Computer simulation of protein folding

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A new and very simple representation of protein conformations has been used together with energy minimisation and thermalisation to simulate protein folding. Under certain conditions, the method succeeds in 'renaturing' bovine pancreatic trypsin inhibitor from an open-chain conformation into a folded conformation close to that of the native molecule.

PROTEIN molecules owe their enormous functional versatility to the fact that they spontaneously fold into complicated and unique conformations determined by the particular amino-acid sequence[1]. Discovering the relationship between protein sequence and conformation is a fascinating theoretical problem of fundamental importance, Most previous theoretical work has used the concept of 'local structure', in which the conformation of a short segment of polypeptide chain is supposed to depend almost entirely on the sequence of that segment. Although this approach has helped understand local secondary structure[2,3], it has not shown how residues distant along the chain can come together to form the overall conformation. The only promising attempt to study the tertiary folding of a protein, in this case myoglobin, was based on the packing of cylinders supposed to represent a helices[4]. The method was not implemented on a computer and cannot be applied more generally to other proteins not built entirely from helices.

centres, the C^{α} atom, and the centroid of the side chain. Interactions are assumed to occur only between side chains, while the C^{α} positions define the chain path (Fig. 1). Each amino-acid residue only has one degree of freedom, the torsion angle about the line joining two adjacent C^{α}s (known here as a). Although a simple representation based on virtual bonds has been used before to study polypeptide random coils[5], it has never been applied to ordered globular proteins. This simplification reduces the degrees of freedom by a factor of four and the number of interaction centres by a factor of fifteen. One might also hope that the reduced space used here to describe different conformations would have many fewer energy minima. The space is of lower dimension and the side chains are smooth spheres without all the minor bumps of the all-atom structures.