SUPPORTING INFORMATION FOR:

Inhibitor Binding of Group IVA Phospholipase A_2 Probed by Molecular Dynamics and Deuterium Exchange Mass Spectrometry

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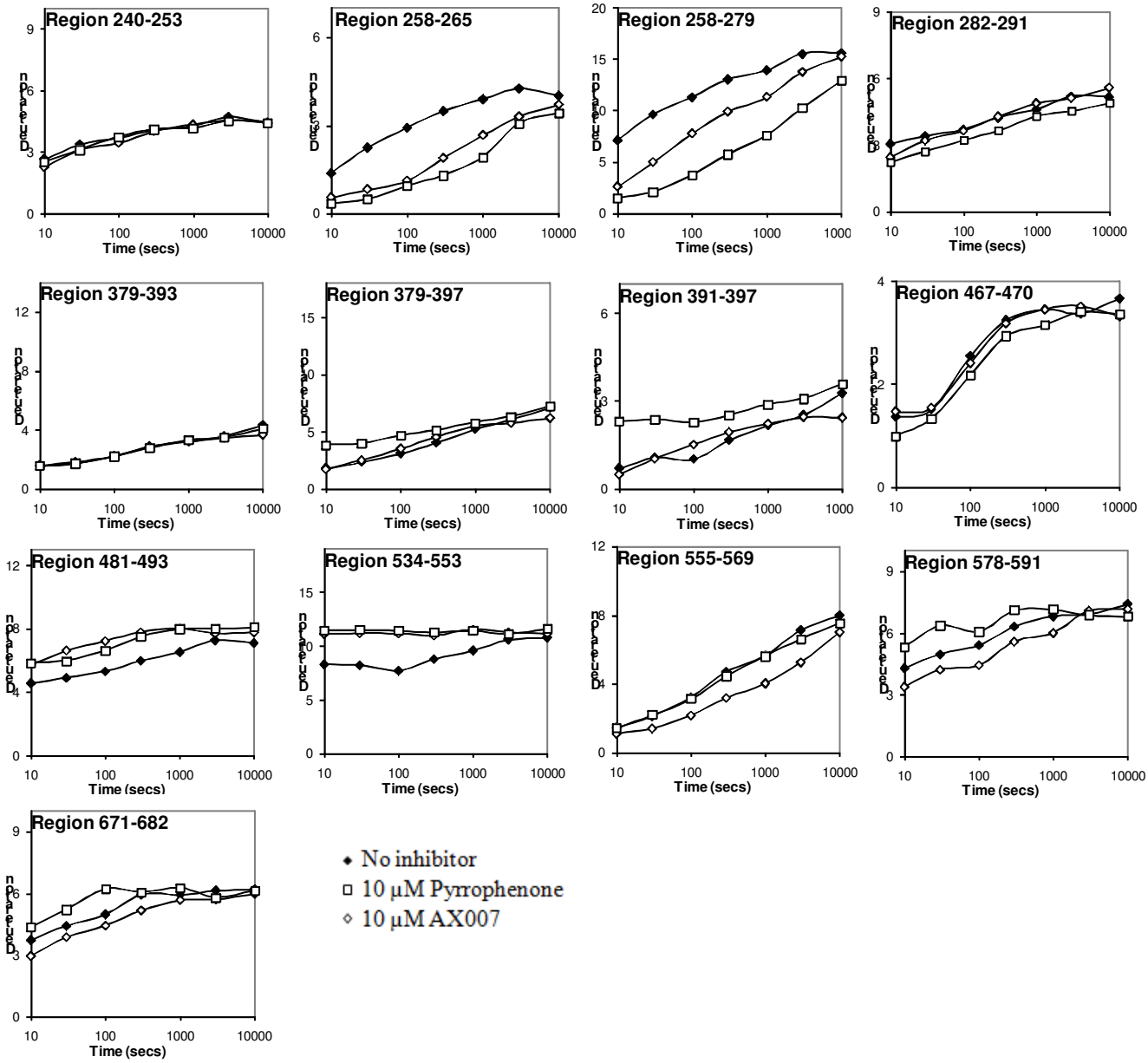
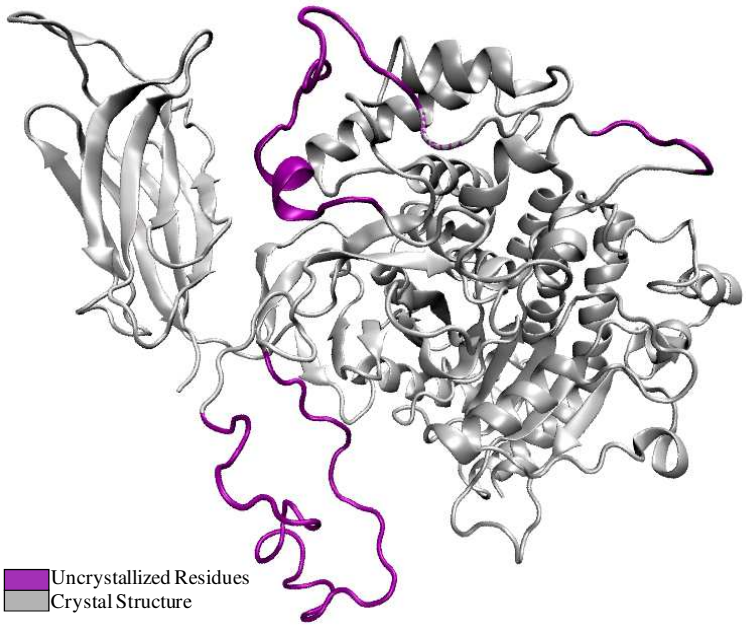
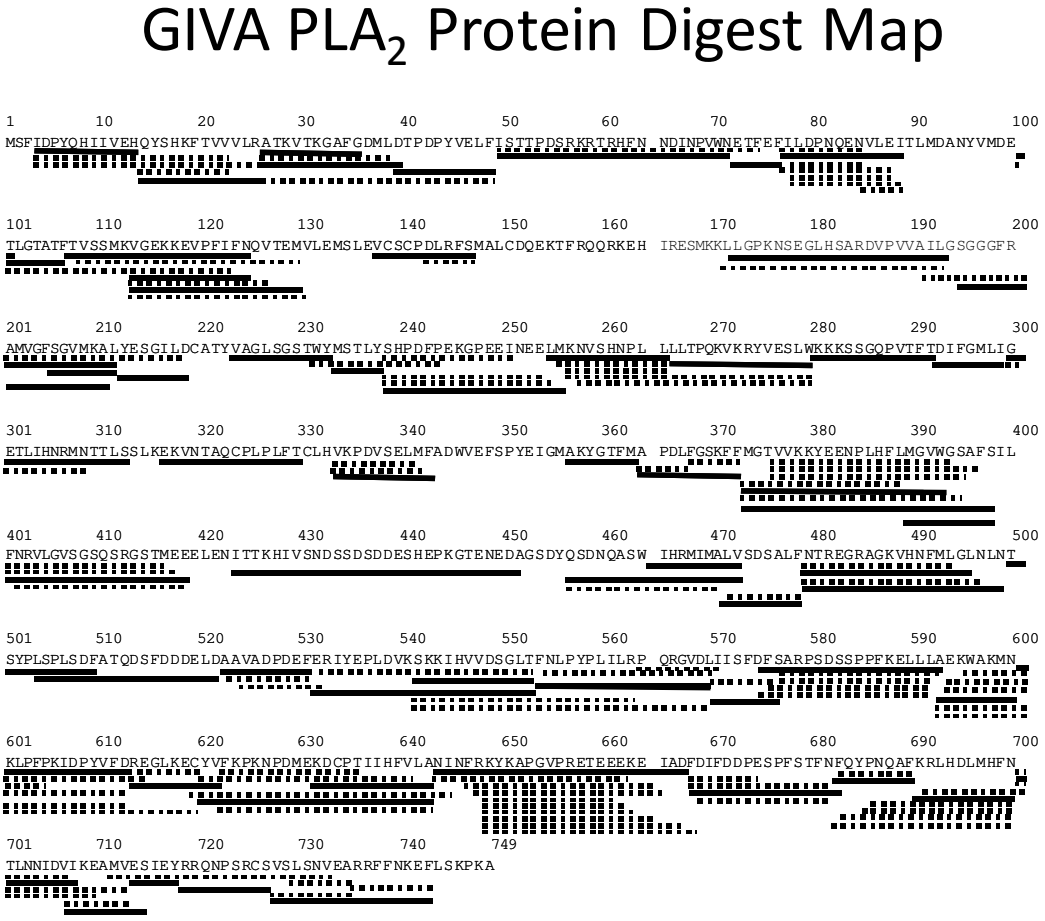


