Electronic Supplementary Information
for
Amide-imide tautomerization in the glutamine side chain in enzymatic and photochemical reactions in proteins

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Section S1. Structures of ES and EP in GTP hydrolysis by the Ras-GAP protein complex

Fig. 1 of the main text shows small fragments of the structures of the enzyme-substrate (ES) and enzyme-product (EP) complexes in GTP hydrolysis by Ras-GAP obtained in QM/MM calculations. Here (Fig. S1) we present a more detailed view on the ES structure.

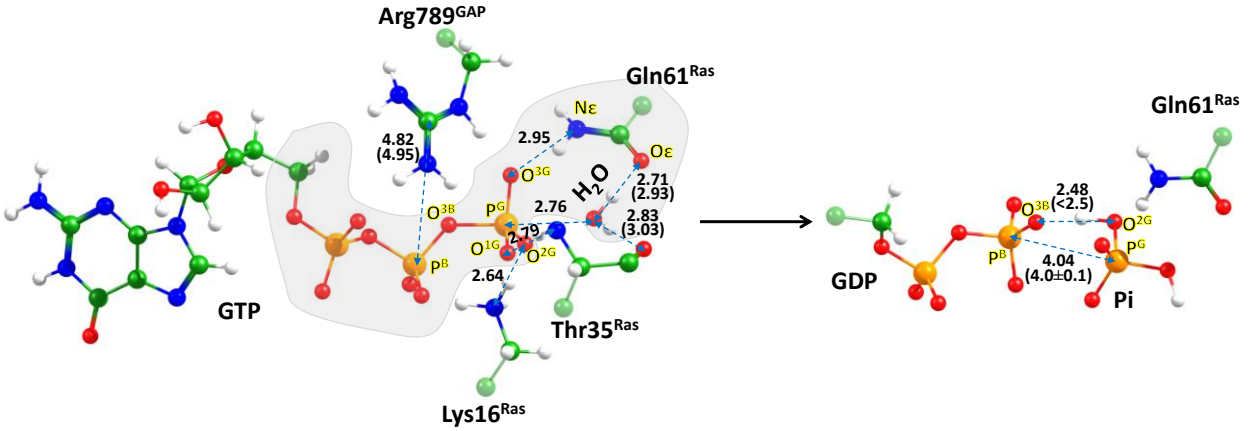

Figure S1. Fragments of the ES complex (left) and of the EP complex (right) in GTP hydrolysis by Ras-GAP. Here and in other figures, carbon atoms are shown in green, oxygen in red, nitrogen in blue, phosphorus in orange, hydrogen in white. Distances between heavy atoms are given in Å; the values in parentheses refer to those in the relevant crystal structures. A fragment of the EP complex shown in the right panel corresponds to the molecular groups of ES contained in the shadowed area in the left panel.

The left panel in Fig. S1 shows several important molecular groups in the enzyme-substrate (ES) complex. The substrate, GTP, is tightly bound in the cavity between Ras and GAP; distances between all oxygen atoms of its terminal phosphate group, O^{1G}, O^{2G}, O^{3G}, and nitrogen atoms of the Ras residues Thr35, Lys16 and Gln61, respectively, indicate typical hydrogen-bond patterns. An important residue from GAP, "arginine finger" Arg789, captures the phosphate groups of GTP and also holds the side chain of Gln61 from Ras in the position favoring the reaction. The hydrogen bonds with the carbonyl groups of Thr35 and Gln61 align the water molecule H_2O for an in-line attack on the terminal phosphate group of GTP. Such arrangement of the reacting species, GTP and H_2O, is beneficial for a low-energy barrier for the cleavage of the O^{3B}-P^G bond in GTP.

A smaller fragment of the model system, corresponding to the enzyme-product (EP) complex, is depicted in the right panel in Fig. S1. We show only the phosphate groups from GDP, the inorganic phosphate, and the side chain of Gln61, i.e., the groups corresponding to those in the shadowed area in the left panel in Fig. S1.

Section S2. Structures of the dark and light states of AppA-BLUF

The computationally derived models for BLUF domains are well consistent with the available crystal structures in the chromophore-binding pockets. For example, Fig. S2 illustrates the computationally obtained [1] geometry parameters of AppA-BLUF compared to the corresponding experimental data.

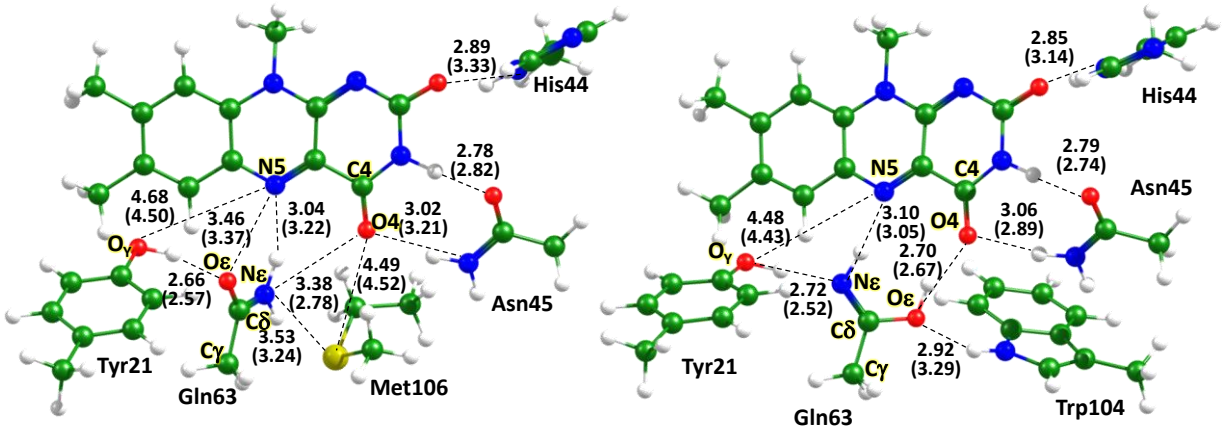

Figure S2. Structures of the dark state (left) and the light state (right) of AppA-BLUF. Distances are given in Å; the values in parentheses refer to the distances in crystals PDB ID 2IYG [2] (left) and PDB ID 1YRX [3] (right).

