

Methods

The receptor was prepared with PDBFixer, where the structure required no rebuilding. Protonation states at pH 7.4 were assigned with PROPKA through PDB2PQR, which also chose each histidine's tautomer and flipped Asn, Gln and His side chains where that improved hydrogen bonding, and hydrogens were added to match. The system was solvated in a truncated octahedral box of OPC water with 1.20 nm of padding, neutralized, and brought to 150 mM NaCl, giving a final system of 23,106 atoms containing 5,232 water molecules. The Amber ff19SB force field was used for the protein. LIG was described by OpenFF Sage 2.2.0, with partial charges from the OpenFF NAGL model `openff-gnn-am1bcc-1.0.0.pt`. Following L-BFGS energy minimization, the system was heated from 50 K to 300 K over 100 ps at constant volume, equilibrated for a further 3.9 ns at constant pressure, and then simulated under NPT at 300 K and 1 bar for 20 ns using a 2 fs timestep with constraints on all bonds involving hydrogen. Long-range electrostatics were treated with particle mesh Ewald and a 1.0 nm real-space cutoff.

Software and data

- 1 Simulation engine: OpenMM 8.6.1. Eastman P. et al., *J. Phys. Chem. B* (2024).
- 2 Preparation: PDBFixer 1.12.0. Eastman P. et al., OpenMM ecosystem.
- 3 Protonation: PROPKA 3.5.1 through PDB2PQR 3.6.1, which chose each titratable residue's state, each histidine's tautomer and the Asn, Gln and His flips. Olsson M. H. M. et al., *J. Chem. Theory Comput.* (2011); Søndergaard C. R. et al., *J. Chem. Theory Comput.* (2011); Jurrus E. et al., *Protein Sci.* (2018); Dolinsky T. J. et al., *Nucleic Acids Res.* (2007).
- 4 Protein: Amber ff19SB, as OpenMM's `amber19-all.xml`. Tian C. et al., *J. Chem. Theory Comput.* (2020).
- 5 Water and ions: OPC, with the Li–Merz 12-6 ions for it, as OpenMM's `amber19/opc.xml`. Izadi S. et al., *J. Phys. Chem. Lett.* (2014).
- 6 Ligand parameters: OpenFF Sage 2.2.0 (`openff-2.2.0.offxml` in `openff-forcefields 2026.09.0`, <https://github.com/openforcefield/openff-forcefields>), © 2016 Open Forcefield Group, licensed under CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>) and provided without warranty. Assigned to LIG in this system by the OpenFF Toolkit 0.19.0 and `openmmforcefields 0.16.0`; `system.xml` holds them as assigned. Boothroyd S. et al., *J. Chem. Theory Comput.* (2023).
- 7 Partial charges: the OpenFF NAGL model `openff-gnn-am1bcc-1.0.0.pt` (`openff-nagl-models 2026.09.0`, <https://github.com/openforcefield/openff-nagl-models>), © 2023 Open Forcefield Group, licensed under CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>) and provided without warranty. Its charges for LIG, computed by OpenFF NAGL 0.6.1, are in `system.xml`.

Reproducibility

Plan hash 94e69e387b0f71f7. Every parameter is in `system.json`. Regenerating this bundle from the same inputs and the same hash yields byte-identical topology.