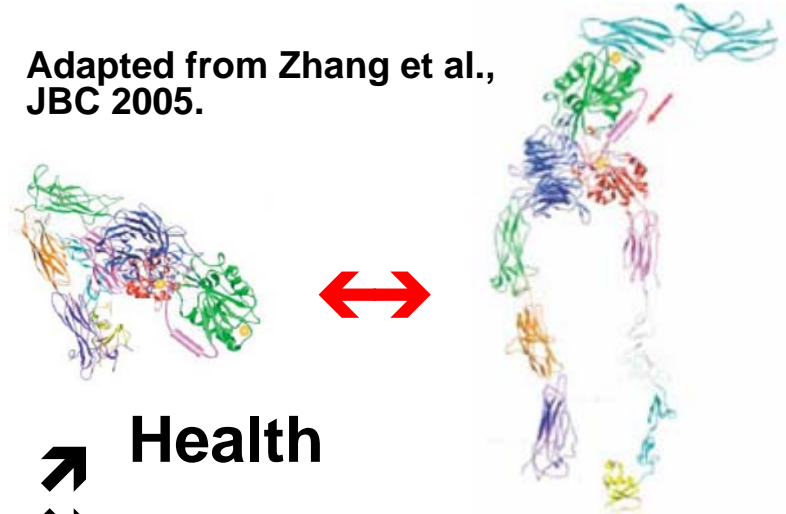


Predicting Functional States of Proteins

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Adapted from Zhang et al.,
JBC 2005.



Protein conformation → Function

↗ Health
↘ Disease

Few crystal structures exist of both functional states.

Can we predict the alternative state of a protein?

Protein engineering → design function

↗ Nanotechnology
↘ Molecular medicine

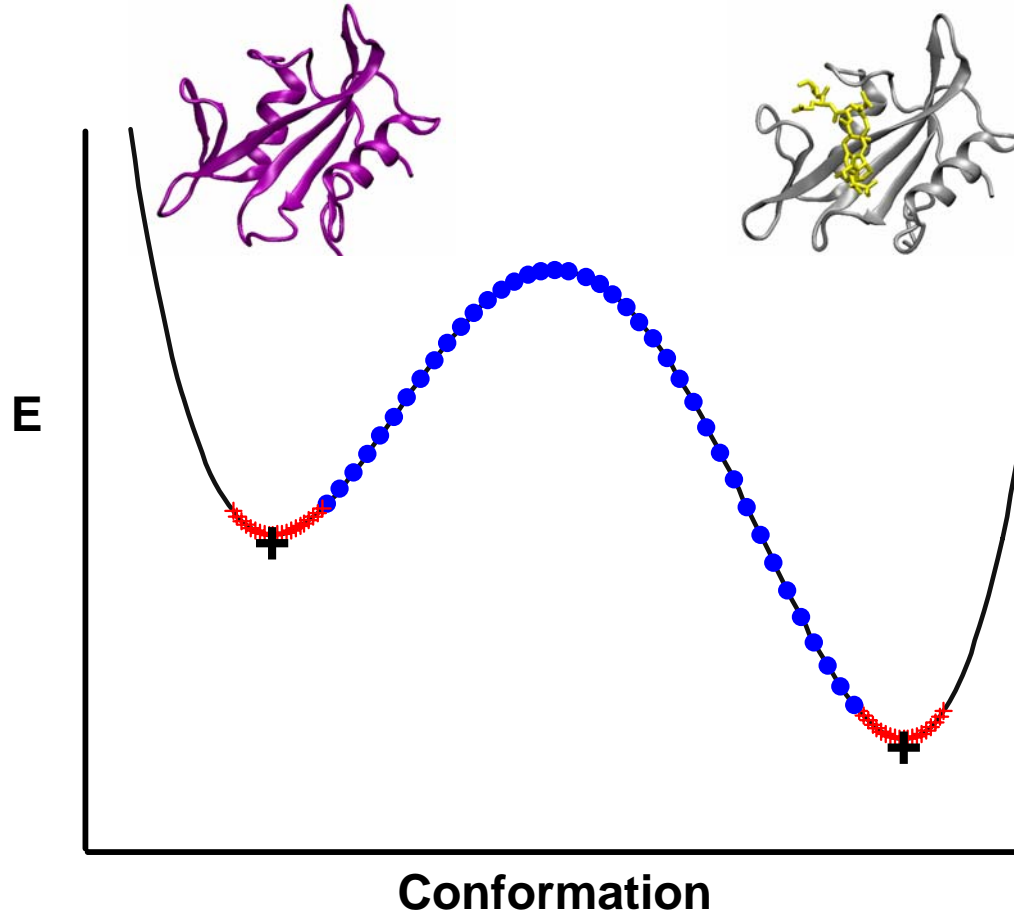


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Predicting Functional States of Proteins

