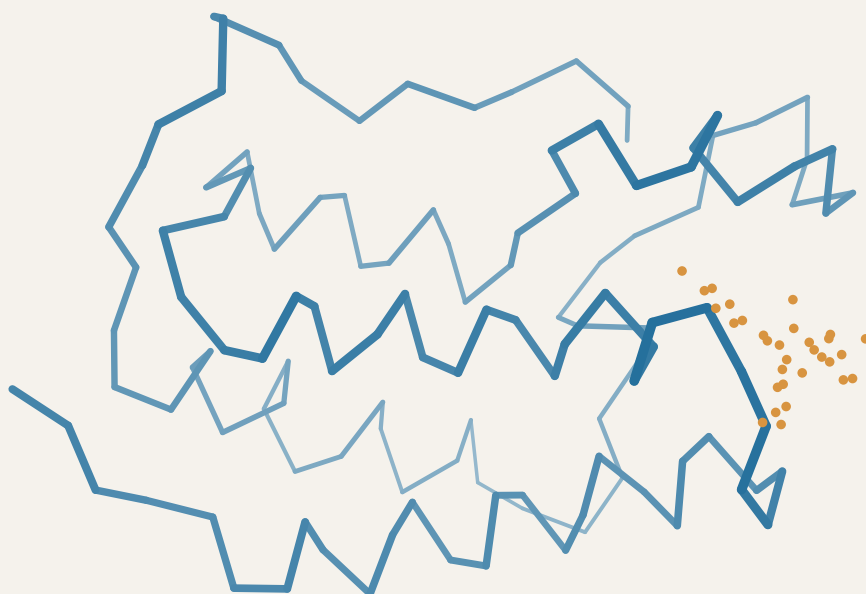


Example study: does JQ1 stay in the predicted BRD4 BD1? (2×20 ns)

JQ1 shifted — in 2 of 2 replicas: it ended 2.5 and 3.9 Å from its starting pose (peaks 3.5 and 6.9 Å). That is a change of pose rather than a leaving event; look at the trajectory before treating the starting pose as the bound one. In replica 2 it reached 6.9 Å, past the 5 Å at which it would count as having left, before coming back to 3.9 Å.



The fold at the end of replica 1: C-alpha trace, nearer is darker

Structure	JQ1 · pose 1 (docked) · predicted model
System	1 chain, 125 residues · LIG
Force field	ff19SB · OPC water
Simulation	20 ns × 2 replicas at 300 K, 2.0 fs steps
Solvent	octahedron, 1.2 nm padding, 150 mM Na ⁺ /Cl ⁻
Run	0c53b82d-43fd-488b-aac7-795398bec64c
Finished	14 October 2026
Prepared for	John

THE ANSWER

Example study: does JQ1 stay in the predicted BRD4 BD1? (2 × 20 ns)

JQ1 shifted — in 2 of 2 replicas: it ended 2.5 and 3.9 Å from its starting pose (peaks 3.5 and 6.9 Å). That is a change of pose rather than a leaving event; look at the trajectory before treating the starting pose as the bound one. In replica 2 it reached 6.9 Å, past the 5 Å at which it would count as having left, before coming back to 3.9 Å. Backbone RMSD ends at 1.30 Å (max 1.38) over 100 frames. Fold is stable on this timescale.

BACKBONE RMSD, END	JQ1 RMSD, END	MOST MOBILE	SIMULATED
1.30 Å	2.5–3.9 Å	PRO52	40 ns
mean of 2 replicas 1.44 ± 0.19 Å	max 6.9 Å from its starting pose, 2 replicas	RMSF 1.64 Å	2 replica(s), 100 frames each

