Study of somuncurin-1 behavior in two membrane models using Molecular Dynamics Simulation

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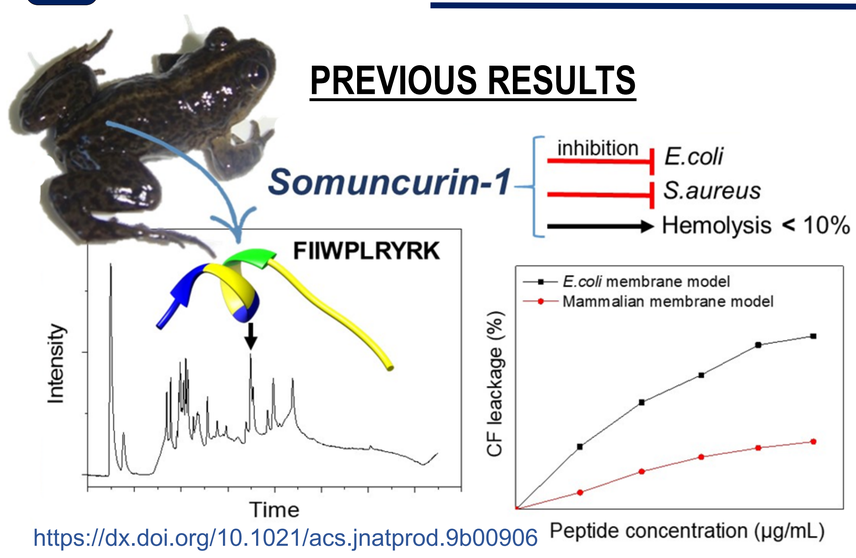
INTRODUCTION

Antimicrobial peptides (AMPs) have the ability to disrupt bacterial membranes. To design AMPs with therapeutic value, is necessary to understand the interaction between AMPs and biological membranes. Molecular dynamics (MD) simulations are a powerful tool to access the atomic level scale of the peptide interaction with biological membranes. In this work we carried out MD simulations considering two lipid bilayers: POPC and POPE/POPG mixtures that mimic mammalian and bacterial membranes respectively. As the AMP model we have chosen somuncurin-1, a peptide identified in the skin secretion of Patagonian frog *Pleurodema somuncurense*.

MD SIMULATIONS AND PEPTIDE CHARACTERISTICS

PREVIOUS RESULTS



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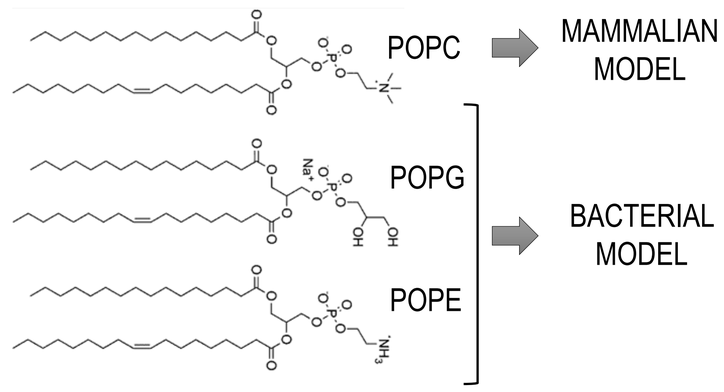
SETUP

NPT ensemble P=1atm
3 temperatures : 303K, 310K and 320K
NAMD program
charmm36 force field
3 initial conditions.
Nº of lipids: 400
Nº of peptides: 11 and 20
Simulation run 700ns

