

Petsko, Structural basis of thermostability in hyperthermophilic proteins, or “there’s more than one way to skin a cat”

Questions to consider

1. What is the difference between thermal denaturation and thermal inactivation?
2. If we are trying to engineer a protein to function at high temperature by directed evolution, why is it important to have a clear definition of what “thermostability” means? In other words, why is it important to have a clear answer for Gertrude Stein’s question, “What is the question?”
3. What do you think about Petsko’s comment that “Extreme thermostability thus seems to be achieved in nature by distributing many different kinds of additional intramolecular interactions throughout the protein rather than by concentrating just one kind in one or a few places (but there is no indication yet that it would be impossible to achieve it in that simpler way artificially).”?
4. Or how about this one, “As is often the case in biology, searches for an overarching principle frequently are doomed to failure from the beginning.”?
5. What connections can you draw between Petsko’s arguments and Maynard Smith’s discussion on how proteins evolve by natural selection?