

## Supporting Information

### Examining the Origin of Catalytic Power of Catechol O-Methyltransferase

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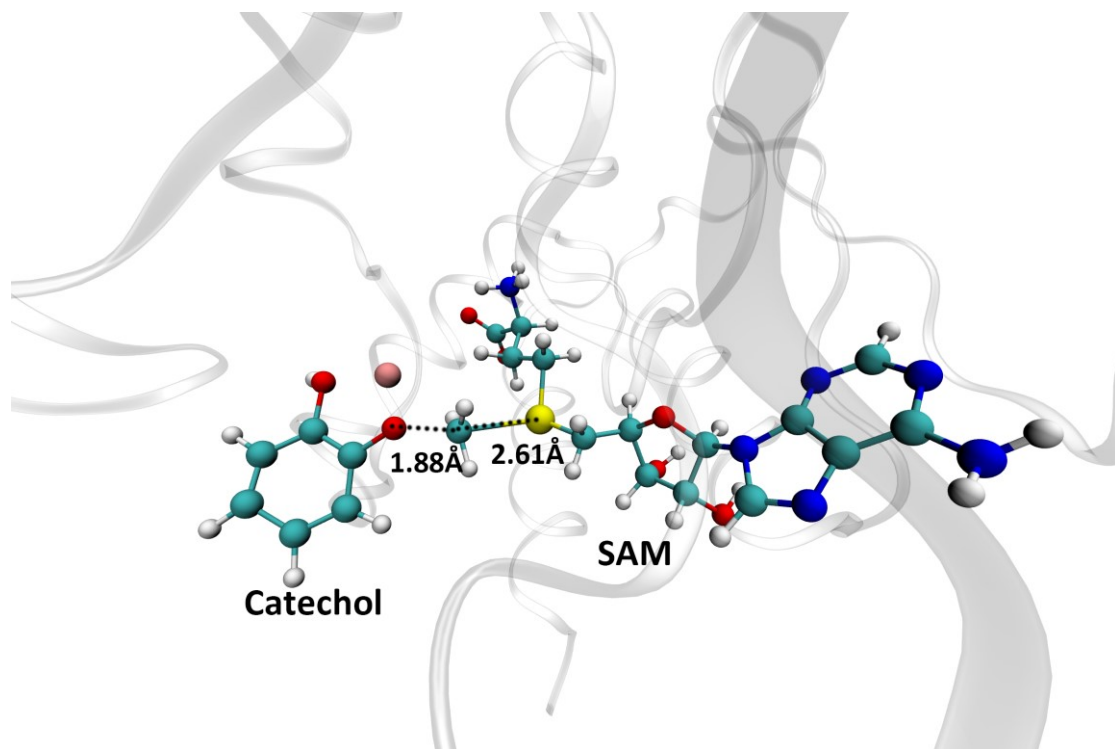
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