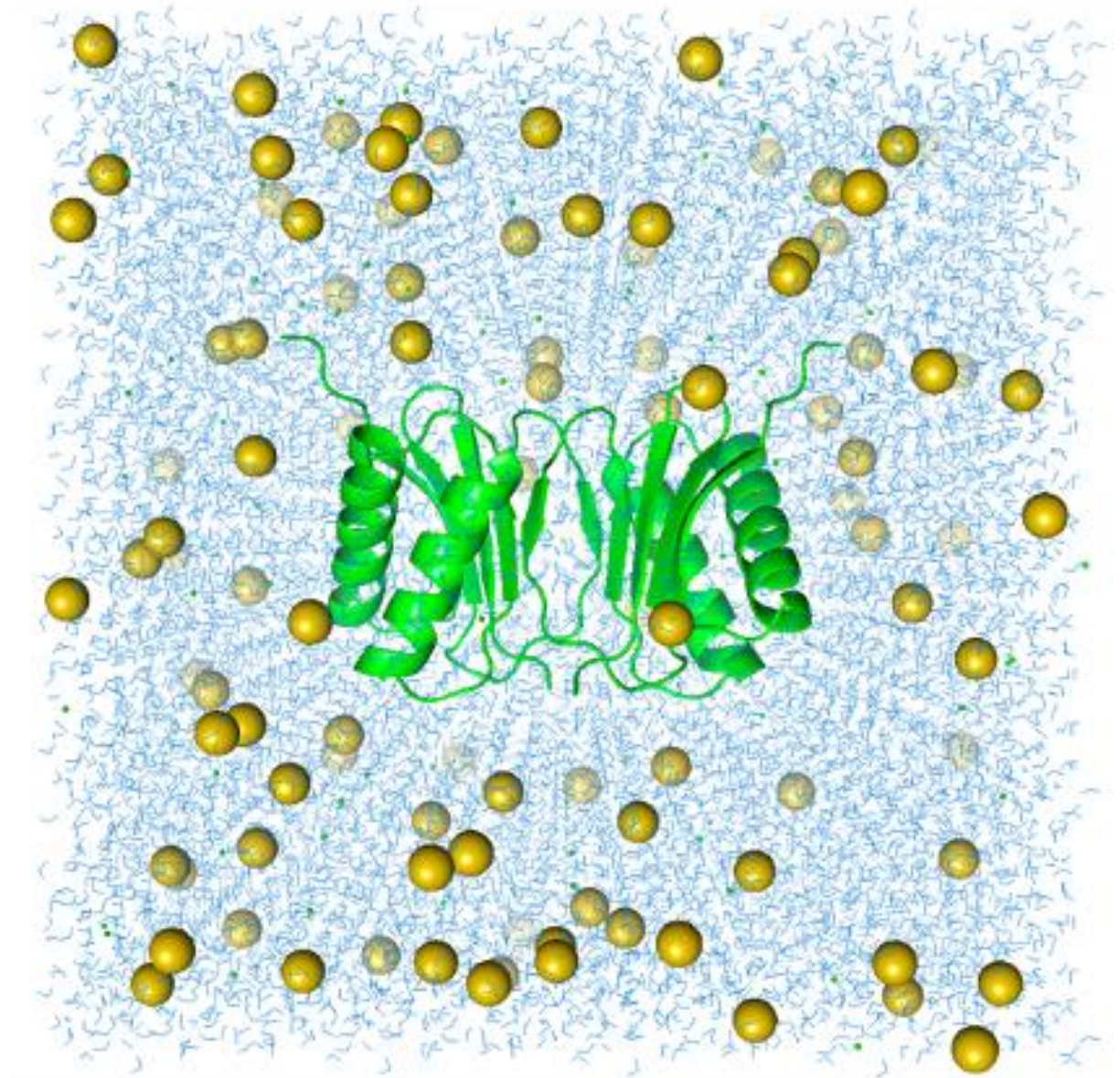


# Introduction and Graduate Studies using Molecular Dynamics Simulations

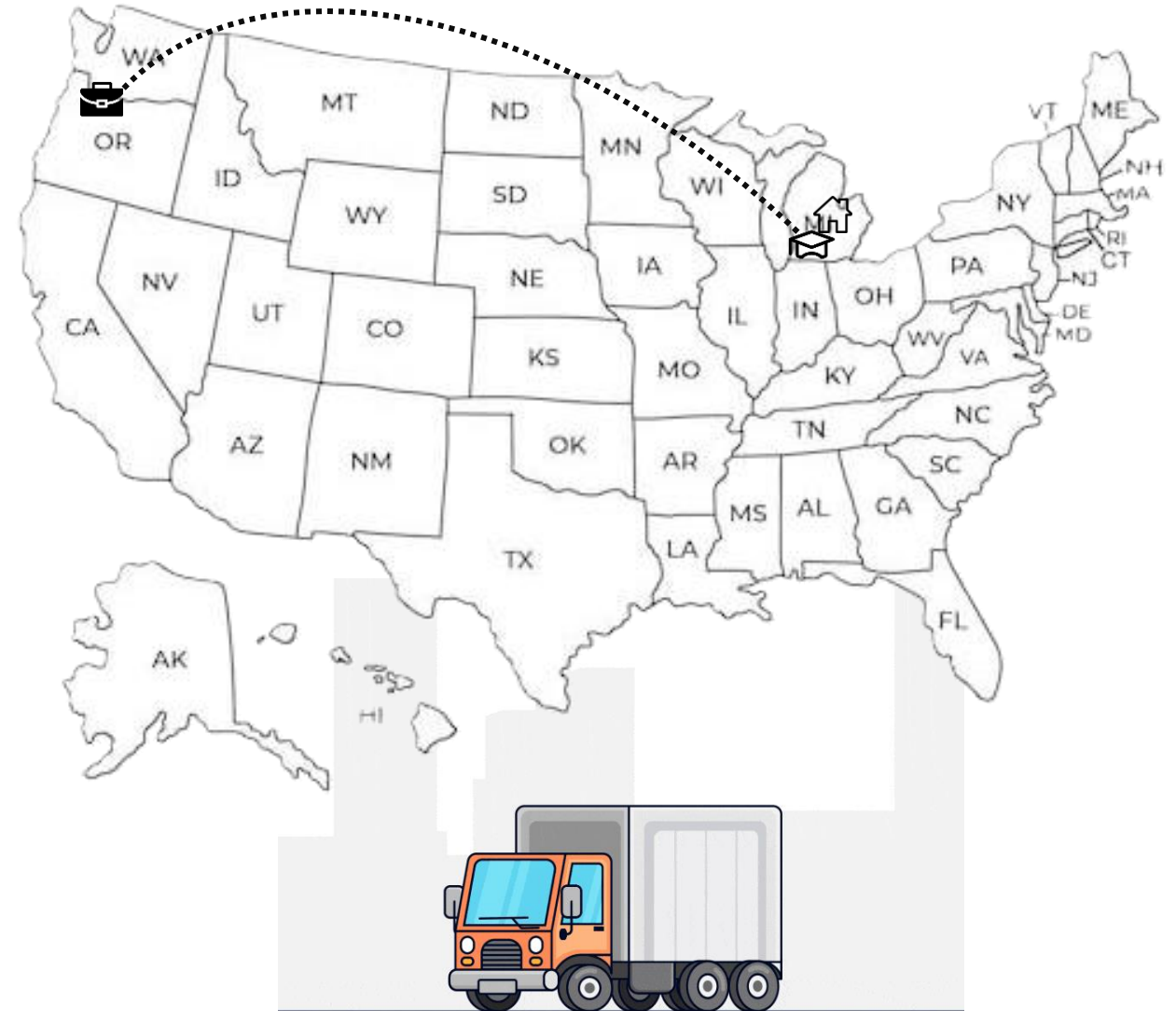
Shelby Santos

Oregon Health and Science University,  
Biomedical Engineering, Zuckerman Lab



# Background

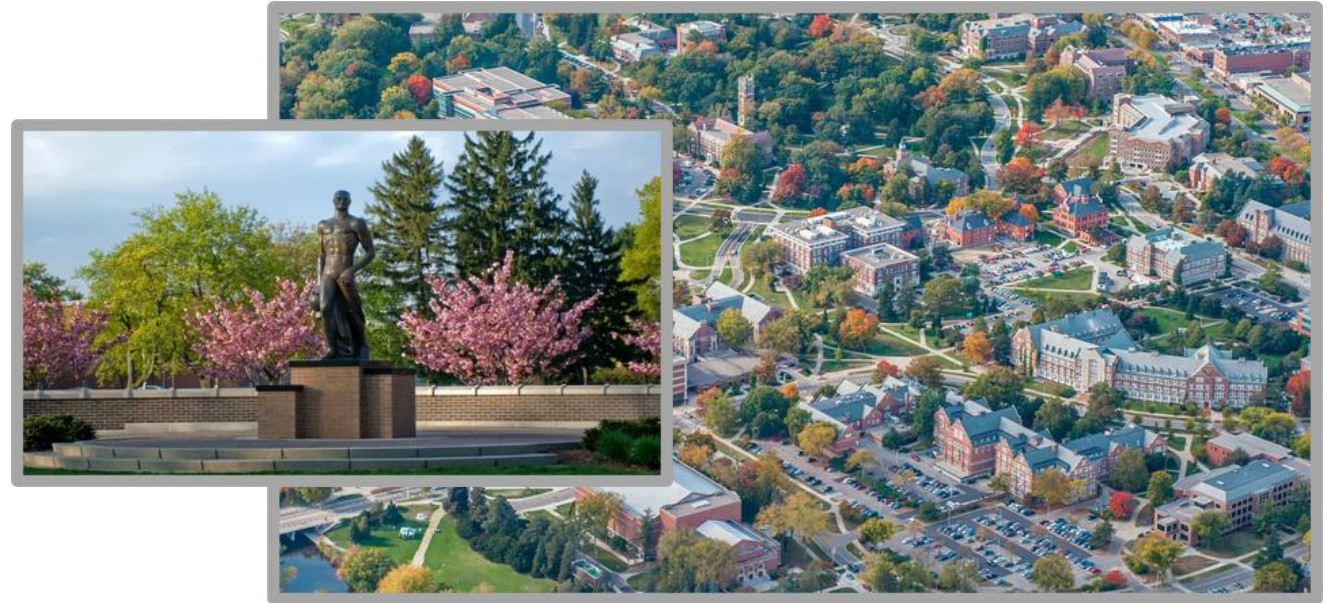
- Grew up in **Saginaw**, Michigan
- Earned my Bachelors in Science at Michigan State University in **Spring 2021**
- After graduation, moved to Portland, Oregon to explore graduate school opportunities
- Began as a **research assistant** in the Zuckerman Lab
- Began the **PhD program** in Biomedical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





