What Happens When a Bee Stings? Using Molecular Dynamics Simulations to Study the Mechanism of Action

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Mellitin is the major component of bee venom. It has been shown to act, at least in vitro, by poration of the lipid membrane. The nanometre size of these pores, however, complicates their structural characterization by experimental techniques. Here we use molecular dynamics simulations, to study the interaction of melittin, with a lipid bilayer in atomic detail. We show that transmembrane pores spontaneously form above a critical peptide to lipid ratio. The lipid molecules bend inwards to form a toroidally shaped pore but with only one or two peptides lining the pore. This is in strong contrast to the traditional models of toroidal pores in which the peptides are assumed to adopt a transmembrane orientation. We find that peptide aggregation, either prior or after binding to the membrane surface, is a prerequisite to pore formation. The presence of a stable helical secondary structure of the peptide, however is not. Using multi-scale simulations, we then corroborate the mechanism of action. The work provides insight into the action of toxins and antimicrobial peptides.