SUPPORTING INFORMATION

Identification of the Crucial Residues in the Early Insertion of Pardaxin into Different Phospholipid Bilayers

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The supplementary data include the van der Waals interactions and hydrogen bonds of each Pardaxin residue in the peptide-lipid complexes. In addition, a specified numbers of snapshots, after the peptide reached the membrane surfaces, are shown in Figure S3.

1. van der Waals forces

The van der Waals interaction values of each Pardaxin residue and the standard deviations are shown in Figure S1. Many of the hydrophobic residues had a significant contribution to the total van der Waals interactions of Pardaxin with the lipid bilayers compared to the total contributions of each residue to the binding free energy (please refer to section 3.4).

In general, Phe 1 and (/or) Phe 3 represent the effective contribution to the total van der Waals interactions of the peptide with the membranes. In the case of the lysine residues, although they are positively charged, they have significant van der Waals interactions with the lipid bilayers because they have long side chain with three methylene groups that can participate in the van der Waals interactions, and the amine group at the end of the side chain often forms hydrogen bonds.

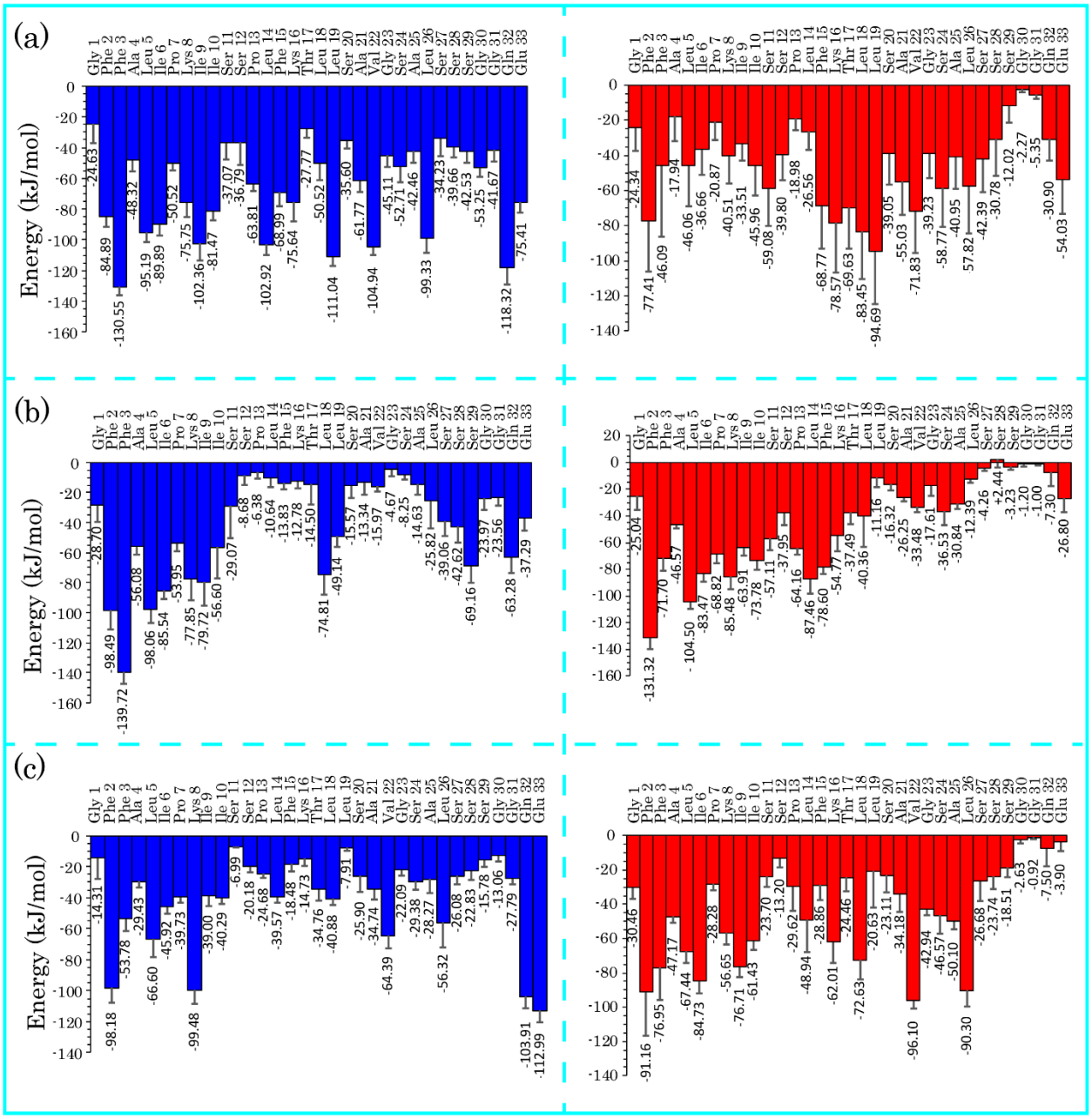

Figure S1. The van der Waals interactions of each Pardaxin residue with lipid bilayers. Blue and red bars represent P1(Pardaxin from its hydrophobic side) and P2(Pardaxin from its hydrophilic side), respectively in (a) Pardaxin-DMPC, (b) Pardaxin-POPC, and (c) Pardaxin-POPG systems. The label numbers represent the van der Walls interaction values.

