

Protein Structure

(a)

MOLECULAR STRUCTURE

Primary (sequence)

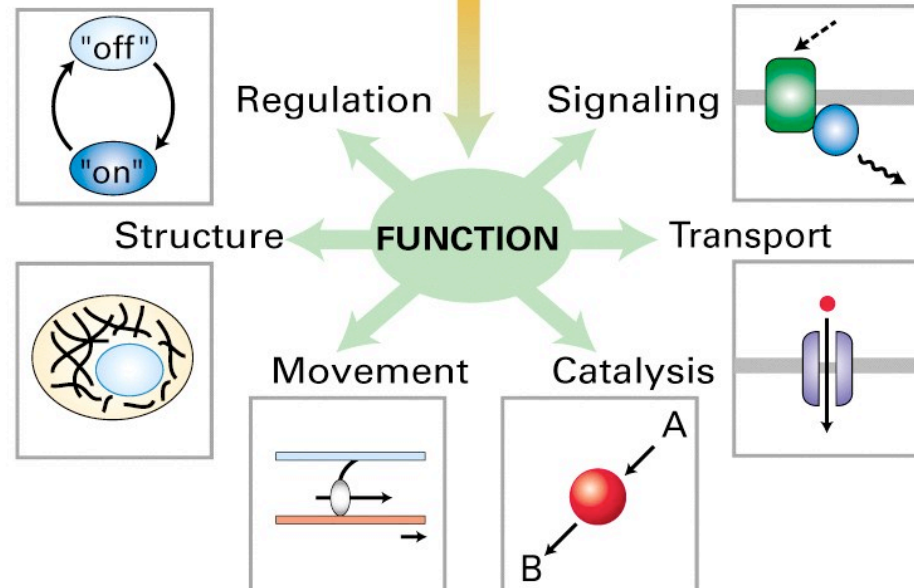
Secondary (local folding)

Tertiary (long-range folding)

Quaternary (multimeric organization)

Supramolecular (large-scale assemblies)

(b)



