

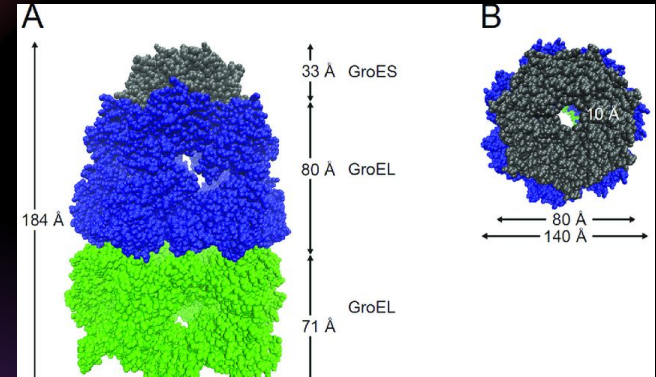
Haytham Zaami

ENM Analysis of GroEL Transitions in E. coli

What is GroEL?

GroEL is bacteria
chaperone protein
(typically found in
E. Coli)

- Required for assisting in protein folding
- One part of two-part chaperone
- Put protein in chamber, come out folded correctly



Carlsen, Thomas & Bennike, Tue & Christiansen, Gunna & Birkelund, Svend. (2013). A role for anti-HSP60 antibodies in arthritis: a critical review. *OA Arthritis*. 1. 10.13172/2052-9554-1-2-879.

Additional animation:
<https://www.youtube.com/watch?v=-NcNeLc1mo>

GroEL–GroES chaperonin complex

T

- Unfolded protein binds inside one of GroEL's rings

T → R

- Taut to Relaxed
- GroES 'cap' not on yet
- Salt Bridges broken to conform

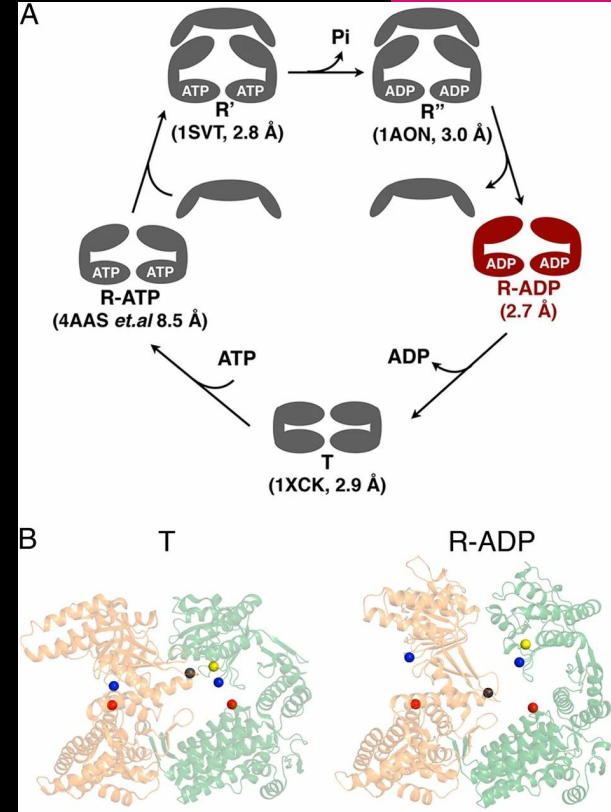
Bind with GroES –
After ATP Hydrolysis

R → R'

- GroES put on

R' → R''

