

# FLEXIBILITY AND PROTEIN FUNCTION

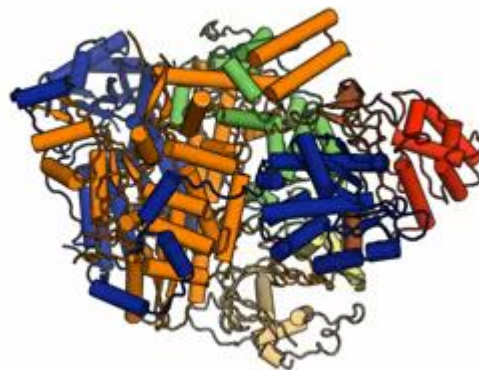
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SUSTC

# Proteins are flexible molecules

- Protein flexibility is the important part of protein function
- Conformational flexibility
  - Binding
  - Catalysis
  - Regulation

Motion	Spatial displacement (Å)	Characteristic time (s)	Energy source
Fluctuations (e.g., atomic vibrations)	0.01 to 1	$10^{-15}$ to $10^{-11}$	$k_bT$
Collective motions (A) fast, infrequent (e.g., Tyr, Phe ring flips) (B) slow (e.g., domain movement; hinge-bending)	0.01 to > 5	$10^{-12}$ to $10^{-3}$	$k_bT$
Triggered conformational changes	0.5 to > 10	$10^{-9}$ to $10^3$	Binding interactions

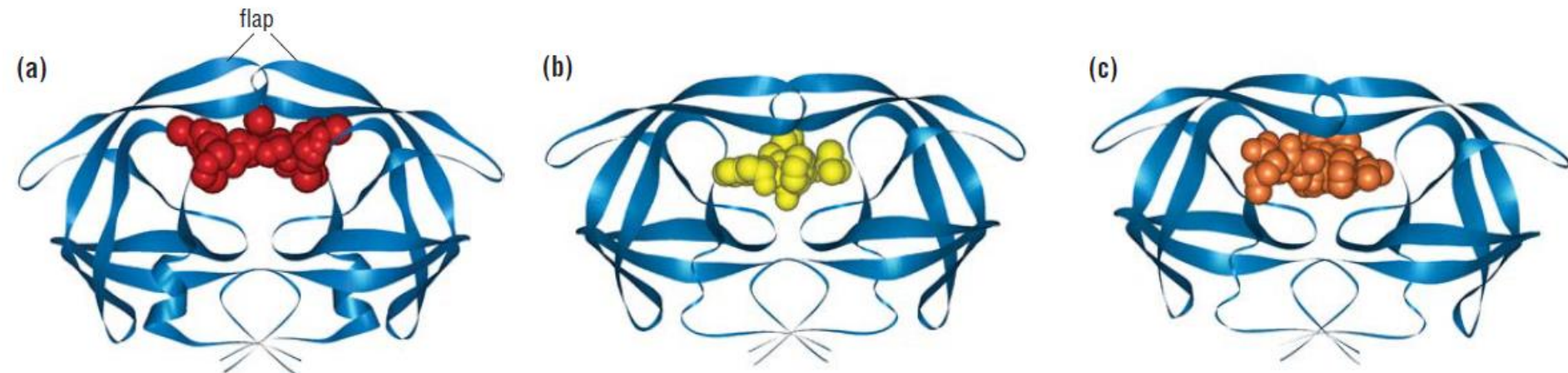


RNA-dependent RNA polymerase from influenza C virus shows large conformational flexibility upon RNA substrate binding

Nature, 2015

# Induced fit

- The flexibility of tertiary structure allows proteins to adapt to their ligands
- Lock-and-key model
- **Induced fit** model
  - Both proteins and their ligands are naturally flexible
- Population shift model



