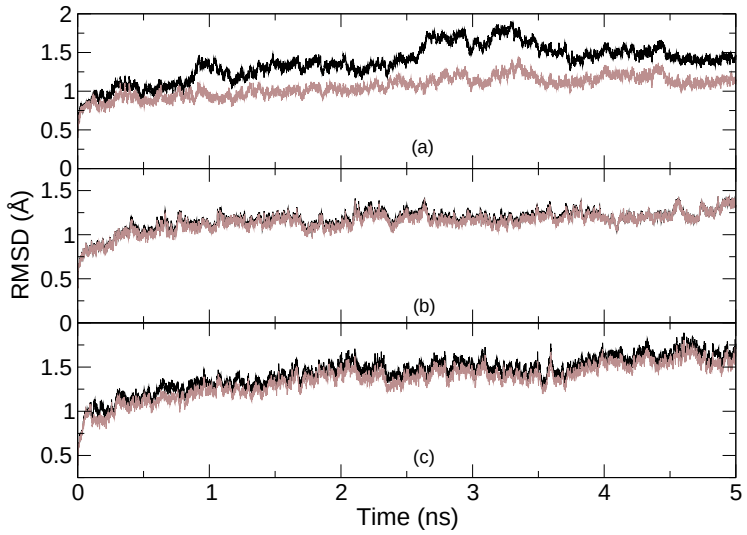
Thermodynamic and Kinetic Stabilities of Active Site Protonation States of a Class C β–Lactamase

