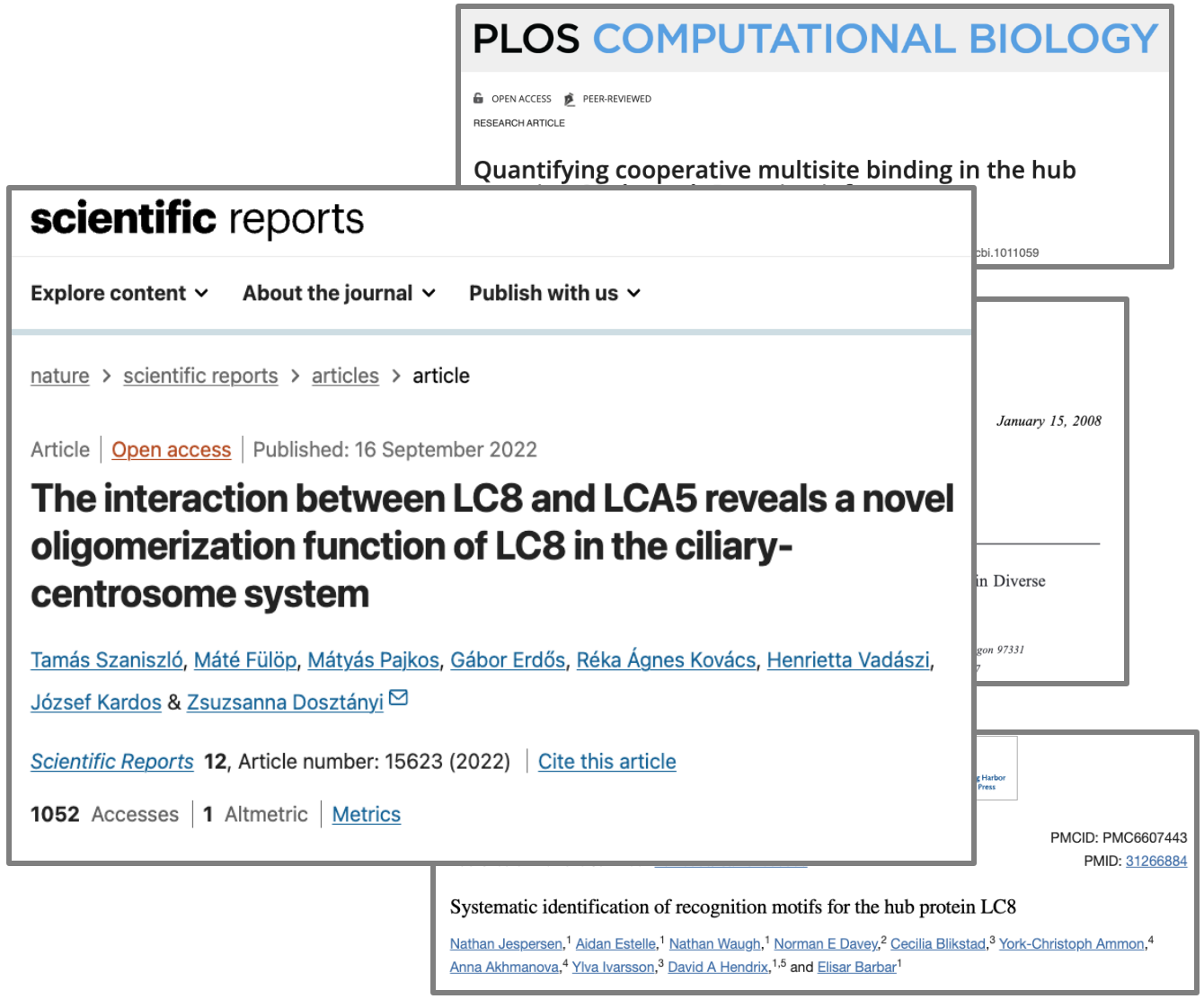




Graduate Research

Many people are interested in LC8

- Intruments like Isothermal Titration Calorimetry (ITC) reveal how *favorable* binding between peptides and LC8 is
- Sometimes the doubly bound state is very favorable
- In fact, a singly bound LC8 can make the doubly bound state more favorable, we call this *cooperativity*
- **Cooperative binding** is one of the most interesting and not fully understood phenomena involved in **control** and **regulation** of biological processes