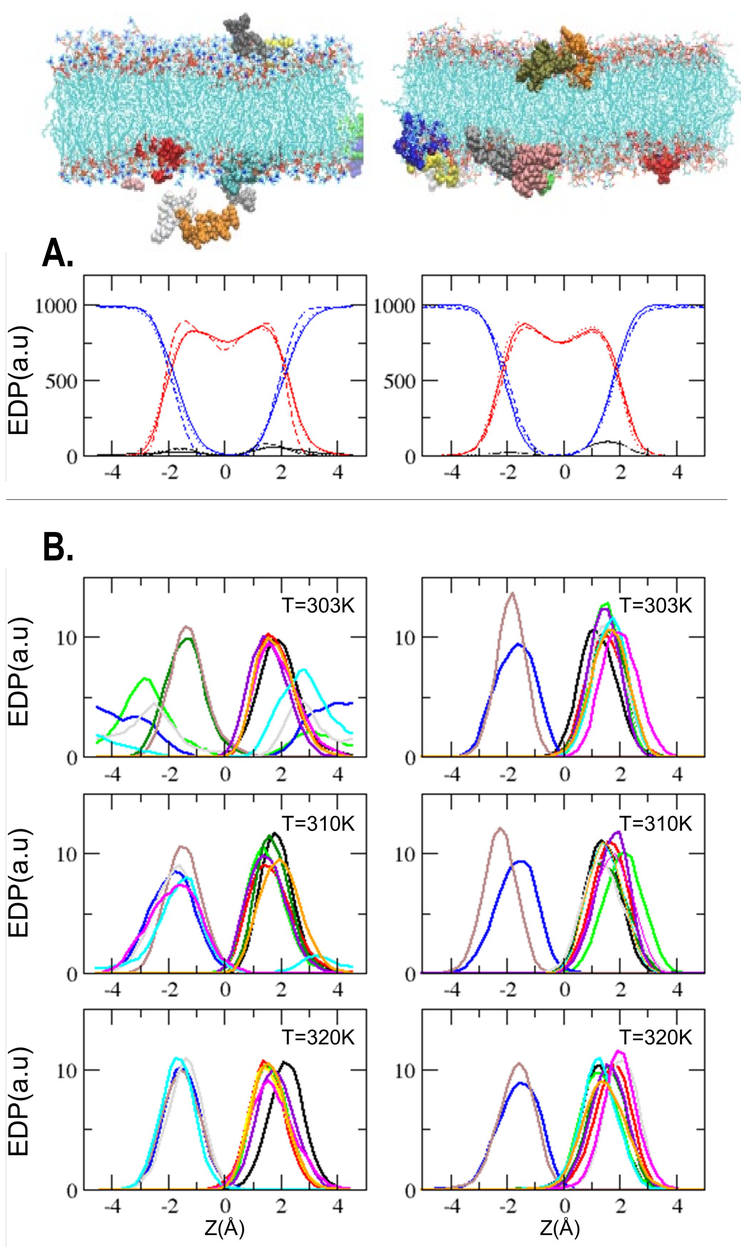
MEMBRANE MODELS



RESULTS

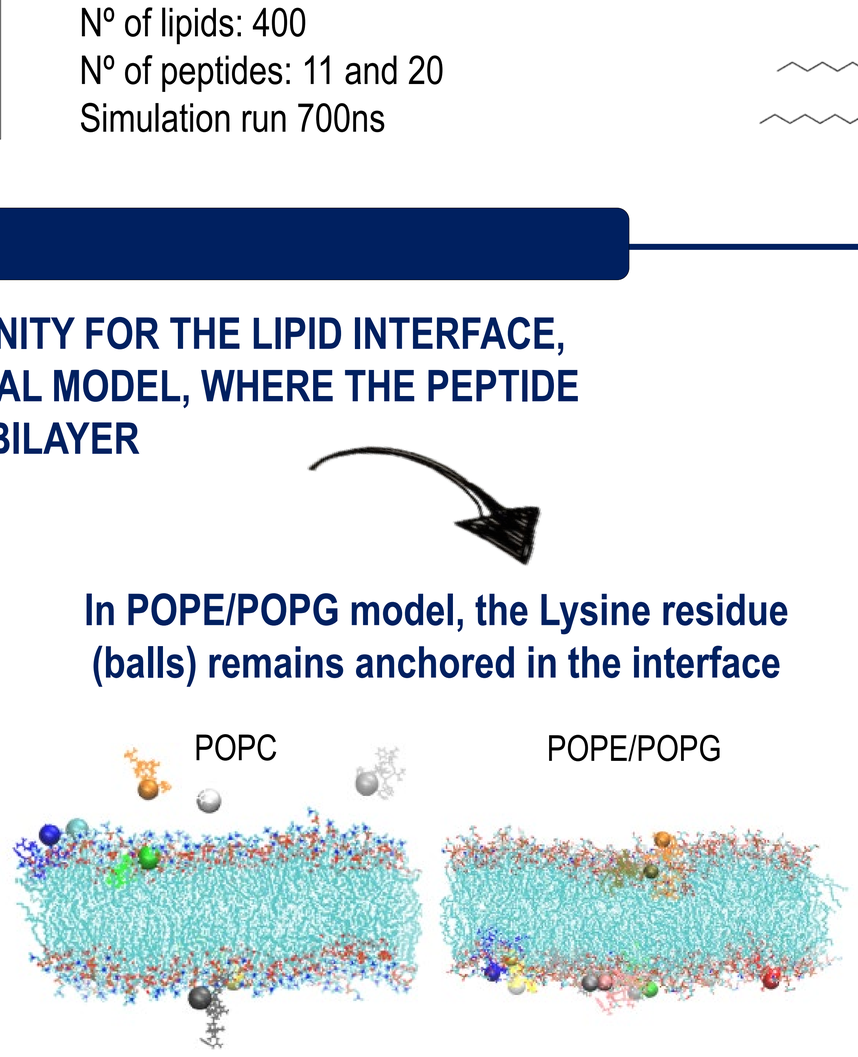
SOMUNCURIN-1 SHOWED A HIGH AFFINITY FOR THE LIPID INTERFACE, MORE PRONOUNCED BY THE BACTERIAL MODEL, WHERE THE PEPTIDE ENTERS THE BILAYER

