Supporting Information for

"Machine Learning Based Implicit Solvent Model for Aqueous–Solution Alanine Dipeptide Molecular Dynamics Simulations"

(18 January 2023)

TABLE S1. Parameters used for the simulation of explicit solvent and vacuum simulations for alanine dipeptide.

System	alanine dipeptide	
Solvation	Explicit	Vacuum
Software	PMEMD	SANDER
Force Field	AMBER ff14SB	AMBER ff14SB
Water model	TIP3P	—
Integrator	Langevin	Langevin
Temperature (K)	300	300
Friction constant (ps^{-1})	0.1	5
Nonbond cutoff (nm)	0.8	—

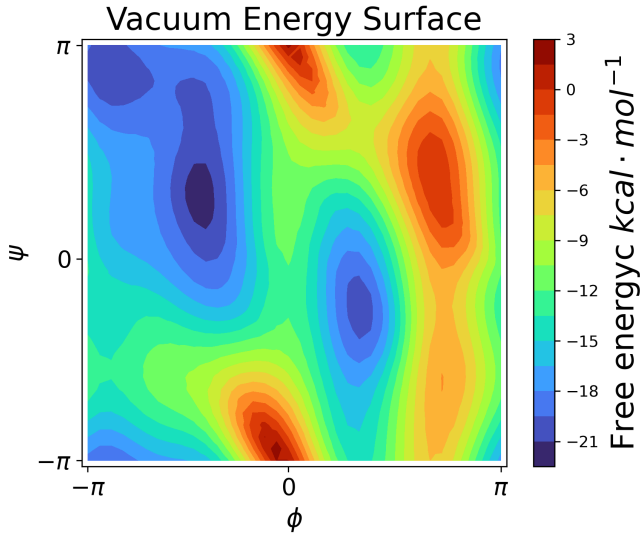

FIG. S1. Energy surface of energy-optimized configurations of alanine dipeptide in the vacuum.

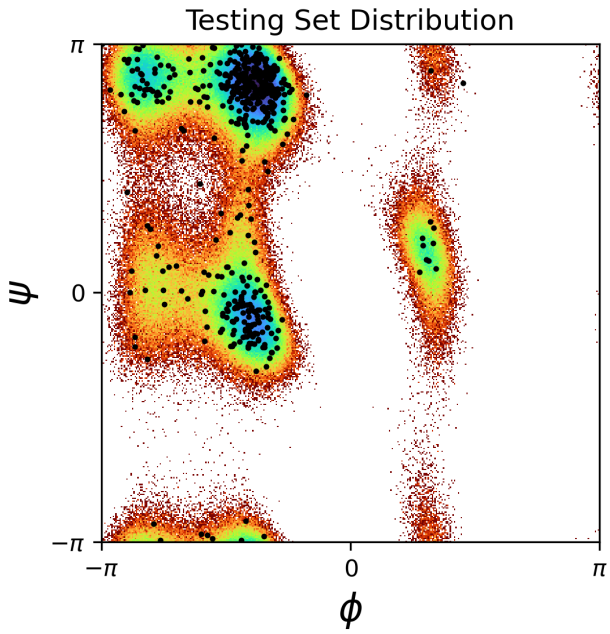

FIG. S2. The distribution of testing set configurations. The configuration locations are indicated by the black dots.

