Protein and Polymer Folding on a Chip

Paul S. Cremer
Department of Chemistry
Texas A&M University
College Station, TX 77843
U.S.A.

Abstract:

We have designed temperature gradient microfluidic devices that allow high throughput, low sample volume assays to be performed on the folding of thermoresponsive polymers and proteins. These macromolecular systems are insoluble at high temperatures, but become hydrated and unfold as the temperature is decreased in a process analogous to the cold denaturation of proteins. Our assays enable highly precise measurements to be made rapidly of the physical behavior of the polymers. The device is specifically used to obtain data on poly (*N*-isopropylacrylamide) and α-elastin at multiple concentrations in the presence of a variety of ions. The results indicate that the folding process follows the Hofmeister series. This series, which dates back to 1888, is a rank ordering of anions and cations based upon their ability to salt-out or salt-in proteins. It had been historically believed that ions affect macromolecule solubility indirectly through their interactions with bulk water. This idea has been largely disproved by a variety of characterization techniques over the last decade. A new theory to explain the mechanism of the Hofmeister effect, however, still needs to be developed. Microfluidic assays in combination with vibrational sum frequency spectroscopy allowed us to develop a model based solely on the direct interaction of the ions with a macromolecule and its first hydration shell. In fact, the protein folding properties can be related to a few simple factors: an ion's hydration entropy, its effect on the surface tension of an aqueous interface, and its ability to interact directly with binding sites on a protein.

References

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