

Supporting Information for:

## **Introducing the Levinthal's protein folding paradox and its solution**

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Suggested questions for student assessment, follow-up assignment, or to stimulate discussions in classroom:

1. A student in the laboratory prepared a sample of purified lysozyme, and let it rest at room temperature for a week. Afterwards, he noted that the activity of the enzyme was lost. What that might imply about the thermodynamic or kinetic stability of the protein?
2. How relevant is it for living organisms that proteins be thermodynamically stable at their functional conformations? How relevant is it that the proteins reach rapidly these conformations? Which is the approximate lifetime of a protein in a cell?
3. Deduce the time required for 50% of the structures of a protein with 100 residues to be folded, for different biasing probabilities towards the native conformation of each residue.
4. Discuss the energetic requirement for the statistical bias towards the native state of each residue to be enough for folding of proteins of realistic length in realistic time. Compare with the typical strength of intermolecular interactions.