Graduate Research

ITC

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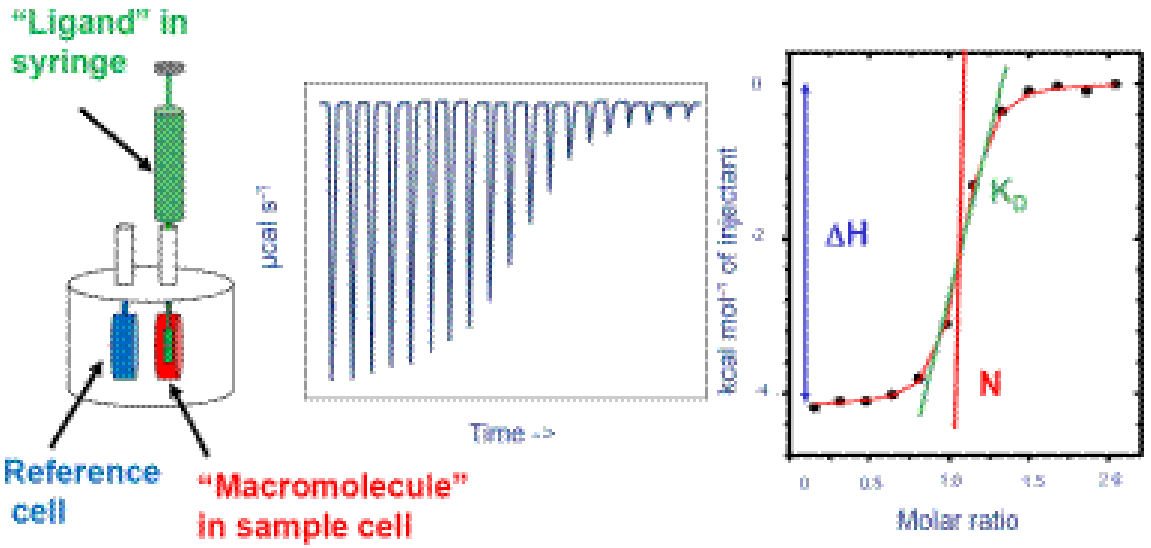

$$p(\theta \mid \text{data}) = \frac{p(\text{data} \mid \theta) \cdot p(\theta)}{p(\text{data})}$$