ELECTRON DENSITY PROFILE'S (EDP)



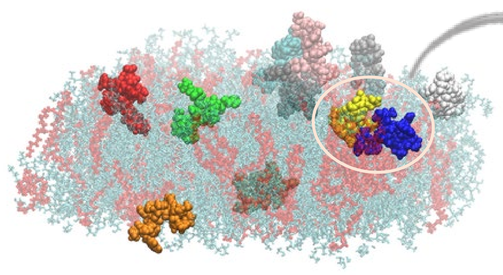
(A) EDP of Bilayers (red), water (blue) and peptides (black). **(B)** EDP of single peptides.

In POPE/POPG model, the Lysine residue (balls) remains anchored in the interface



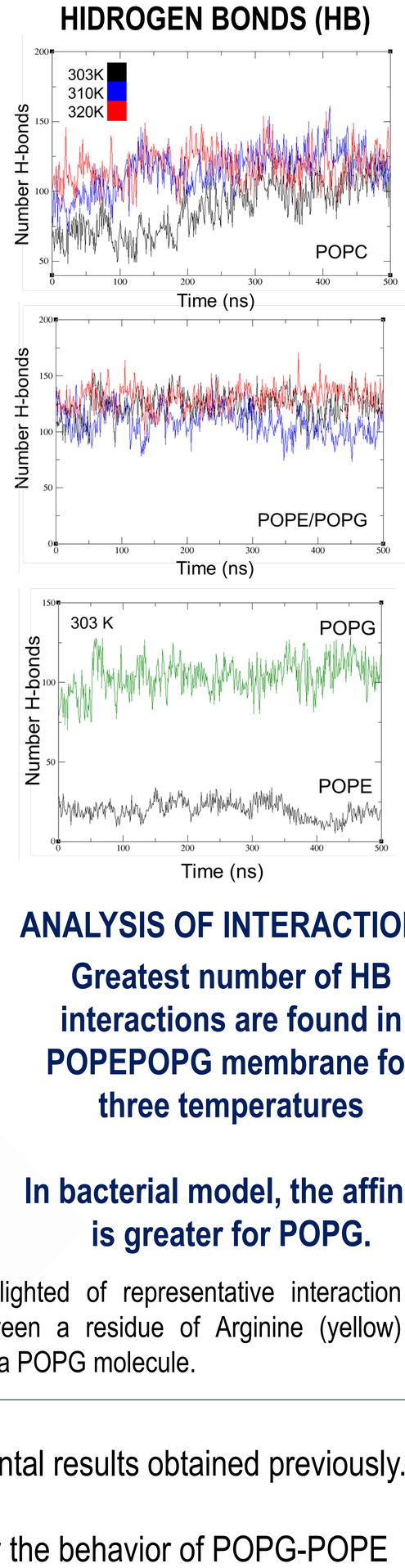
In POPC model is possible observed any peptides in the water

In POPE/POPG model, somuncurin-1 molecules form clusters on the bilayer surface



A representative snapshot of the bacterial membrane model during the production run. Each peptide is depicted in a different color.

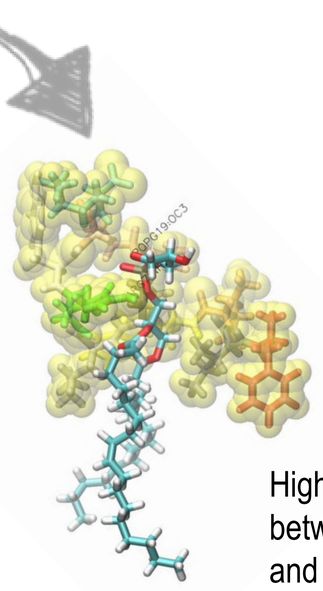
HIDROGEN BONDS (HB)



ANALYSIS OF INTERACTIONS

Greatest number of HB interactions are found in POPEPOPG membrane for three temperatures

In bacterial model, the affinity is greater for POPG.



Highlighted of representative interaction between a residue of Arginine (yellow) and a POPG molecule.

REMARKS AND PERSPECTIVES

- ✓ Somuncurin-1 shows greater affinity for the bacterial membrane model in coincidence with the experimental results obtained previously.
- ✓ Peptides enter the bilayer with the Lys residues remain anchored to the interface.
- ✓ The next step is to correlate the structure of the peptide with their location in the membrane and to study the behavior of POPG-POPE liposomes as a function of peptide concentration