- Convert ATP to ADP after GroES on
- Won't cover during research

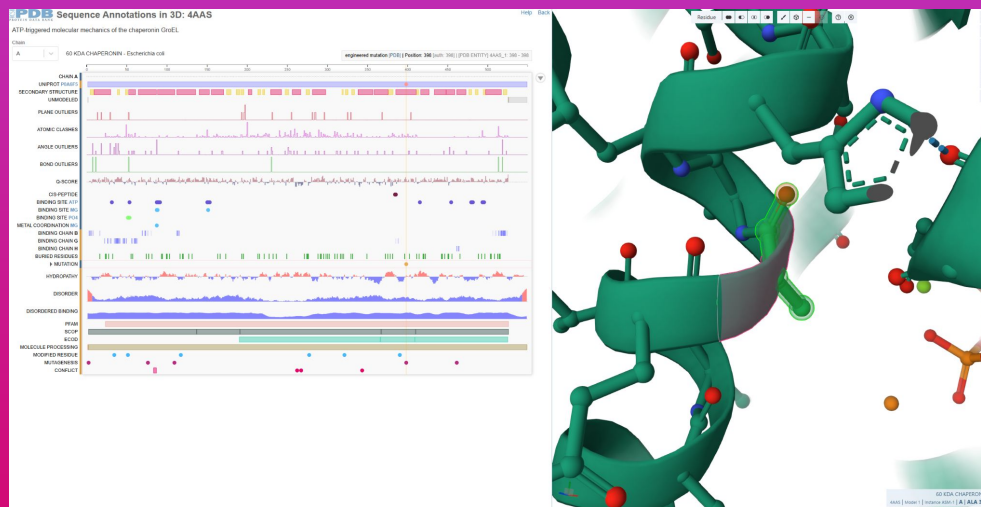
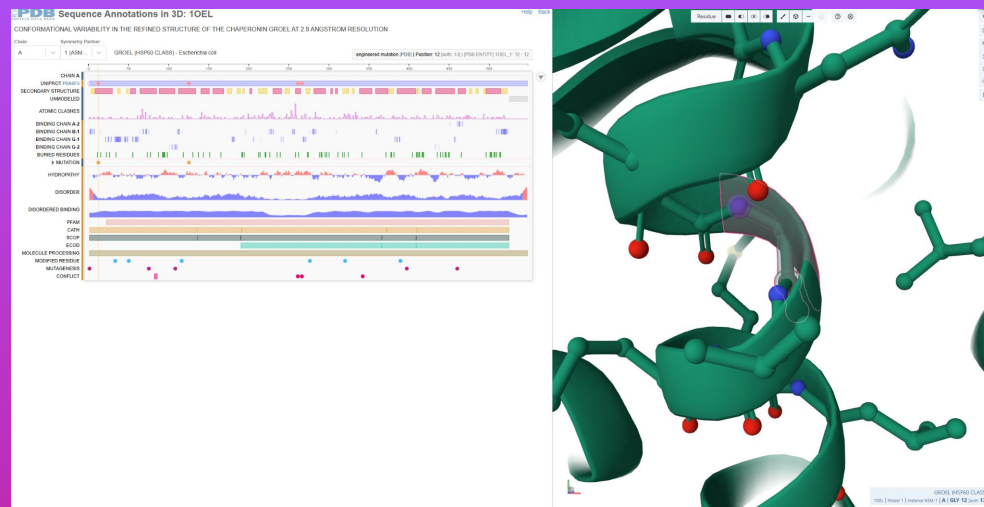


X. Fei, D. Yang, N. LaRonde-LeBlanc, & G.H. Lorimer, Crystal structure of a GroEL-ADP complex in the relaxed allosteric state at 2.7 Å resolution, *Proc. Natl. Acad. Sci. U.S.A.* 110 (32) E2958-E2966, <https://doi.org/10.1073/pnas.1311996110> (2013).

Proteins Used/ Caveates

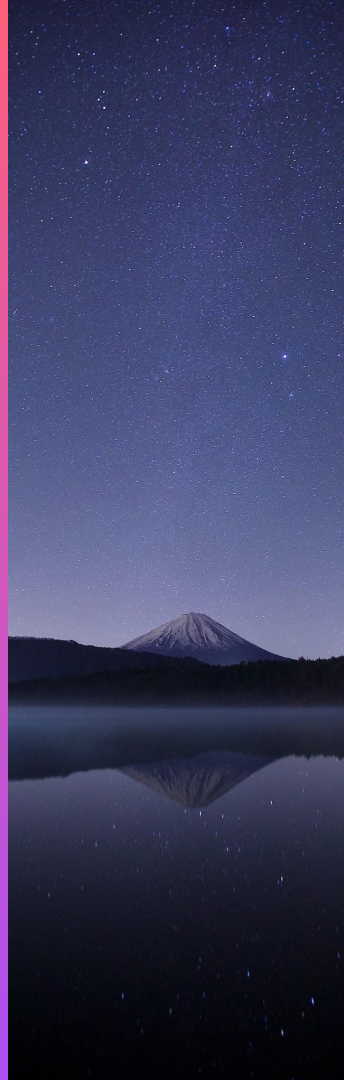
- T State: PDB ID 1OEL
 - Mutated; potentially for protein stabilization/disease study
 - Will neglect mutation
- R State: 4AAS
 - Mutated
 - Will neglect mutation
- R' State: 1SVT
 - Non Mutated

*Mutations could potentially impact research, but minimally



Central Topic:

How well do different types of Normal Mode Analysis predict the transitions that the chaperone protein goes through?



