Supplementary Information

Molecular insights into the trapping effect of Ca^{2+} in protein kinase A: A molecular dynamics study

Jocelyn Solorza,[†] Rodrigo Recabarren[†]* and Jans Alzate-Morales*

Centro de Bioinformática, Simulación y Modelado (CBSM), Facultad de Ingeniería, Universidad de Talca, 1 Poniente 1141, Talca, Chile

[†] These authors contributed equally to this work.

Email: rrecabarren@utalca.cl (R.R), jalzate@utalca.cl (J. A-M.)

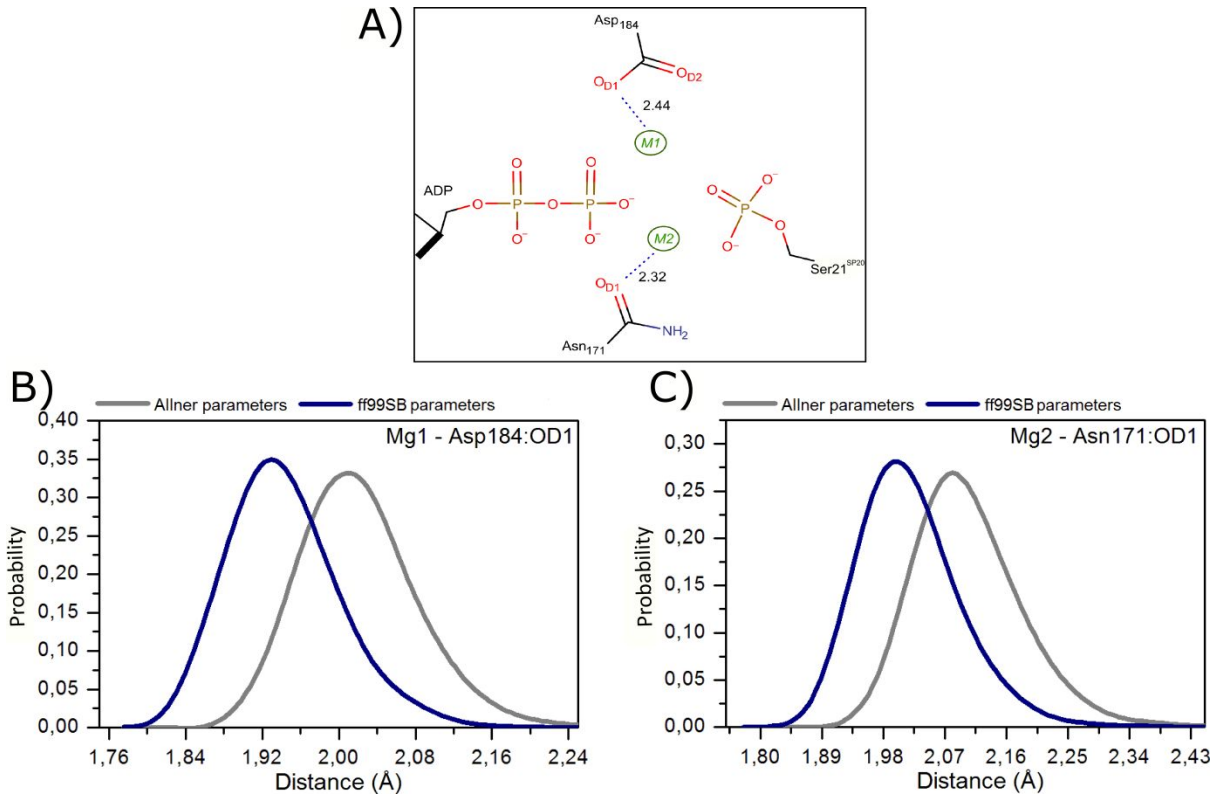

Figure S1. Probability histograms of occurrence for the distances Mg1-Asp184:OD1 and Mg2-Asn171:OD1 in MD simulations of 20 ns considering state I. A) Representative sketch of crystallographic distances Mg1-Asp184 and Mg2-Asn171. B) Distance distribution between cofactor Mg1 and oxygen OD1 from residue Asp184 using Allnér and ff99SB parameters. C) Distance distribution between cofactor Mg2 and oxygen OD1 from Asn171 using Allnér and ff99SB parameters. Distances are given in Angstroms (Å).

