Agonist dynamics and conformational selection during microsecond simulations of the A_{2A} adenosine receptor

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Supporting Material

FIGURE S1 Error estimation of MSD (σ(MSD) in Table 1) of (A) adenosine and (B) UK432097. There are data for two independent trajectories of each ligand: The first trajectory results are shown in red and the second trajectory results in blue. The estimation was calculated using the blocking approach as described in the main text. The second trajectory of adenosine (blue in (A)) and the first trajectory of UK432097 (red in (B)) show plateaus around 1.51 and 0.07 $Å^2$, respectively, which are estimates for σ(MSD) (see Table 1). The first trajectory of adenosine (red in (A)) and the second trajectory of UK432097 (blue in (B)) show no clear plateaus, indicating an unreliable estimate σ(MSD) for the entire trajectory. As discussed in the main text, performing the same analysis on each half of the trajectories separately yields converged error estimates.

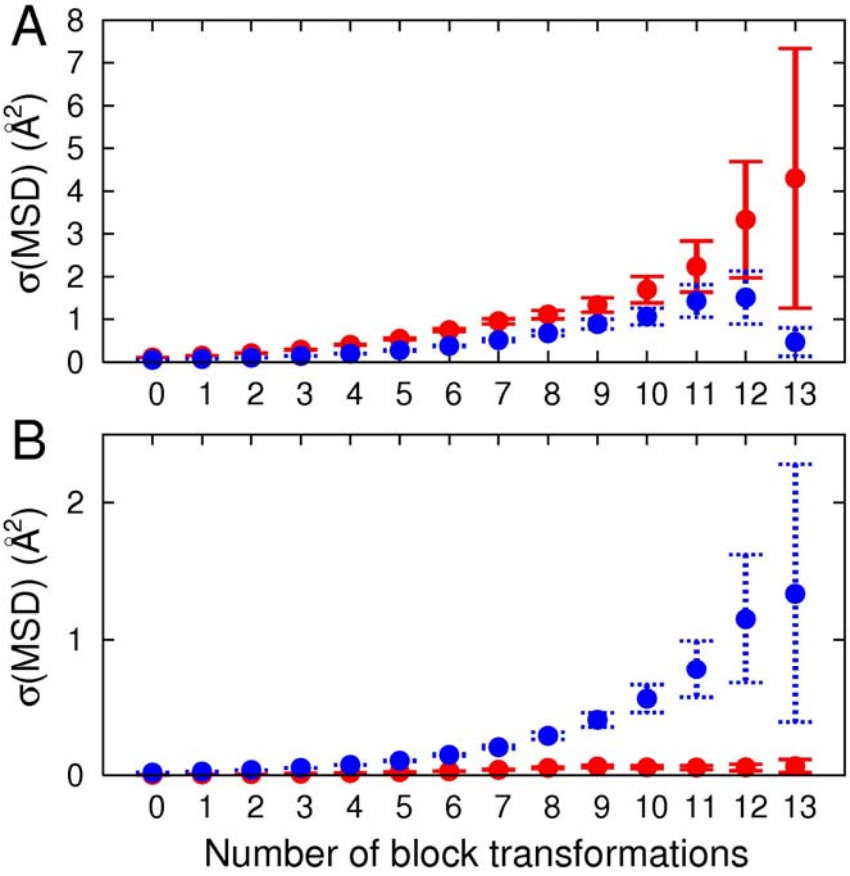

FIGURE S2 Contacts of (A) adenosine and (B) UK432097 with A_{2A} for two independent trajectories. A contact (heavy atom distance less than 4 Å) is indicated by a thin vertical black line, stable contacts appear as horizontal solid black bars. The residues shown in Table 2 are indicated, with residues identified by mutagenesis to be important for ligand binding indicated by an (*), and those that form the binding site for our hypothesized inverted pose indicated by an (†). The vertical arrows indicate the transmembrane helices.

