



Supplementary information, Fig. S14| Similar to norepinephrine, epinephrine also takes a different binding pathway in the β_1 AR and β_2 AR.

a, The norepinephrine (orange sticks) binding pathway to the β_1 AR revealed by metadynamics simulations. b, The norepinephrine (orange sticks) binding pathway to the β_2 AR revealed by metadynamics simulations. c, The epinephrine (green sticks) binding pathway to the β_1 AR revealed by metadynamics simulations. d, The epinephrine (green sticks) binding pathway to the β_2 AR revealed by metadynamics simulations. e, Convergence of the metadynamics simulations sampling binding pathways for norepinephrine and epinephrine at β_1 AR and β_2 AR. The convergence of metadynamics simulations shown for the sampling of the distance between the core of the receptor (center of mass of V117^{3,36} and W286^{6,48}) and ligand (center of mass of ligand atoms). Convergence is demonstrated by a small change in the free energy surface between different intervals of sampling time.