

# Supporting Information

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## SI Text

Animations of structural motions along normal modes 24–27 in B2AR. The brown tube shows the protein backbone, green spheres indicate the ligand binding site, orange spheres indicate the DRY motif (the G-protein binding site), and yellow spheres indicate the assumed  $\beta$ -arrestin binding site. Normal modes 25 (that dominates signaling propagation to the  $\beta$ -arrestin binding

site; Movie S1) and 26 (that dominates signal propagation to the DRY motif; Movie S2) do not appear significantly different from normal modes 24 (Movie S3) and 27 (Movie S4), which are not strongly involved in signal transduction between key allosteric sites. As such, an assessment of site-to-site protein-mediated interactions (Eq. 3 of the article text), rather than simple analysis of normal mode displacements, is essential for assessing allosteric couplings (even when a single mode dominate the allostery).



Movie S1.

[Movie S1 \(MPG\)](#)



Movie S2.

[Movie S2 \(MPG\)](#)



Movie S3.

[Movie S3 \(MPG\)](#)





Movie S4.

[Movie S4 \(MPG\)](#)