General principles and selected applications of scanning calorimetry: ultrafast folding, kinetic stability and ancestral proteins

Jose M. Sanchez-Ruiz

Departamento de Quimica Fisica, Facultad de Ciencias, Universidad de Granada. 18071-Granada, Spain

Differential scanning calorimetry (DSC) is one of the most informative experimental approaches to the analysis of protein folding and stability because it is sensitive to the energetics of all conformations that are significant populated during protein thermal denaturation [1,2]. DSC has thus provided much of our current understanding of the fundamental factors that determine protein stability and energetics [3-6]. Furthermore, important problems related with protein folding/denaturation kinetics and molecular evolution are best addressed when DSC is used to complement other experimental methodologies. DSC has thus contributed to establish a connection between the experimental data and the landscape view of protein folding and has led to the assessment of the marginal free energy barriers that determine the ultrafast folding of some proteins [2,7,8]. Also, DSC studies have shown that the stability of many proteins is determined by kinetic factors and have provided evidence for the evolutionary role of protein kinetic stability [9]. Finally, DSC experiments have demonstrated the much-enhanced stability of many resurrected ancestral proteins [10-12] and have thus contributed to the current interest in the biotechnological applications of ancestral sequence reconstruction [13,14].

1. Freire, Biltonen (1978) Biopolymers 17:463-479.
2. Sanchez-Ruiz (2011) Annu Rev Phys Chem 62:231-255.
3. Privalov (1979) Adv Prot Chem 33:167-241.
4. Freire (2001) Meth Mol Biol 168:37-68.
5. Makhatadze, Privalov (1995) Adv Prot Chem 5:507-510.
6. Robertson, Murphy (1997) Chem Rev 97:1251-1267.
7. Muñoz, Sanchez-Ruiz (2004) Proc Natl Acad Sci USA 101:17646-17651.
8. Naganathan, Sanchez-Ruiz, Muñoz (2005) J Am Chem Soc 127:17970-17971.
9. Sanchez-Ruiz (2010) Biophys Chem 148:1-15.
10. Risso, Gavira, Mejia-Carmona, Gaucher, Sanchez-Ruiz (2013) J Am Chem Soc 135:2899-2902.
11. Risso, Gavira, Sanchez-Ruiz (2014) Environ Microbiol 16:1485-1489.
12. Romero-Romero, Risso, Martinez-Rodriguez, Ibarra-Molero, Sanchez-Ruiz (2016) Biochem J 473:3611-3620.
13. Risso, Sanchez-Ruiz, Ozkan (2018) Curr Opin Struct Biol 51:106-115.
14. Trudeau, Tawfik (2019) Curr Opin Biotechnol 60:46-52.