

Protein Stability, Folding, and Dynamics

Protein Stability, Folding, and Dynamics

Two-state model:

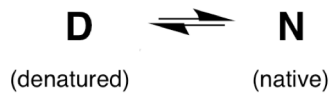


What is favored in this equilibrium, D or N?

What forces operate?

Which forces are the most important?

Protein Stability, Folding, and Dynamics



What is the equilibrium?

Lies to the right

Therefore, ΔG is negative

What forces operate?

Non covalent:

H-bonds?

yes, definitely, but those with water in D-state

Ionic (salt-bridges)?

yes, but not that many and non specific

van der Waals?

yes, but not a driving force until there is compaction

Hydrophobic?

YES, bury hydrophobic residues

Covalent:

Disulfide bonds?

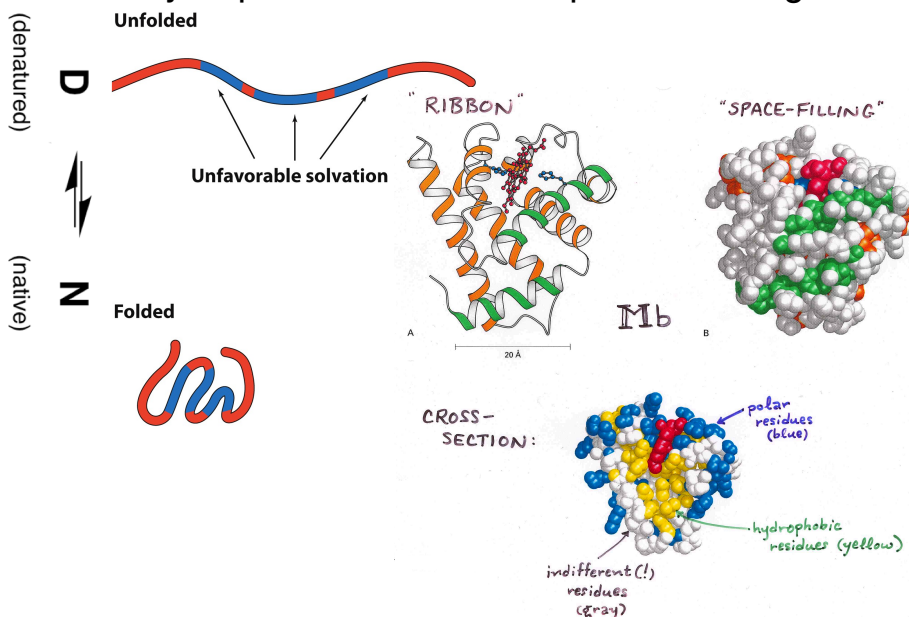
yes, but most proteins don't have any

Which force(s) are the most important?

Hydrophobic!

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Hydrophobic effect drives protein folding



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[TABLE 4-3] Hydrophobicity Scales

Residue	Scale A ^a	Scale B ^b
Phe	2.8	3.7
Met	1.9	3.4
Ile	4.5	3.1
Leu	3.8	2.8
Val	4.2	2.6
Cys	2.5	2.0
Trp	-0.9	1.9
Ala	1.8	1.6
Thr	-0.7	1.2
Gly	-0.4	1.0
Ser	-0.8	0.6
Pro	-1.6	-0.2
Tyr	-1.3	-0.7
His	-3.2	-3.0
Gln	-3.5	-4.1
Asn	-3.5	-4.8
Glu	-3.5	-8.2
Lys	-3.9	-8.8
Asp	-3.5	-9.2
Arg	-4.5	-12.3

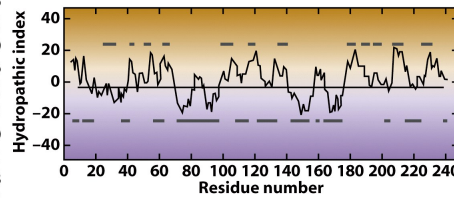


Figure 6-35 Fundamentals of Biochemistry, 2/e
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^aScale A is from Kyte, J., and Doolittle, R.F., *J. Mol. Biol.* 157, 105–132 (1982).

^bScale B is from Engelman, D.M., Steitz, T.A., and Goldman, A., *Annu. Rev. Biophys. Chem.* 15, 321–353 (1986).

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7

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Hydrophobic effect drives protein folding

What about membrane proteins?