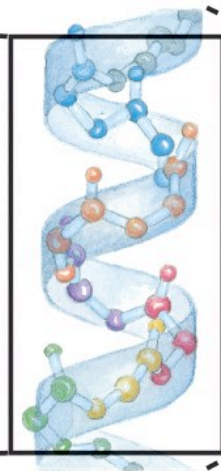
Protein Structure

Primary structure



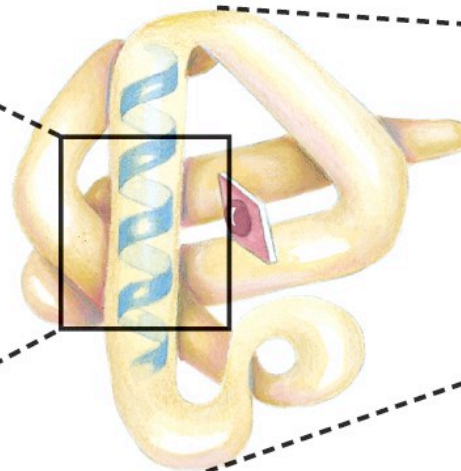
Amino acid residues

Secondary structure



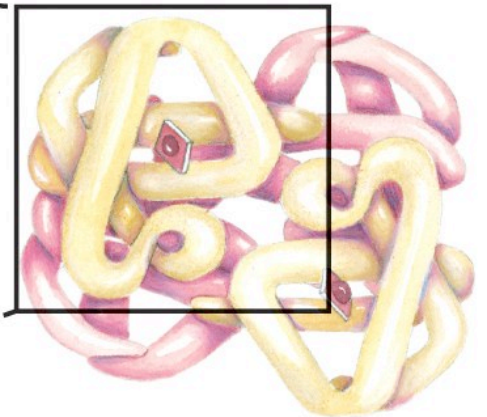
α Helix

Tertiary structure



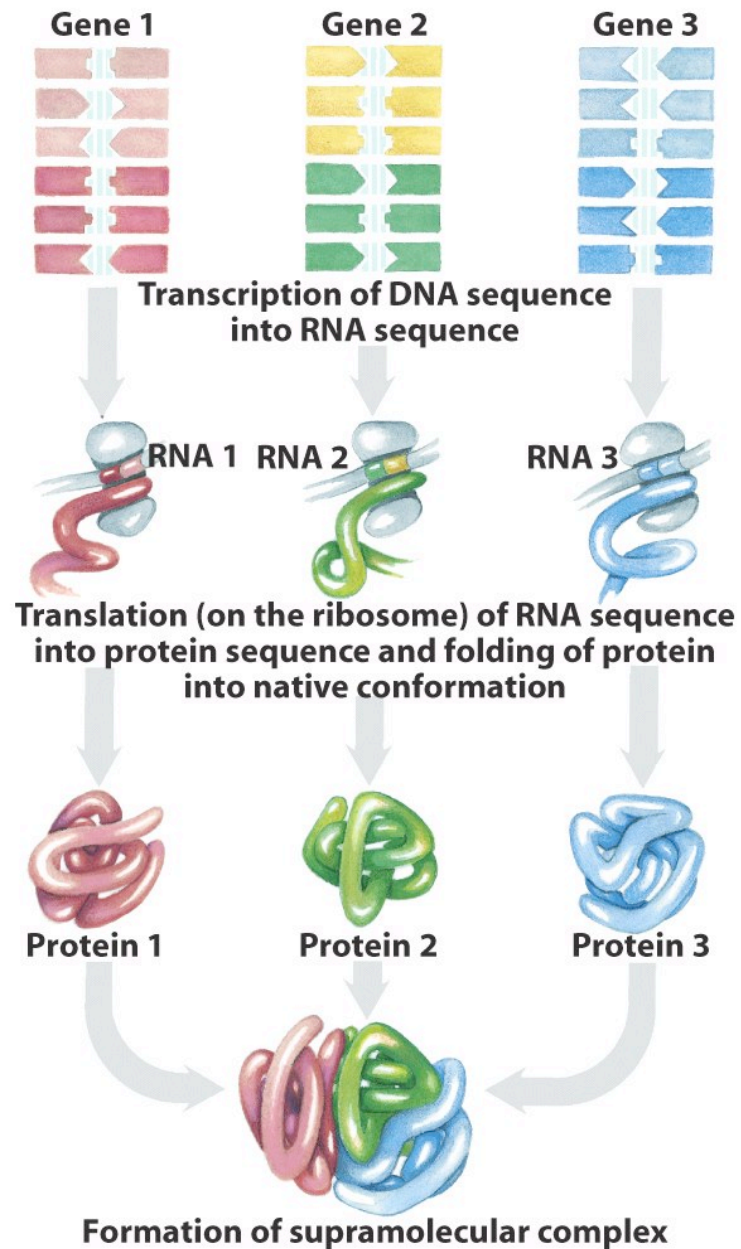
Polypeptide chain

Quaternary structure

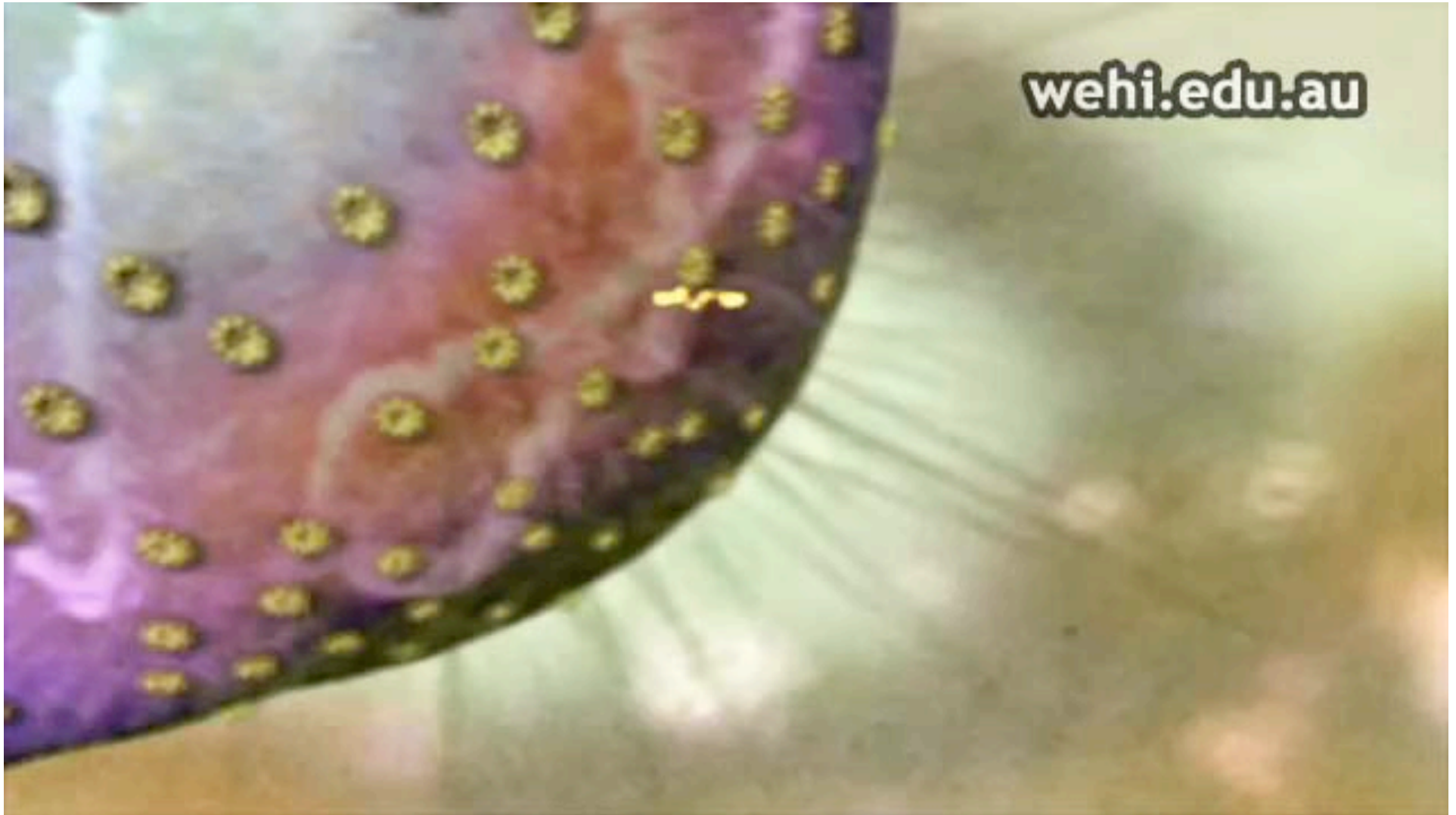


Assembled subunits

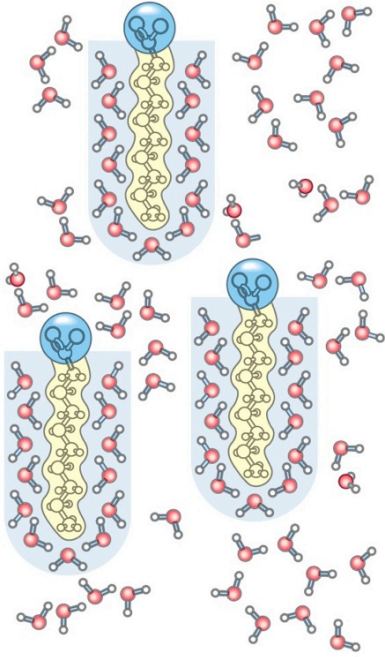
Central Dogma of Biology



Protein Folding in the Cell

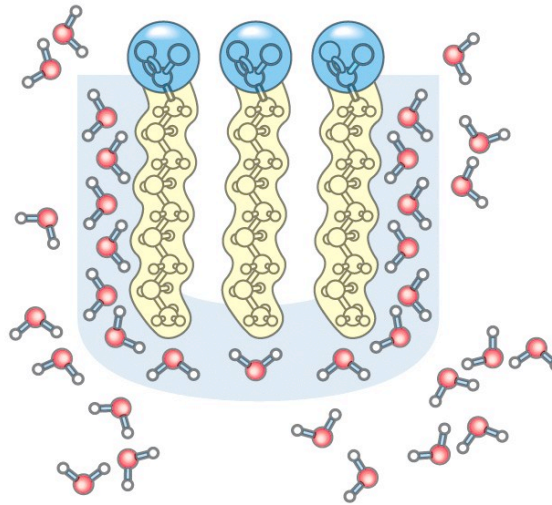


The Hydrophobic Effect



Dispersion of lipids in H₂O

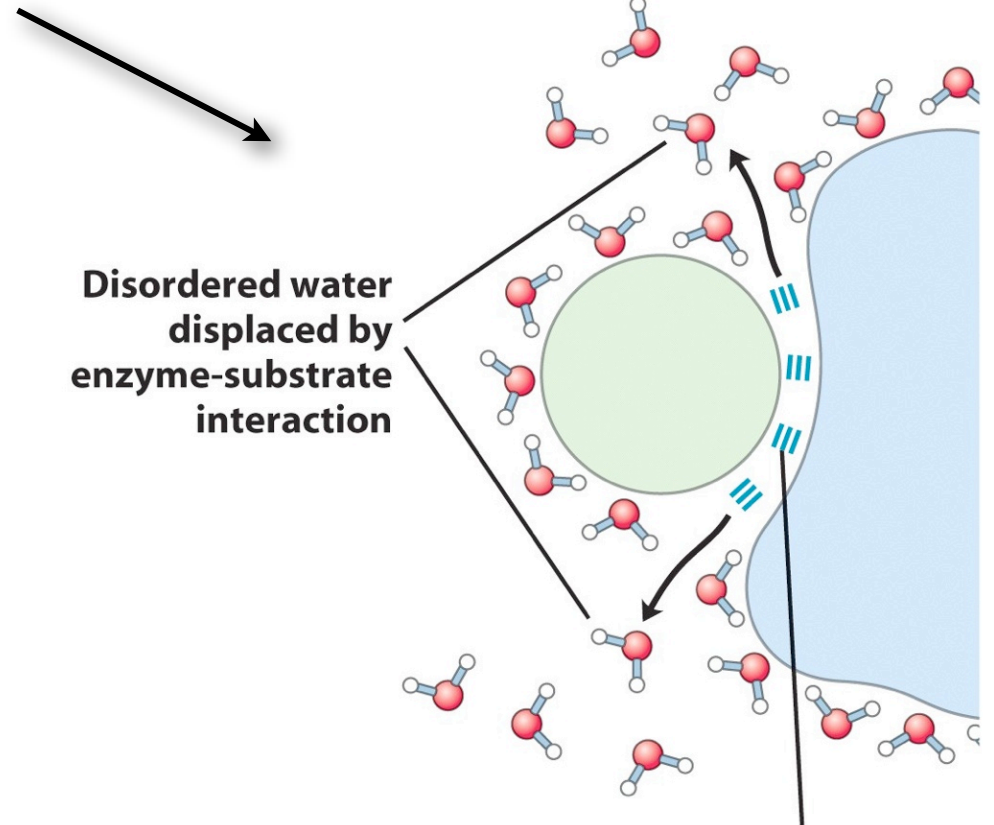
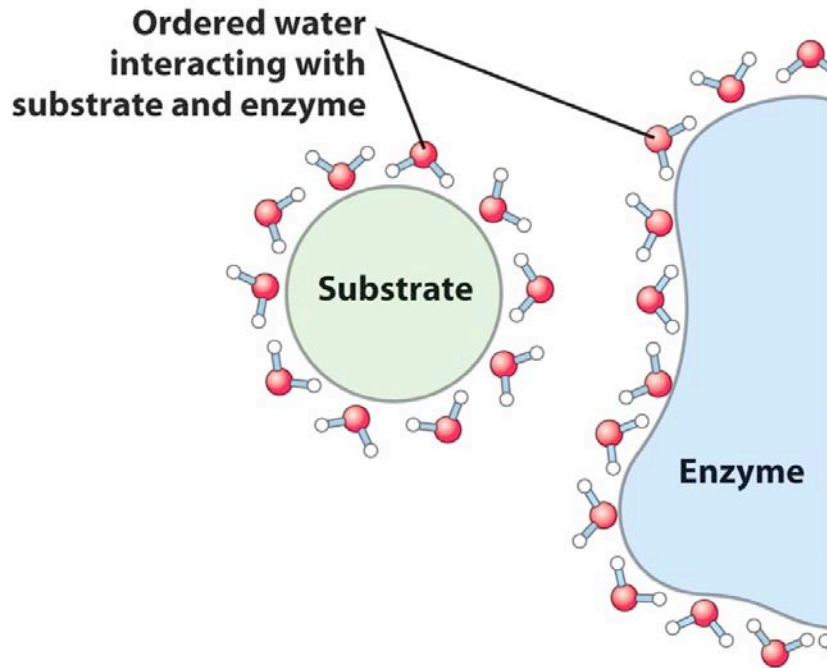
Each lipid molecule forces surrounding H₂O molecules to become highly ordered.



Clusters of lipid molecules

Only lipid portions at the edge of the cluster force the ordering of water. Fewer H₂O molecules are ordered, and entropy is increased.

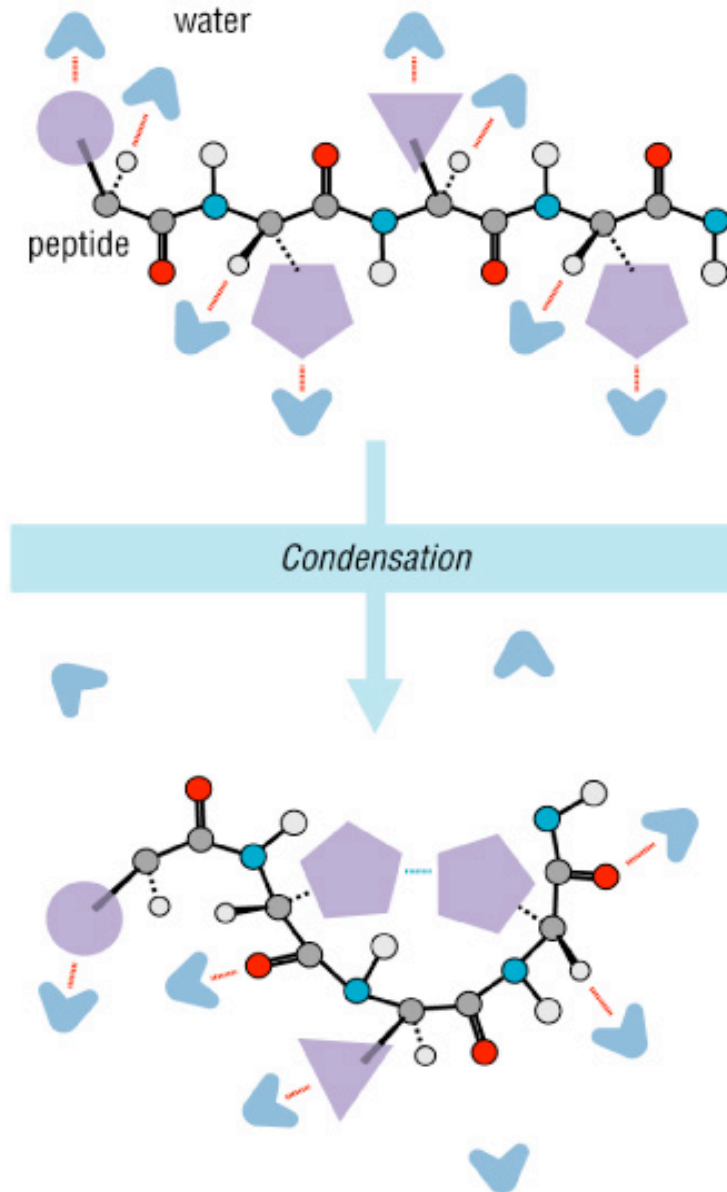
The Hydrophobic Effect it drives binding