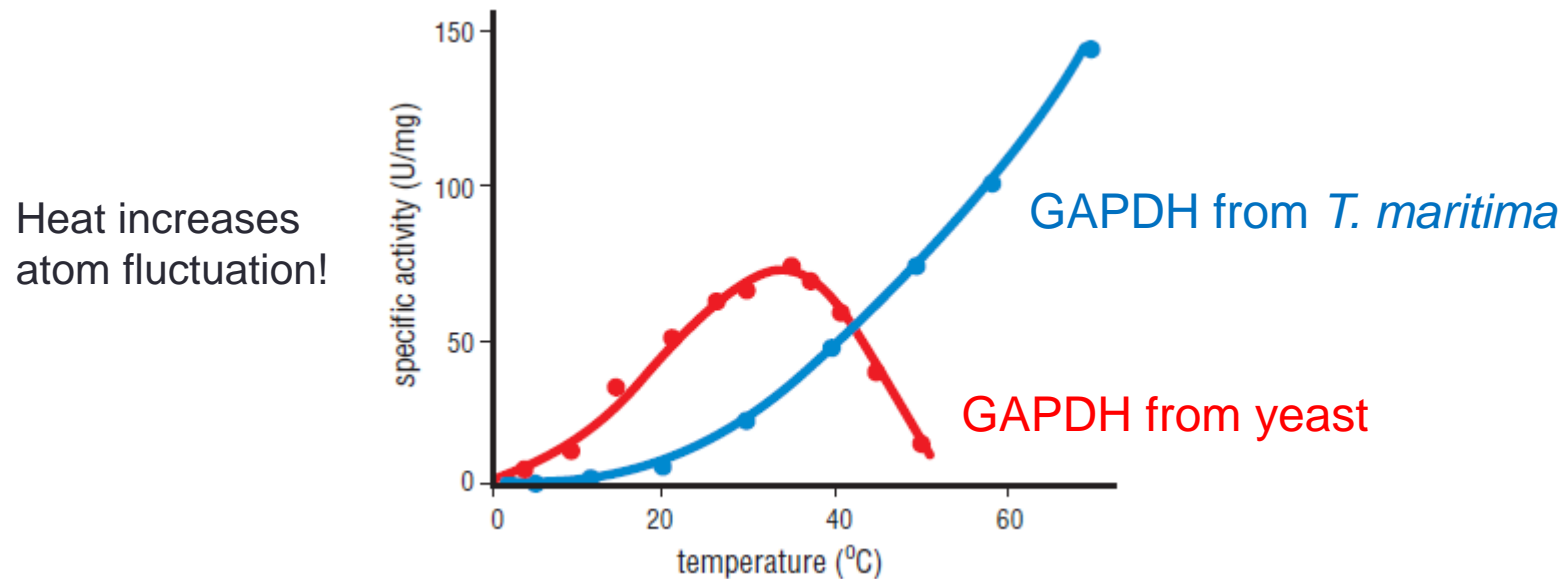
HIV protease, an enzyme from the virus that causes AIDS, bound to three different inhibitors