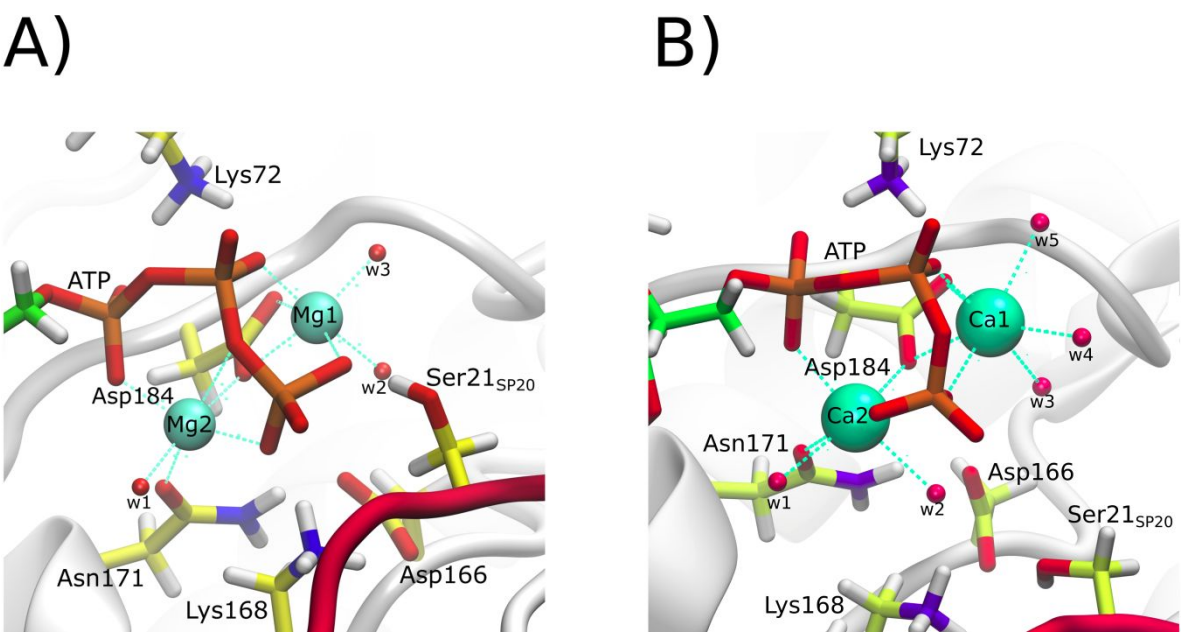

Figure S2. Comparative description of the active site of PKA with Mg^{2+} and Ca^{2+} ions as cofactors in the reactant state. A) Active site of PKA with Mg^{2+} ions in reactant state. Mg1 is coordinated by the β- and γ-phosphates of ATP, in a bidentate way by residue Asp184, and two water molecules (w2 and w3). Mg2 is coordinated by the α-, β- and γ-phosphates of ATP, Asp184, Asn171, and one water molecule (w1) (PDB ID: 3X2W). B) Active site of PKA in reactant state with Ca^{2+} ions in replacement of Mg^{2+} ions. Ca1 is coordinated by the β- and γ-phosphates of ATP, in a bidentate way by residue Asp184, and three water molecules (w3, w4 and w5). Ca2 is coordinated by the α- and γ-phosphates of ATP, Asp184, Asn171, and two water molecules (w1 and w2) (PDB ID: 4XW4, AMPPNP is replaced by ATP).

