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Molecular Dynamics of Jaburetox in a POPC Bilayer

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INTRODUCTION

Jaburetox (Jbtx) is an insecticidal peptide derived from the *Canavalia ensiformis* urease (JBU).[1] Its mechanism of action involves disruption of the cell membrane, especially in the stomach walls of the insect. Through NMR studies[2], Jbtx was shown to be an intrinsically disordered peptide. Jbtx forms cation-selective pores inside POPC bilayers[3]. It is interesting, therefore, to analyze the interaction of Jbtx with membrane bilayers.

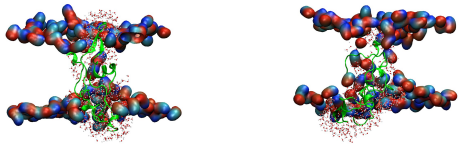
METHODS

Jbtx was modeled initially by homology in the PHYRE2 server. The molecular dynamics and analysis were performed with the Gromacs 4.5 suite. The peptide was initially inserted in an aqueous box with physiological concentration of NaCl. After energy minimization and position restrained equilibration steps, the system was subjected to 200 ns molecular dynamics simulation. After 50 ns, the peptide structure was then inserted in two geometries inside a POPC bilayer with the *g_membed* algorithm of the Gromacs suite.

RESULTS AND DISCUSSION

Jbtx was correctly modeled as an intrinsically disordered peptide. Its backbone consists mostly of coils and transient regions as inferred from DSSP analysis. The only three regions with permanent secondary structure are consistent with NMR[2] studies and X-ray[4] experiments with JBU.

When inserted into the POPC bilayer, Jbtx anchors into the bilayer surface. When inserted in transmembrane fashion, Jbtx remained anchored to both interfaces. When inserted completely submerged in the hydrophobic region, it migrated into one of the interfaces. In both cases, Jbtx attracts some polar heads of the phospholipids, forming a ionic pathway, resembling a pore. Water molecules are present inside this pore throughout the simulation. The last snapshot of both simulations are shown in Figure 1.



(a) (b)

Figure 1. Last snapshot of the bilayer simulations. (a) Transmembrane insertion; (b) Submerged insertion.

CONCLUSIONS

The molecular dynamics simulations performed display formation of a pore, even when the peptide is completely submerged in the hydrophobic region of the bilayer. The presence of the peptide draws the polar heads of the POPC molecules inside of the bilayer itself, thus allowing water molecules to flow inside.

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