# Education

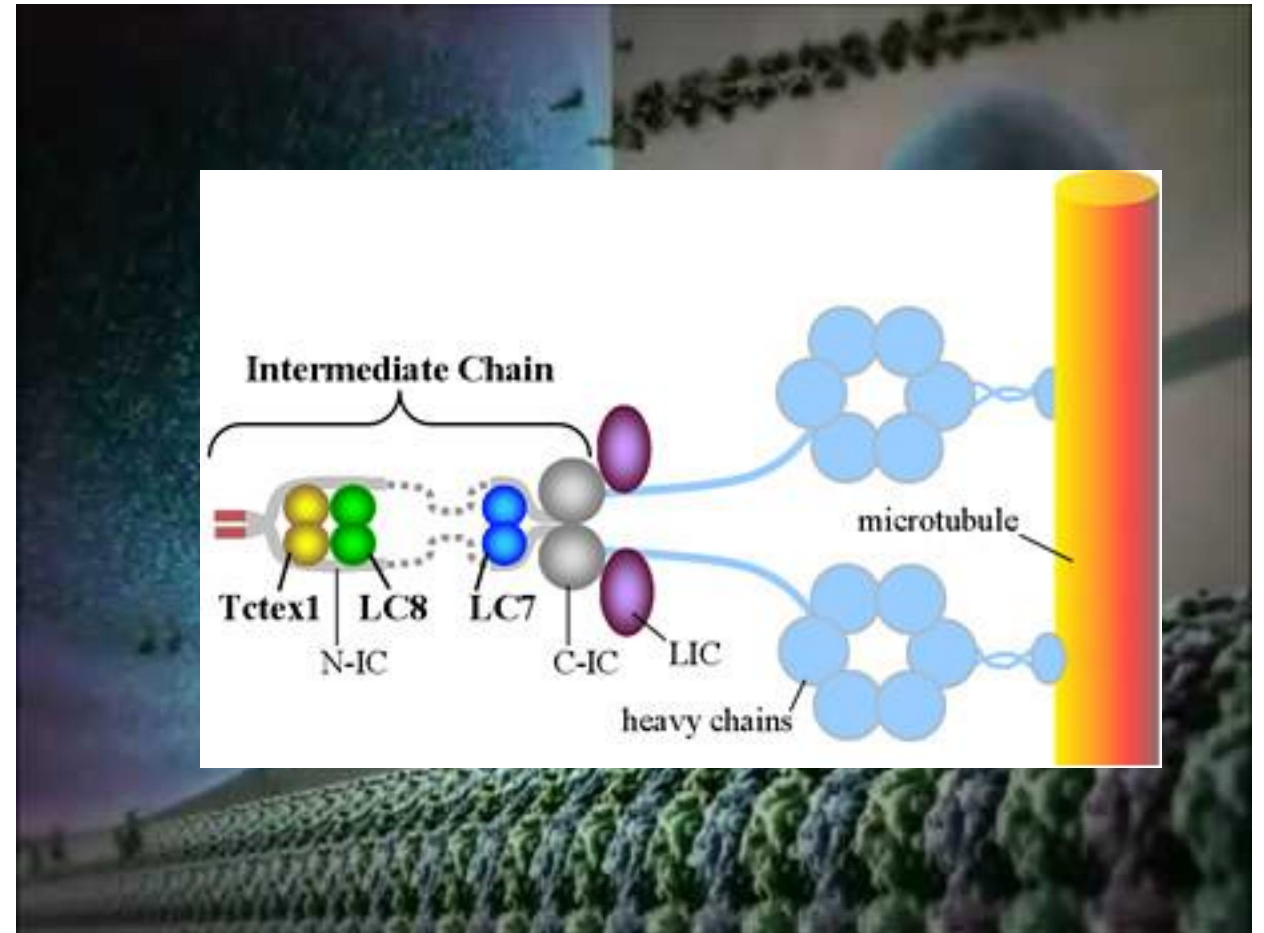
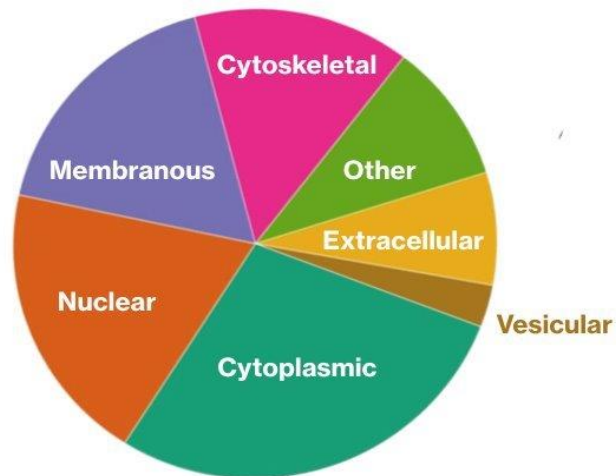
- During my undergraduate, I **majored** in Biochemistry and Molecular Biology and Biotechnology and **minored** in Computational Mathematics, Science, and Engineering
- As a PhD student, I have taken courses on Probability and **Statistics**, Scientific Writing, Data Visualization, Software **Engineering**, 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**

