Supporting Information

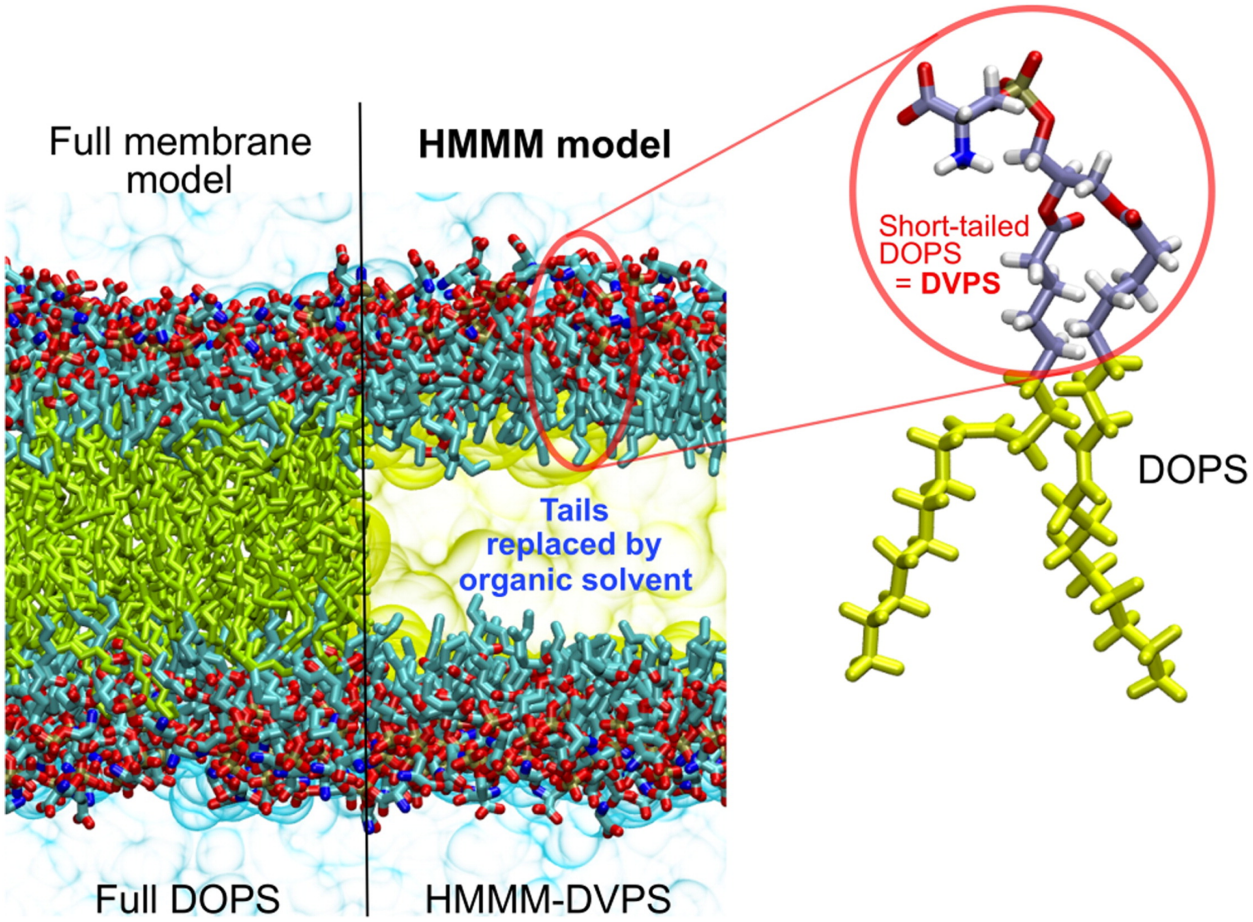

Figure S1: Brief description of the HMMM model.The HMMM model is a biphasic solvent system composed of a core of organic solvent molecules and interfacial regions of short-tailed lipids. The short-tailed lipid are created by removing C_6 to C_{18} (left, yellow sticks) on the phospholipid acyl tail and replacing C_6 with a hydrogen to statisfy the C_5 to C_6 bond. Stort-tailed lipids are represnted in full atomistic detail. The formal chemical name for these short-tailed lipids, which do not occur in vivo, is divalerylphosphatidylserine (the circled fraction of the inset molecule). The oranic solvent, 1,1-dichloroethane (right, yellow area), fills the space left by removal of C_6 to C_{18}, ie the membrane core [31]. Figure originally published in [31], and reprinted with permission of the Biophysical Society, Copyright 2012.