Posterior · Likelihood · Prior · Normalization

Graduate Research

Collaborators' Experimental Data

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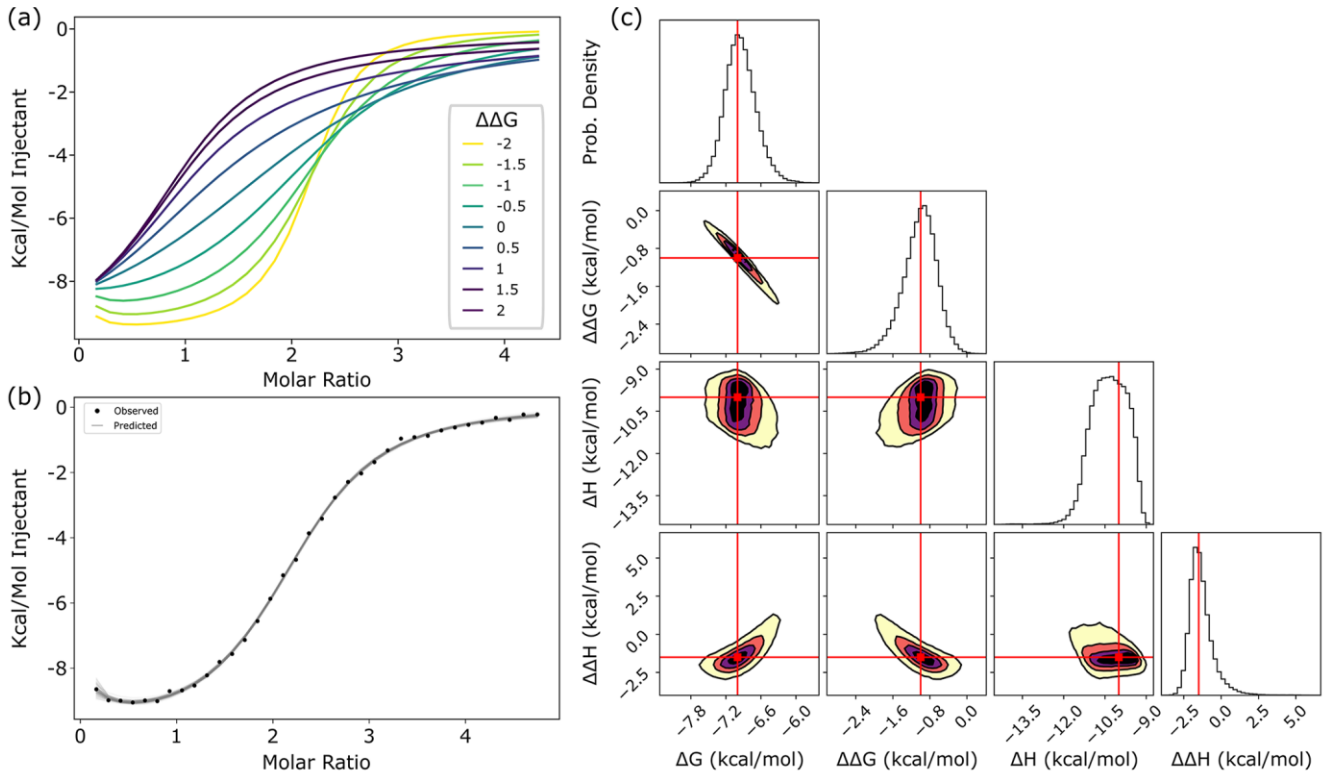
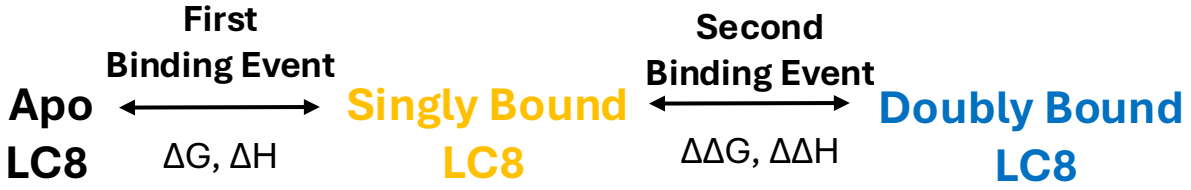


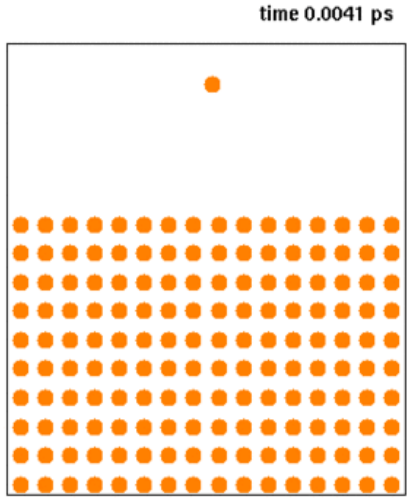


Graduate Research

Why continue studying it?

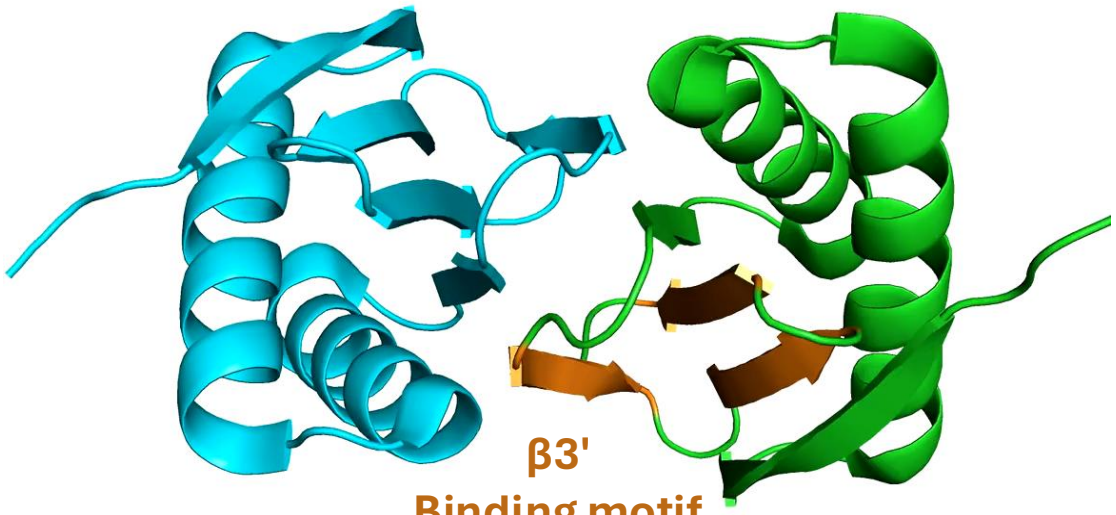
- The **atomistic mechanisms** of LC8's cooperative behavior is unknown
- In other words, we know that *LC8 is cooperative* but we don't know *why or how it is acting cooperatively*
- We explore this using **Molecular Dynamics**