2. Hydrogen bonds

We calculated the number of hydrogen bonds made by each residue with all three model membranes over the last 40 ns of the MD simulations. Thereafter, we considered the median of the number of hydrogen bonds that were formed by each residue during this time as the final number of hydrogen bonds. As can be observed in Figure S2, the maximum number of hydrogen bonds made by all the hydrophobic residues was 1. It should not be ignored that the number of hydrogen bonds for the N-terminal glycine (Gly 1) was 2 or 3 because, unlike the rest of the glycine residues, the amine group of its side chain is free and can form hydrogen bonds. In addition, for the lysine residues, we can see a large number of hydrogen bonds, equal to 3 in many cases, for both P1 (Pardaxin from the hydrophobic side) and P2 (Pardaxin from the hydrophilic side). This is because the amine group of the lysine side chains could form salt bridges with the lipid bilayer head groups. Although the alcoholic residues (serine and threonine) and glutamine lack ionic side chains like the lysine residues, the polar side chains can form hydrogen bonds. Figure S2 demonstrates that the number of hydrogen bonds for serine 11 and 12 was 2, and glutamine 32 had 2 or 3 in many cases, which was nearly the same as the lysine residues.

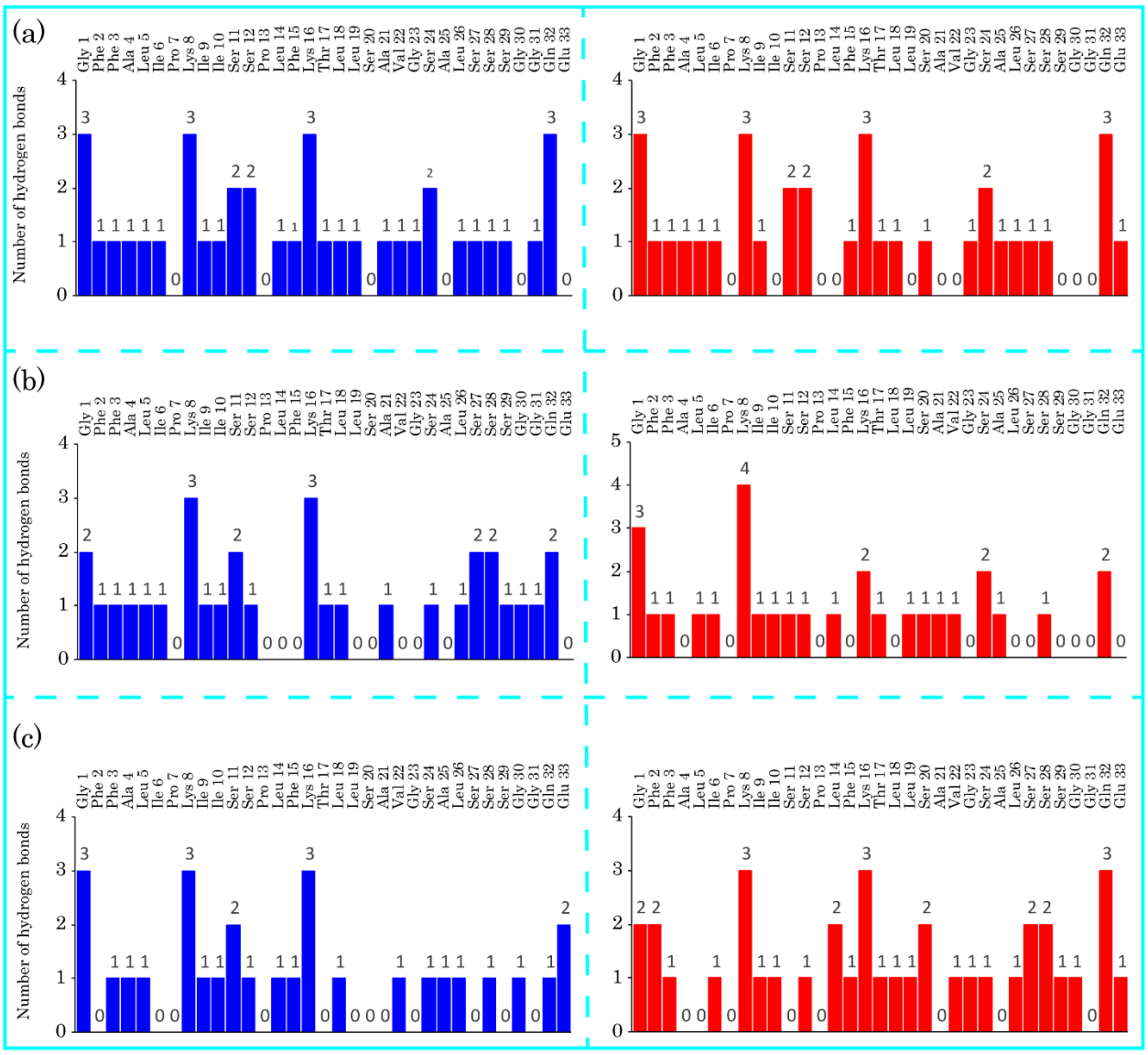

Figure S2. Represents the number of hydrogen bonds of each Pardaxin residue with the lipid bilayers over last 40 ns of the MD simulations. Blue bars represent the number of hydrogen bonds for P1 (Pardaxin hydrophobic face) and red bars the number of hydrogen bonds for P2 (Pardaxin hydrophilic face). (a), (b), and (c) represent Pardaxin-DMPC, Pardaxin-POPC, and Pardaxin-POPG systems, respectively.

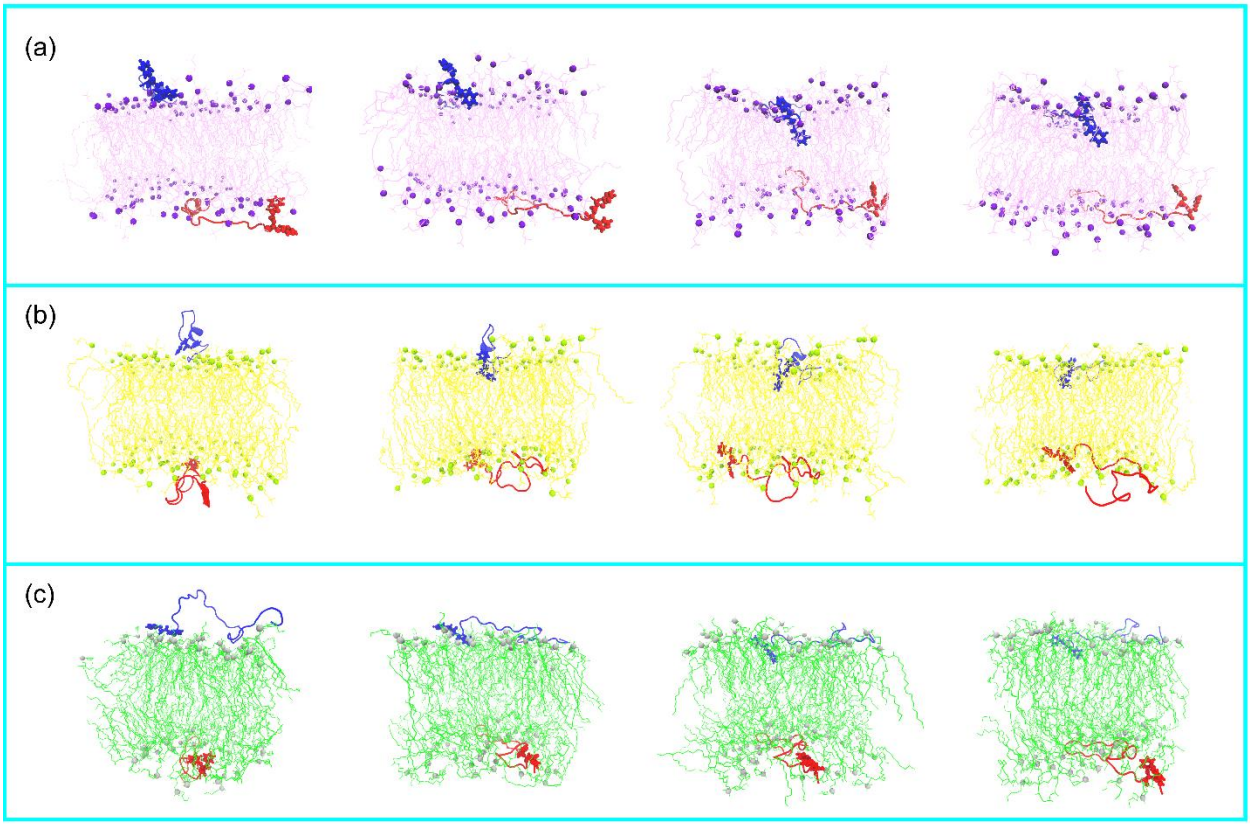

Figure S3. Specified numbers of snapshots, after Pardaxin reached the membrane surfaces, derived from (a) Pardaxin-DMPC, (b) Pardaxin-POPC, and (c) Pardaxin-POPG simulation systems. The simulation time in each panel increases from left to right. Pardaxin from the hydrophobic and hydrophilic faces are shown as blue and red colors, respectively. The phenylalanine residues are shown as CPK model. For clarity the water molecules and ions are omitted.