The role of Gln 61 in HRas GTP hydrolysis: a Quantum Mechanics/Molecular Mechanics (QM/MM) study.

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SUPPORTING MATERIAL

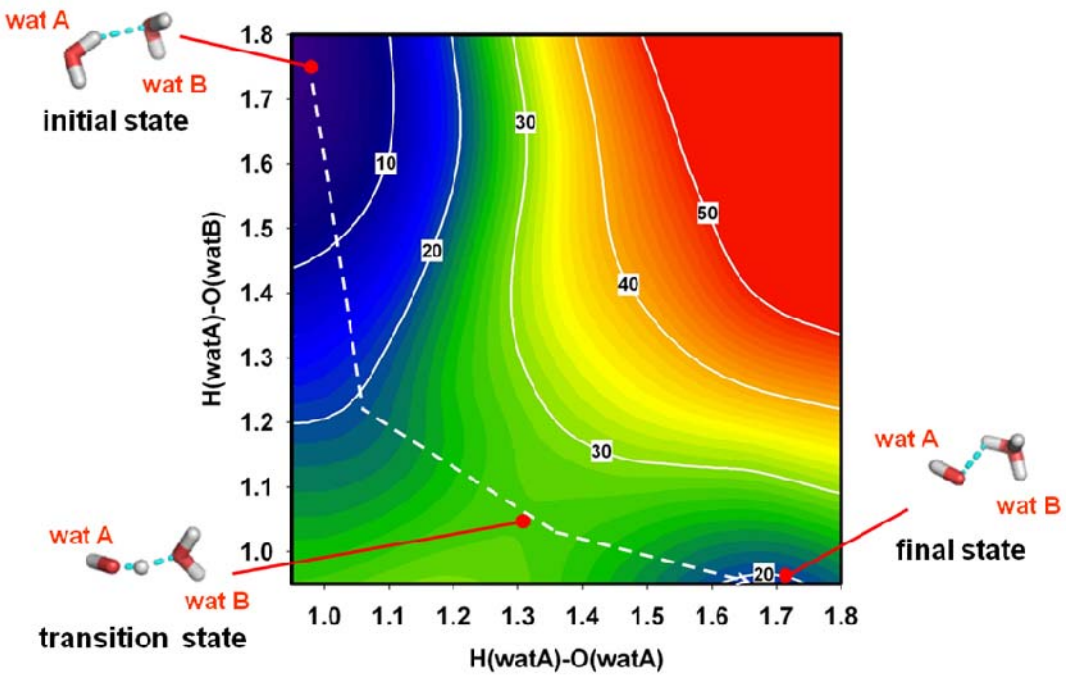


Figure S1. Free energy landscape for the ionization of water. ΔG^{o} values of the system are shown for the different states corresponding to the following distances: x–axis, from proton to oxygen atom in the attacking water molecule (wat A); y–axis, from the same proton to the oxygen atom in the second water molecule (wat B). The structures of the two water molecules in the initial state (ΔG^{o} value adjusted to 0), the transition state ($\Delta G^{o} \approx 28$ kcal·mol^{-1}) and final state containing OH^{-} plus H_3O^{+} molecules ($\Delta G^{o} \approx 19$ kcal·mol^{-1}) are represented.