Molecular Dynamics (MD) is a computational simulation technique used to study the **physical movements of atoms** and molecules over **time**, providing insights into the structure, dynamics, and interactions of biological systems at an atomic level.



Simplified Example of Dynamics

Molecular Dynamics Simulation Demonstration of **Unbound** LC8

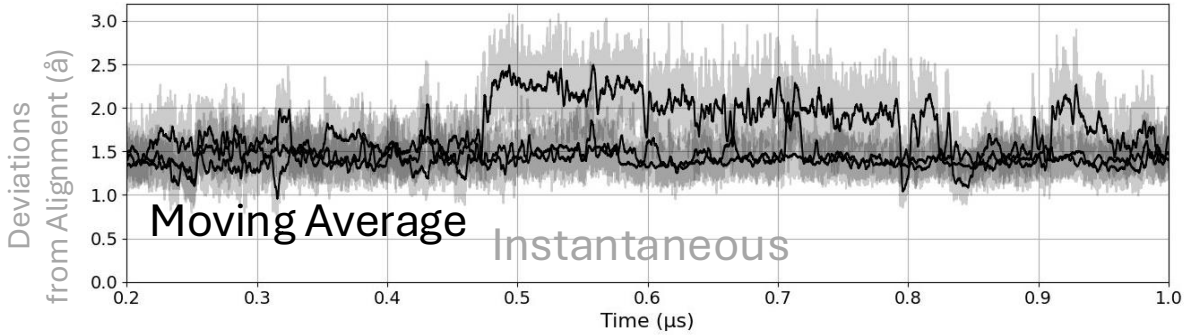


Graduate Research

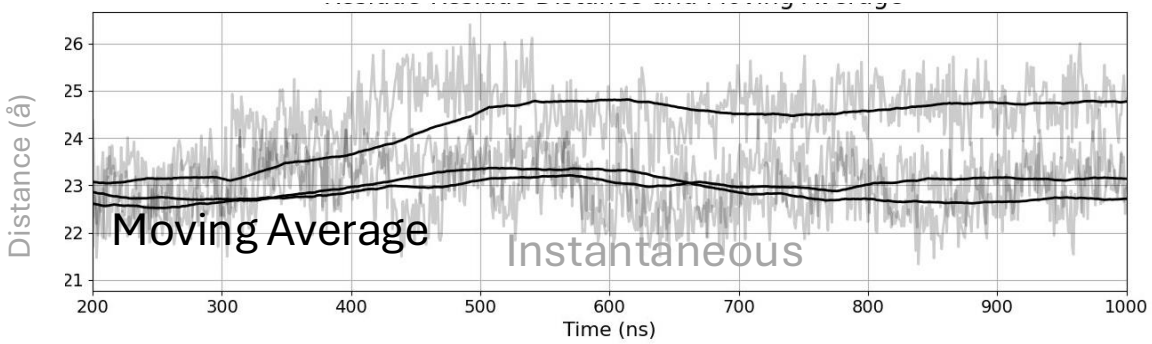
We can use MD data to do tons of things

- MD data includes the **coordinates** of atoms, how they **change** over time, and at what **speed** they move between each time point
- We can look at how the protein changes as a **whole** (Global Fluctuations)
- … and how **specific parts** of the protein changes (Local Fluctuations)