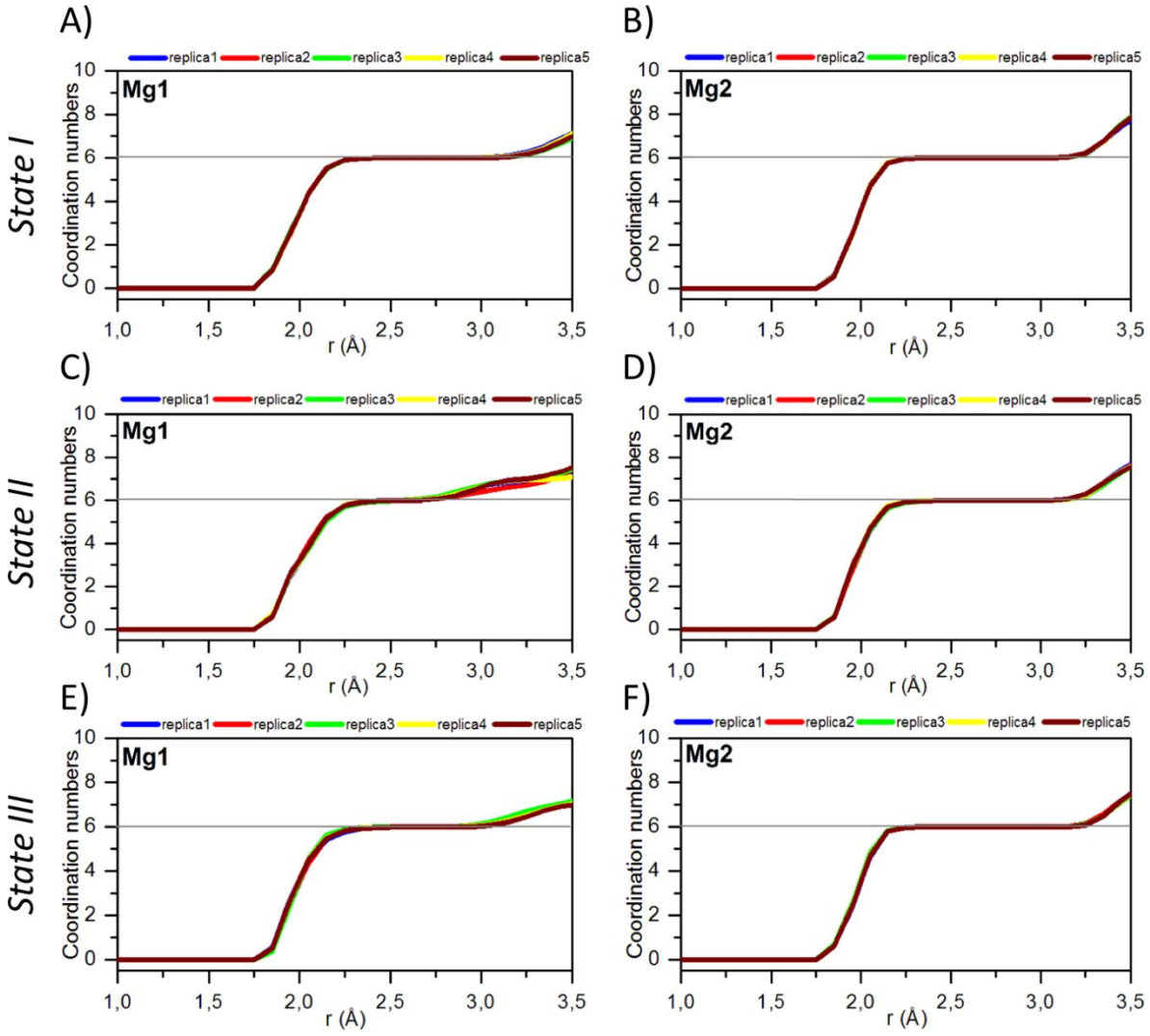

Figure S3. Coordination numbers for Mg1 and Mg2 cofactors respect to oxygen atoms present in the coordination spheres of the three studied states. Coordination numbers of oxygen atoms in state I for Mg1 (A) and Mg2 (B). Coordination numbers of oxygen atoms in state II for Mg1 (C) and Mg2 (D). Coordination numbers of oxygen atoms in state III for Mg1 (E) and Mg2 (F). The horizontal gray line in all graphics describes the crystallographic number of oxygen atoms in the coordination spheres of both ions.

