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Structure and Functions of Simple Peptides at Membrane-Water Interfaces

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Even the simplest protocell must have had the capability to catalyze the chemical reactions needed for its survival and growth, and to communicate with its environment. One group of potential early catalysts and signalling molecules were peptides - possible precursors of contemporary enzymes and receptors. Unfortunately, short peptides typically do not exhibit any secondary structure in an aqueous solution and, therefore, do not appear to be suitable for the desired cellular functions. There is, however, a growing body of evidence that peptides, which are disordered in water, acquire an amphiphilic secondary structure at water–air, water–oil or water–membrane interfaces, providing that they have a proper sequence of polar and nonpolar residues. Similarly, hydrophobic peptides can readily organize into α–helices inside a nonpolar phase (*e.g.* lipid bilayer). The specific identity of the residues is of lesser importance, which is a desirable property in the absence of information molecules.

To examine the ability of small peptides to organize at aqueous interfaces, we performed a series of large–scale computer simulations on several small peptides constituted of two residues: nonpolar leucine (L) and polar glutamine (Q). The peptides differed in size and sequence of amino acids. Among the molecules studied were the dipeptides LL, LQ, QL, and QQ. Although these peptides were too short to form secondary structures, they represented very good models for examining conformational preferences of the peptide backbone as a function of the environment. For these molecules, the changes in free

energy were calculated as a function of the ϕ and ψ dihedral angles characterizing the backbone. Next, we studied the two heptamers (LQQLLQL) and (LQLQLQL), designed to maximize the amphiphilicity of an α–helix and a β–strand, respectively, burying their polar side chains in the aqueous phase, and exposing their nonpolar residues towards air. Finally, a transition of a 11-mer, composed entirely of leucine residues, from a disorder structure in water to an α–helix in a nonpolar phase modeling the interior of the membrane was investigated.

The results of our simulations illuminate three important properties of small peptides at aqueous interfaces. First, peptides that contain both polar and nonpolar amino acids tend to accumulate at the interface. Second, amphiphilicity provides a strong force driving the peptides towards specific, organized structures. This force is absent in bulk water. The tendency to organize at the interface, driven by the amphiphilicity of the structure rather than by a specific sequence, is consistent with the concept of an active interface, and might have been conducive to primitive catalysis under protobiological conditions. Finally, the degree of structural organization of the peptide backbone changes with the position in the sequence. The backbone is considerably more disordered at the ends of the peptide than in the middle.

The existence of secondary structure in membrane–bound peptides does not necessarily imply their biological activity. Only a few protobiologically relevant examples of such activity are known to date. The link between the interfacial structure of peptides and their catalytic and signalling activity is an important area of future studies on the origins of cellular life.