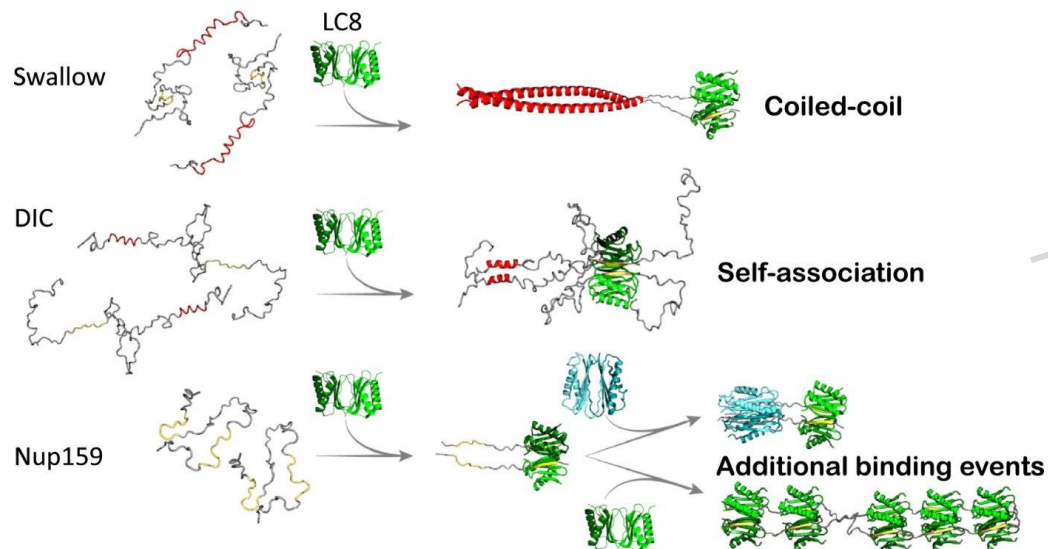




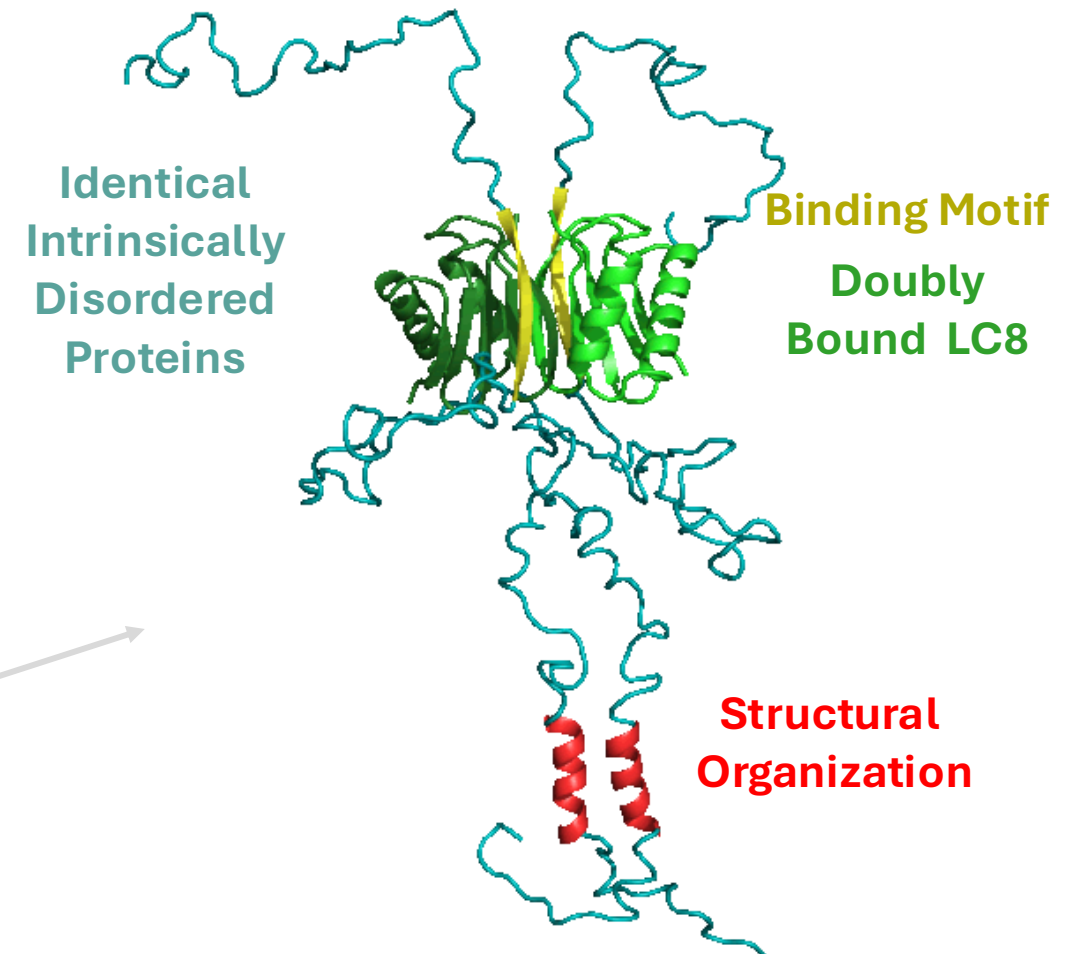
# Graduate Research

## LC8 is a Dimerization Hub

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



Trends in Biochemical Sciences



# Graduate Research

## Many people are interested in LC8

- Instruments 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

### PLOS COMPUTATIONAL BIOLOGY

OPEN ACCESS PEER-REVIEWED  
RESEARCH ARTICLE

#### Quantifying cooperative multisite binding in the hub

doi:10.1371/journal.pcbi.1011059

January 15, 2008

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g Harbor Press

PMCID: PMC6607443  
PMID: 31266884

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Article | [Open access](#) | Published: 16 September 2022