Section S3. Acetamide-acetamidic acid tautomerization in a small model cluster

Section 3 in the main text describes modeling of the reaction step Int1 → TS2 → Int2 in the Ras-GAP catalyzed hydrolysis of GTP using a model molecular cluster mimicking the enzyme active site. Here we simulate this reaction step even for a smaller cluster composed of two acetamide molecules, metaphosphate (PO_3^-) and a water molecule (left panel in Fig. S3). Calculations at the PBE0/cc-pVTZ level allows us to locate a transition state TS in reactions of proton transfer shown in the top central panel in Fig. S3. The full energy profile connecting the minimum energy points separated by this TS is computed by using the intrinsic reaction coordinate (IRC) method as realized in the Firefly program package. [4]

The results obtained for both cluster models are much alike, showing that the system with the imide tautomer is lower in energy than that with the amide tautomer in this particular environment.

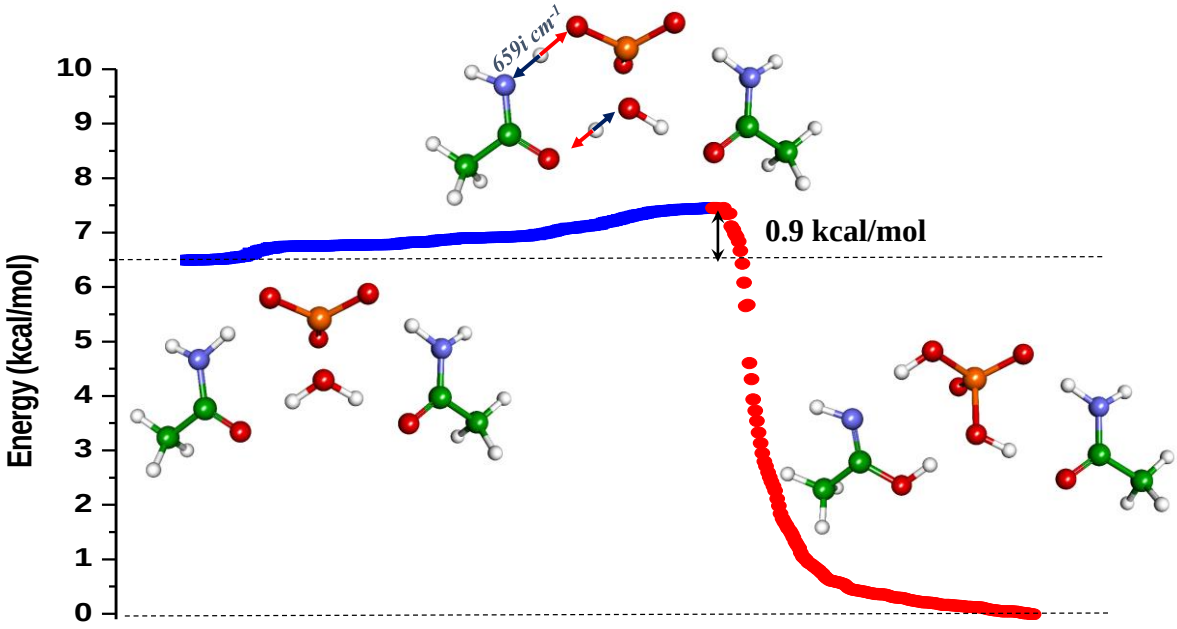

Figure S3. Energy profile for the reaction step Int1 → TS2 → Int2 (see Fig. 2 in the main text) modeled with a small molecular cluster.

Section S4. A protein model system inside the shell of water molecules

To simulate effects of water shells surrounding proteins, model systems analyzed in the present work were inserted into boxes of explicit water molecules. Fig. S4 shows a model system prepared for molecular dynamics simulations in the Ras-GAP-GTP complex.

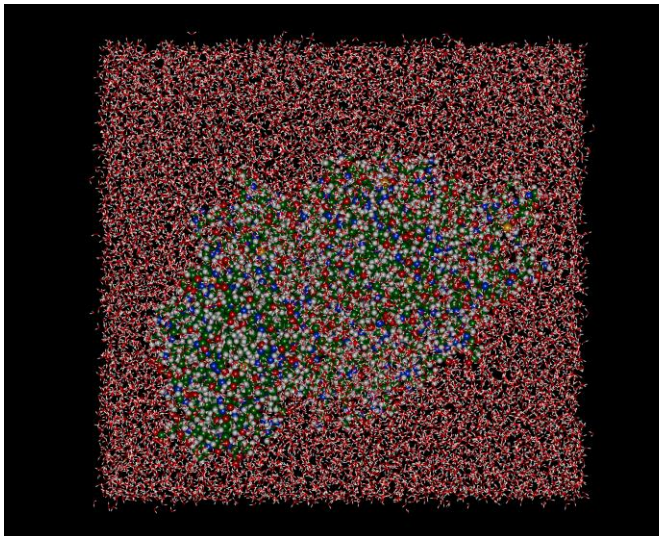

Figure S4. Model system used for molecular dynamics simulations in the Ras-GAP-GTP complex. Protein atoms are shown in balls.

References

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