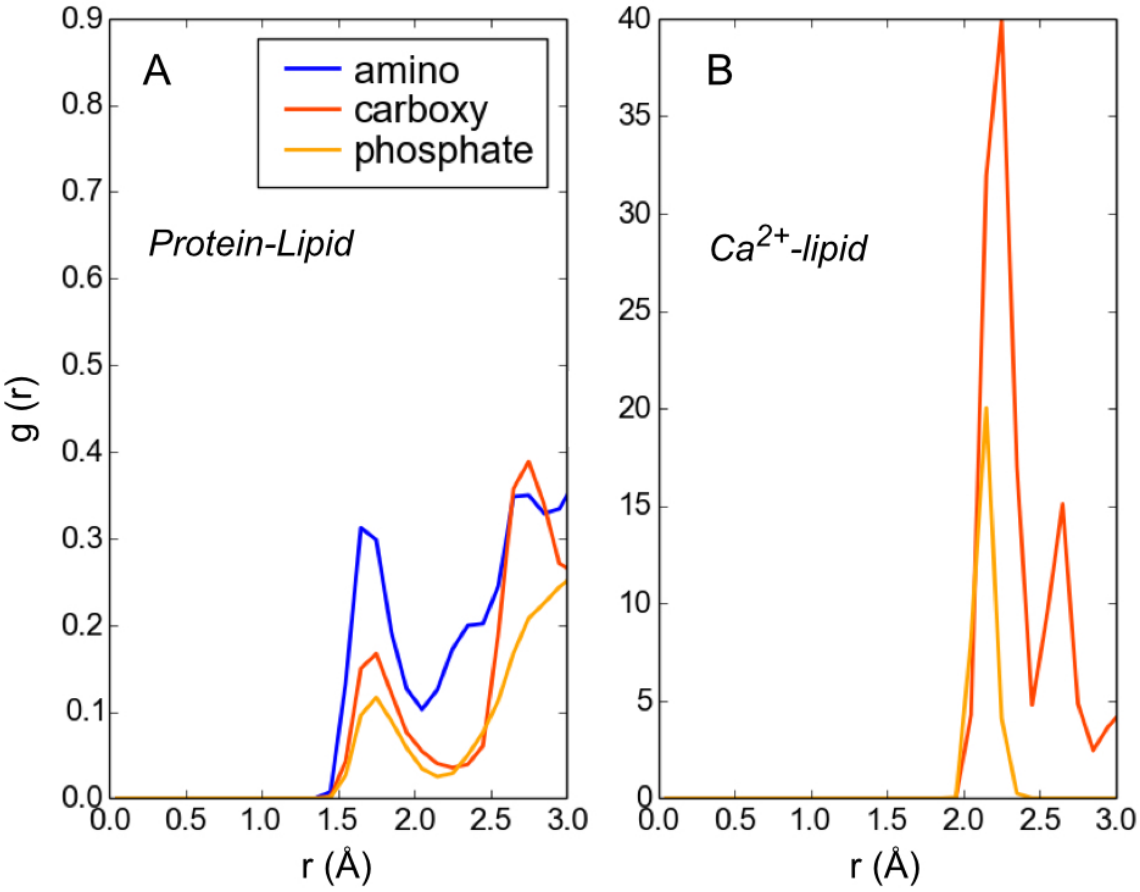

Figure S2: The radial distribution function for A) distances between protein residues and lipid charged functional groups, and B) distances between Ca^{2+} ions (bound to the GLA domain) and lipid charged groups. All contact calculations used the cut-off values derived from this analysis, namely 2.25 Å for protein-phosphate contacts, 2.5 Å for protein-carboxyl contacts, 2.25 Å for protein-amino contacts, 2.5 Å for Ca^{2+}-phosphate contacts, and 3.0 Å for Ca^{2+}-carboxyl contacts. Every 10th frame of a representative 100 ns conventional simulation was used to calculate the radial distribution function. Atoms used for each moiety were: all Ca^{2+} ions for Ca^{2+}, all protein atoms for protein residues, the carbon and two bound oxygen atoms for carboxyl groups, the phosphorus atom and four bound oxygen atoms for phosphate groups, the nitrogen atom and three bound hydrogen atoms for amino groups.