Enzyme-substrate interaction stabilized by hydrogen-bonding, ionic, and hydrophobic interactions

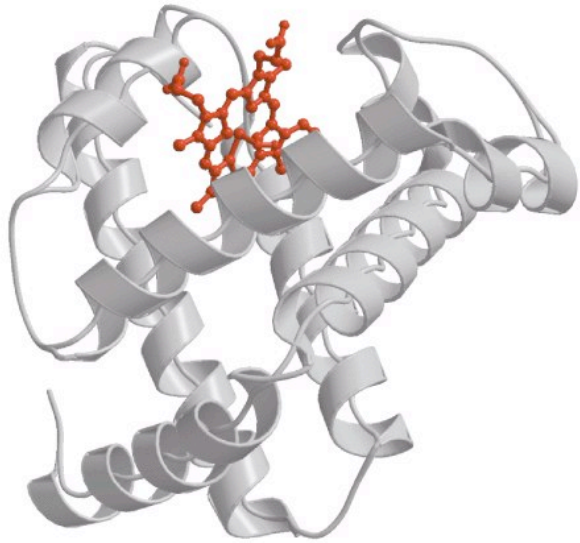
The Hydrophobic Effect

it drives folding

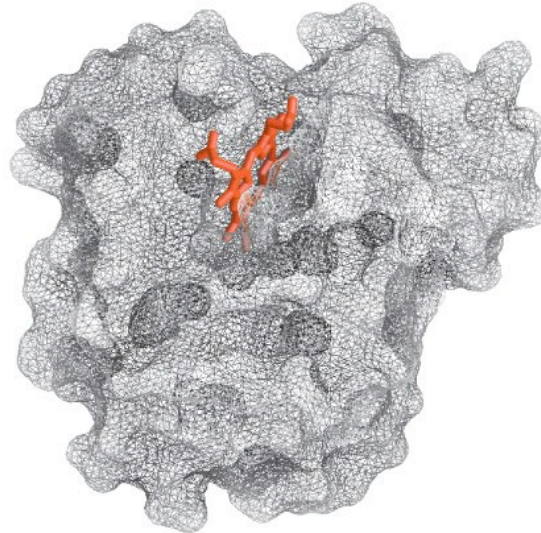


Protein Structure

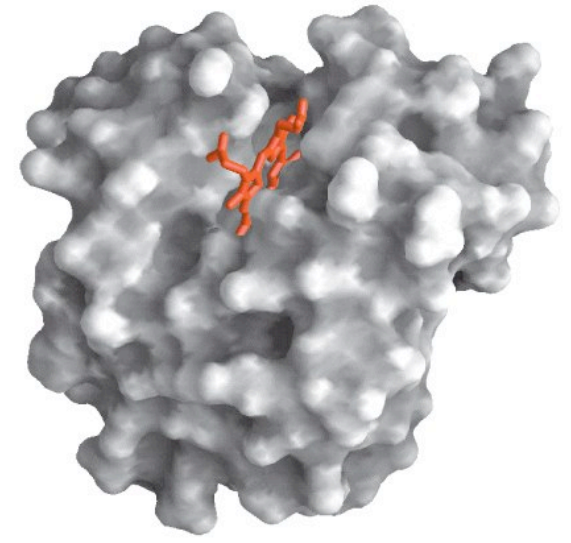
hydrophobic residues are buried



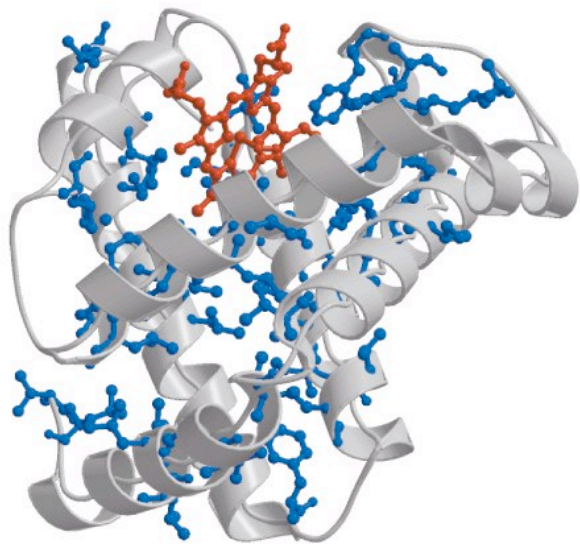
(a)



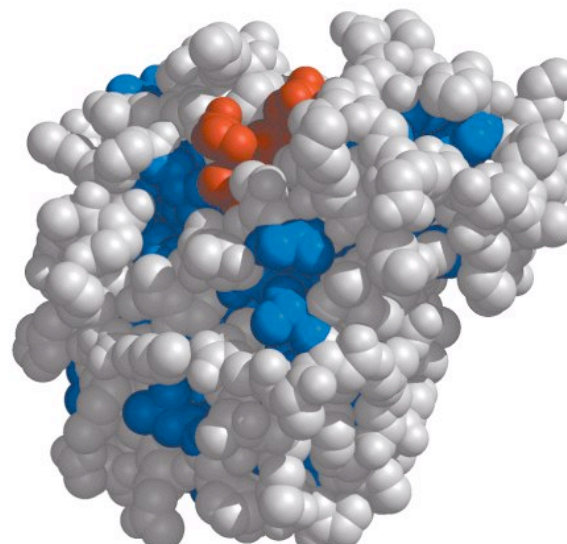
(b)



(c)



(d)

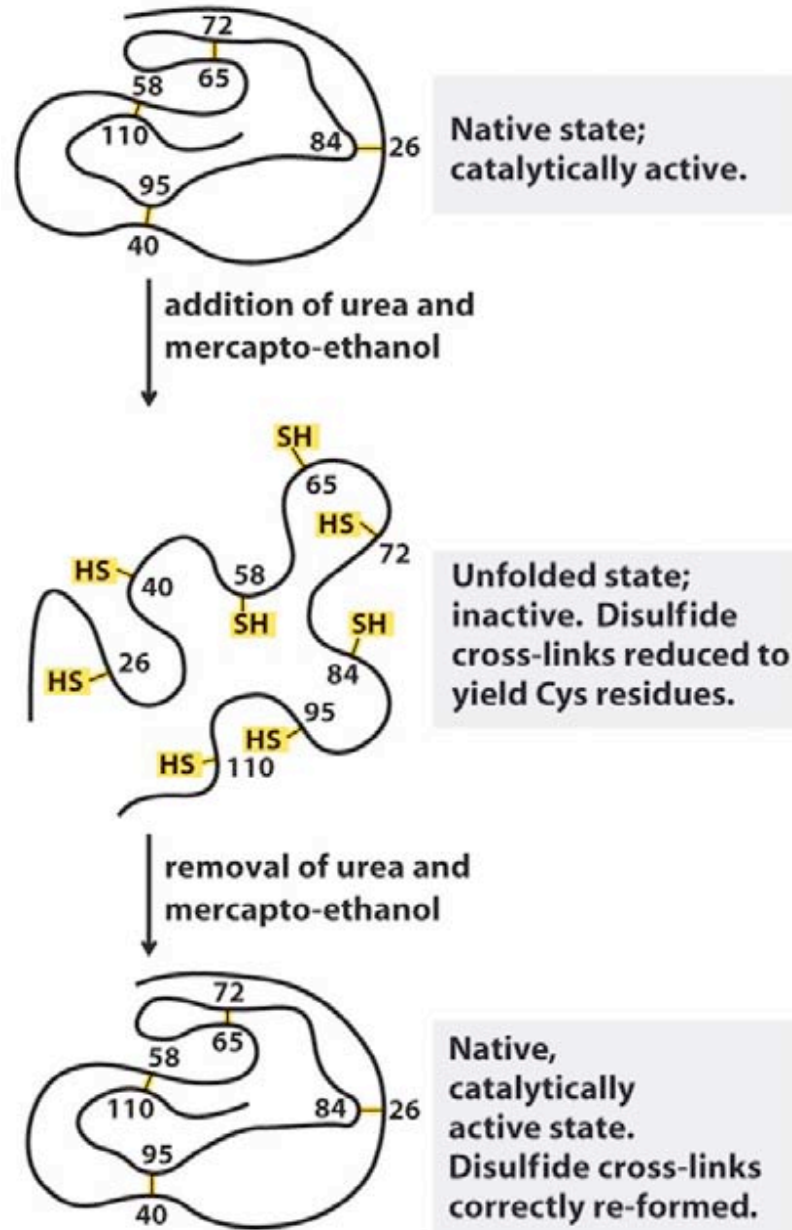


(e)