What the run found

- Temperature held at 300.3 K (sd 2.2, range 292-307). Thermostat is controlling.
- Box volume moved +0.02% between the first and last third (176.4 to 176.4 nm³). Density has settled.
- Backbone RMSD ends at 1.30 Å (max 1.38) over 100 frames. Fold is stable on this timescale.
- Most mobile residues: PRO52, ILE57, ASP53 (up to 1.64 Å RMSF).
- JQ1 shifted — in 2 of 2 replicas: it ended 2.5 and 3.9 Å from its starting pose (peaks 3.5 and 6.9 Å). That is a change of pose rather than a leaving event; look at the trajectory before treating the starting pose as the bound one. In replica 2 it reached 6.9 Å, past the 5 Å at which it would count as having left, before coming back to 3.9 Å.
- 2 replicas: backbone RMSD 1.44 +/- 0.19 Å (range 1.30-1.57). They agree, so this is a property of the system rather than of one trajectory.

Its limits

- A classical force field: no bonds break or form, and no electronic polarisation.
- An interaction's share of frames is how often its geometry held, not how strong it is.
- Stability over this timescale is not binding affinity.

FIGURES

How the structure moved

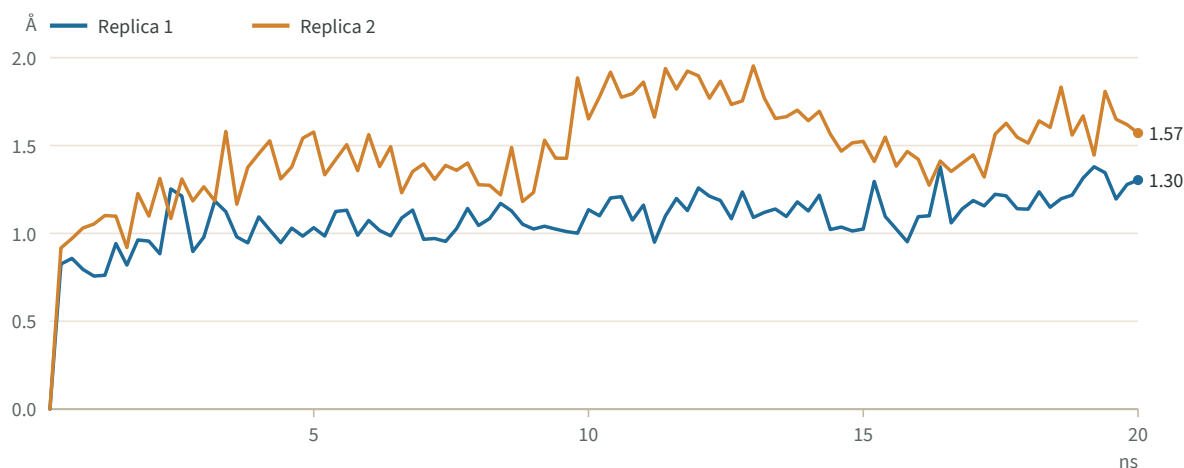


Figure 1. Backbone RMSD from the starting structure, aligned on frame 0, per replica. A plateau means the structure has settled; a climb that has not levelled off means it is still changing.

