Bilayers at the ILL

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AMP monomers or aggregates - Which is more effective on antimicrobial: an insight from coarse-grained simulations and experiments

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Over the past few decades, extensive studies have been devoted to the use of peptides as antimicrobials, with a focus on rationally designed short peptides composed of a sequence shorter than 20 amino acids, due to their relatively low synthesis costs and ease of manipulation1,2. A more complete understanding of how these short cationic antimicrobial peptides brings about bacterial cell death is needed to further their optimization and development for practical applications.
Several synthetic antimicrobial peptides (AMPs), including G(IIKK)3I (G3), G(IIKK)4I (G4), GLLDLLKLLLKAAG□LDKA□and naturally existing Melittin were studied using both molecular dynamics simulations in MARTINI coarse-grained models and experimental approaches. Among them, G3, G4 were shown to have better membrane selectivity than Melittin and LDKA. Meanwhile, their aggregate behaviours in the bulk solution also effect their interaction modes with lipid bilayers in some degree.
Among them, melittin shows a "detergent-like" action to disrupt DPPG membrane, while LDKA self-assembles to form long fibres which become inserted into membranes by means of a non-pore carpet mechanism. Simulations revealed that G3 molecules are widely distributed on the DPPG bilayer in single or oligomer states, divide the whole outer membrane into small parts, but do not penetrate through the bilayer in the timescale of modelling. On the other hand, G4 molecules interact with the DPPG bilayer in a manner similar to melittin, with G4 nano-assemblies disrupting the lipid membrane in a "detergent-like" mode. LDKA are more hydrophobic with less net positive charges than G3 and G4. As a result, they have more preference to self-assemble on the DPPG bilayer but they interact with the membrane differently: LDKA's fibre aggregation can even roll up lipid micelle from DPPG bilayer under a high peptide concentration. These observations provide a rich information base for devising systematic studies in future work.

References:
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2. Porcelli, F.; Verardi, R.; Shi, L.; Henzler-Wildman, K. A.; Ramamoorthy, A.; Veglia, G., line. Biochemistry 2008, 47 (20), 5565-5572.

Primary authors: LIAO, Mingrui; GONG, Haoning

Presenter: LIAO, Mingrui

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