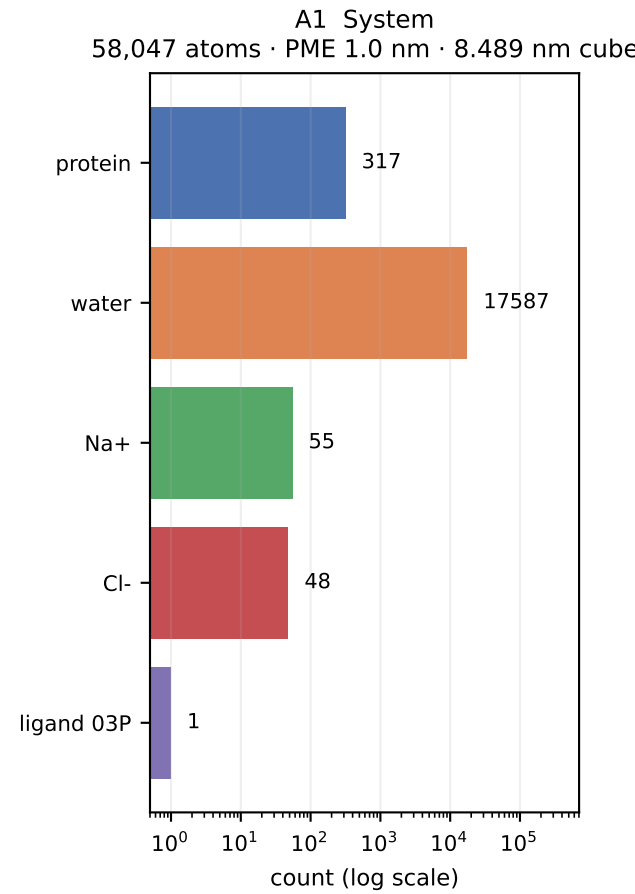


A What was actually simulated — system composition (A1: protein counted in residues; water, ions and ligand in molecules), protocol (A2) and preparation evidence (A3)



A2 Protocol – source chapter (T019) vs this run

|              |                         |              |
|--------------|-------------------------|--------------|
| force fields | amber14-all + tip3pfb   | names reused |
| ligand FF    | GAFF 2.2.20 + AM1-BCC   | REGENERATED  |
| water model  | TIP3P, rigid (default)  | same         |
| nonbonded    | PME, 1.0 nm cutoff      | same         |
| integrator   | Langevin 300 K, 1/ps    | same         |
| timestep     | 2 fs, standard H masses | same         |
| barostat     | none -> NVT ensemble    | same         |
| solute X-H   | HBonds (source: unset)  | ADAPTED      |

Provenance

- UPSTREAM coordinates were REUSED as the starting structure;
- ligand parameters were REGENERATED (the source System XML was never shipped) – force-field NAMES match, the parameter set does not;
- the source set no explicit SOLUTE constraint. That is NOT the same as rigid water being unconstrained: TIP3P is rigid by engine default;
- the physical model is therefore not bit-identical, so differences from the upstream trajectory cannot be attributed to sampling alone.

A3 Preparation checks

|                   |                |
|-------------------|----------------|
| formula           | C26H25ClF3N5O3 |
| CCD 03P           | TAK-285        |
| InChIKey match    | True           |
| atoms mapped      | 63/63          |
| bond disagreement | 0              |
| min lig-prot dist | 0.190 nm       |
| System atoms      | 58,047         |
| constraints       | 55,360         |

Chemical state used for parameterisation was matched to RCSB CCD 03P (TAK-285): same InChIKey, all atoms mapped, no genuine bond disagreement.