Global Fluctuations of Unbound LC8



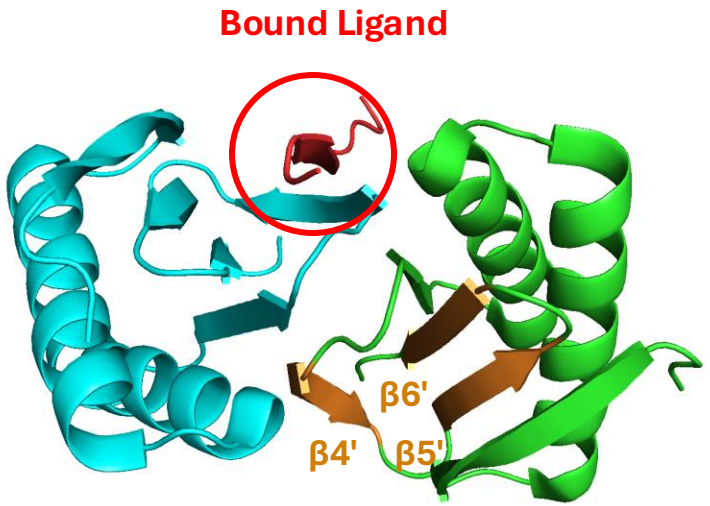
Local Fluctuations of Unbound LC8



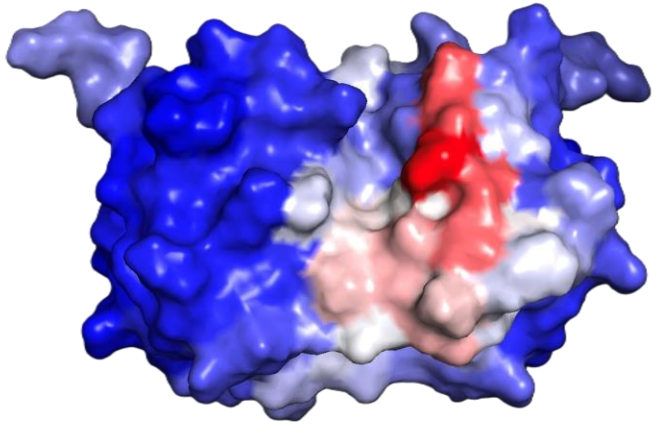
Graduate Research

Results!

- LC8 is **cooperative** if we see changes induced at the unbound binding region of the **singly bound LC8**
- We can measure this by calculating how similar (or different) the **singly bound** is from the **unbound** LC8
- We can then match those values to the amino acids on the protein and plot!

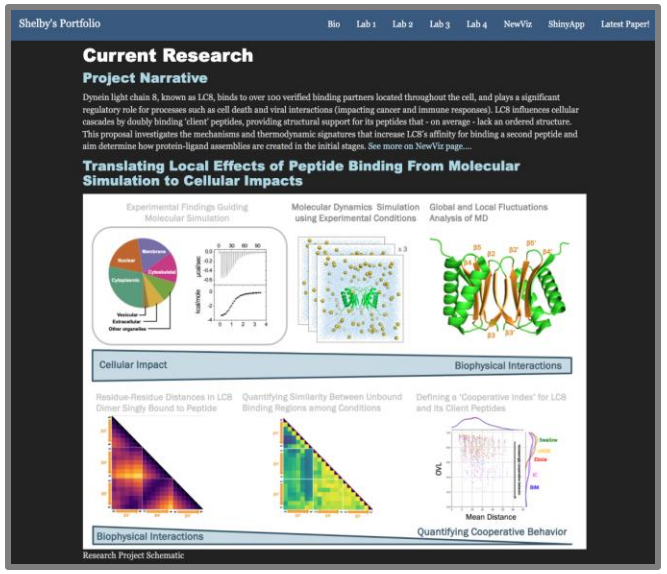


Lower Similarity → Higher Cooperative Behavior



Experience

- Beyond research, there are many ways to get involved in science to broaden and deepen your skill base
- Taking an opportunity to explore an interest or gain more experience is never a waste of time



BPS2025 los angeles
February 15–19, 2025 california

Outreach

Opportunities and communities everywhere!

Lighting the Pathway

The "Lighting the Pathway to Faculty Careers for Natives in STEM" (LTP) program supports the Indigenous peoples of North America and the Pacific Islands who are pursuing careers in academia.

Advancing Chicanos/Hispanics & Native Americans in Science

ADVANCING INDIGENOUS PEOPLE IN STEM

Oregon State Biophysics Society Student Chapter