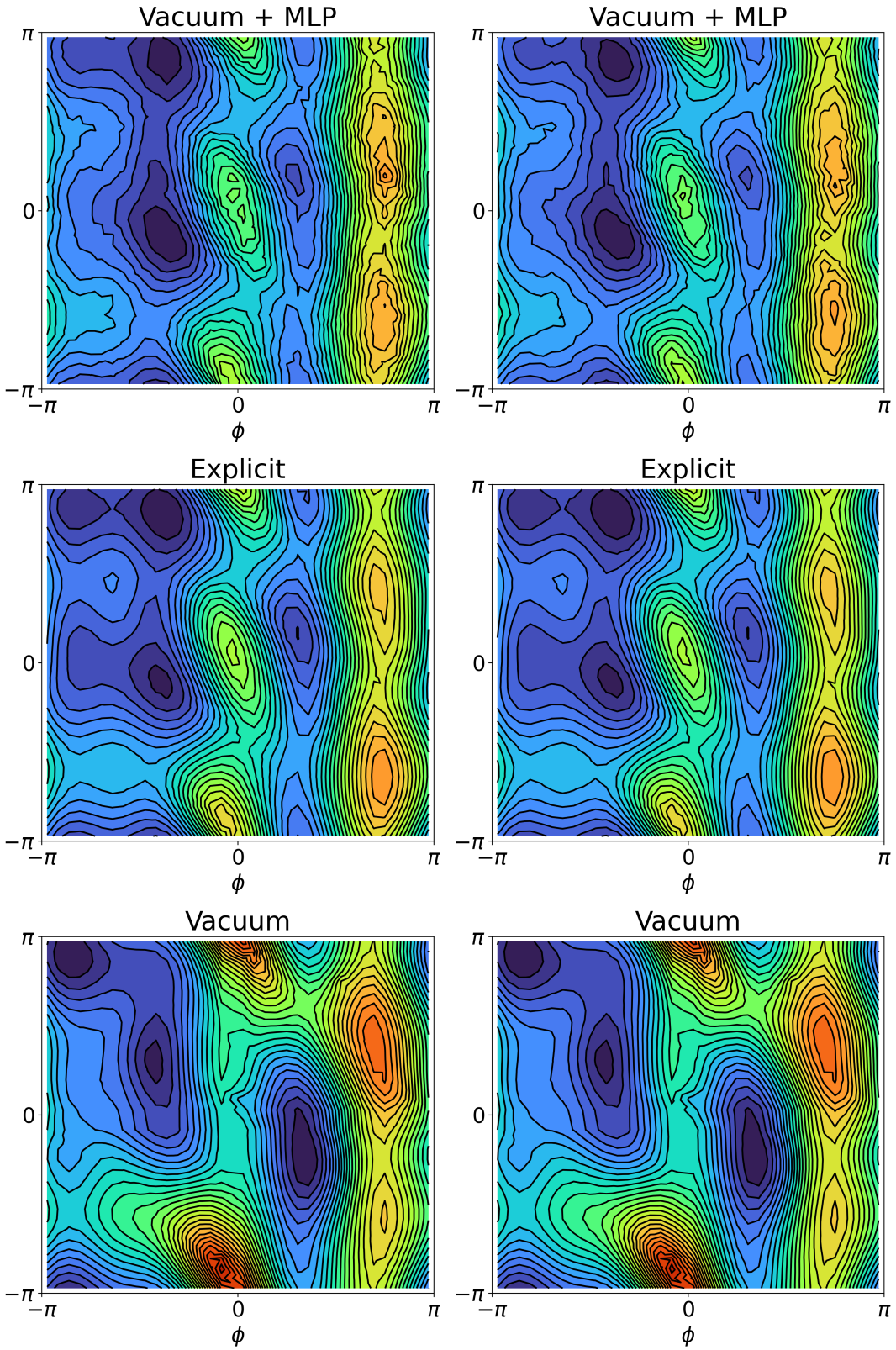

FIG. S3. Free energy surfaces of solvated alanine dipeptide based on umbrella sampling configurations from the 100-300 ps trajectory (left column) and 300-500ps (right column). The first 100 ps of each trajectory was treat as the equlibration stage.