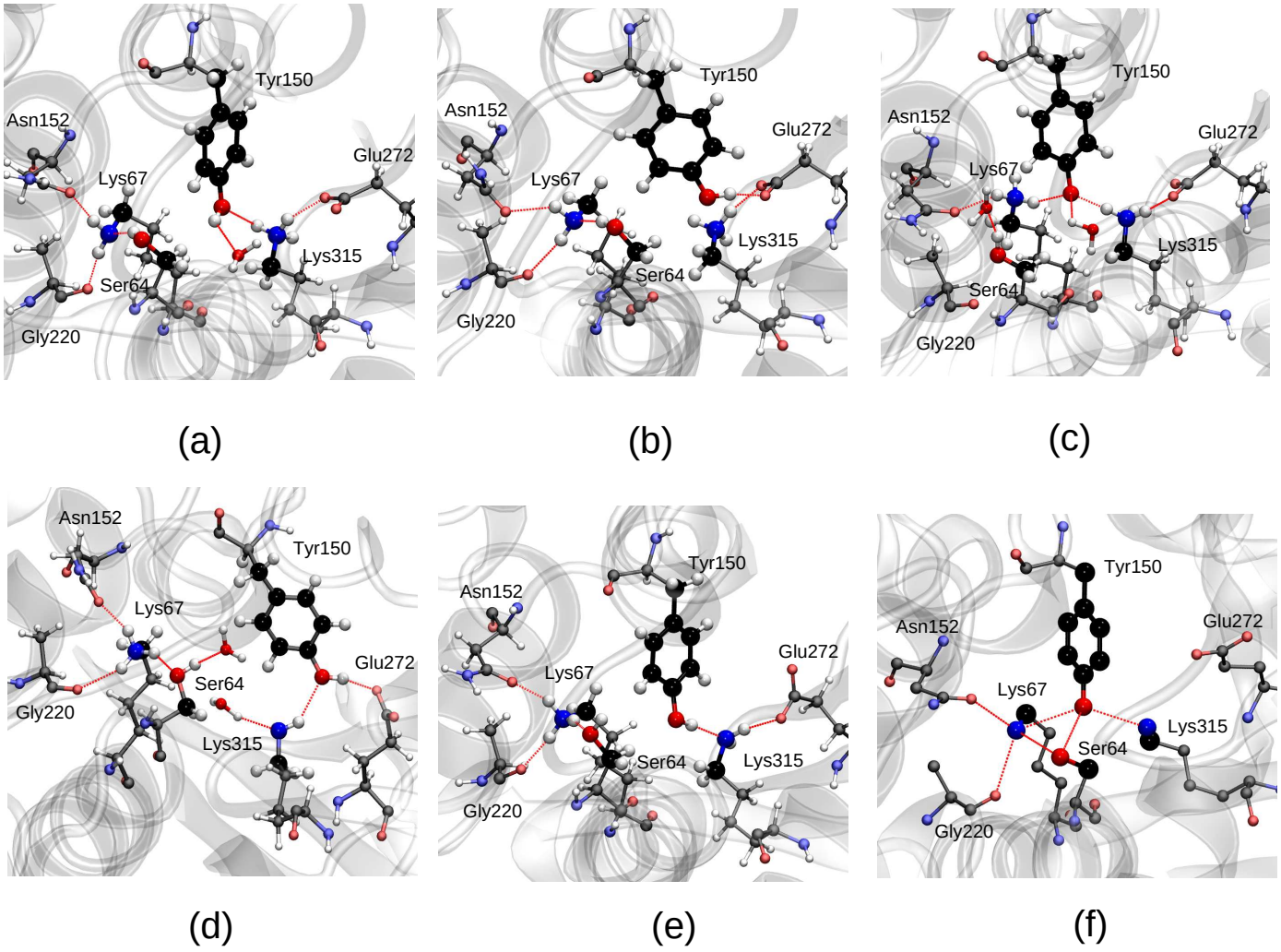
Ravi Tripathi and Nisanth N. Nair

Department of Chemistry Indian Institute of Technology Kanpur, Kanpur, India

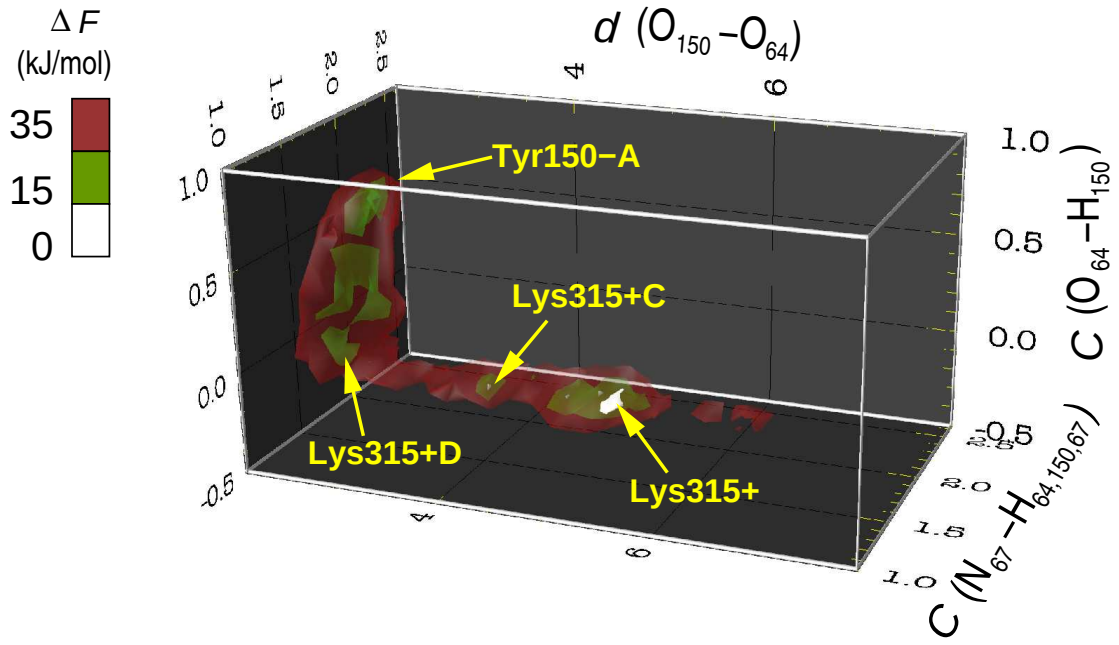
Supporting Information



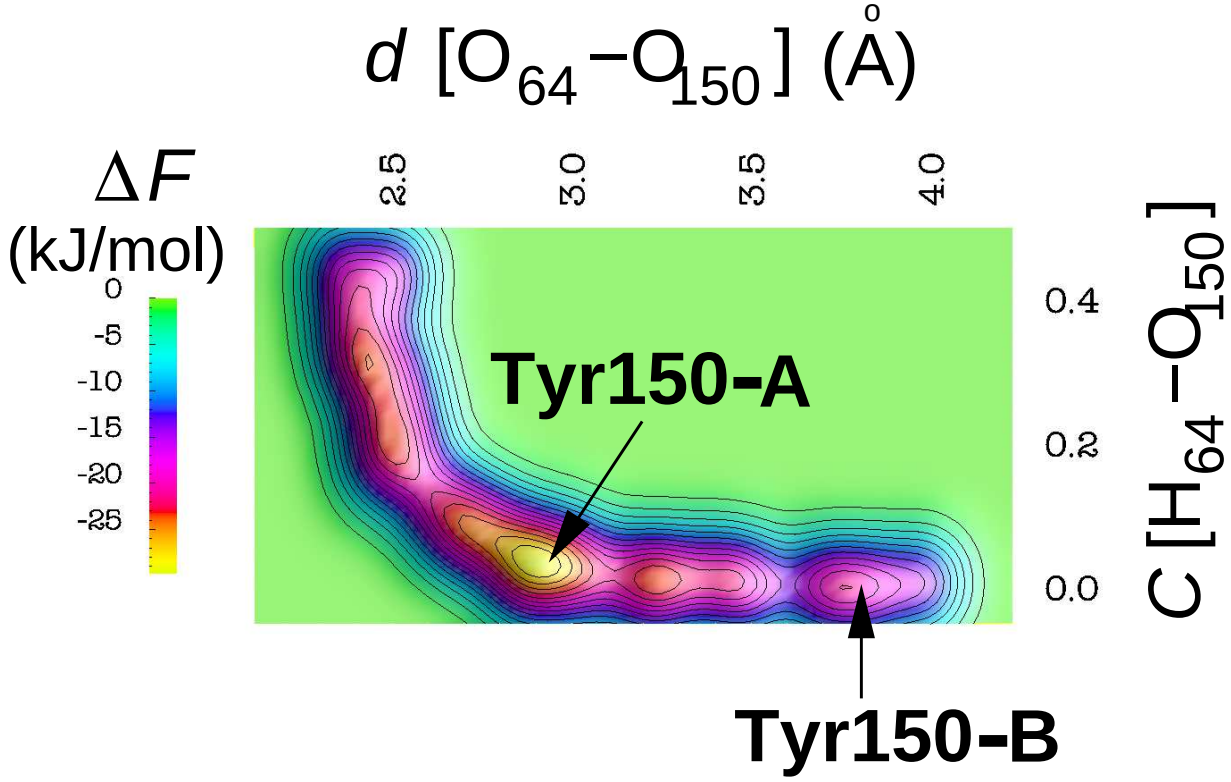
FigSI 1: RMSD of the protein backbone with respect to the starting structure of the NVT simulation during the empirical force field based MD simulation for (a) **Lys315+**, (b) **Tyr150-**, and (c) **Lys67+** protonation states. Black line indicates the RMSD of whole protein whereas brown line is for residues 5-361.



