Molecular Dynamics of LC8

OHSU BME Coding Bootcamp

About Me

Undergrad

Michigan State University 2021

Biochemistry, Molecular Biology and Biotechnology

Minor in Computational Mathematics, Science, and Engineering

Research

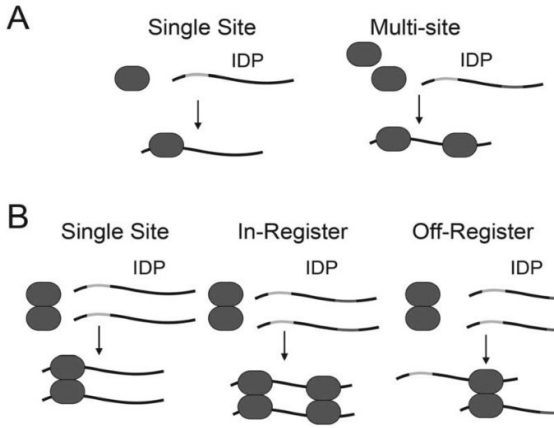
Oregon Health and Science University

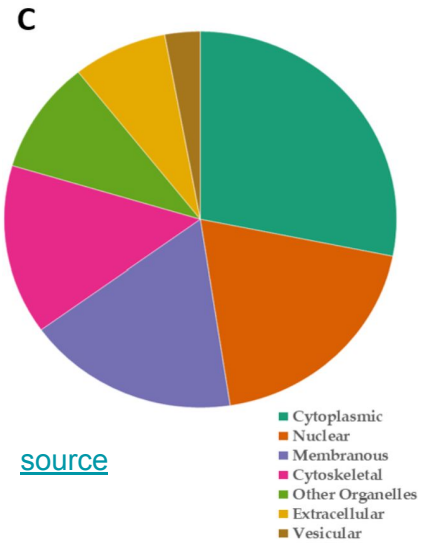
Molecular Dynamics RA

Important as assembly scaffold or molecular sensor

What is LC8?

- Homodimer, with binding groves for 8 - 10 residue long peptides, capable of symmetrically binding ligands
- Intrinsically disordered proteins (IDPs) dimerization 'hub' protein

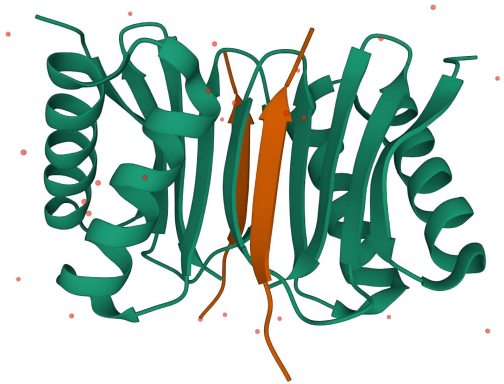




source

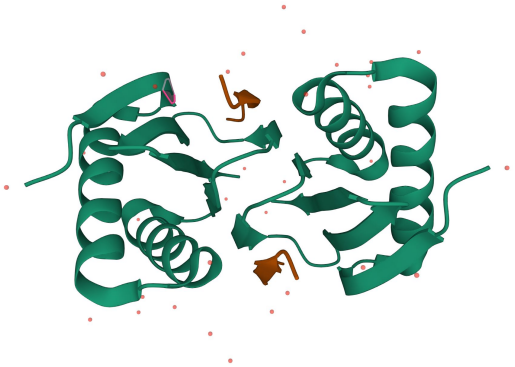
100+ verified partners found in the cellular compartments

source



Side view

source



Top view

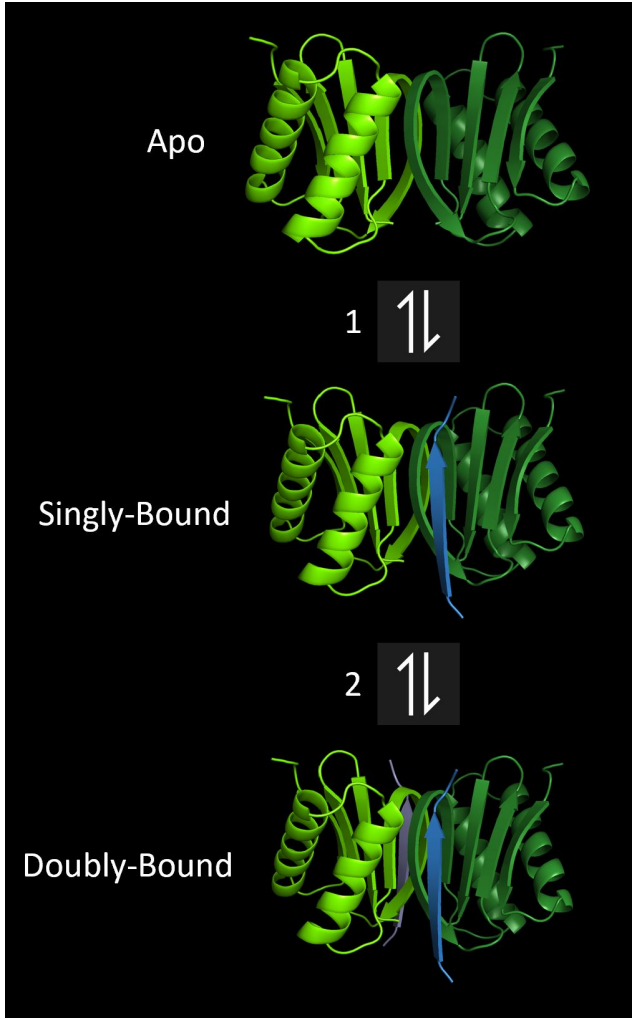
Project Goals

From ITC data, we know the second binding **2** event is more favorable than **1**