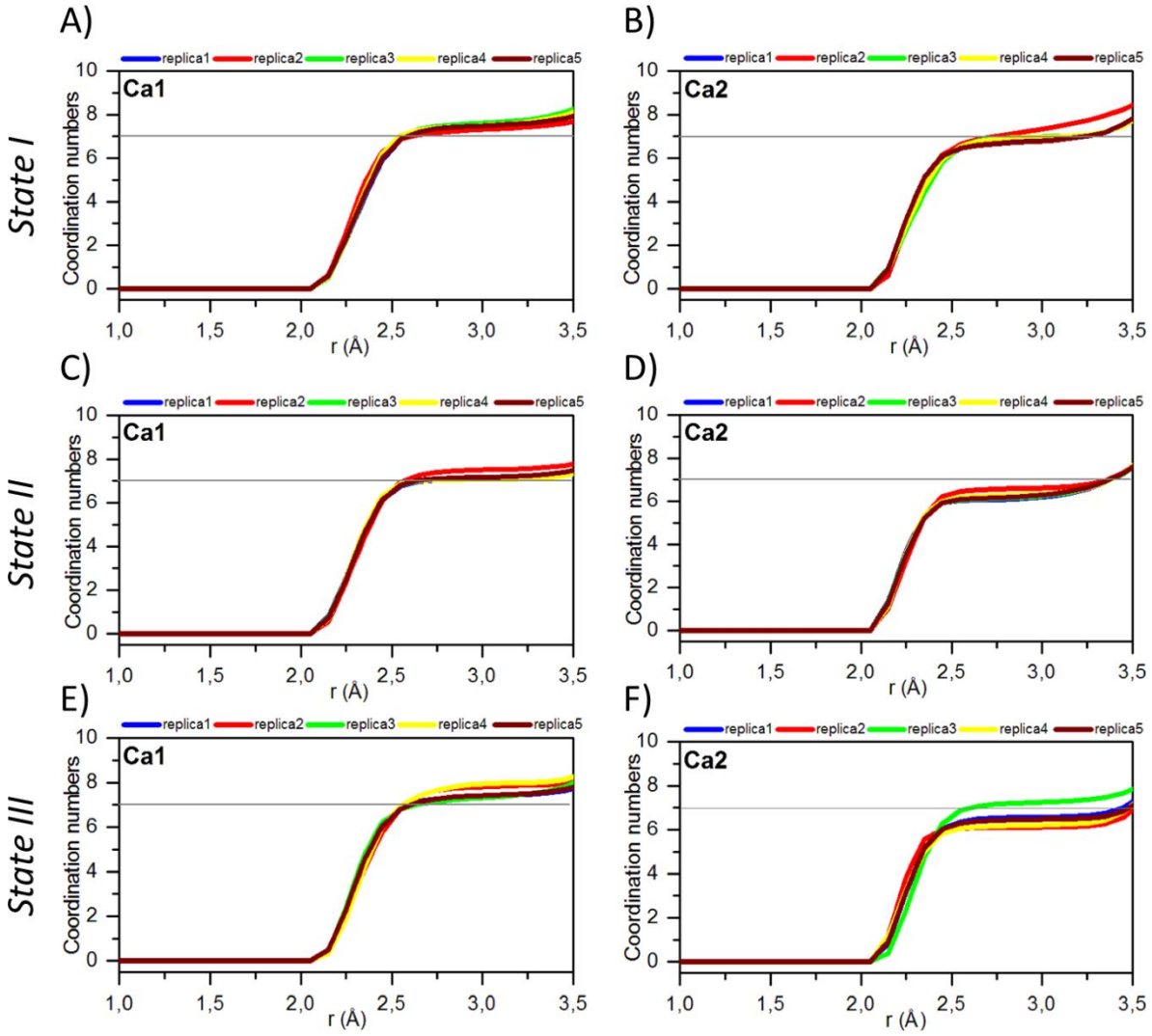

Figure S4. Coordination numbers for Ca1 and Ca2 cofactors respect to oxygen atoms present in the coordination spheres of the three studied states. Coordination numbers of oxygen atoms in state I for Ca1 (A) and Ca2 (B). Coordination numbers of oxygen atoms in state II for Ca1 (C) and Ca2 (D). Coordination numbers of oxygen atoms in state III for Ca1 (E) and Ca2 (F). The horizontal gray line in all graphics describes the crystallographic number of oxygen atoms in the coordination spheres of both ions.

