Structure and function relationship: The case of defensins and allergens

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Abstract
Our major goal has been to correlate the tertiary structure of proteins with its function. For this purpose, we have studied proteins using solution NMR. We study proteins such as defensins, allergens, globins and thioredoxins. The structure determination combined with dynamic profiles is used to understand the proteins properties and conformational diversity of their binding sites.
The new generation of biologically active compounds developed during the 20th century relied on knowledge of enzymology and protein structure, and were based initially, on the understanding that protein-protein interactions occurred through a lock-and-key mechanism. Later, evidence suggested that this mechanism was usually followed by a conformational change, known as induced fit. Recent studies on protein dynamics, mainly by nuclear magnetic resonance (NMR) relaxation measurements, have shown that proteins are not structured in a unique conformation. Rather, they frequently have regions of conformational diversity.
In the present talk I will discuss a novel view of binding, put forward in by several research groups in the last 5 to 10 years. In the free state, protein regions displaying conformational diversity exhibit equilibrium among pre-existing conformations. In the presence of a ligand, one of these conformations is stabilized, so that the ligand does not need to induce a new conformation. Upon ligand binding there is a population shift toward the bound conformational state. Conformational diversity of binding sites of several proteins has been measured and has important practical as well as thermodynamic consequences: binding sites can be mapped without prior knowledge of the ligand and also evolution of binding sites depends mostly on the free state, occurring at least partially independently of the ligand.