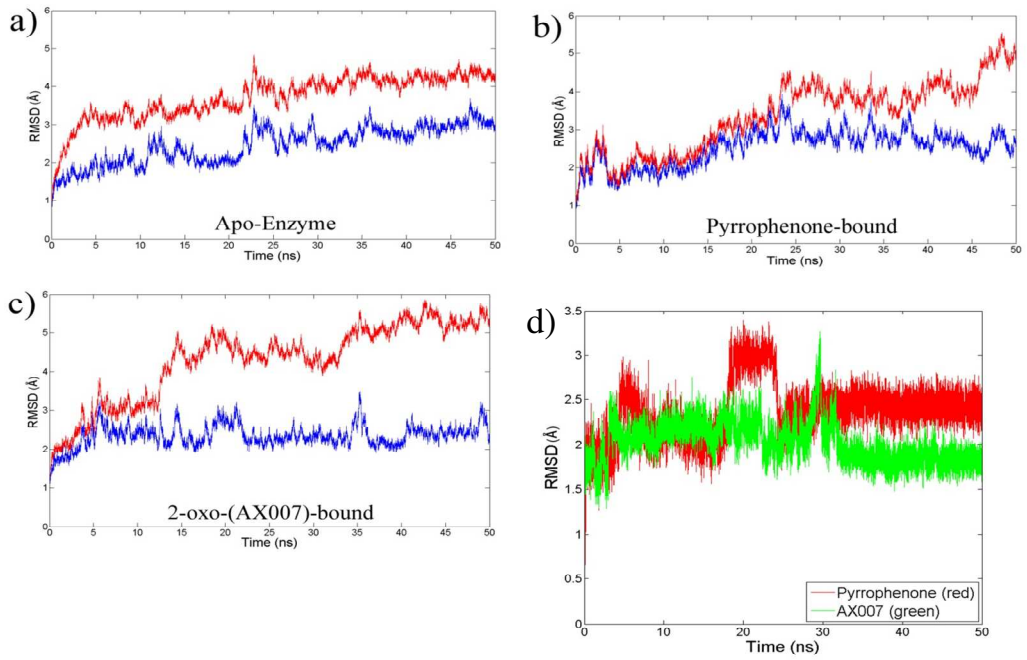
Supplemental Figure 1 Deuterium exchange upon binding of 10 µM pyrrophenone or AX007. The number of incorporated deuterons at seven time points are displayed in peptides that overlap peptides displayed in Figures 3 and 5. Peptides 240-253, and 379-393 are given as examples of peptides with no change in exchange upon inhibitor binding.