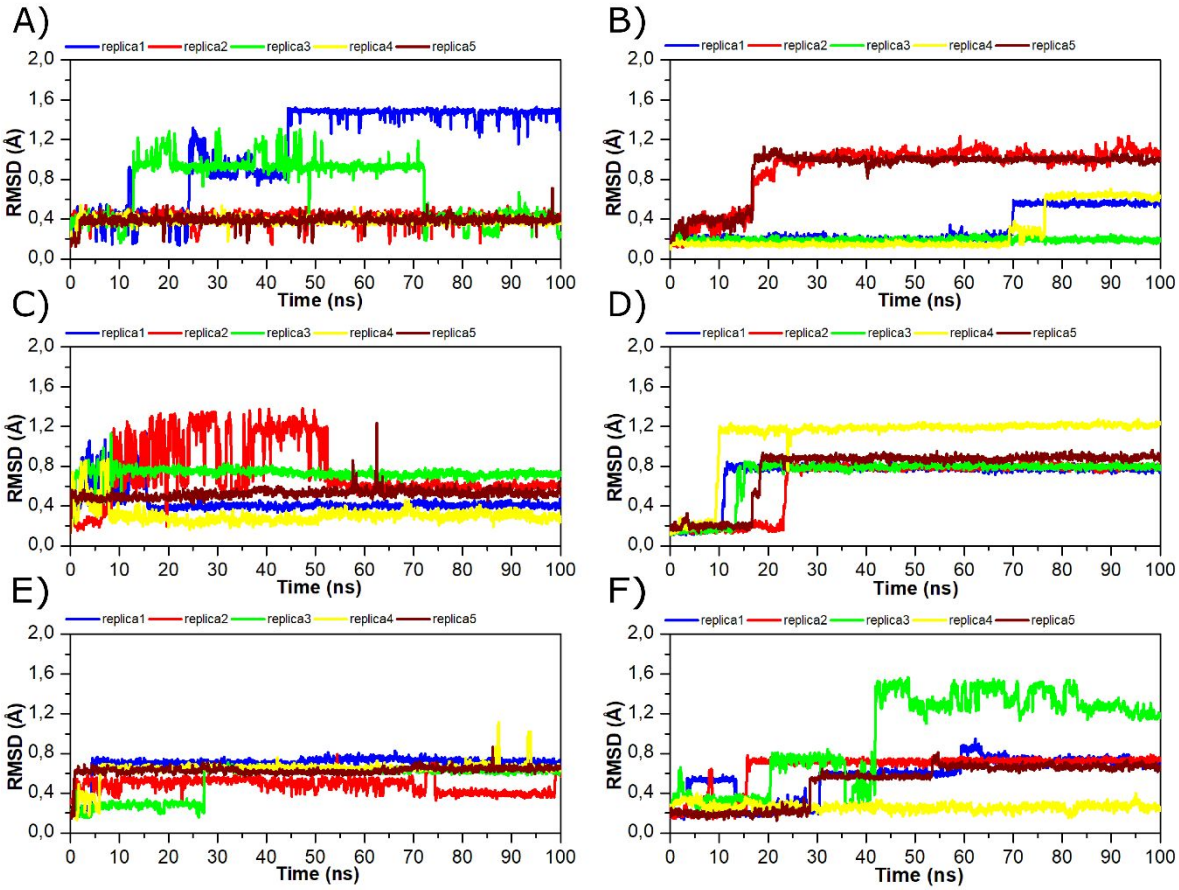

Figure S5. Evolution over time of the RMSD (root mean square deviation) on the pSer21 residue. A), C) and E) describe MgADP system in states I, II and III, respectively. B), D) and F) describe CaADP system in states I, II and III, respectively. All graphs are smoothed with an adjacent averaging function considering 10 points.

