Impact of the Electrical Double Layer and Ionic Strength on Antimicrobial Peptides' Mode of Action

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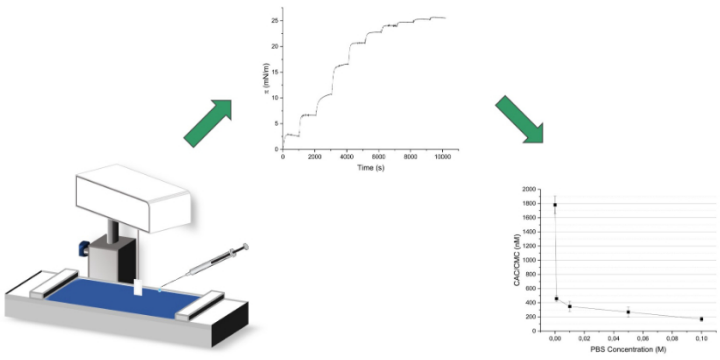
The global emergence of multi-drug-resistant (MDR) bacteria has raised serious concerns about the future effectiveness of currently used antibiotics [1]. A possible solution to this issue lies in peptide-based antimicrobial agents known as antimicrobial peptides (AMPs). Most AMPs share a similar main mode of action, focused on disrupting or dispersing bacterial membranes [2]. Regardless of the exact mechanism of a given peptide, initial interactions of the compound with the membrane require accumulation of peptides on the membrane surface [2]. We propose that this aggregation is driven by locally elevated ionic strength arising from the electrical double layer formed on the membrane surface [3]. Additionally, the outer layer of the membrane is rich in anionic polymers, such as teichoic acids and lipopolysaccharides, which induce polyelectrolyte-like properties to the surface [4].

To validate this hypothesis, we employed the Langmuir technique to determine the aggregation behavior of model peptides in environments with an increasing ionic strength. These results were then correlated with experiments on compressed monolayers containing an increasing content of anionic lipids. We compared the changes in required peptide concentration to achieve a plateau in the surface pressure. Furthermore, peptide adsorption and aggregation on the model membrane systems were monitored using a quartz crystal microbalance (QCM). The compiled experimental data allowed us to estimate the peptide-to-lipid (P/L) ratio across all studied scenarios.

Our initial findings indicate that AMPs' aggregation characteristics are similar to the critical micellization concentration (CMC) of surfactants [5]. A clear trend emerged, showing a decrease in the peptide concentration required for aggregation as the ionic strength of the environment increased. The presence of the lipid mono- and bilayer systems further alters these mechanisms. It manifests as a plateau in the surface pressure at lower peptide concentrations.

In summary, we have defined the relationship between the ionic environment and the aggregation behavior of model AMPs, both in the absence and presence of model lipid systems. It provides a foundation for further research regarding the specific interactions of the peptides with different membrane components and the dependence of these interactions on membrane surface potential and ionic environment at the membrane interface.

Keywords:
Electrical double-layer, Antimicrobial peptides, Ionic strength, Langmuir monolayers



Schematic overview of the experimental workflow to determine model antimicrobial peptides aggregation behavior using the Langmuir technique.

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