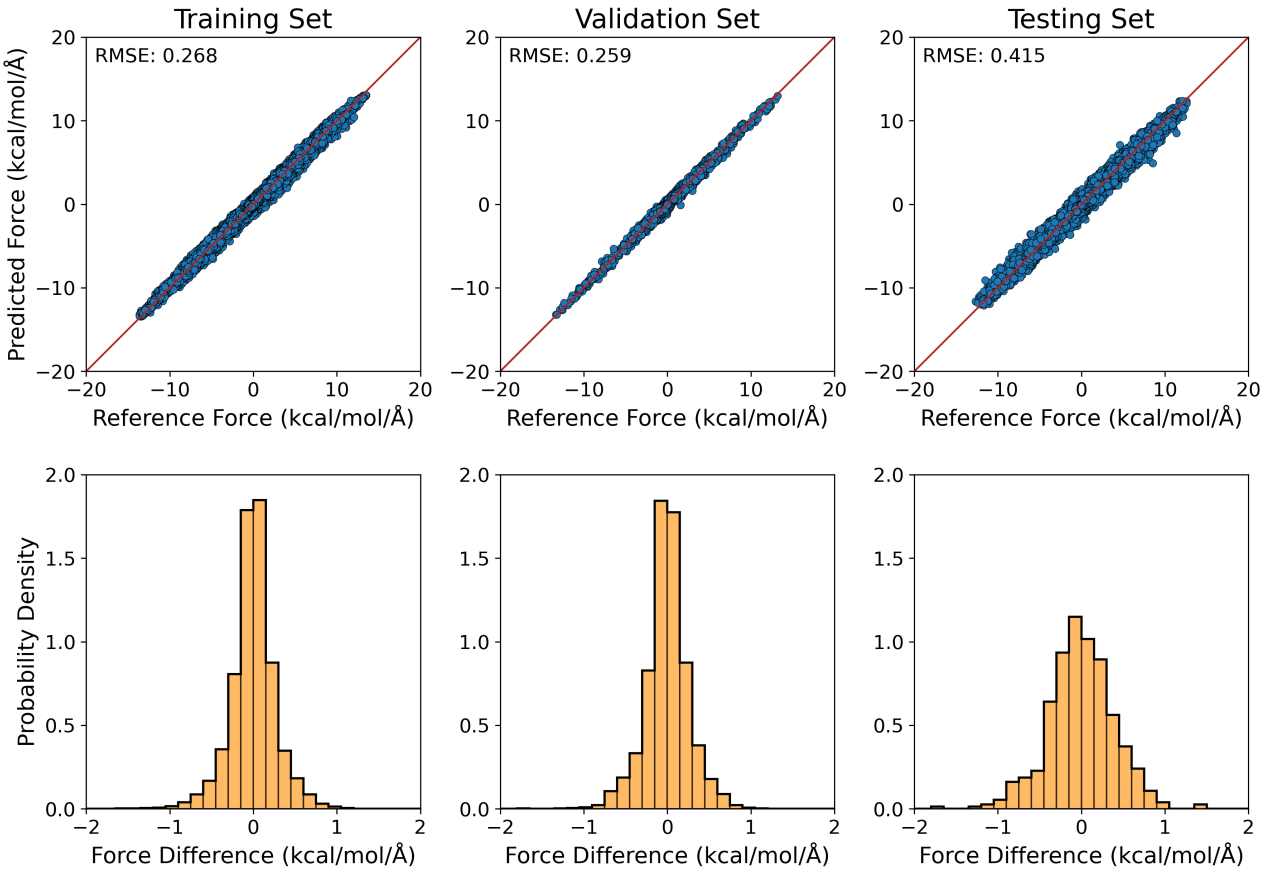

FIG. S4. ML-predicted solvation forces acquired for gas-phase-energy-minimized solute structure within their ASEC environment. Top: ML-predicted solvation forces versus reference values (in kcal/mol/Å) for the training, validation, and testing sets, which consist of 1245, 51, and 500 configurations, respectively. Bottom: the distribution of errors in the ML-predicted forces.

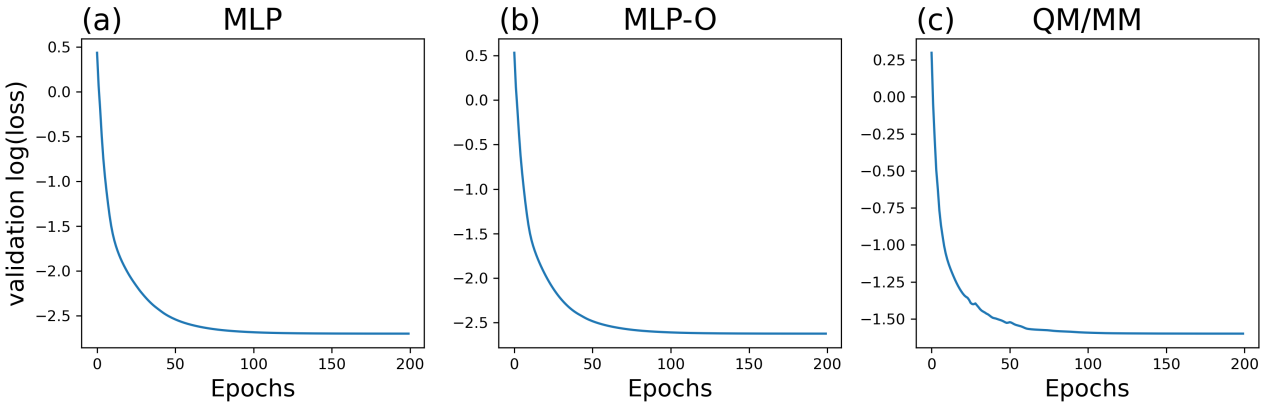

FIG. S5. Decay of the loss function of the validation set during the training of different models: (a) MLP, (b) MLP-O, (c) QM/MM.