blue: hydrophobic

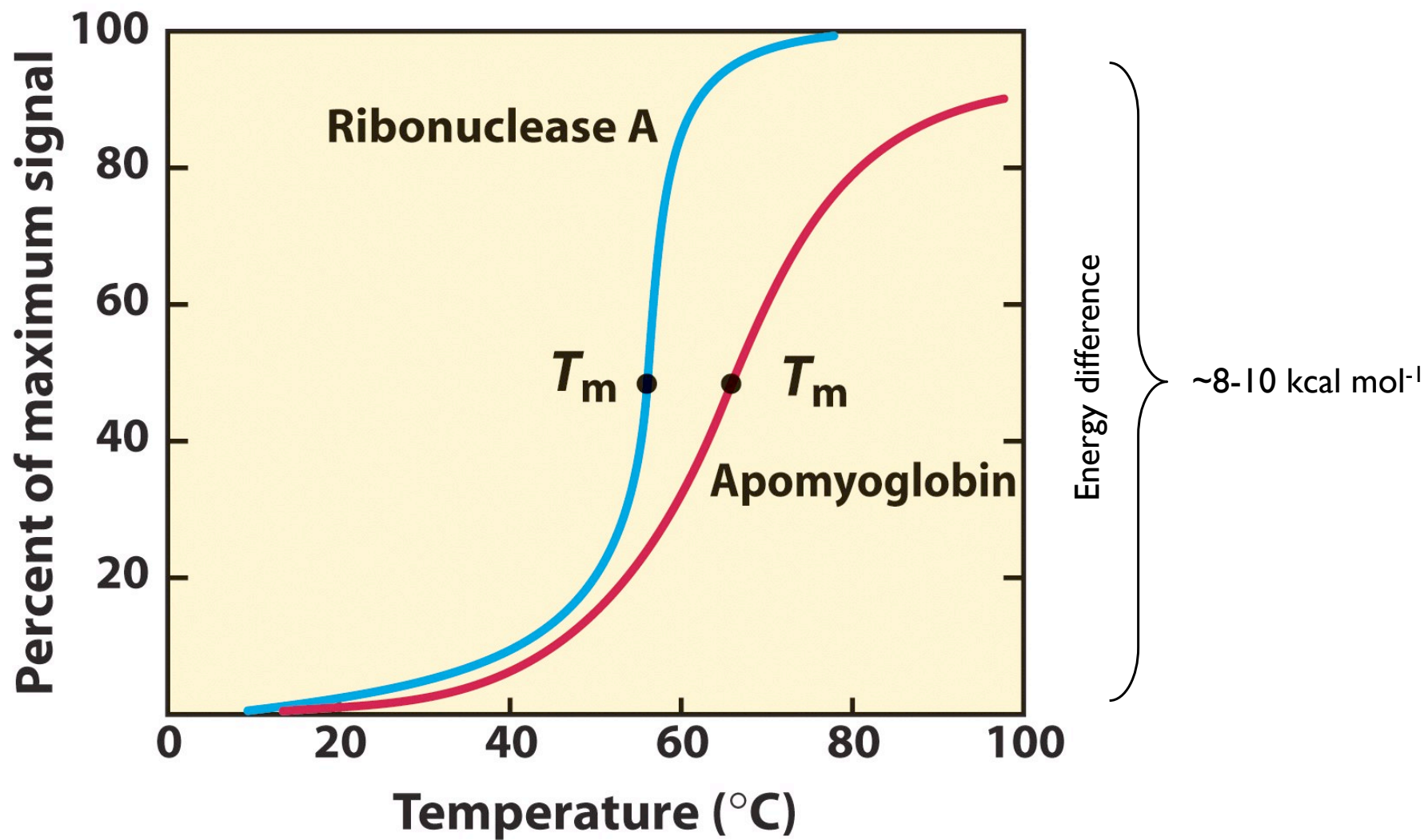
Protein Folding

Protein unfolding results in loss of function



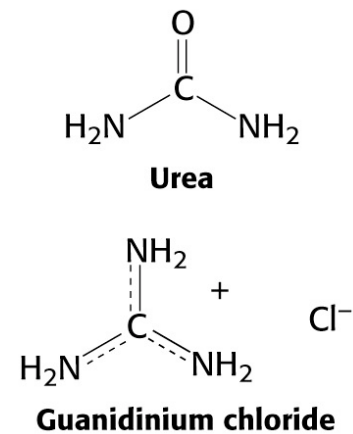
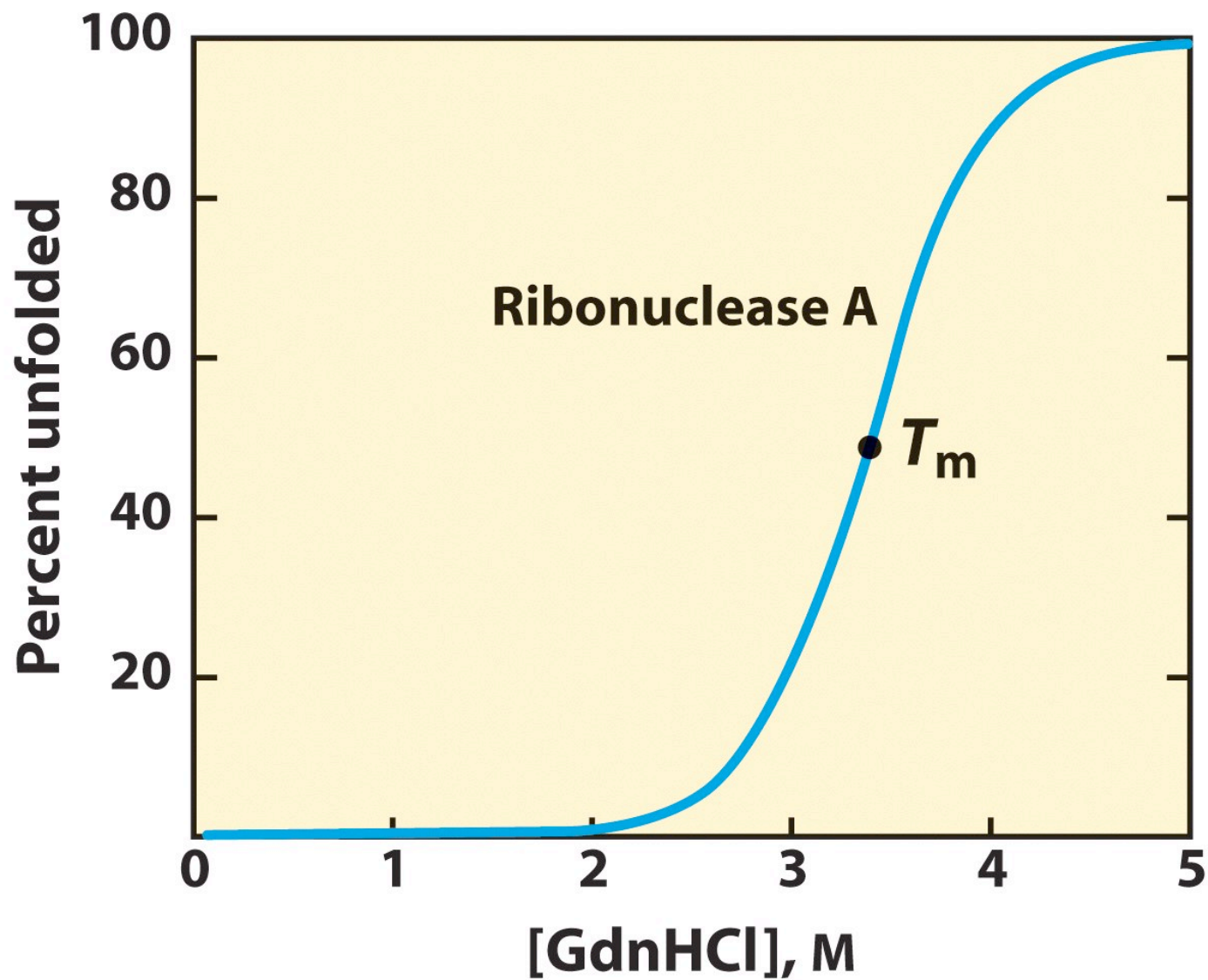
Protein Folding

