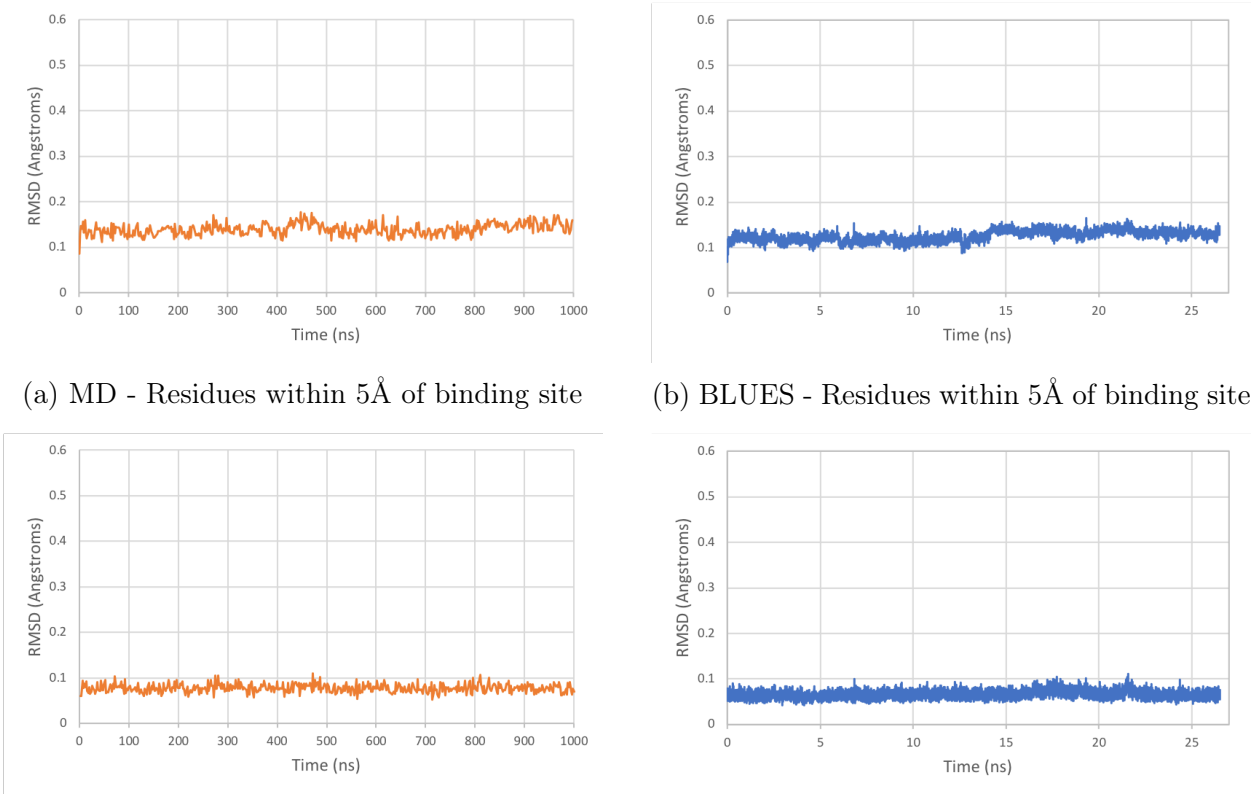
Supplementary Figures: Enhancing Sidechain Rotamer Sampling Using Non-Equilibrium Candidate Monte Carlo



(a) MD - Residues within 5Å of binding site

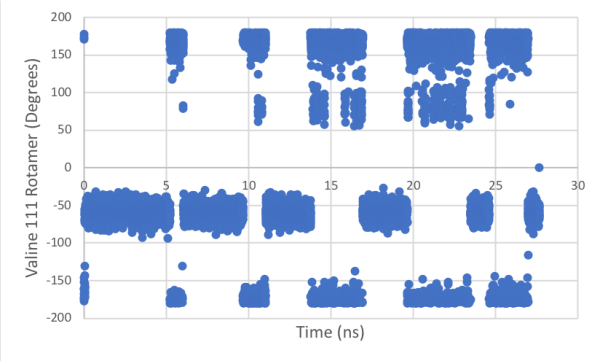
(b) BLUES - Residues within 5Å of binding site

(c) MD - Val111 only

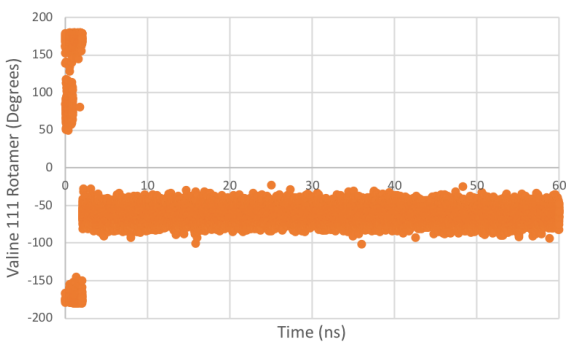
(d) BLUES - Val111 only

Supplementary Figure 1: **RMSDs of T4 lysozyme L99A backbone atoms in BLUES and MD simulations** RMSDs of backbone atoms from the microsecond MD simulation of T4 lysozyme L99A with p-xylene bound are plotted in orange while those from the shorter BLUES simulations are plotted in blue. (*a*) and (*b*) RMSDs of all backbone atoms residues within 5Å of the p-xylene binding site. (*c*) and (*d*) RMSDs of backbone atoms from Val111.