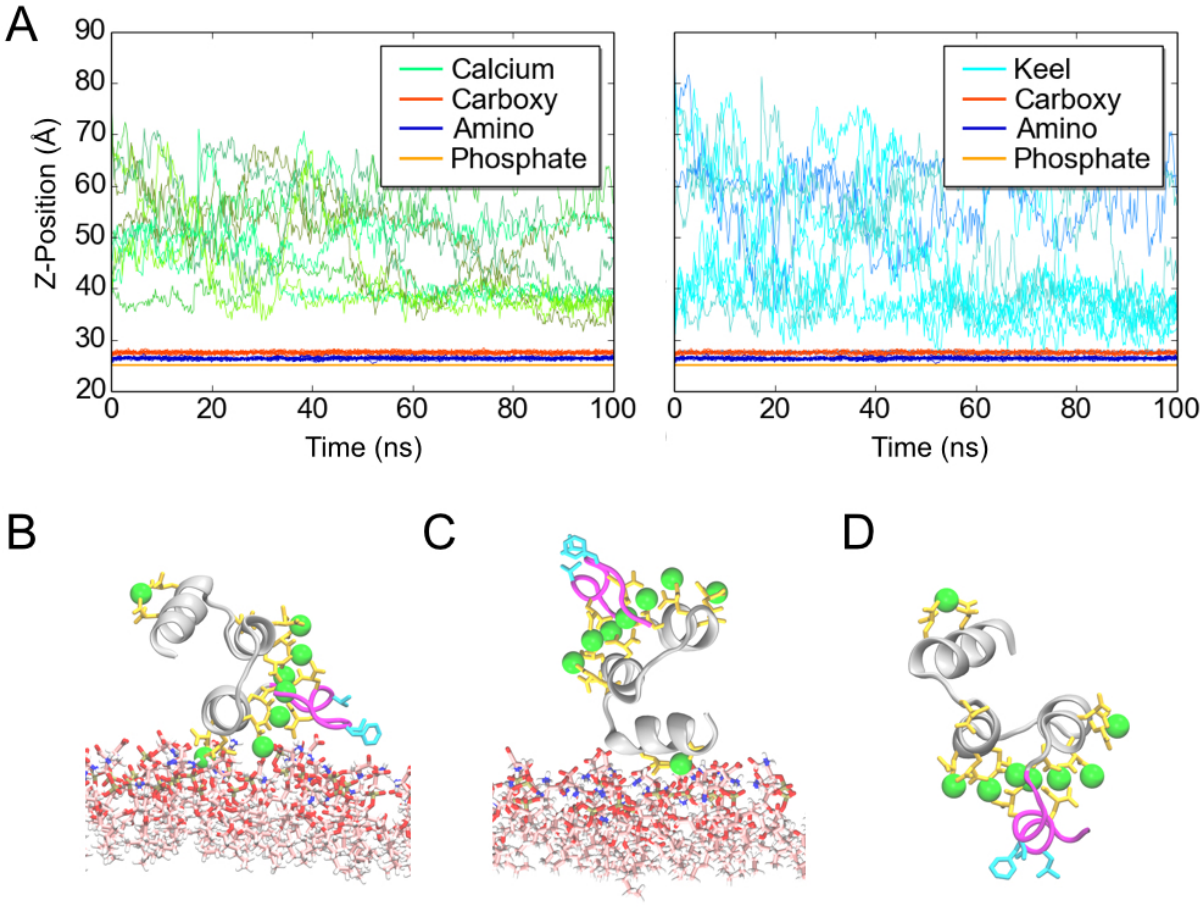

Figure S3: Membrane insertion and binding for improperly bound and discarded trajectories. Binding and penetration depth relative to the membrane for these trajectories are shown (A). B) and C) show examples of binding from these trajectories, which are representative of binding found in 9 trajectories discarded for failing the criteria of membrane penetration of the keel residues below the phosphate head-group region. Of the simulations with keels above the hydrophobic membrane core, 9 FX-GLAs interacted with the membrane but represented nonspecific binding poses which would be incompatible within the context of the full-length coagulation FX. Poses of these 9 simulations were either bound sideways to the membrane, as in (B) or upside down, as in (C). Two simulations showed no membrane interaction. An additional two trajectories were rejected as they showed partial unfolding of the omega loop (D).