Two-State Model



Method

Use crystal structure

1. Perturb structure
2. Repack side chains
3. Minimize energy
4. Accept or reject structure

Repeat 1000s of cycles

+ Crystal structure

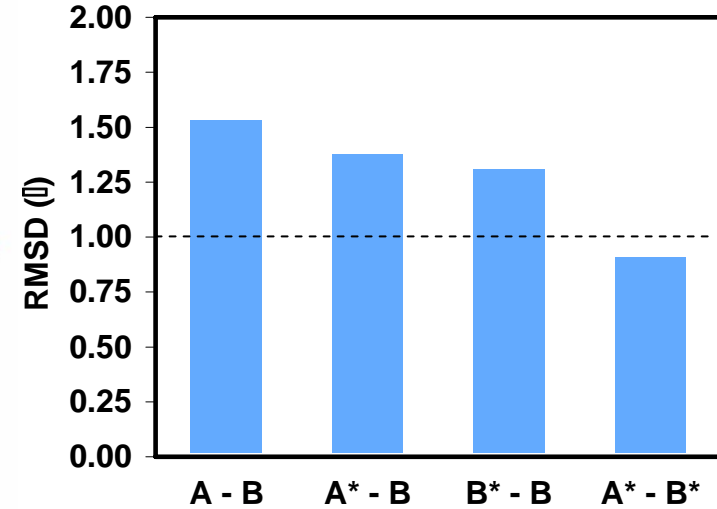
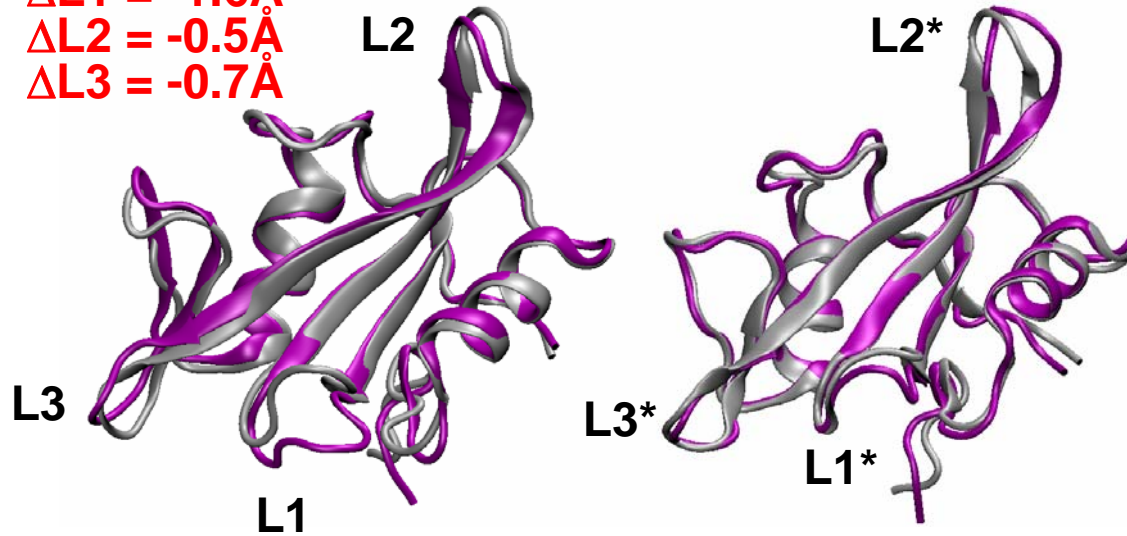
+ First round

● Second round



Predicting Functional States of Proteins

$\Delta L1 = -1.6\text{\AA}$
 $\Delta L2 = -0.5\text{\AA}$
 $\Delta L3 = -0.7\text{\AA}$



Conclusions

- Predict states of small conformational changes
- Map energy landscape of two-state protein

Next Steps

- Increase size of proteins and degree of difference
- Apply to proteins where alternative state is unknown