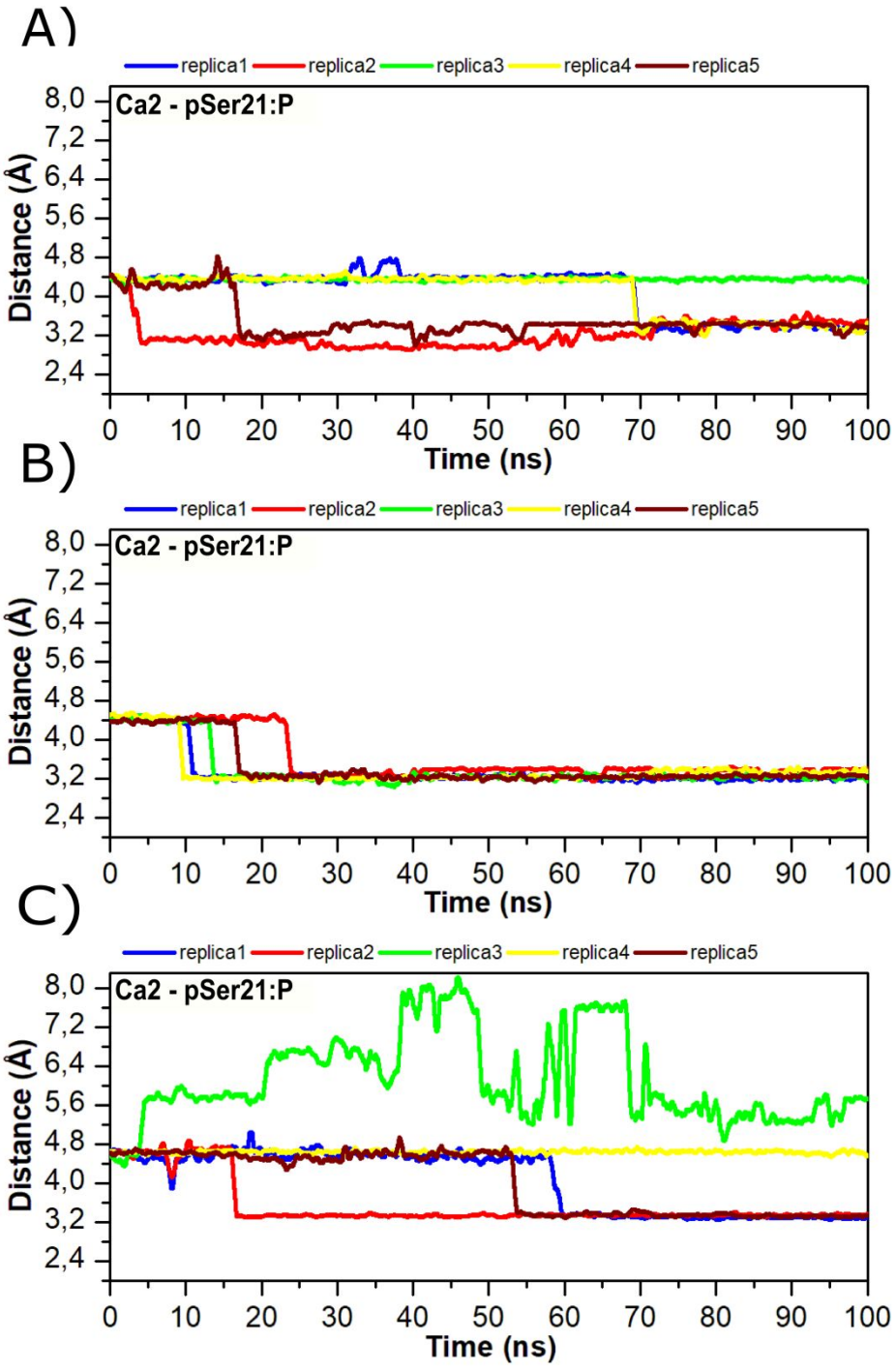

Figure S6. Evolution over time of the distance between Ca2 and the phosphorus atom of pSer21 (pSer21:P) in state I (A), state II (B) and state III (C) in CaADP. All graphs are smoothed with an adjacent averaging function considering 60 points.