Type of analysis used



Analysis to see if theoretical motion matches biological reality

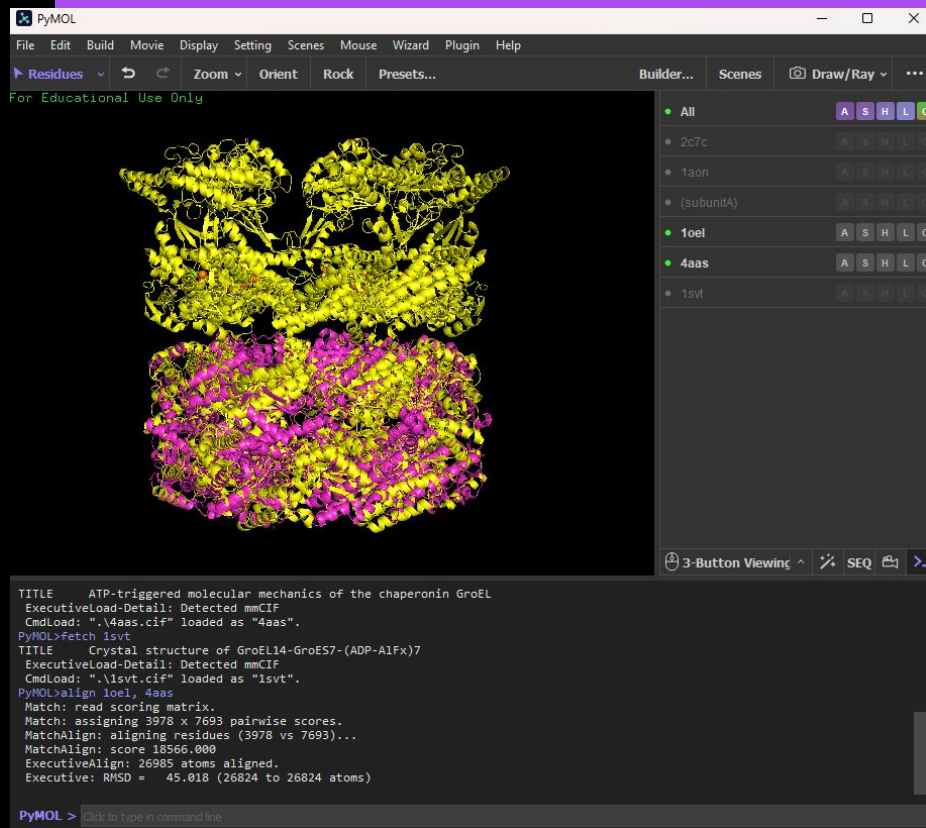
- ANM
- GNM
- *parameter-free ANM
- *RTB