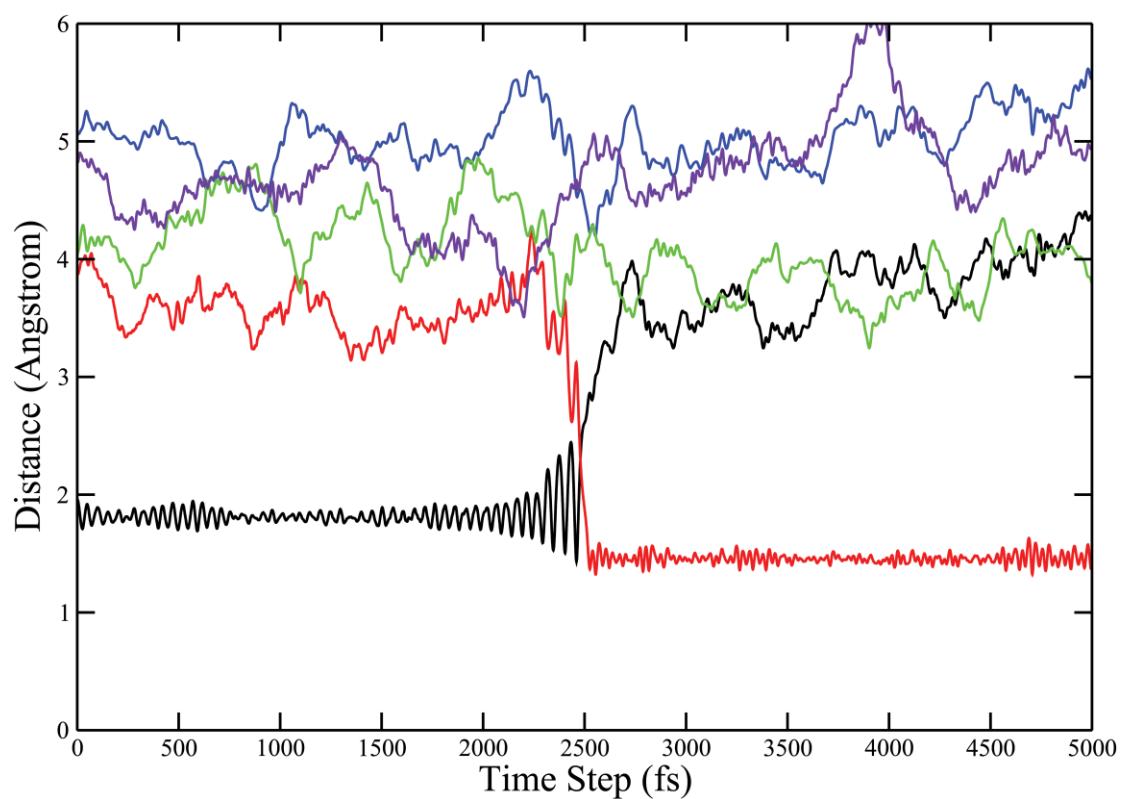
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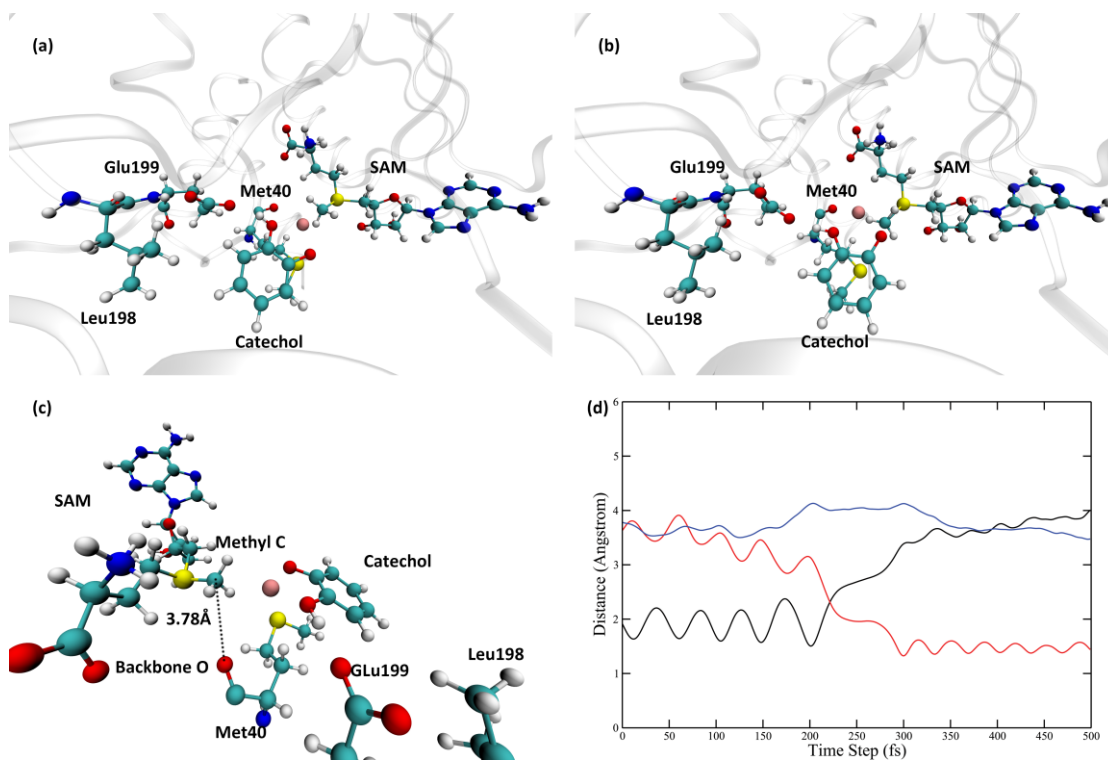
**Figure S1. Transition state structure of the wild type COMT from a representative trajectory**

