Conformational energies and entropies of peptides, and the peptide-protein binding problem

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Abstract. A novel statistical thermodynamics approach is applied to the free peptide segments in order to classify them according to their conformational energies and entropies and heat capacities. Our approach employs the rotational isomeric states (RIS) model in which the states are described by the Ramachandran map of backbone torsion angles. The statistical weight matrices for the pairwise dependent states are derived from the torsion angle probabilities of the consecutive dipeptides in Coil library. The partition function is determined for a given sequence via RIS multiplication of the pre-determined matrices. The conformational partition function, Helmholtz free energy, energy, entropy and heat capacity are obtained. The model is applied to randomly produced peptides and also to known peptide inhibitors to analyze their thermodynamic properties. Peptides with low energy, low entropy and low heat capacity are determined to be essential for a peptide to be a good candidate inhibitor. Free energy changes in peptide binding are also discussed.