- Learn details of the of experimentally observed allostery
  - Using GROMACS, VMD, and MDAnalysis
- Compare Apo “free”, Singly Bound, and Doubly Bound LC8

Research Question

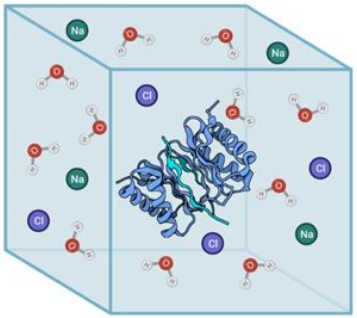
What detailed atomistic behavior can reveal allostery in LC8?



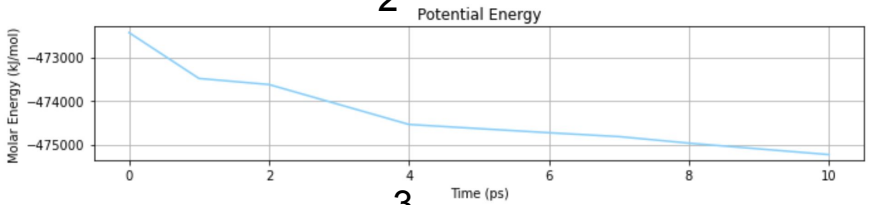
Molecular Dynamics Simulation

To understand allostery from singly bound to doubly bound LC8, we will want to look at the changes in shape, or conformation, of the protein through time, known as dynamics

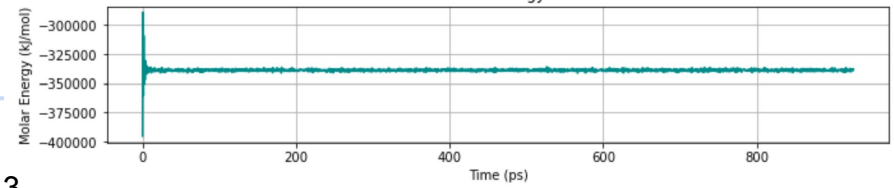
1



2



3



1

Preprocessing

Generating Topology

Solvation and Ionization

2

Energy Minimization

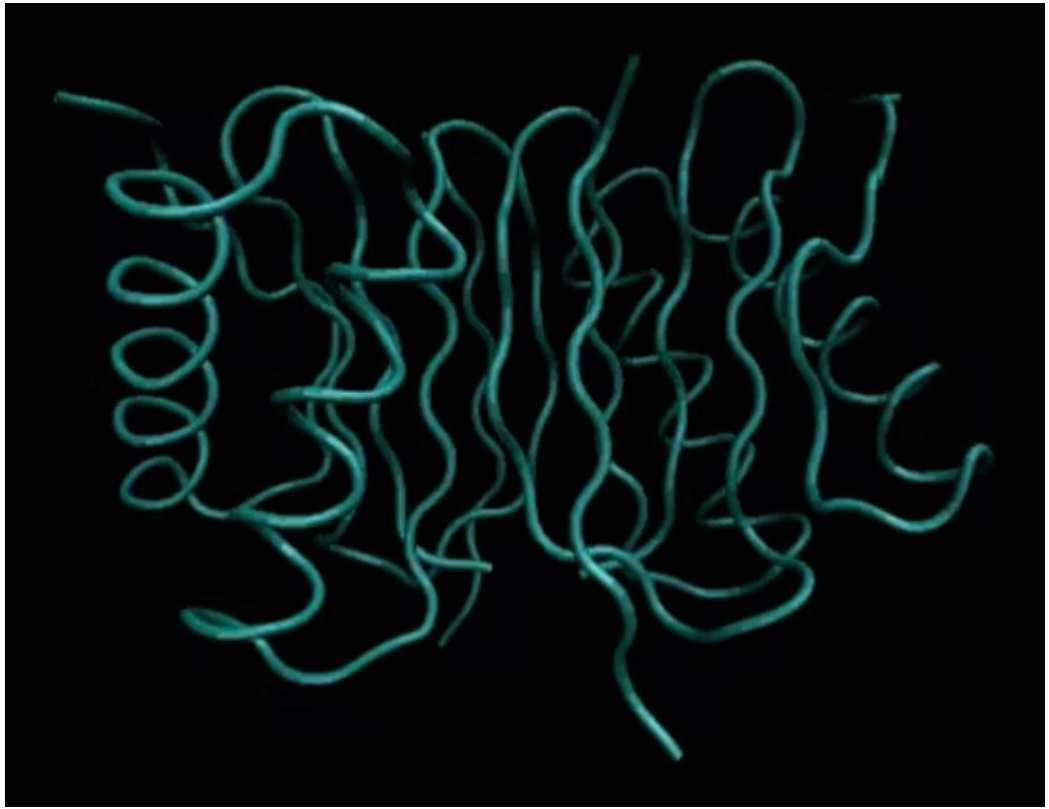
3

Equilibration

Production Molecular Dynamics

Analysis

Trajectory Movie



https://vimeo.com/730038994

Evidence of Allostery

Root Mean Square Fluctuations

What is RMSF?

Measure of the displacement of residues relative to the crystal structure, averaged over time

$$RMSF = \sqrt{\frac{1}{N}\sum_{j}^{N}\left(x_{i(j)} - \langle x_i \rangle\right)^2}$$