<http://www.bahargroup.org/prody/>



Predictions

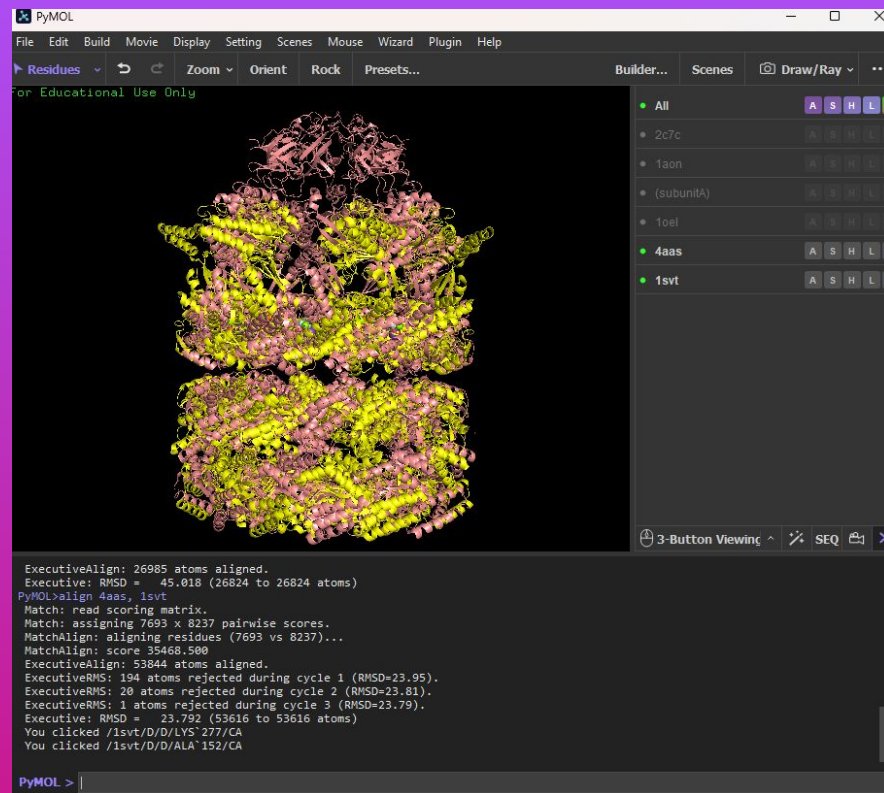
- 1OEL will conform similar, stretching
- May need to combine low frequency modes



1OEL - magenta
4AAS - Yellow

Predictions

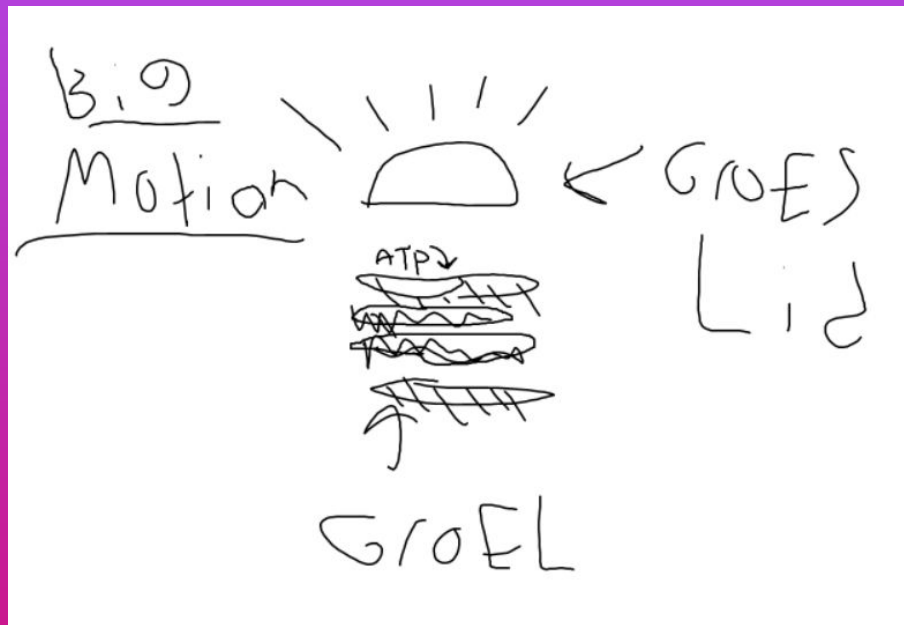
- 4AAS does not have the GroEL cap, will not get it from doing NMA
 - Has opening at top for ATP and protein to enter
- More overlap as structures similar in size/width



4AAS - Yellow
1SVT - Pink/Peach

Anticipated Issues

- Computation time
 - Based on method
- ATP Energy
 - NMA Constraint
 - Single energy minimum
- Large Scale motion prediction accuracy



Timeline of research*

NMA on 1OEL

- Try different methods
- Compute different modes
- Test for accuracy

NMA on 4AAS

- Try different methods
- Obtain different modes
- Test for accuracy

Visualize

- Visualize data to obtain insights
- Interpret accordingly
- Make changes if needed

Put Together

- Make inferences from findings

Current sources

Inspiration for proteins to use

[Crystal structure of a GroEL-ADP complex in the relaxed allosteric state at 2.7 Å resolution | PNAS](#)

Python library for analysis

[ProDy Project - Protein Dynamics and Sequence Analysis](#)

Chaperone protein transitions

[Dynamics of allosteric transitions in GroEL - PubMed](#)

More soon!