#### The interaction between LC8 and LCA5 reveals a novel oligomerization function of LC8 in the ciliary-centrosome system

[Tamás Szaniszló](#), [Máté Fülöp](#), [Mátyás Pajkos](#), [Gábor Erdős](#), [Réka Ágnes Kovács](#), [Henrietta Vadászi](#), [József Kardos](#) & [Zsuzsanna Dosztányi](#) 

[Scientific Reports](#) 12, Article number: 15623 (2022) | [Cite this article](#)

1052 Accesses | 1 Altmetric | [Metrics](#)

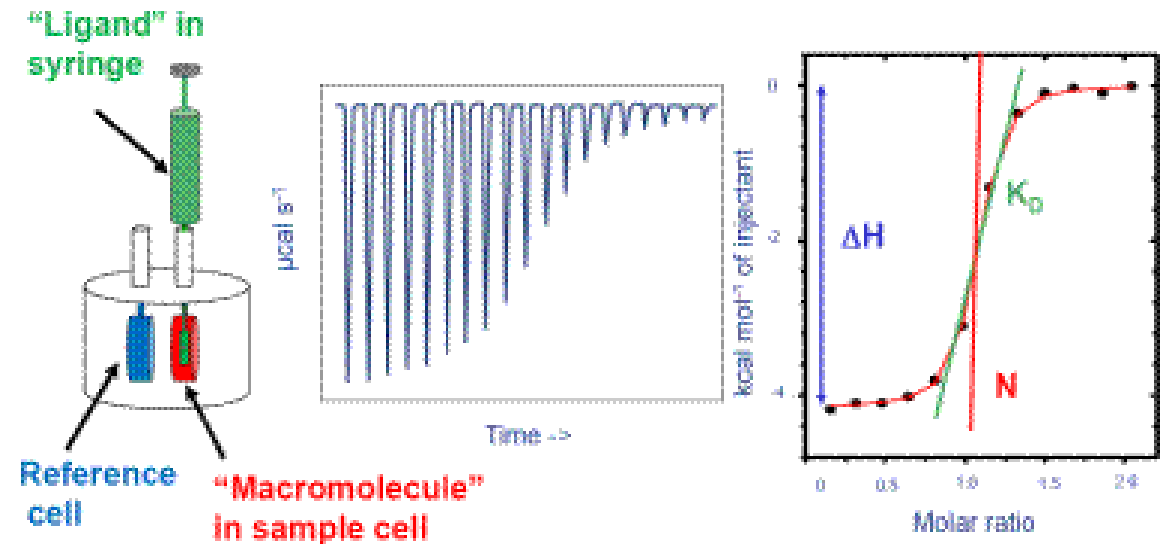
#### Systematic identification of recognition motifs for the hub protein LC8

[Nathan Jespersen](#),<sup>1</sup> [Aidan Estelle](#),<sup>1</sup> [Nathan Waugh](#),<sup>1</sup> [Norman E Davey](#),<sup>2</sup> [Cecilia Blikstad](#),<sup>3</sup> [York-Christoph Ammon](#),<sup>4</sup> [Anna Akhmanova](#),<sup>4</sup> [Ylva Ivarsson](#),<sup>3</sup> [David A Hendrix](#),<sup>1,5</sup> and [Elisar Barbar](#)<sup>1</sup>