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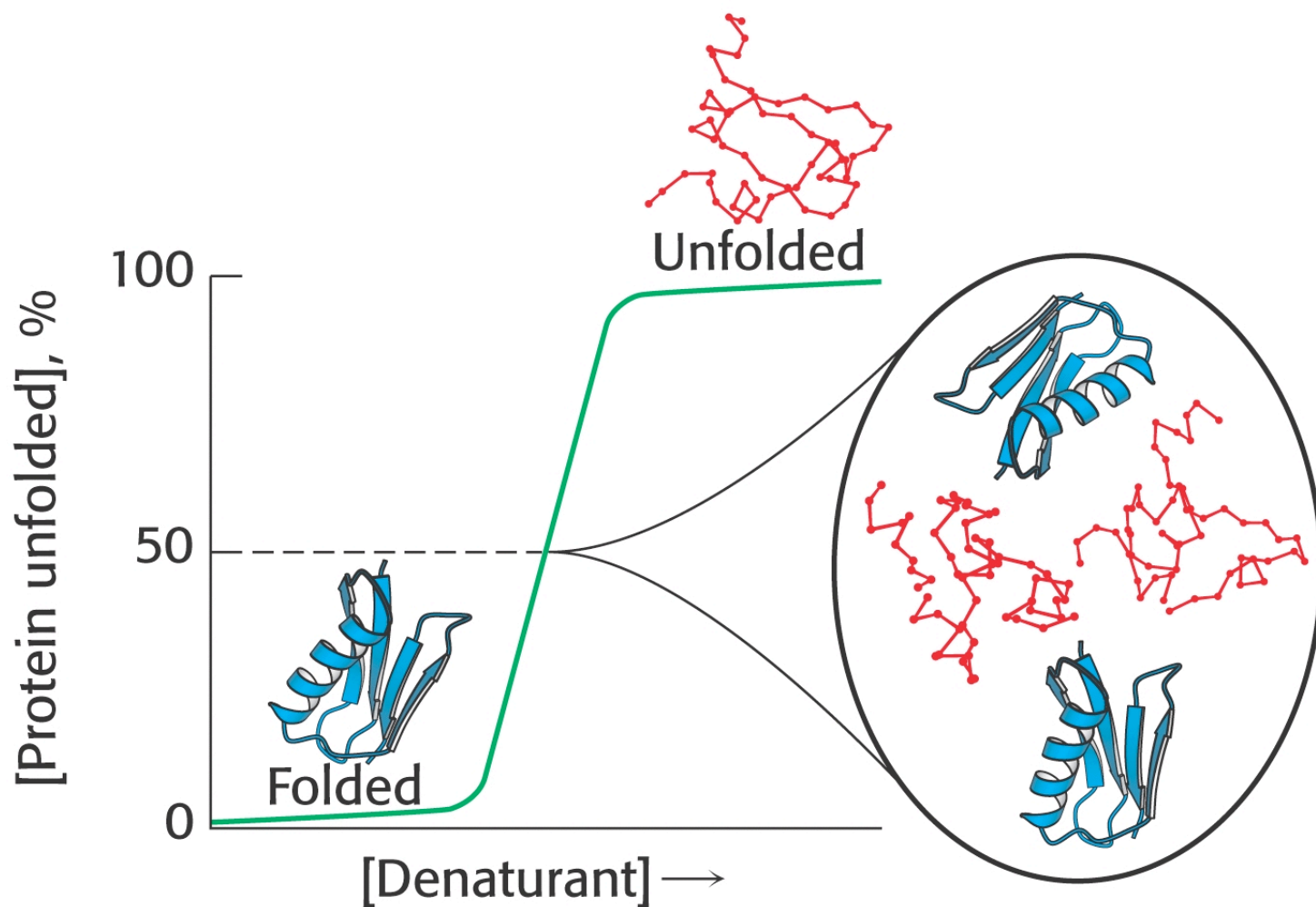
Protein Folding

Protein unfolding results in loss of function



Protein Folding

Protein (un)folding is highly cooperative

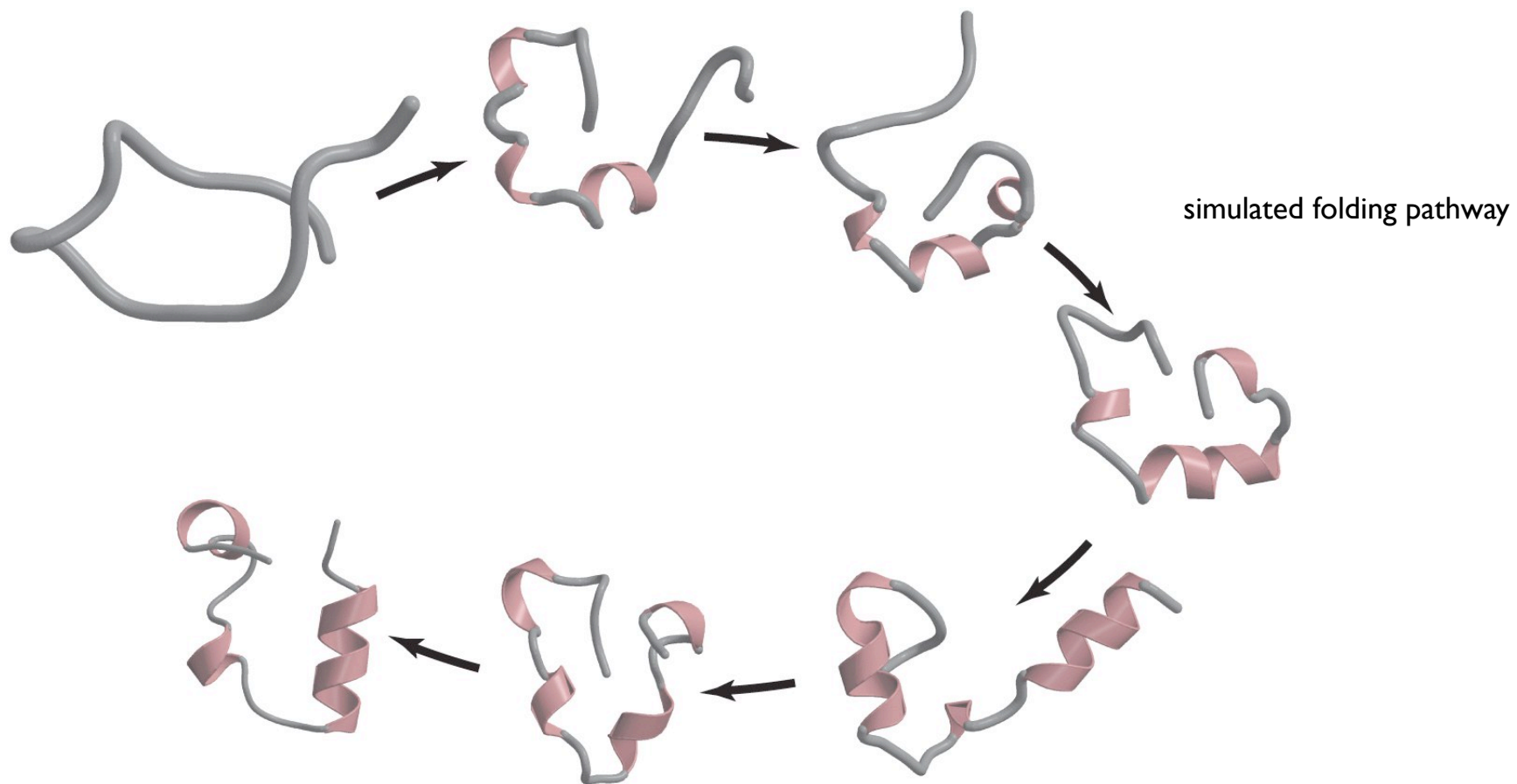


Protein Folding

How does a protein arrive at its native structure?

The Levinthal's paradox: a protein would take $\sim 10^{77}$ years to fold

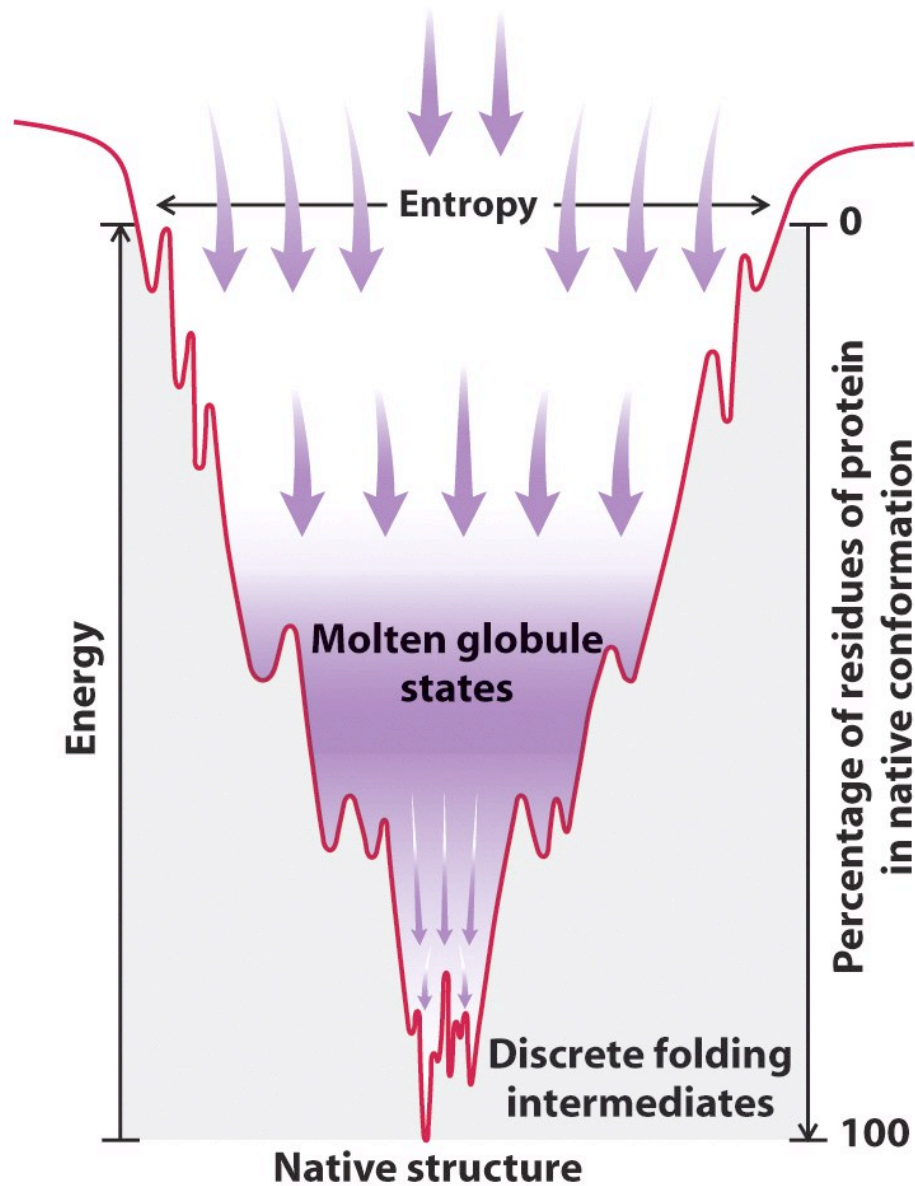
Two folding models: the hierarchical and through the "molten globule"



