

## *Protein structure and folding in the gas phase.*



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The chemical environment of a protein can have profound effects on its structure and folding, but the relative contributions of intrinsic protein stability and external forces are difficult, if not impossible, to separate from each other in condensed phase experiments. In this seminar, insight into the intramolecular interactions that stabilize protein structure, and drive protein folding, in the complete absence of solvent water, are discussed. Data from structural probing experiments reveal that native, globular protein folds are thermodynamically unstable in the gas phase, which eventually causes them to unfold. Once a solution structure is lost after desolvation, folding in the gas phase can produce more compact structures, but these bear no or little resemblance to the native fold. Moreover, our data on protein folding in the gas phase suggest that fast folding, on a ms to ms timescale, or even the formation of structural elements involving ~10 or more residues neighboring in sequence, is highly unlikely in the absence of hydrophobic interactions.