# Graduate Research

## ITC

- Instruments like Isothermal Titration Calorimetry (ITC) reveal how *favorable* binding between peptides and LC8 is
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- **Cooperative binding** is one of the most interesting and not fully understood phenomena involved in **control** and **regulation** of biological processes



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

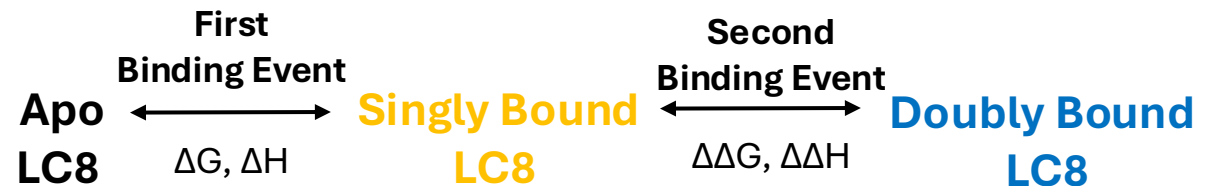
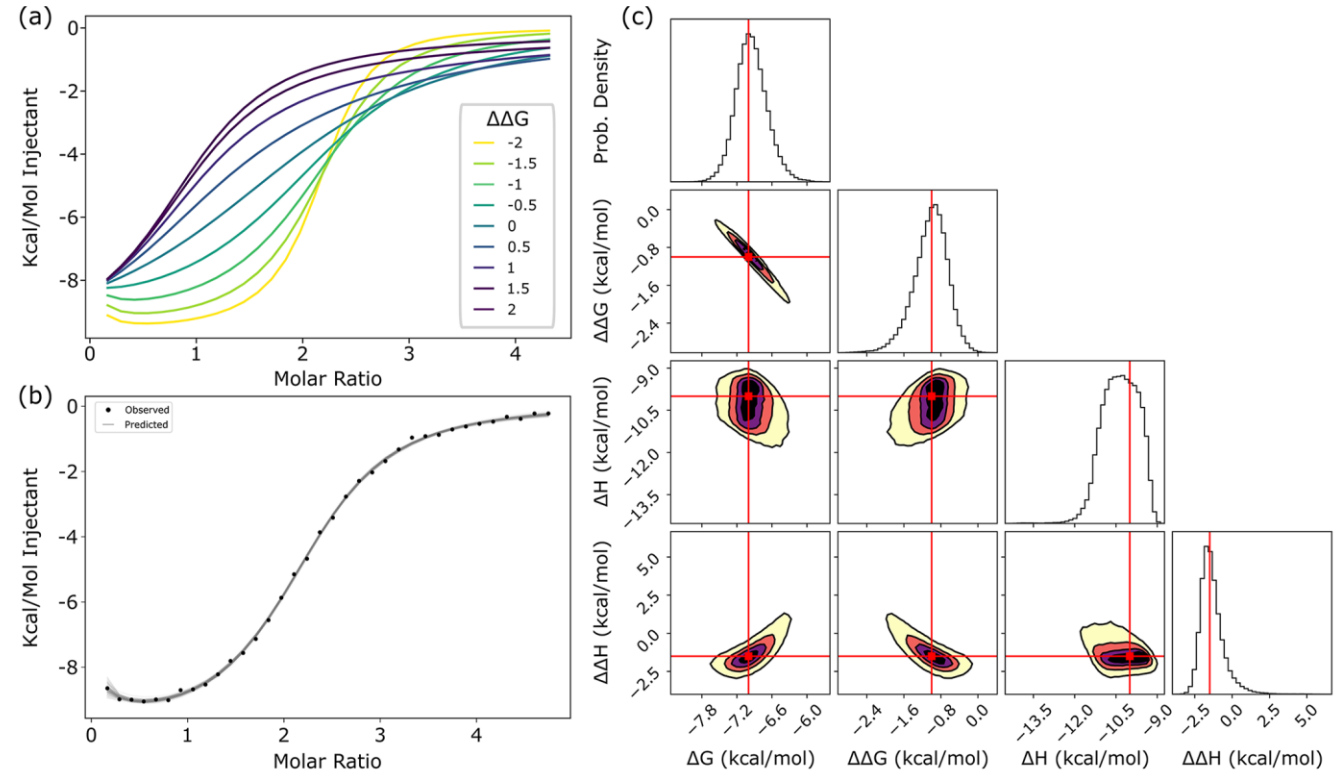
Posterior      Likelihood      Prior

Normalization

# Graduate Research

## Collaborators' Experimental Data

- Instruments like Isothermal Titration Calorimetry (ITC) reveal how *favorable* binding between peptides and LC8 is
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Background