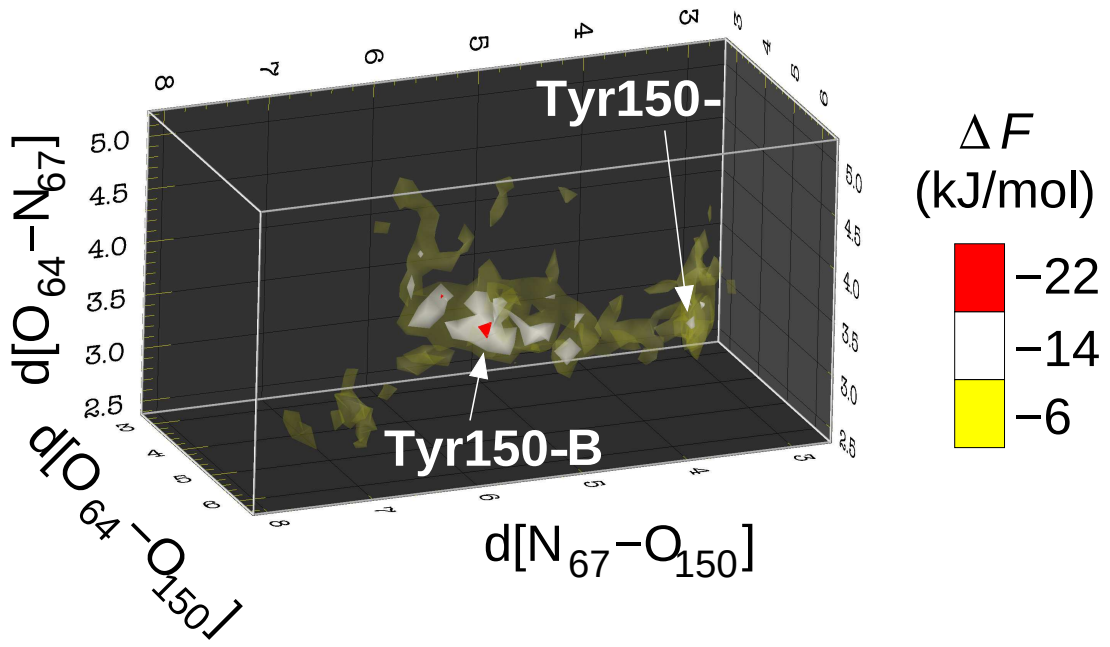
FigSI 2: Average active site structures after *NVT* simulation using empirical force field (a-e) and X–ray crystallographic structure (f). Structures are labeled as (a) **Lys315+**, (b) **Lys315+A**, (c) **Tyr150-**, (d) **Lys67+** (e) **Lys67+A**; see also Figure 5 of the manuscript.



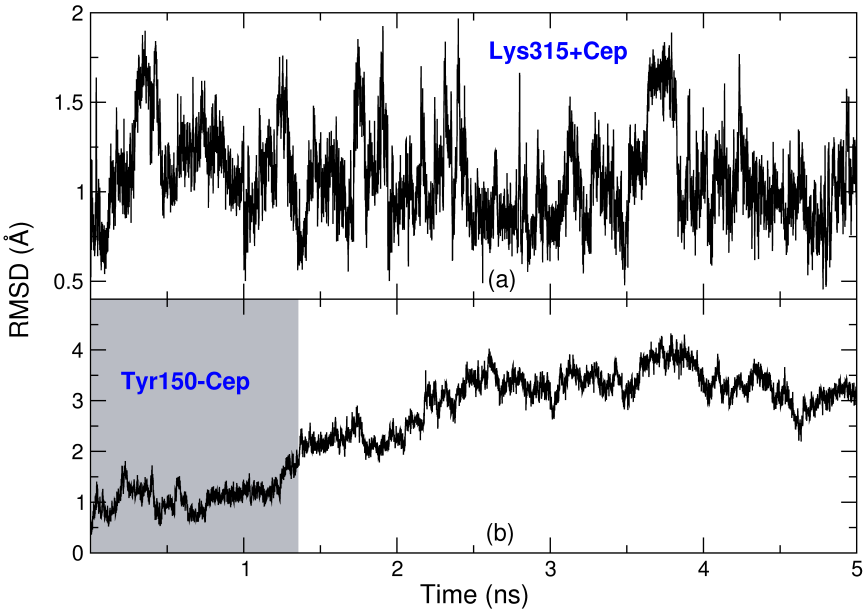
FigSI 3: Four dimensional reconstructed free energy surface for the reaction **Lys315+** → **Tyr150-A**, visualized as a volumetric data for selected isovalues. See Figure 10 of the manuscript for other further details.



