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On the Effects of Surface Charge of Amphiphilic Peptides on Peptide-Lipid Interactions in the Gas Phase and in Solution

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Abstract (max. 2000 characters)

The interactions between peptides and lipids are fundamental for many biological processes. Therefore, exploring the non-covalent interactions that govern these interactions has become increasingly important. Native mass spectrometry is a valuable technique for the characterisation of specific peptide-lipid interactions. However, native mass spectrometry requires the transfer of the analyte into the gas-phase and non-covalent interactions driven by the hydrophobic effect might be distorted. We, therefore, address the importance of electrostatic interactions for the formation of peptide-lipid interactions. For this, we make use of the amphipathic, antimicrobial peptide LL-37 as well as a positively and negatively charged variant thereof, and study binding of a variety of lipids by native mass spectrometry. We found that the surface charge affects the transfer of peptide-lipid interactions into the gas phase. We further compare our findings observed in the gas phase with interactions formed in solution between the peptides and lipid monolayers using a Langmuir film balance. The two approaches deliver

comparable results and revealed a clear trend in the lipid preferences of all variants for those lipids with opposite charge. Notably, the unmodified wild type peptide was more flexible in the formation of peptide-lipid interactions. We conclude that native mass spectrometry is indeed well-suited to explore the interactions between peptides and lipids, and that electrostatic interactions as expressed by the surface charge of the peptides play an important role in the formation of peptide-lipid interactions.