Supplementary information

Enzymatic GTP Hydrolysis: Insights from an *Ab initio* Molecular Dynamics Study

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Protein/water system. This model was based on the X–ray structure of AlF_3/GDP/Cdc42GAP/Cdc42 complex (PDB code 1GRN[1]). In this complex, Cdc42 is bound to the active form of GAP, with transition state mimic AlF_3 in the active site. As we used this model to estimate the protein electrostatic field on the reactants (the catalytic water and GTP), we did not include the following groups in the model: AlF_3, GDP and WAT. Water molecules present in the X–ray structure were included. Hydrogen atoms were added to the complex assuming standard structural parameters. The complex was immersed in a 60x70x77 $Å^3$ box containing 7,950 water molecules. The positions of the protein hydrogens and of the water molecules were equilibrated by carrying out a molecular dynamics simulation based on the AMBER 5 suite of programs[2]. The all–atom AMBER force field[3] and the TIP3P model[4] were used for the protein and water, respectively. The dielectric constant was set equal to 1. Long range electrostatic interactions were calculated with particle mesh Ewald method[5]. Short range electrostatic and van der Waals interactions were truncated within a 12 Å cutoff. Constant temperature simulations were carried out by coupling the system to a Berendsen bath[6] with 0.2 ps relaxation time. The hydrogen atoms and the water molecules underwent 5,000 geometry optimization steps followed by 30 ps of MD.

References

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CAPTION TO THE FIGURE

Figure 1SI. Three dimensional structures of models **a** and **b**. Removal of V36 amide group in model **a** resulted in a change of the WAT O–H Bond Ionicity Indexes[7] and of the electric field on the reactants as small as ~ 2 %.

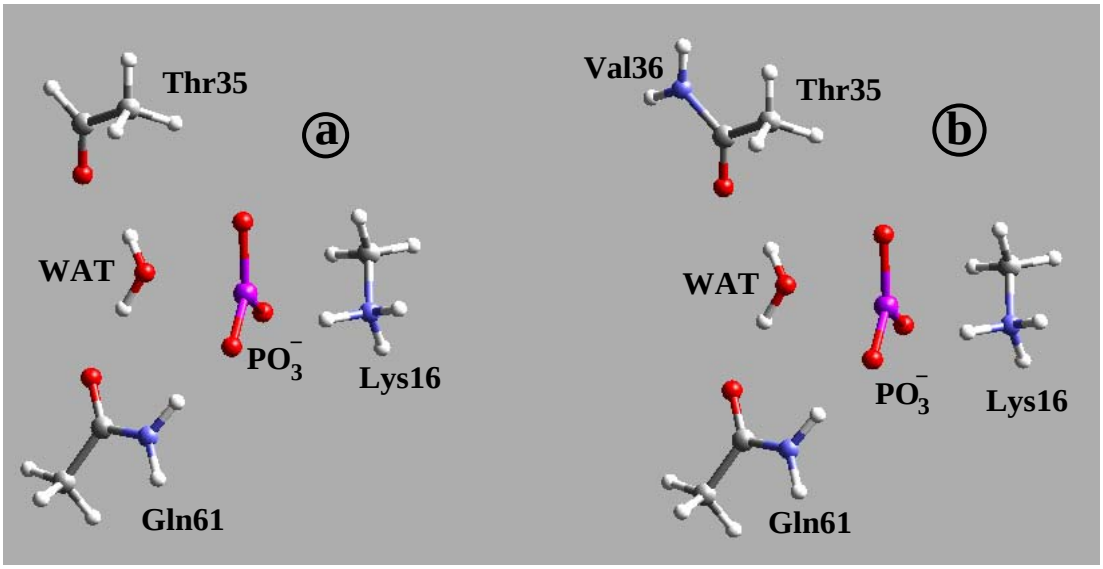

Figure 1 SI