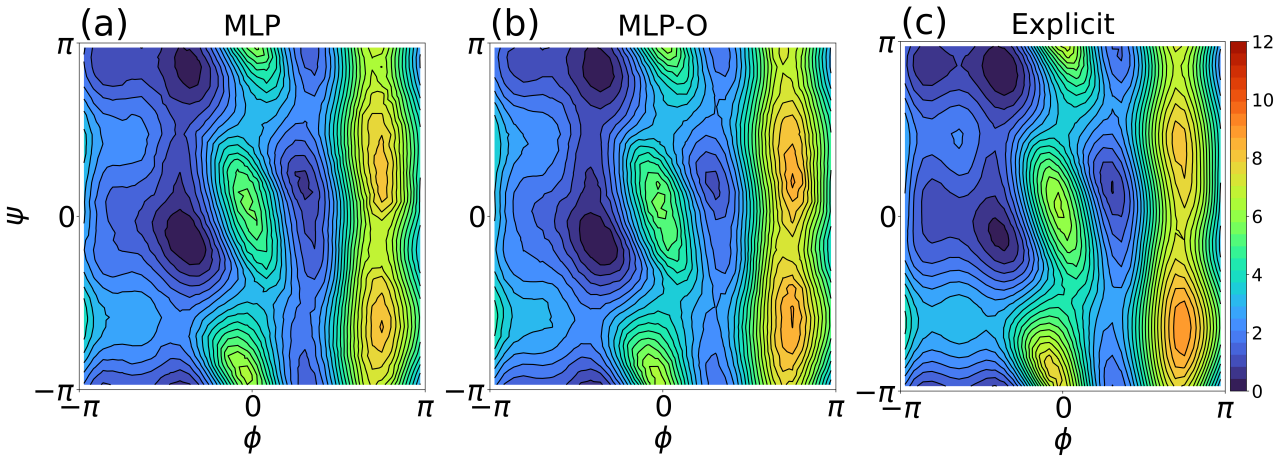

FIG. S6. Free energy surface of solvated alanine dipeptide using (a) MLP, (b) MLP-O, and (c) explicit solvent models.

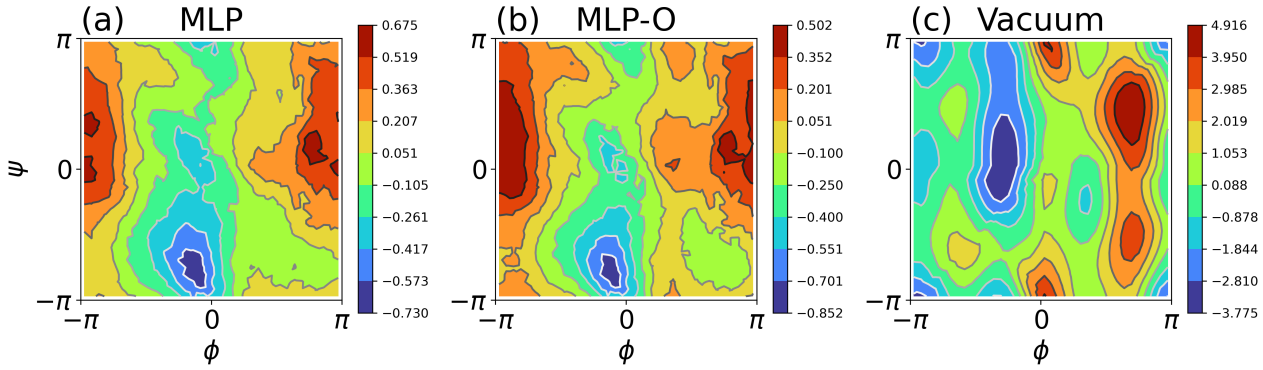

FIG. S7. Difference in (a) MLP, (b) MLP-O, and (c) vacuum free energy surfaces against the explicit-solvent model. All values are in kcal/mol.