Protein Folding

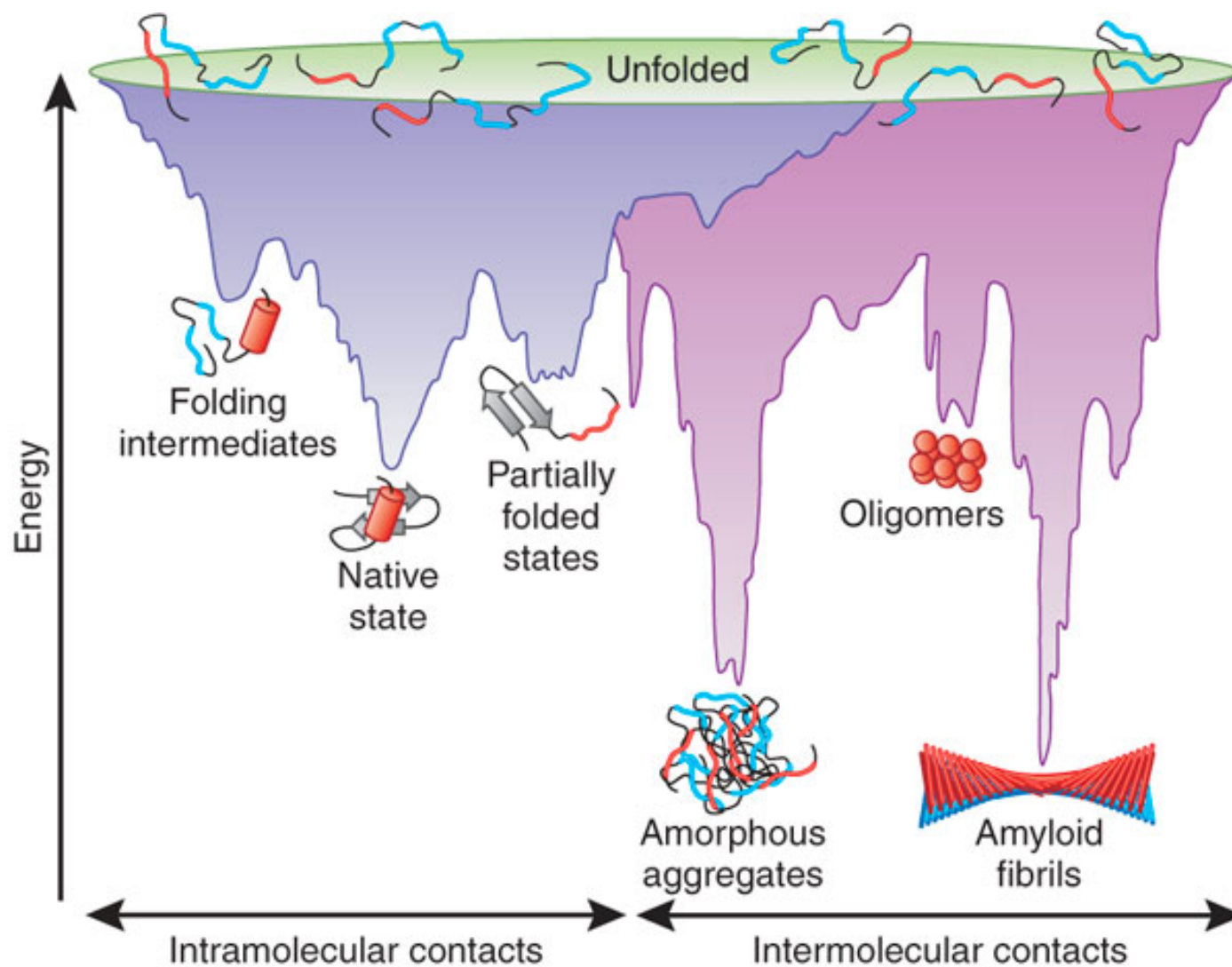
Energy landscape

Beginning of helix formation and collapse



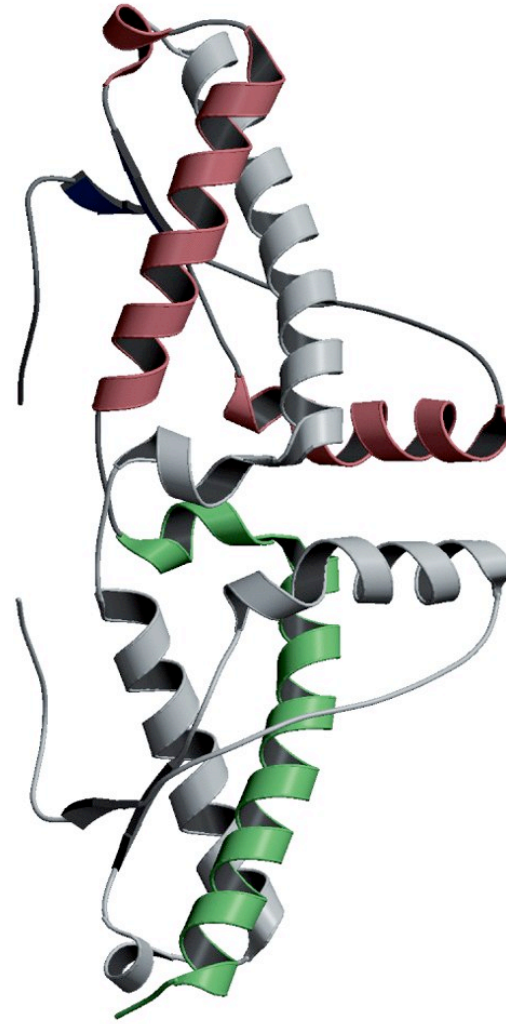
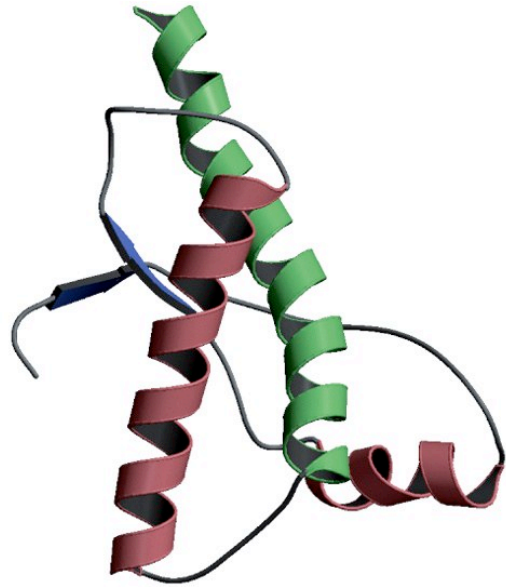
Protein Folding