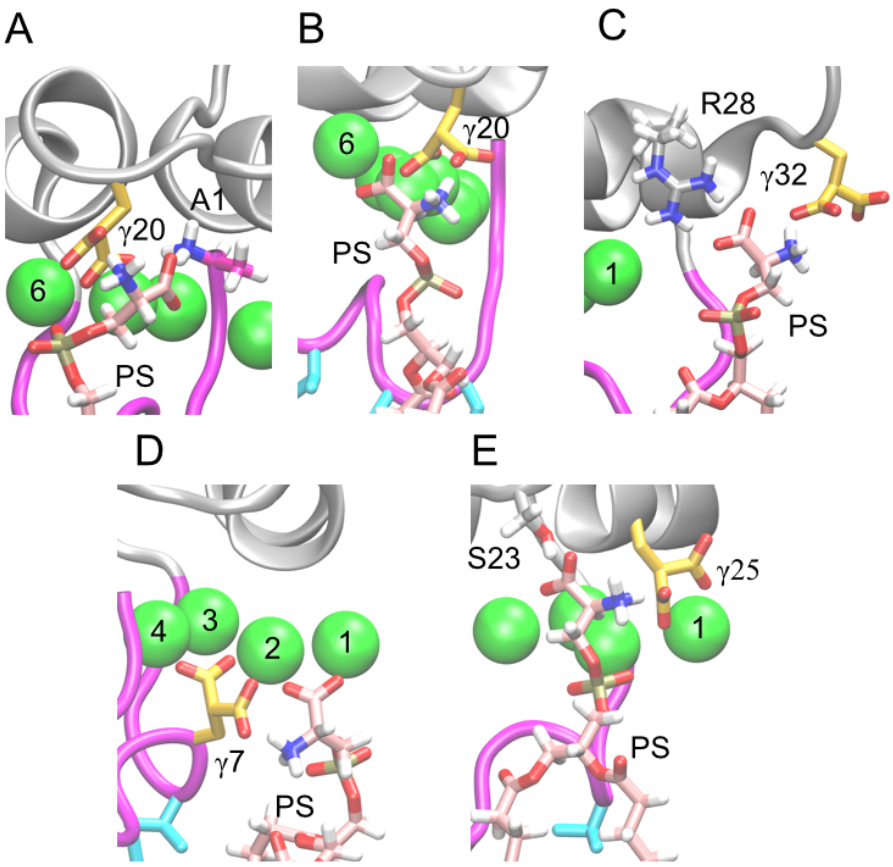

Figure S4: PS binding modes. A-E show various PS binding modes we identified in which two or more charged groups on the same lipid interact with the protein/Ca^{2+}. Specific residues interacting are A) N-terminal (ALA1) with carboxyl, GLA420 with amino, and Ca-6 with phosphate, B) GLA20 with amino, Ca-6 with carboxyl, C) GLA32 with amino, ARG28 with carboxyl, D) GLA7 with amino, Ca-1 and 2 with carboxyl, E) GLA25 with amino and SER23 with carboxyl.

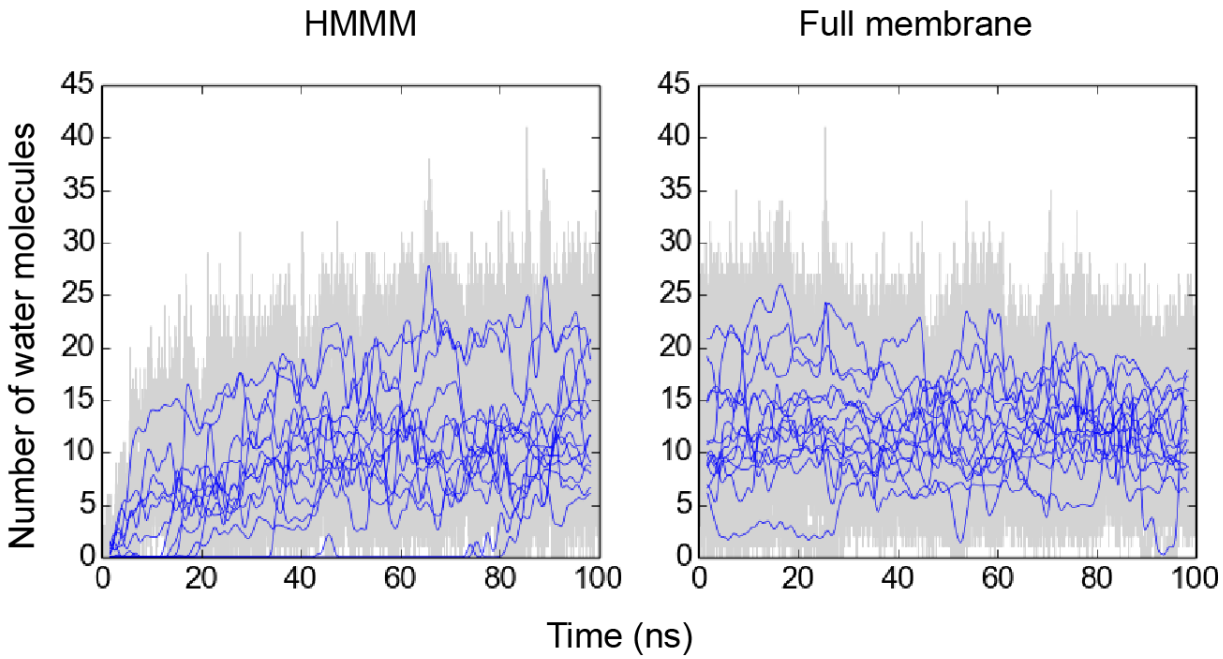

Figure S5: Water at the interface between the membrane and the GLA domain. Raw contact data is show in grey, while smoothed data (Gaussian running average) is shown in blue. We define water in the interface as water molecules both within 2 Å of GLA residues (protein or calcium) and 2 Å of POPS. Data for all 14 fully bound trajectories is included. Left panel shows data from the HMMM simulations, right panel shows data from the full membrane simulations. There is significant fluctuation throughout the trajectories, but by the end of the fullmembrane simulation between 10 and 15 water molecules are present.