Towards well-defined antimicrobial nanoparticles through controlled peptide and polymer assembly

Antimicrobial resistance (AMR), known as the silent pandemic, is a serious threat to modern medicine and public health. Antimicrobial peptides (AMPs) effectively target a broad range of bacteria, including resistant strains, by disrupting bacterial cell membranes. However, their therapeutic use is constrained by challenges such as slight host cell toxicity (e.g., haemolytic effects), vulnerability to enzymatic degradation, and passivation by serum proteins, which restricts their circulation in the bloodstream.

This project seeks to overcome these obstacles by developing antimicrobial nanoparticles through methods such as self-assembly [1] or co-assembly with oppositely charged block copolymers using coacervation [2]. We employ techniques like small-angle neutron/X-ray scattering (SAXS/SANS), circular dichroism spectroscopy, and molecular dynamics simulations to investigate the nanostructure, stability, and molecular exchange of antimicrobial peptide nanosheets. Our results show that these nanostructures are remarkably stable, resist enzymatic degradation, and effectively disrupt bacteria as intact sheets.

Moreover, we study the complexation of colistin with poly(ethylene oxide)-b-poly(methacrylic acid) (PEO-b-PMAA) block copolymers to form complex coacervate core micelles (C3Ms) with tunable sizes and high loading capacity for potent antimicrobial peptides [2-3]. Using time-resolved SAXS, we analyze the kinetics of micelle formation with colistin [4] and its prodrug undergoing hydrolysis [5]. In our presentation, we will discuss nanoparticle stability, peptide-lipid-membrane interactions, and biological activity.

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