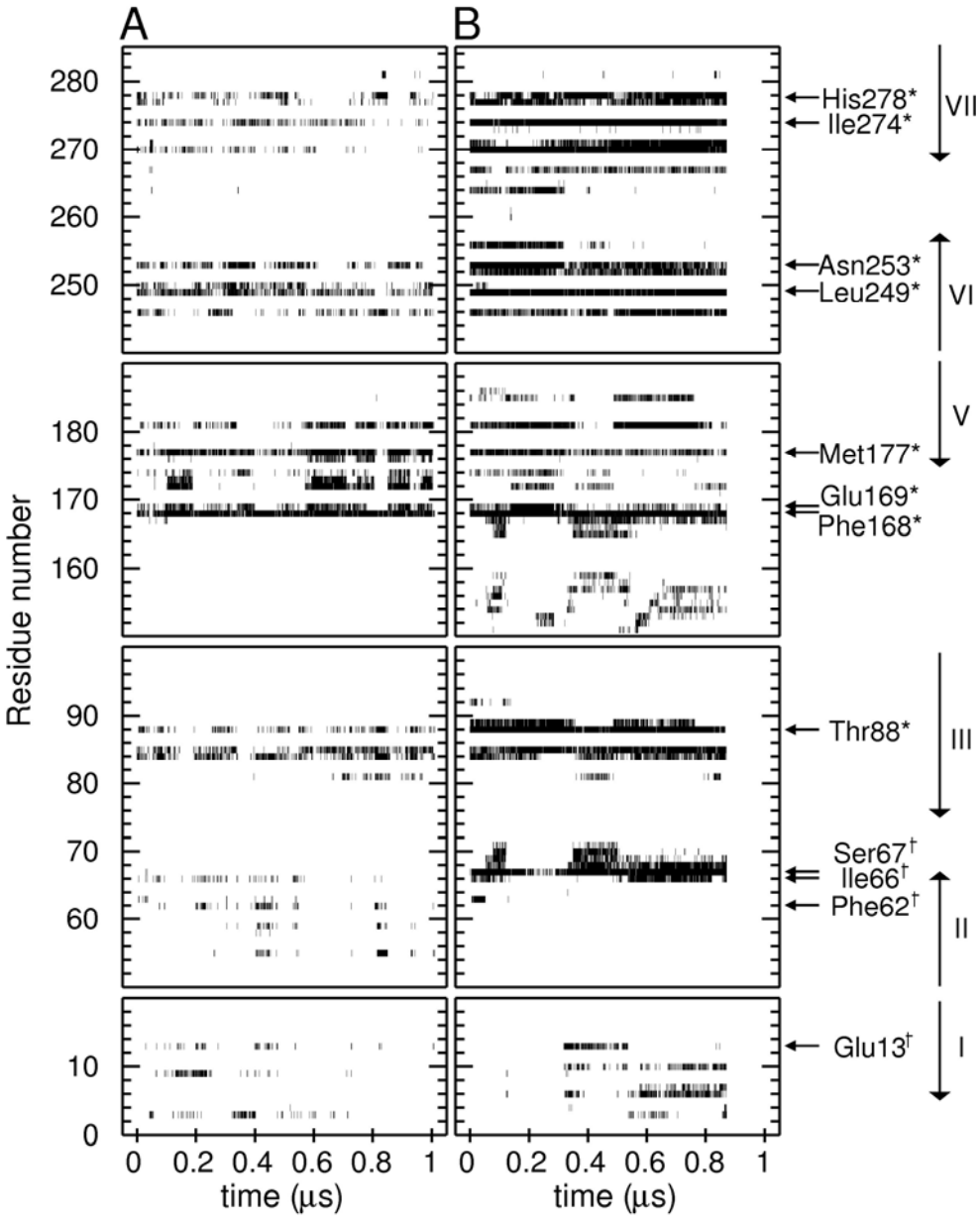

FIGURE S3 Number of water molecules in the ligand binding pocket of A_{2A} with adenosine or UK432097 for two additional independent trajectories.

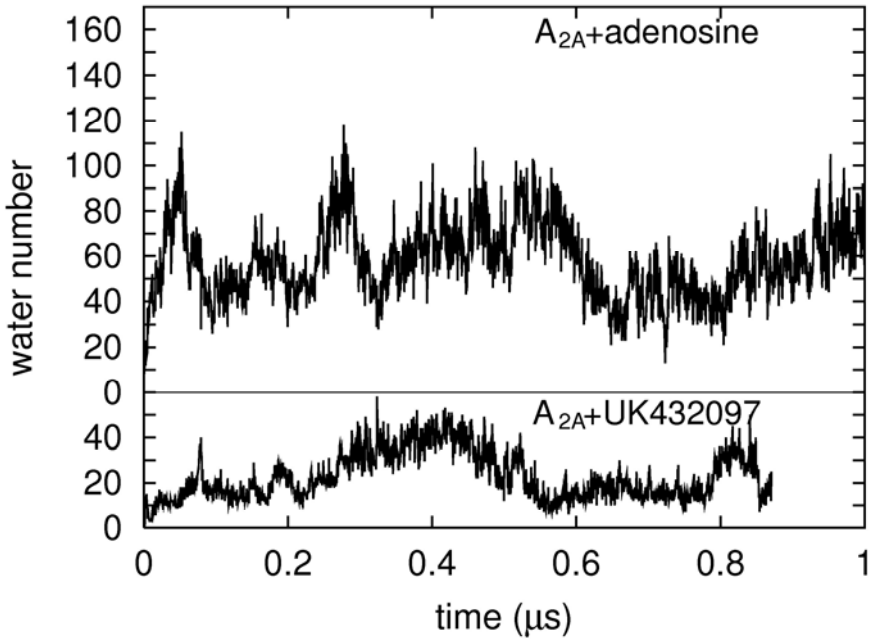

FIGURE S4 Isosurface of water density in the ligand binding pocket of A_{2A} with (A) adenosine or (B) UK432097 for two independent trajectories. The water density is averaged over 0.1-0.9 μsec, and the isosurface with 0.3 of the bulk water density is drawn in green. In each figure, H6 and H7 are marked by VI and VII, respectively, the ligand is shown in red, and Asn253 on H6 and His278 on H7 are shown in blue. The portion buried in isosurface is rendered with thinner lines.