The degree of flexibility varies in different proteins



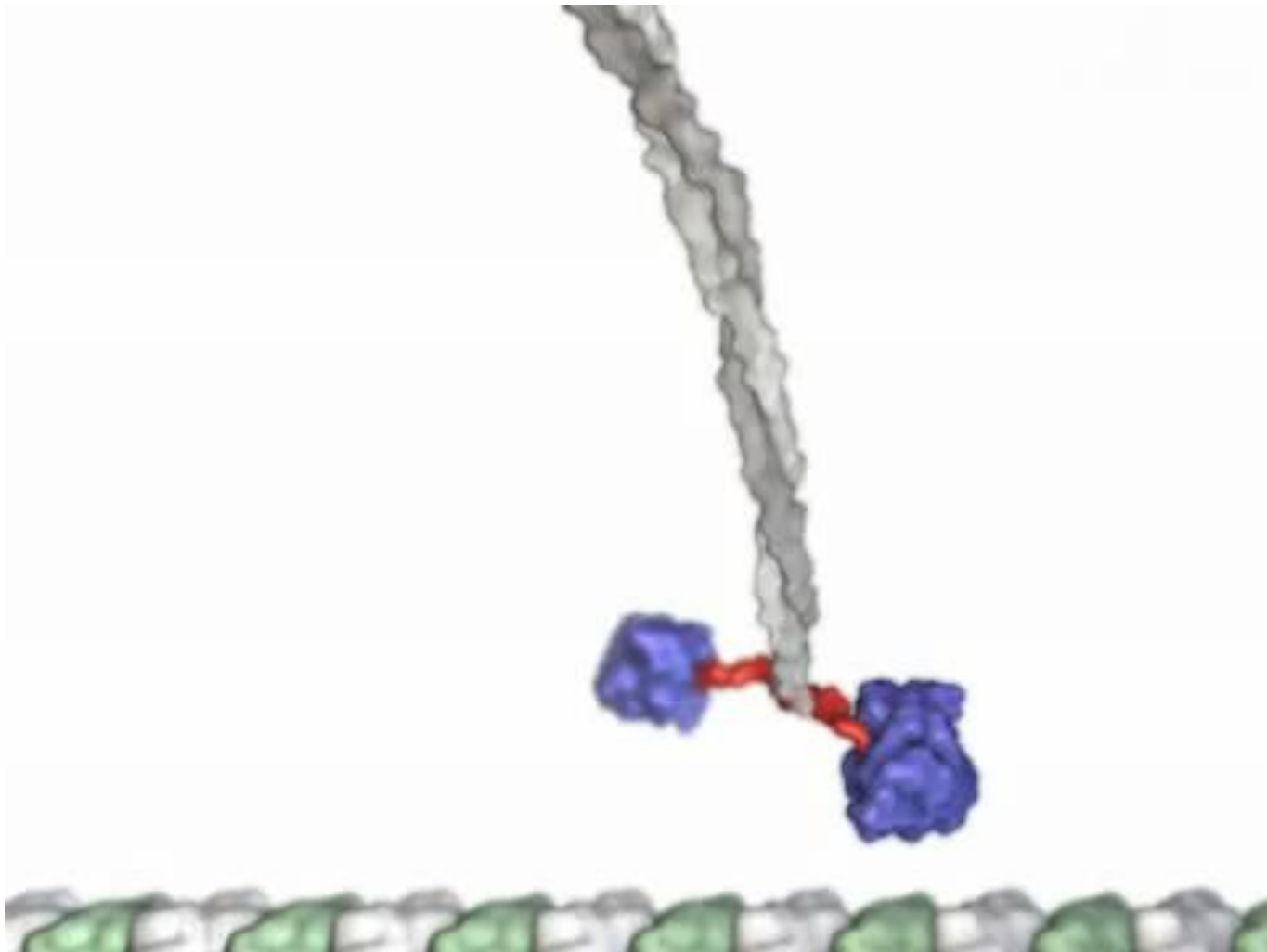
## Protein flexibility is essential for biochemical function

