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Exploring the Interaction of Endogenous Therapeutic Peptides with Lipid Membranes: Insights from Biased calculations.

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Understanding the behaviour of endogenous therapeutic peptides (ETPs), short cationic peptides that have the ability to target and disrupt the pathological membranes, which typically contain a high concentration of anionic lipids, is crucial for the development of effective therapeutic strategies [1,2]. This study investigates multiple ETPs and their interaction with model lipid membranes.
The main objective of this research is to characterise the free energy profiles associated with the interactions between various ETPs and lipid bilayers. Here, we employ advanced computational techniques, including Metadynamics [3], which allows a comprehensive exploration of the configurational space, overcoming the limitations of conventional molecular dynamics methods, where the system can be trapped in local or global minima, which leads to poor sampling of the configurational space. Using Metadynamics, we can effectively capture the peptide-membrane approach, the tilt or rolling motion of ETPs and obtain a more accurate sampling of their membrane interaction states.
Energy calculations play a key role in this study, as they allow us to assess the relative stability of different conformations and interaction states. The resulting free energy profiles provide valuable information on the favourable interactions between ETPs and lipid membranes. These findings are crucial for identifying ETPs, thus facilitating the rational design and development of therapeutic peptides. As a result, an optimized, reproducible and easy to automate protocol to get the free energy profile corresponding to the interaction between ETPs and lipid bilayers is obtained. The protocol here presented is sensitive both to the ETP sequence and the lipid composition of the membrane model.

References

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