Protein electrostatics: Do salt bridges stabilize proteins?

Summary / Zusammenfassung
The contribution of salt bridges (ion pairs) to protein stability is a difficult problem for which no simple answer is in reach. We have solved the NMR structure of a designed leucine zipper with a maximized number of salt bridges between its component peptide chains. The high resolution NMR structure features salt bridges between the helices. Determination of pKa-values of Glu and His side chains by NMR titration, pKa calculations using the continuum electrostatic model and thermodynamic experiments indicate that electrostatic interactions are destabilizing rather than stabilizing. The reason is that desolvation of a charged side chain and its interaction with the protein multipole exacts a large energetic cost that is only rarely compensated by the gain in Coulombic attraction to the potential salt bridge partner. Stability difference bewteen leucine zippers were shown to originate from different ionic interactions in the unfolded state, demonstrating the importance of residual structure in the unfolded protein when assessing protein stability. We have reviewed mutational and thermodynamic approaches for measuring electrostatic effects in proteins and have clarified discrepancies regarding protein stabilization by salt bridges.

Weitere Informationen unter http://www.biochem.uzh.ch/research/bosshard/index.html

Publications / Publikationen


Keywords / Suchbegriffe
Electrostatics, protein structure, computational chemistry, NMR, spectroscopy, protein design

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Funding Source(s) / Unterstützt durch
SNF (Personen- und Projektförderung)

Duration of Project / Projektdauer
Aug 1997 to Jul 2005