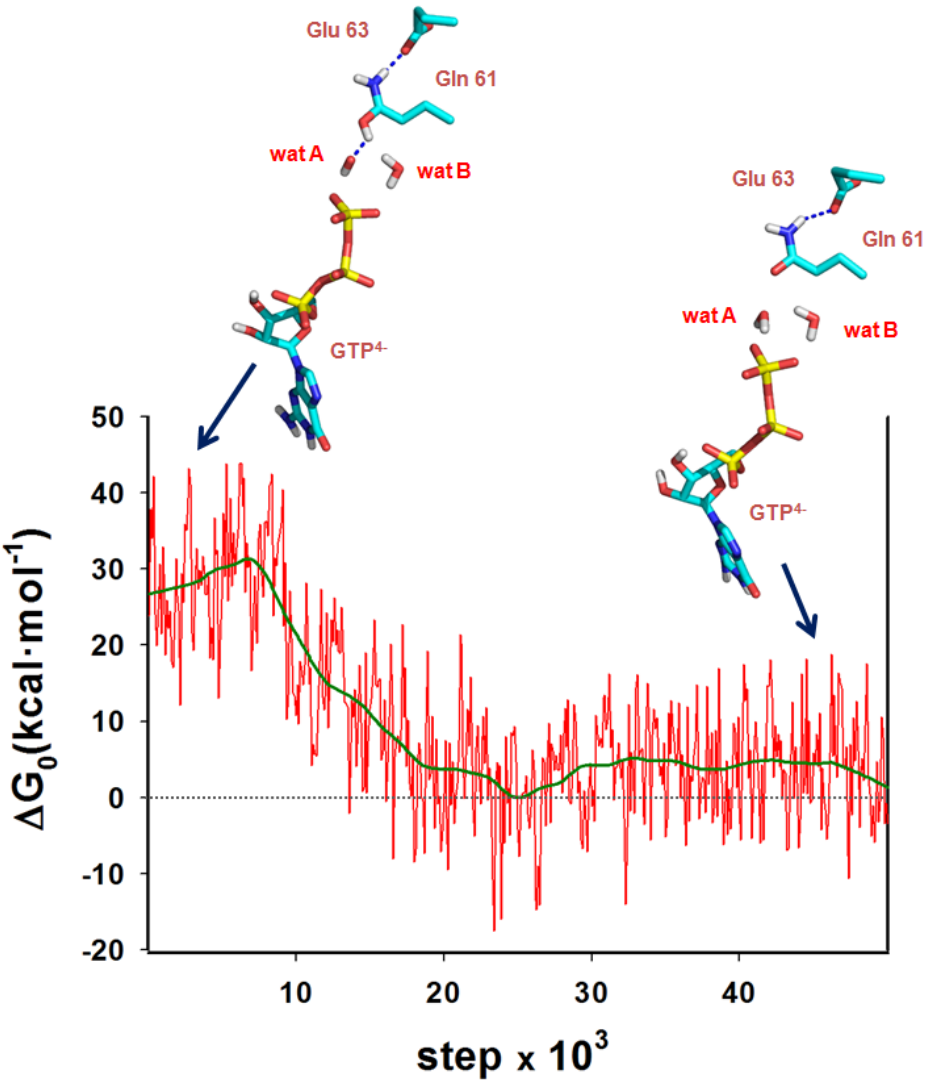
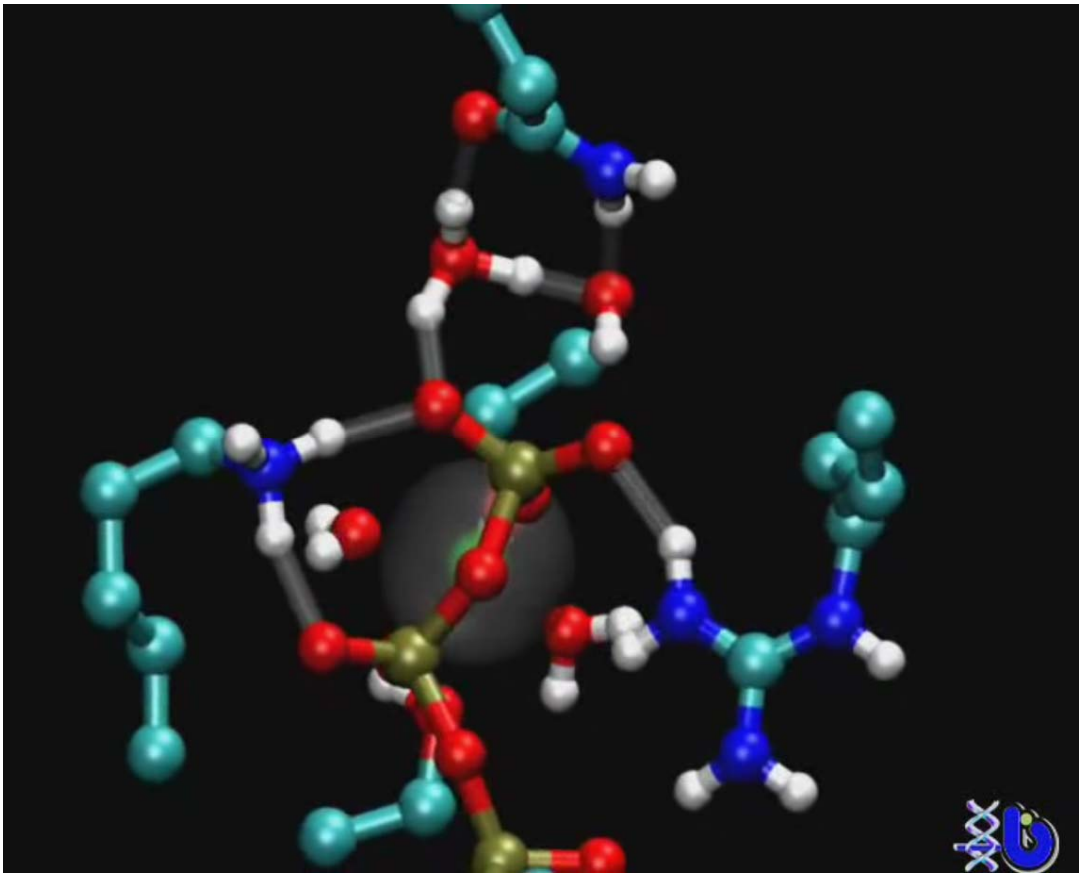


Figure S2. Unconstrained simulation of protonated Gln61. Final state of the experiment shown in Figure 2 was subjected to 5.000 steps of unconstrained simulation and ΔG^o variation (in kcal•mol-1) was continuously measured. The structure of the active center at the beginning (protonated Gln 61) and after the simulation process in absence of constrains (unprotonated Gln61 plus two water molecules, equivalent to the initial reaction substrates), are represented.



Movie S1. Video demonstrating proton movements in the QM region of the QM/MM system. First: a proton is transferred from the attacking water molecule (wat A) to the second water molecule (wat B). Second, a different proton is transferred from wat B to GTP. The role of Gln 61 in stabilizing proton movements and transient molecules is highlighted.