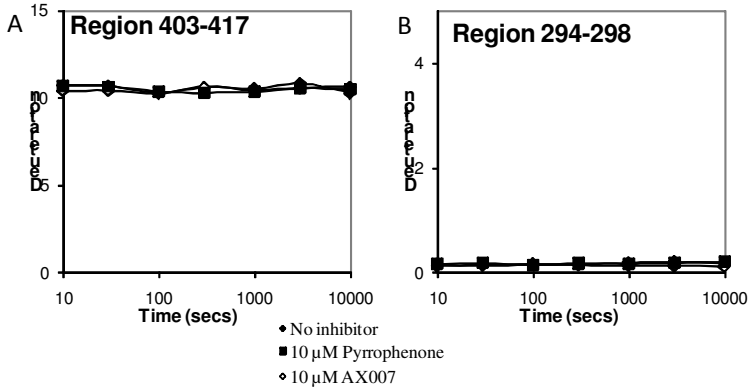
Supplemental Figure 2 Modeling uncrystalized residues in PLA_2. The residues without defined electron density in the crystallographic structure were modeled and are shown in purple.



Supplemental Figure 3 Peptide digest map of GIVA PLA_2. Identified and analyzed peptides resulting from pepsin-digestion are shown below the primary sequence of GIVA PLA_2. All peptides were analyzed, but to prevent redundancy only the peptides shown as solid lines were used in this study.



Supplemental Figure 4 Root mean square distance of protein and inhibitor. For all C_α RMSD measurements the red represents the RMSD of all residues, with crystallized residues RMSD shown in blue (excluding 407-414, 431-462, 498-538, and 626-632). a) The RMSD of the C_α in the apoenzyme over the simulation time course (50 ns). b) The RMSD of the C_α in the pyrrophenone bound enzyme. c) The RMSD of the C_α in the oxoamide bound enzyme. d) The RMSD values of both the oxoamide (green) and pyrrophenone (red) over the simulation time course is plotted.



Supplemental Figure 5 Regions in contact with inhibitors with extremely fast or slow rates of exchange. Region 403-417 (A) and 294-298 (B) are plotted showing extremely fast rates of exchange (region 403-417), or extremely slow rates (region 294-298), with or without pyrrophenone or oxoamide present.