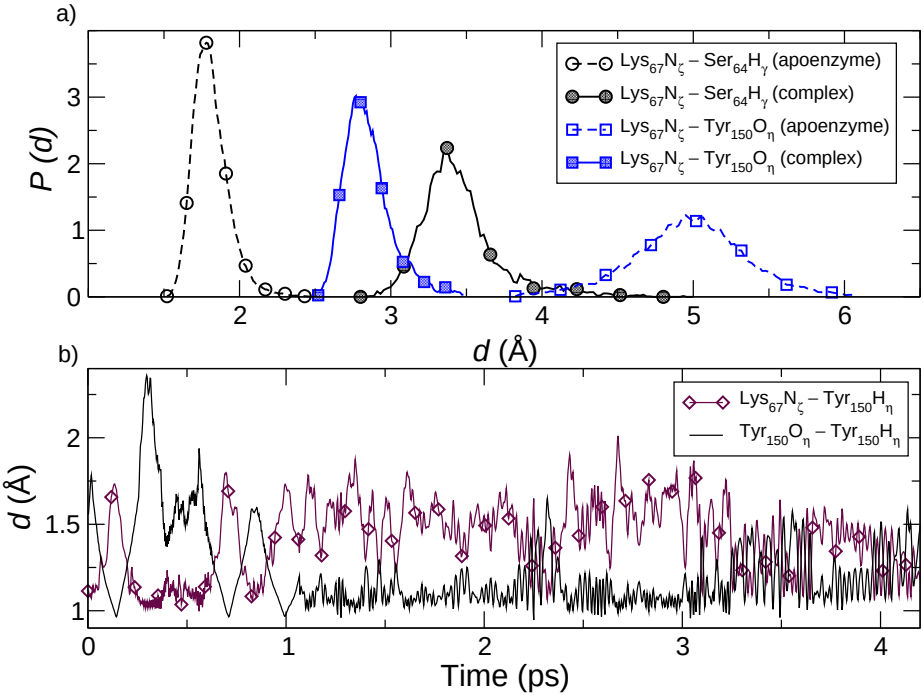
FigSI 4: Four dimensional reconstructed free energy surface for the conversion of **Tyr150-A** to **Tyr150-B** is visualized here as three dimensional surface by making a cut at $d[O_{64} - N_{67}] = 2.70$ Å. See Figure 10 of the manuscript for further details.



FigSI 5: Five dimensional reconstructed free energy surface for the conversion of **Tyr150-B** to **Tyr150-** is visualized here as volumetric data for the cut at $d[\mathrm{O}_{152} - \mathrm{N}_{67}] = 2.84$ Å, for selected isovalues. All the three coordinates are in Å. See Figure 10 of the manuscript for further details.



FigSI 6: RMSD of the active site including cephalothin with respect to the starting structure of the NVT simulation during the empirical force field based MD simulation for (a) **Lys315+Cep**, (b) **Tyr150-Cep** protonation states.



FigSI 7: (a) Distribution of selected distances during the empirical force field simulation for **Lys315+** (dotted line) and **Lys315+Cep** (solid line) protonation state. (b) The distance between $\mathrm{Lys_{67}N_\zeta \cdots Tyr_{150}H_\eta}$ (diamond) and $\mathrm{Tyr_{150}O_\eta \cdots Tyr_{150}H_\eta}$ during the QM/MM canonical ensemble simulation of **Lys315+Cep** protonation state.