Research

Experience

Outreach

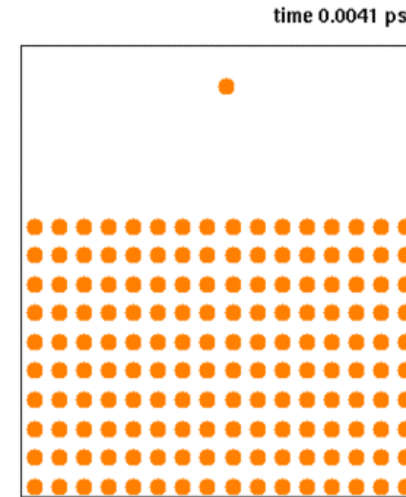
Conclusions

# Graduate Research

## Why continue studying it?

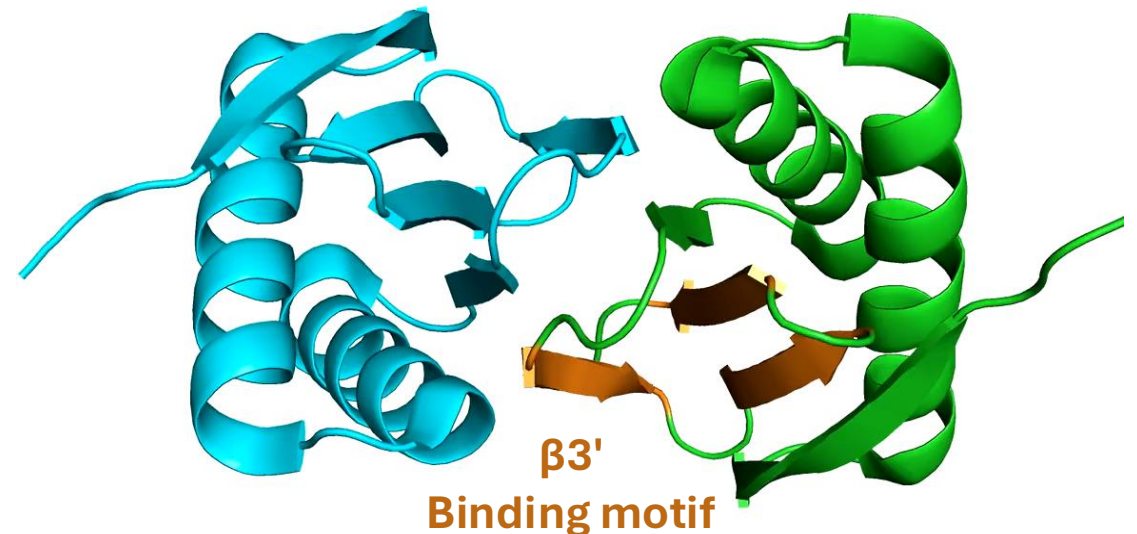
- The **atomistic mechanisms** of LC8's cooperative behavior is unknown
- In other words, we know that *LC8 is cooperative* but we don't know *why or how it is acting cooperatively*
- We explore this using **Molecular Dynamics**

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



Background

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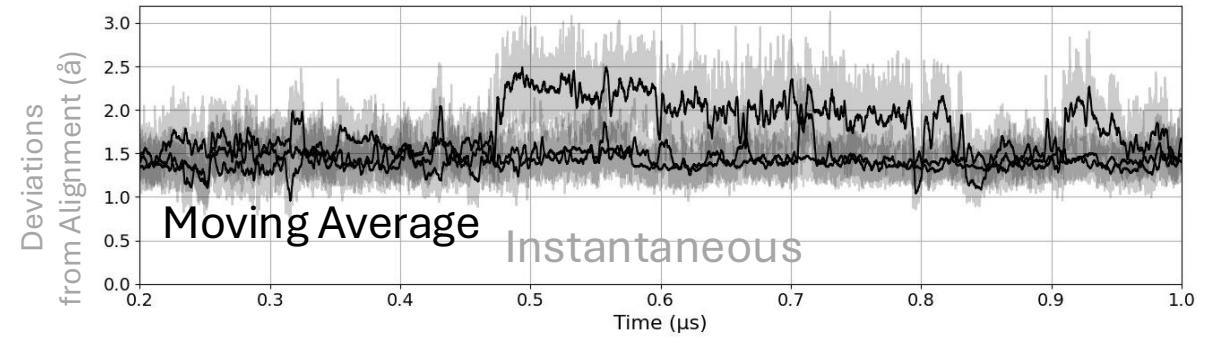
Conclusions