**Table S1 Average Transition States Structures of Y68A**

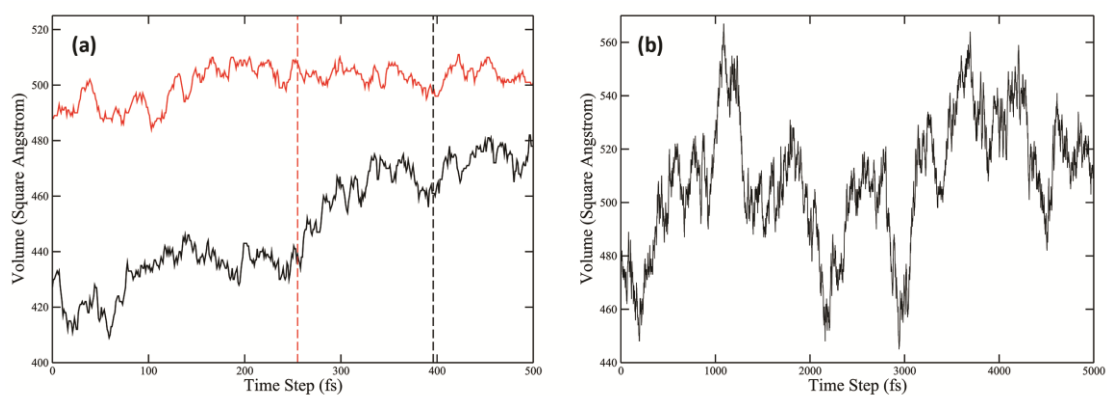
Donor-Methyl Group Distance (Å)	Acceptor-Methyl Group Distance (Å)	Donor-Acceptor Distance (Å)
2.71	1.96	4.59



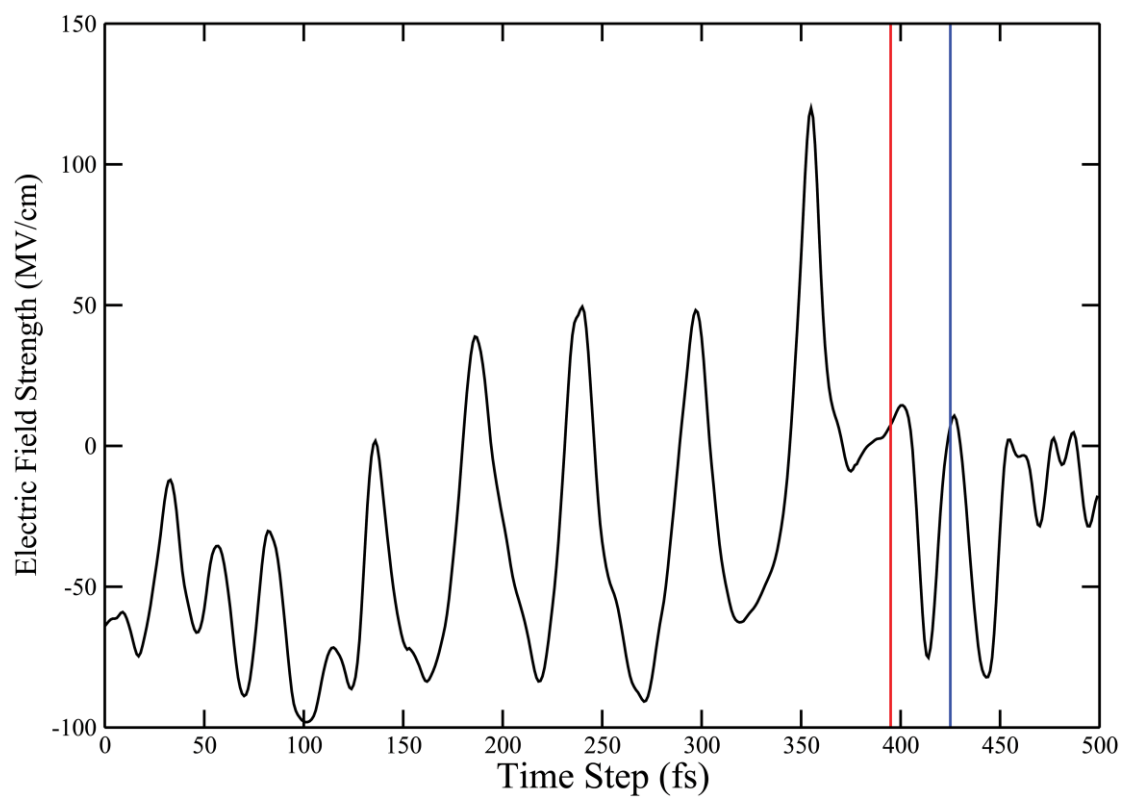
**Figure S2. Reaction progress of a 5000 fs TPS trajectory of the wild type COMT.** Donor-methyl group and acceptor-methyl group distance are shown as the black and red solid lines. The blue solid line is the donor-acceptor distance. The green solid line is the distance between Leu198 C $\gamma$  and catechol C61. The purple solid line is the distance between Tyr68 C $\beta$  and the donor sulfur atom.



