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Coarse-grained molecular dynamics simulations of antimicrobial peptides against membrane models

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The increasing emergence of resistant bacteria is a great concern in terms of public health as available conventional antibiotics drugs are not able to kill them. One strategy proposed is the use of bacterial membranes as a therapeutic target so that their basic properties are perturbed, altering the membrane potential and inhibiting the control functions on the signalling, communication or production bioenergy processes. In this sense, antimicrobial peptides (AMPs) exhibit unique properties, which include broad-spectrum activity, rapid action and difficult development of resistance. They are part of the innate immune system in a large number of species, where they form the first line of defence against pathogenic invasion, still maintaining its effectiveness after being present in nature for thousands of years. Despite these advantages, AMPs have, in general, a small therapeutic window, and can hardly be used systemically because of their high toxicity. A detailed understanding of the molecular details of the membrane permeabilization process would allow the rational design of new molecules with the same mechanism of action, but with improved activity, selectivity, and bioavailability.
Computational studies play an increasingly important role in understanding the structure and dynamics of biomolecular systems. For example, Molecular Dynamics simulations using coarse-grained (CG-MD) resolution is able to systematically explore events that take place into ranges where direct comparison and experimental testing are starting to be feasible. In this study, we performed CG-MD simulations (5 μs) of series of AMPs in the presence of different membrane models containing different mixtures of1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol (POPG) and 1-Palmitoyl-2oleoyl-sn-glycero-3-phosphoethanolamine (POPE), imitating bacterial, and 1-palmitoyl-2-oleoyl-snglycero-3-phosphocholine (POPC) representing mammalian membranes. The outcome of this study should provide the basis to design better AMPs that will disrupt the bacterial membrane and ultimately cause the death of their cells.

Keywords: Antimicrobial peptides (AMPs), membranes, molecular dynamics, antimicrobials, coarse grained.

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