Synthetic Lipid Bilayers as Versatile Platforms for Investigating Ion Channels and Membranolytic Antimicrobial Agents

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Synthetic lipid bilayers mark a substantial advancement in membrane architecture research, serving as vital platforms for elucidating the complex interactions between membranes and biologically active molecules, including antimicrobial agents and ion channel-forming peptides. Biomimetic membranes enable the investigation of structural and functional properties of lipid bilayers such as permeability, stability, and hydration using advanced surface-sensitive techniques including electrochemical impedance spectroscopy (EIS), surface-enhanced infrared absorption spectroscopy (SEIRAS), quartz crystal microbalance (QCM-D), and atomic force microscopy. [1]

Our recent studies demonstrate that supported bilayers prepared via liposome spreading or bicelle self-assembly can accommodate membrane-active compounds while preserving functionality, especially when polymer cushions such as PEG, PLA or chitosan derivatives are used.[2,3] These architectures ensure sufficient submembrane hydration and spatial separation from the solid support, which are essential for reconstitution of ion channels like antimicrobial peptide gramicidin A. In particular, we show that gramicidin A channel activity can be modulated not only via steric blockage at the pore entrance, but also through alterations of the lipid matrix that shift peptide conformation toward inactive states. Such multifactorial modulation highlights the importance of the lipid environment in ion channel regulation. Additionally, artificial lipid membranes were used as platforms for studying the activity of membranolytic compounds such as antibiotic peptides or peptidomimetics. In particular, lipooligourea foldamers, which are synthetic mimics of antimicrobial peptides, demonstrate concentration-dependent membranolytic effects on model bacterial membranes composed of DPPG/POPG/cardiolipin.[4] At low concentrations, these compounds interact superficially, while at higher levels, they disrupt acyl chain packing, induce solubilization, and ultimately disintegrate the bilayer.

Together, these findings underscore the utility of synthetic lipid bilayer models in understanding membrane dynamics and in supporting the development of novel antimicrobial agents. Integrating such systems with sensitive analytical techniques offers a robust framework for elucidating molecular mechanisms of membrane-targeting therapeutics, particularly in the context of combating antibiotic resistance.

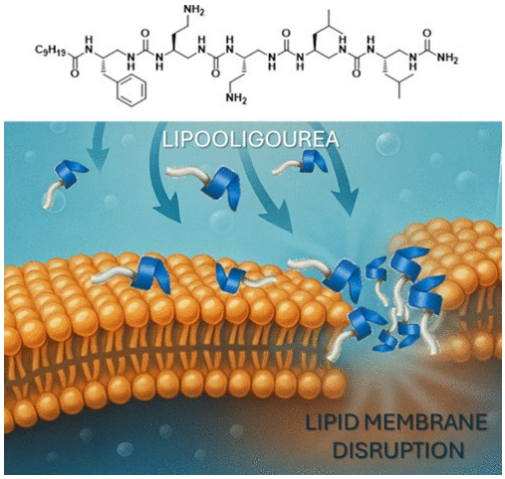

Figure 1: Structure of lipooligourea foldamer and illustration of its disruptive action on artificial lipid membrane. Adapted from reference [4] under CC-BY 4.0 license.

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References

[1] Lipkowski, J. *Phys. Chem. Chem. Phys*., **2010**,*12*, 13874-13887.
[2] Dziubak, D.; Sek, S. *Bioelectrochemistry* **2023**, *153*, 108482.
[3] Paria Pashazadeh Panahi et al. *Electrochim. Acta* **2025**, 528, 146292
[4] Kinga Burdach *et al. J. Phys. Chem. B* **2025**, 129, 26, 6517-6527