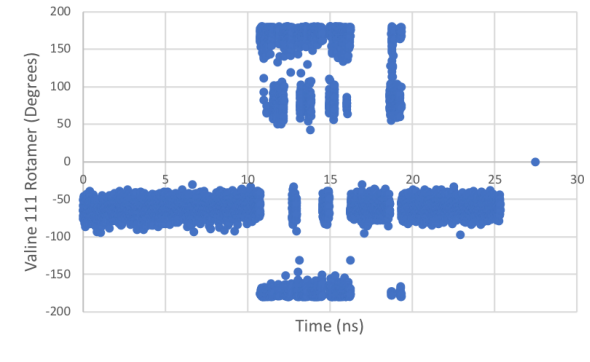
Val111 χ_1 Transitions: Comparison of Starting Conformations



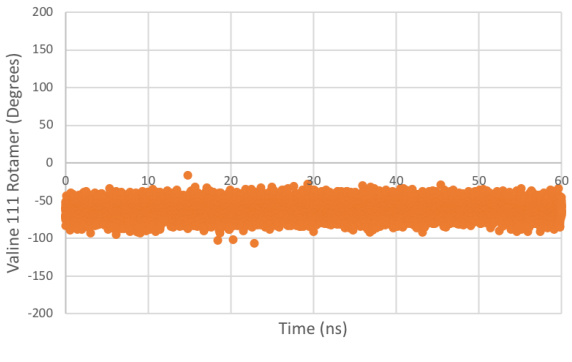
(a) Val111 χ_1 rotamers: BLUES [T0]



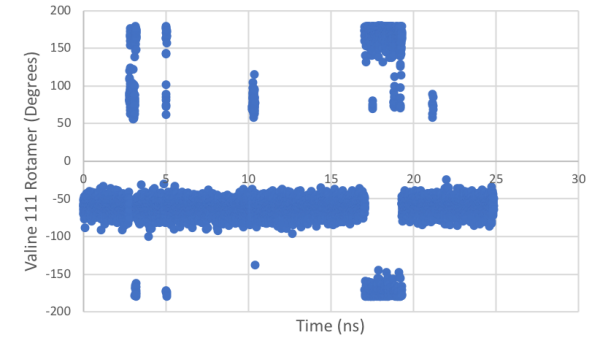
(b) Val111 χ_1 rotamers: MD [T0]



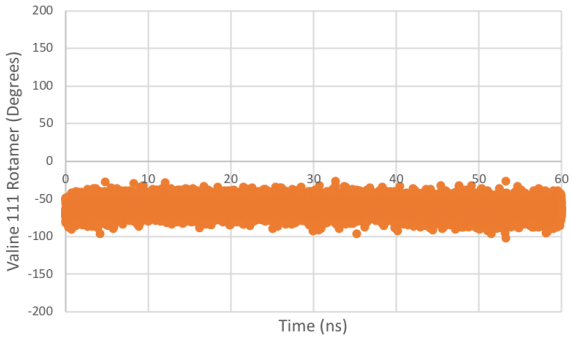
(c) Val111 χ_1 rotamers: BLUES [T250]



(d) Val111 χ_1 rotamers: MD [T250]



(e) Val111 χ_1 rotamers: BLUES [T1000]



(f) Val111 χ_1 rotamers: MD [T1000]

Supplementary Figure 2: **Val111 χ_1 rotamer data for BLUES and MD simulations of p-xylene bound T4 lysozyme L99A in explicit solvent from three starting states.** The BLUES simulations are plotted in blue (a,c,e) and the MD simulations are plotted in orange (b,d,f). (a) and (b) These simulations started from the initial input files generated from the p-xylene bound T4 lysozyme L99A crystal structure. The BLUES simulation was 27.7ns, with 23.9×10^6 FEs, and a total of 91 rotamer transitions. The MD simulation was 60ns, with 30×10^6 FEs, and a total of 15 rotamer transitions. (c) and (d) These simulations started from a snapshot of p-xylene bound to T4 lysozyme L99A after 250ns of MD simulation. The BLUES simulation was 25.3ns, with 22.7×10^6 FEs, and a total of 47 rotamer transitions. The MD simulation was 60ns, with 30×10^6 FEs, and 0 observed rotamer transitions. (e) and (f) These simulations started from a snapshot of p-xylene bound to T4 lysozyme L99A after 1 µs of MD simulation. The BLUES simulation was 24.8ns, with 22.5×10^6 FEs, and a total of 30 rotamer transitions. The MD simulation was 60ns, with 30×10^6 FEs, and 0 observed rotamer transitions.