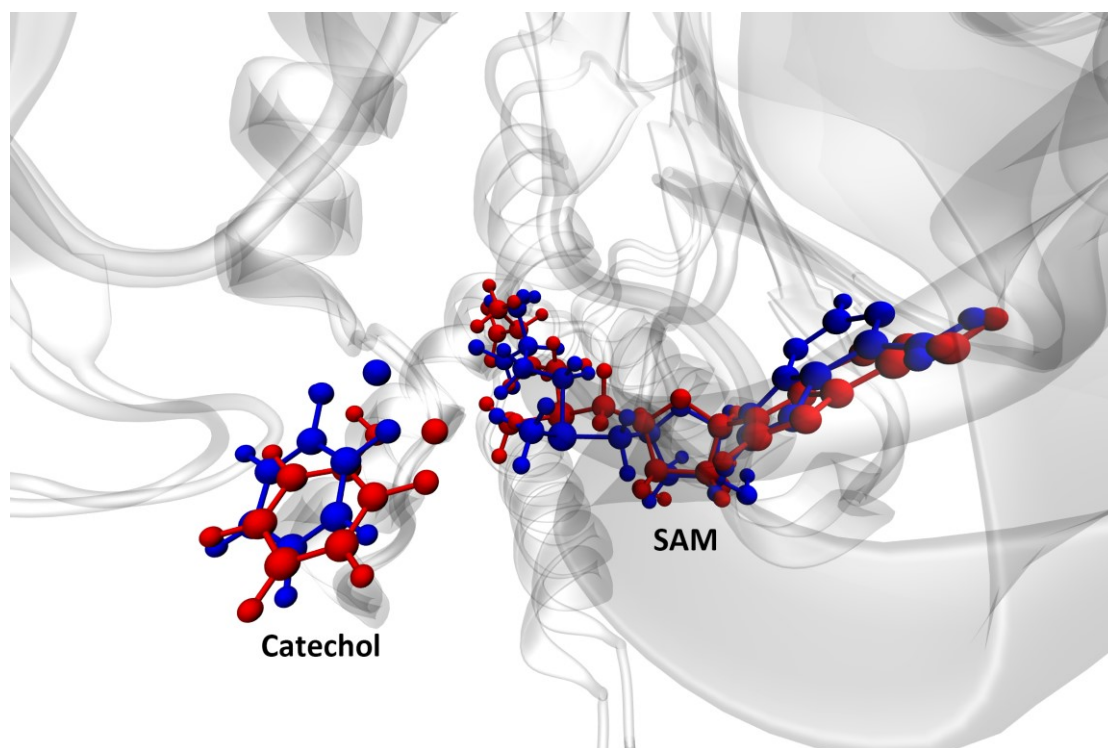
**Figure S3. Reaction Progress in the Y68A Mutant.** Figure S3(a) and S3(b) are the system before and after the change of orientation of the catechol molecule, respectively. Figure S3(c) shows the hydrogen bond between Met40 backbone oxygen and hydrogens on the transferred methyl group. The distance between Met40 backbone oxygen and the transferred methyl group carbon is labeled by the black dashed line. Figure S3(d) shows the distance labeled in Figure S3(c) (blue) along with the donor-methyl group distance (black) and acceptor-methyl group distance (red).



**Figure S4. Volume of the Active Site Calculated by POVME3.** Figure S4(a) shows the volume of the active site along 500fs reactive trajectories of wild type COMT (solid black line) and Y68A mutant (red solid line). Time slice of the transition state of each trajectory were marked by the corresponding dashed line. Figure S4(b) shows the volume of the active site along a 5000fs reactive trajectory of wild type COMT.



**Figure S5. Calculated Electric Field of the Wild Type COMT.** Black solid line indicates the calculated field. Red and blue vertical line represents the transition state and maximum donor-acceptor compression, respectively.



**Figure S6. Overlay of the QM region of wild type COMT and Y68A mutant.** Wild type COMT is displayed in blue, Y68A mutant is displayed in red