The proper balance between flexibility and rigidity is a must for proteins

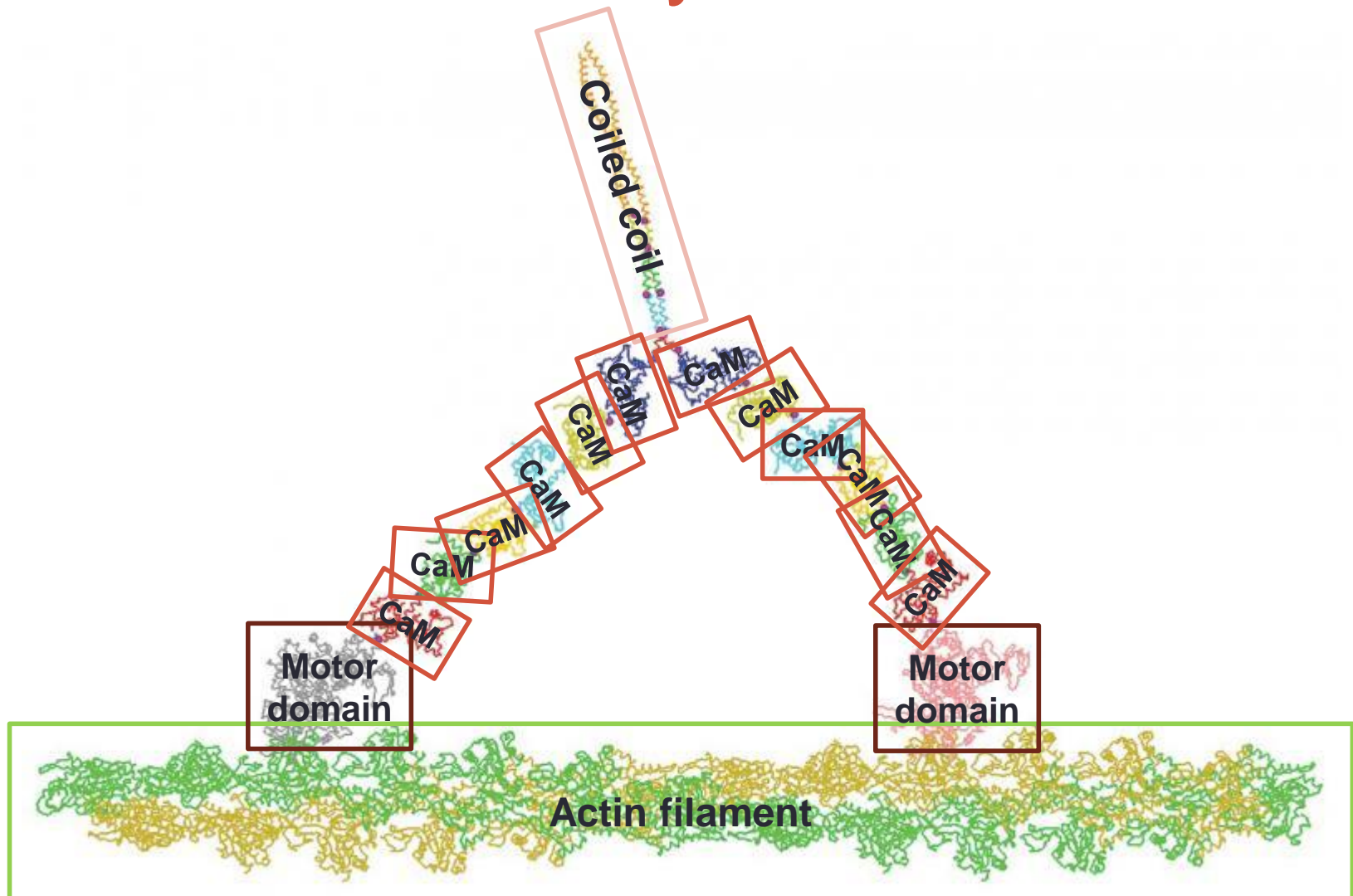


Differences in the temperature dependence of the specific activity of D-glyceraldehyde-3-phosphate dehydrogenase (GAPDH) from two organisms

# Cytoskeleton motors are flexible proteins

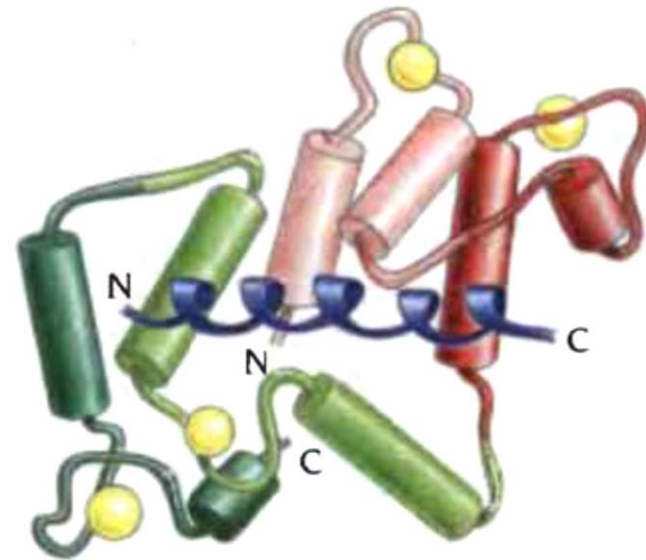
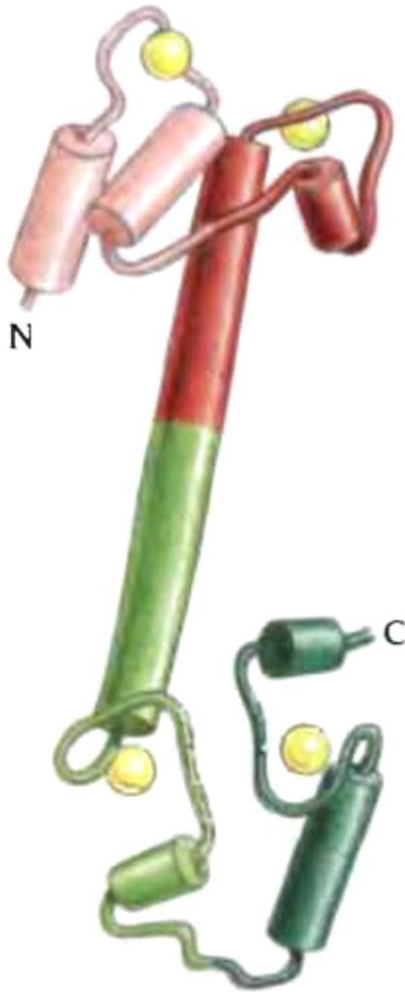


# Calmodulin and myosin





## Calmodulin



Free form and peptide bound form of calmodulin



