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Investigating Lipid Phase Transitions and the Insertion of the Antimicrobial Peptide Gramicidin S Via Time-resolved Temperature-jump IR Spectroscopy

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Antibiotic resistance is a growing global health threat, stressing the need for novel antimicrobial strategies. Antimicrobial peptides (AMPs) disrupt bacterial membranes, primarily through lipid insertion, and provide a promising platform for next-generation antibiotics. Gramicidin S (GS), a potent AMP, has been clinically used for over 80 years without resistance, making it a valuable model for AMP development. While most insights into GS insertion come from equilibrium data, time-resolved experimental data remain scarce.

Here, we use a laser-induced temperature-jump to trigger lipid phase transitions and GS insertion in biomimetic membranes. With time-resolved quantum cascade laser infrared spectroscopy, we track lipid rearrangements, GS conformational changes, and water dynamics from nanoseconds to milliseconds.

Our results reveal that at the phase transition, the membrane exhibits slower, highly stretched-exponential dynamics, suggesting strong intermolecular coupling and large domain fluctuations with poor packing properties. In contrast, water dynamics accelerate at the phase transition, indicating changes in membrane hydration. Transient data of GS insertion shows a coupling to the lipid dynamics, revealing that the insertion dynamics are highly lipid-phase dependent.