# Graduate Research

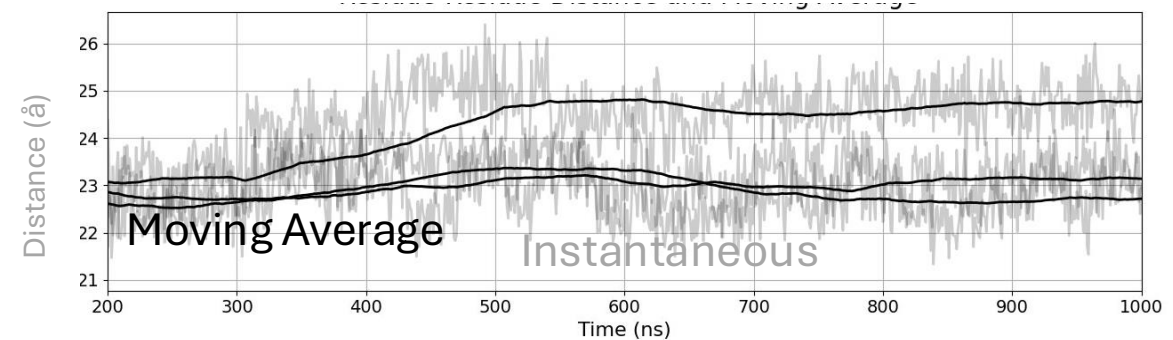
We can use MD data to do tons of things

- 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



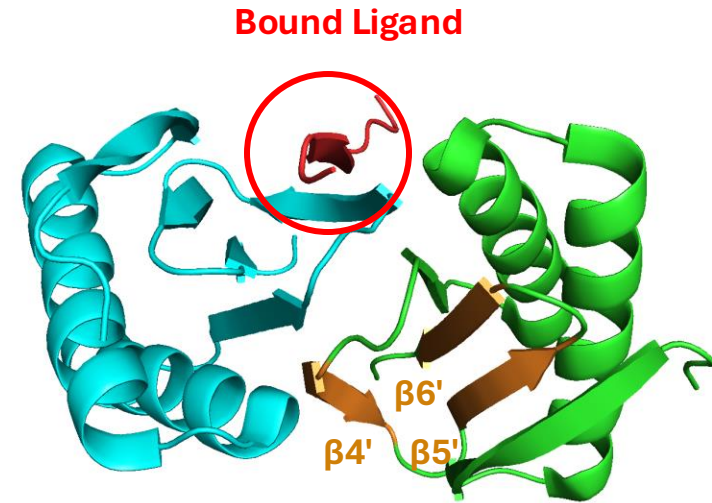
Local Fluctuations of Unbound LC8



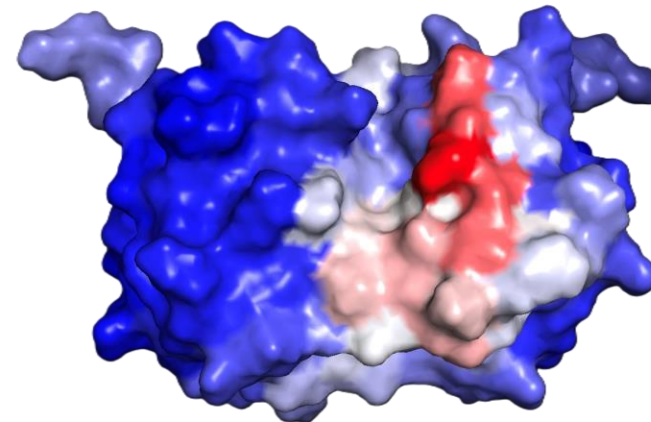
# Graduate Research

## 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!



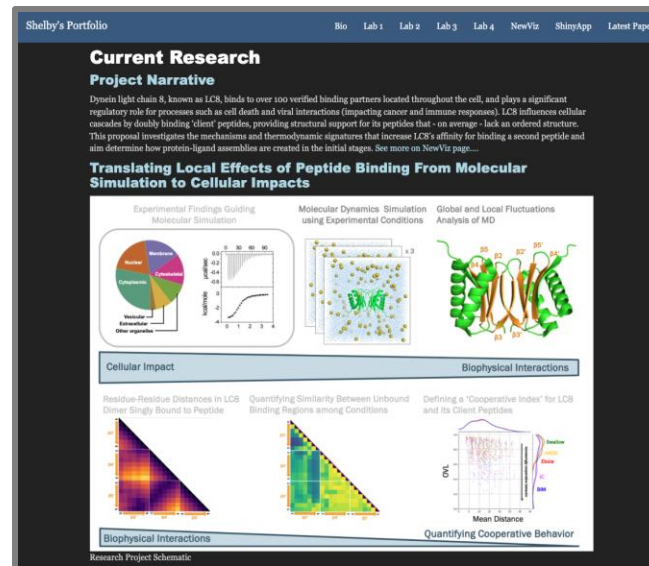
**Lower Similarity → Higher Cooperative Behavior**





# 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

Background

Research

Experience

**Outreach**

Conclusions

# Outreach

Opportunities and communities everywhere!

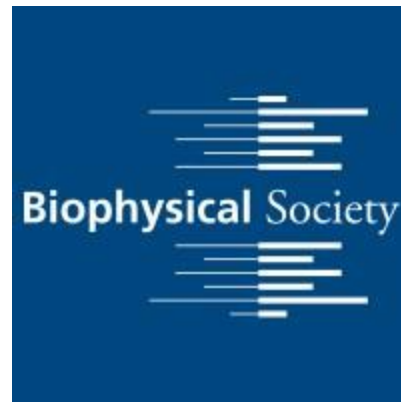


## Lighting the Pathway

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*



Oregon State



Biophysics Society  
Student Chapter