

Check: Thermodynamic Cycles

Construct a thermodynamic cycle for the ΔG of folding and mutating an amino acid residue of a protein (i.e., you have the transition going from unfolded to folded and the transition going from wild type to point mutant).

Write the formula for the $\Delta\Delta G$ of folding free energy due to a mutation.

Pretend that the only thing that matters is the configurational entropy. The table below provides per-residue ΔS values:

- $\Delta S_{\text{bu} \rightarrow \text{ex}}$: the entropy change associated with the transfer of a side chain that is buried in the interior of the protein to its surface
- $\Delta S_{\text{ex} \rightarrow \text{u}}$: the entropy change from a surface exposed side chain transitioning from a folded protein to an unfolded protein
- ΔS_{bb} : the entropy change of the backbone when transitioning from a folded protein to an unfolded protein

That is, the ΔS of unfolding for a buried residue is $\Delta S = \Delta S_{\text{bu} \rightarrow \text{ex}} + \Delta S_{\text{ex} \rightarrow \text{u}} + \Delta S_{\text{bb}}$.

TABLE II. Conformational Entropies for Amino Acids*

Amino acid	$\Delta S_{\text{bu} \rightarrow \text{ex}}$ (cal/K · mol)	$\Delta S_{\text{ex} \rightarrow \text{u}}$ (cal/K · mol)	ΔS_{bb} (cal/K · mol)
ALA	0.00	0.00	4.1
ARG	7.11	-0.84	3.4
ASN	3.29	2.24	3.4
ASP	2.00	2.16	3.4
CYS	3.55	0.61	3.4
GLN	5.02	2.12	3.4
GLU	3.53	2.27	3.4
GLY	0.00	0.00	6.5
HIS	3.44	0.79	3.4
ILE	1.74	0.67	2.18
LEU	1.63	0.25	3.4
LYS	5.86	1.02	3.4
MET	4.55	0.58	3.4
PHE	1.40	2.89	3.4
SER	3.68	0.55	3.4
THR	3.31	0.48	3.4
TRP	2.74	1.15	3.4
TYR	2.78	3.12	3.4
VAL	0.12	1.29	2.18

D'aquino JA, Gómez J, Hilser VJ, Lee KH, Amzel LM, Freire E. The magnitude of the backbone conformational entropy change in protein folding. *Proteins: Structure, Function, and Bioinformatics*. 1996 Jun;25(2):143-56.

Compute the $\Delta\Delta S$ of

1. buried TRP to buried PHE
2. buried ILE to buried VAL
3. surface ARG to surface ALA
4. buried ARG to surface GLY

Check+

<https://colab.research.google.com/drive/1A6ubGV70w7UNC9FI1TPDAAYPunCYj163?usp=sharing>