**Description of Additional Supplementary Files**

File Name: Supplementary Movie 1

Description: The structure of norepinephrine bound dDATmfc morphed over the structure of dopamine bound dDATmfc (PDB id: 4XP1) highlighting the structural changes in the substrate bind pocket. The TM6 linker undergoes an inward movement by 2.4 Å in the dopamine bound state relative to the norepinephrine bound state. This inward movement positions the F325 side-chain closer to dopamine, which is bound in proximity to subsite B relative to norepinephrine, which is bound closer to subsite C. This structural change is accompanied by ~260° flip in the χ1 torsional angle of D46 side chain and a 16° χ2 torsion angle shift in the side chain of D121.