Energy landscape



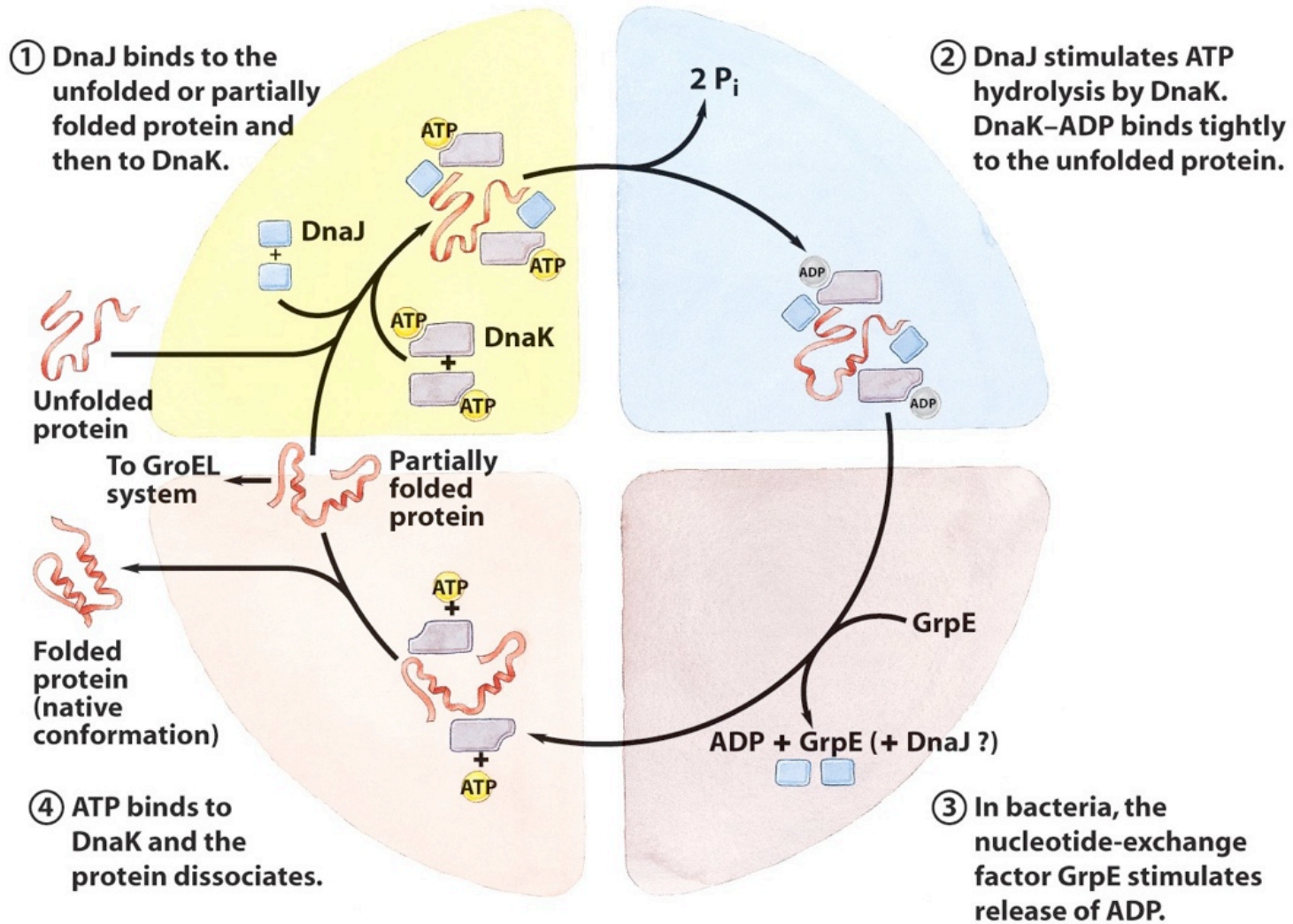
Protein Folding

Death by misfolding: the Prion diseases



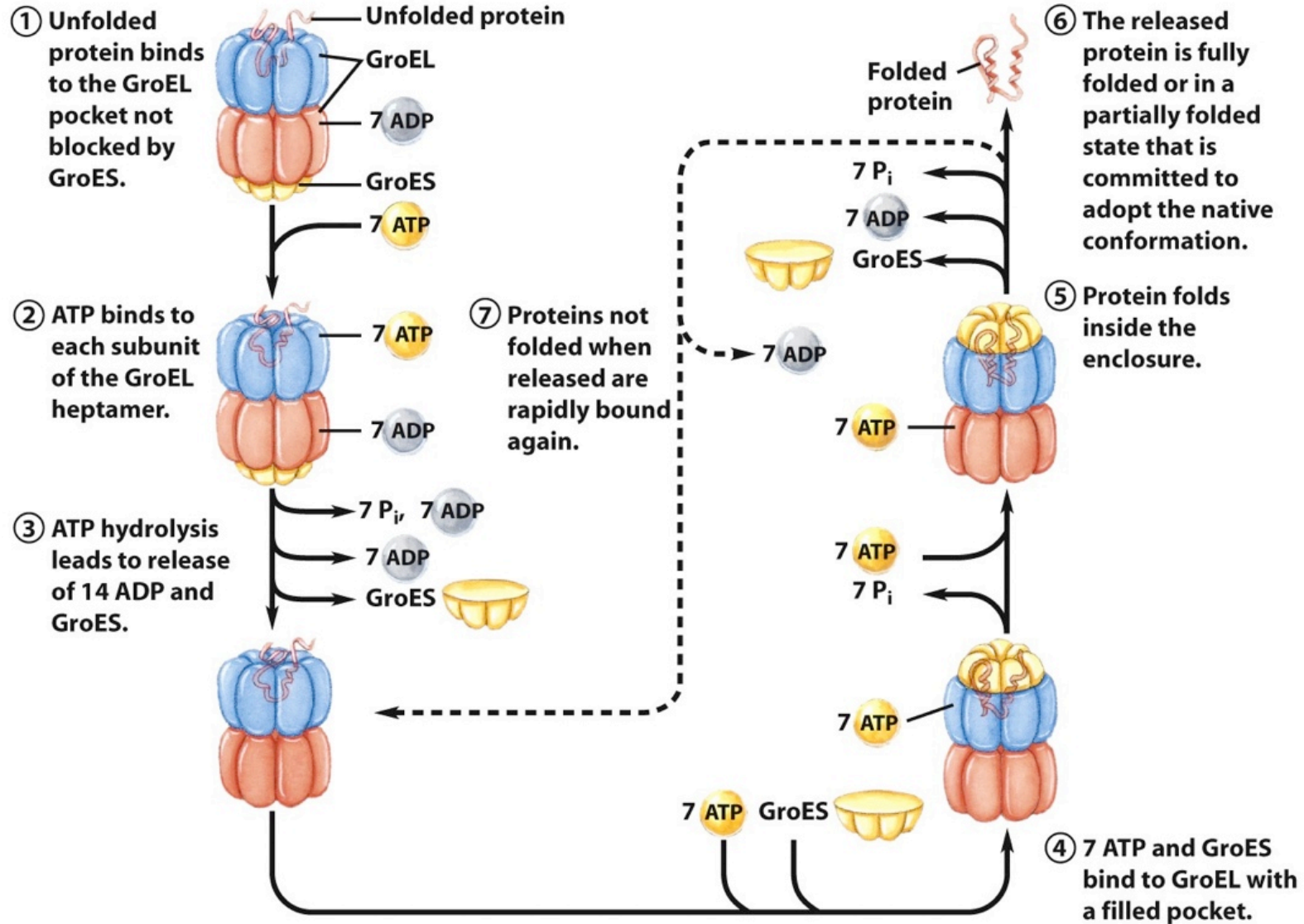
Protein Folding

Chaperones assist newly synthesized proteins to fold



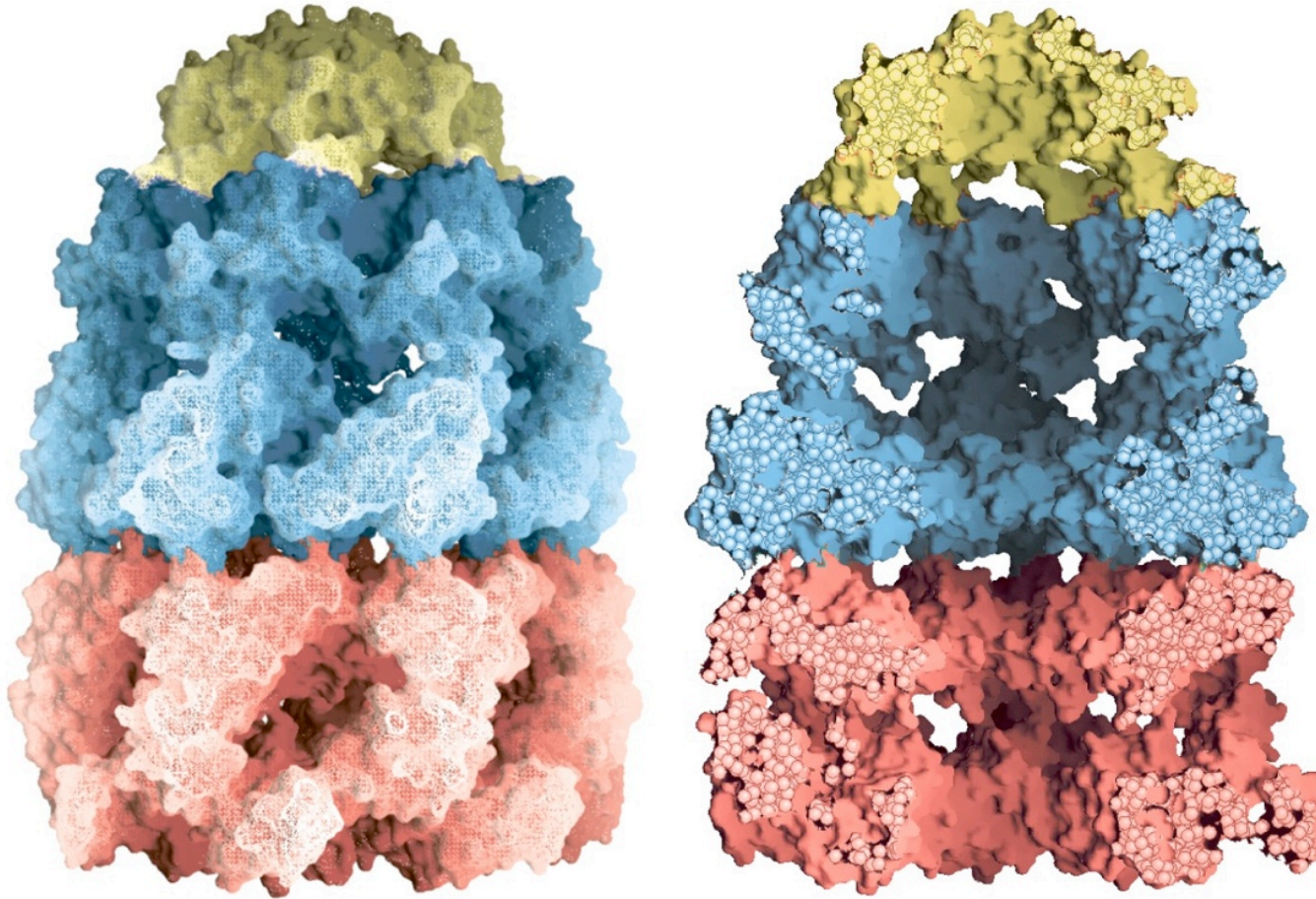
Protein Folding

Chaperones assist newly synthesized proteins to fold



Protein Folding

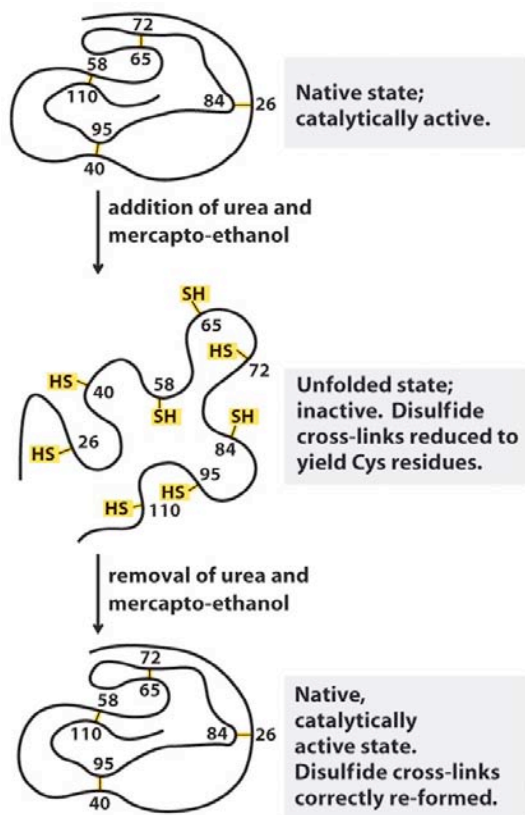
Chaperones assist newly synthesized proteins to fold



The GroES-EL chaperonin

Protein Folding

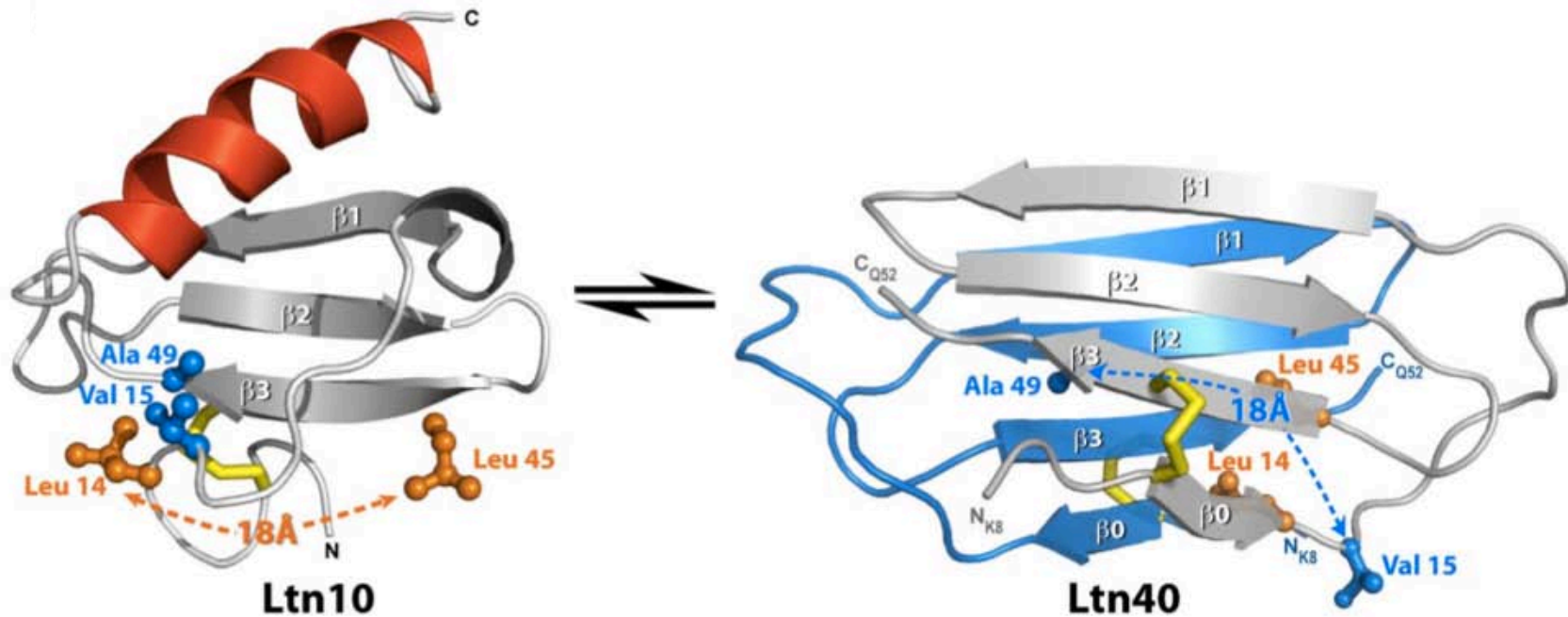
Anfinsen's hypothesis: Sequence determines structure



One sequence, one fold

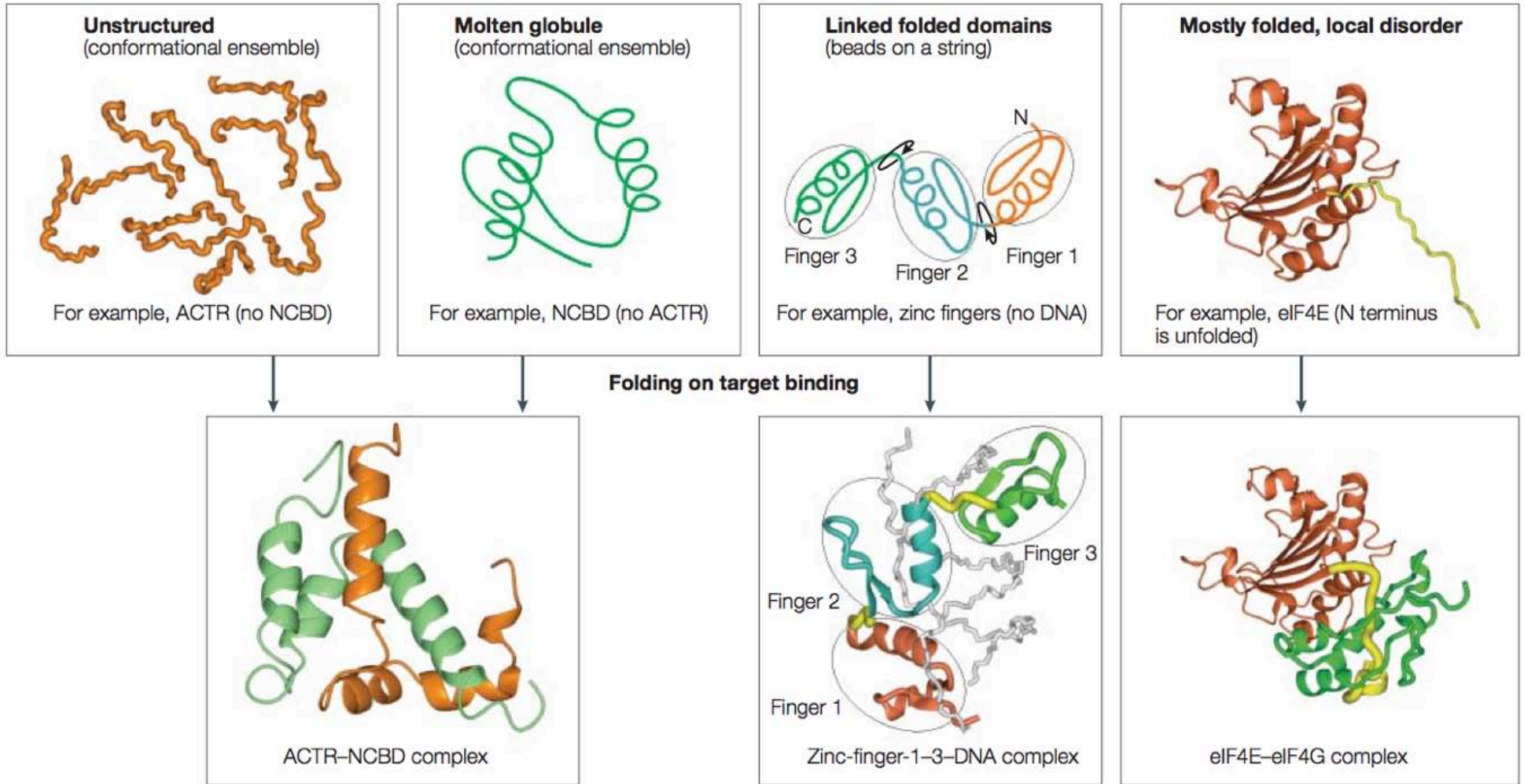
Protein Folding

One sequence, one fold?



Intrinsically Unstructured Proteins

Increasing content of stable three-dimensional structure →



Intrinsically Unstructured Proteins

Coupled folding and binding