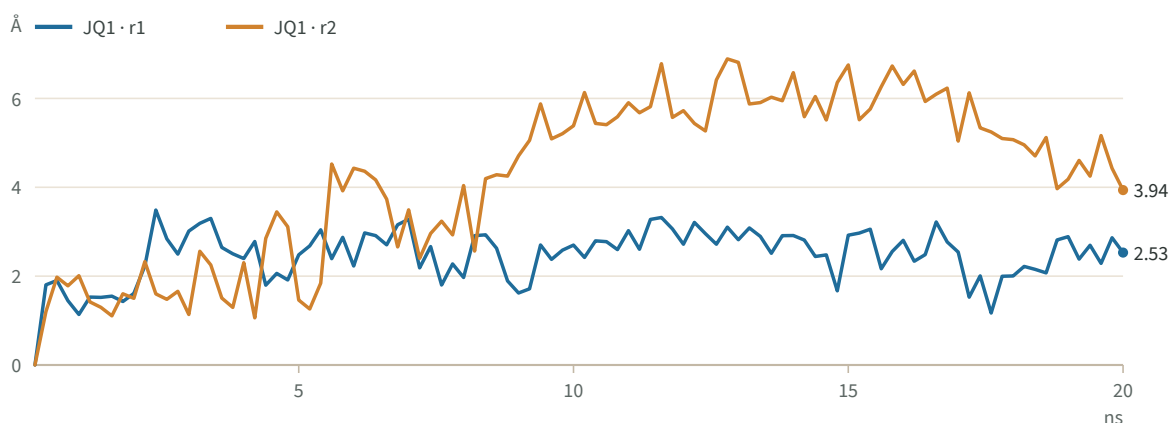


Figure 2. Ligand RMSD from its starting pose, measured after aligning on the protein: movement within the site, not the protein moving. Under 2 Å is the pose holding; past 5 Å it has left.

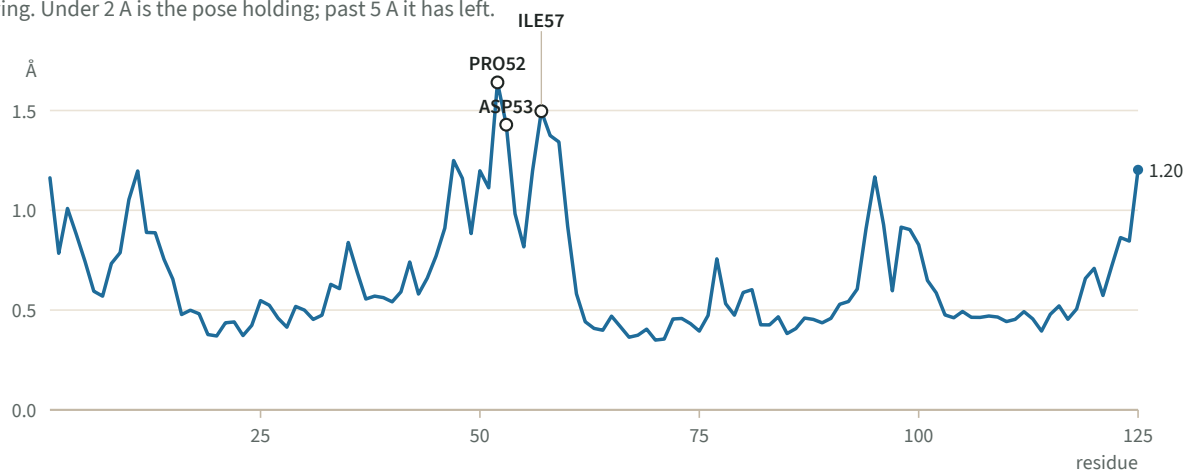


Figure 3. Per-residue flexibility (C-alpha RMSF), replica 1. Peaks are loops and termini that move most; the three highest are named: PRO52, ILE57, ASP53.

What holds it together



 π -stacking, T-shaped
  Water bridge
  Hydrophobic contact
  Hydrophobic
 Negatively charged (-)

Figure 4. The ligand JQ1 and the residues holding it: interactions present in at least 30% of frames (the mean of 2 replicas). Each line ends at the atom, ring or charged group involved and is labelled with its share of frames; the residues around are coloured by kind.

Interactions that last

Every interaction between the bound molecule and the rest present in at least 30% of frames, from the mean of 2 replicas, specific ones first. For hydrogen bonds the arrow runs from donor to acceptor.

Residue	Partner	Interaction	Atoms	r1	r2	Share
A:TRP38	JQ1	π -stacking, T-shaped	ring · ring	63%	10%	36%
A:ASP102	JQ1	Water bridge	N · N3	78%	77%	78%
A:ASP101	JQ1	Water bridge	OD2 · O1	62%	19%	40%
A:ILE103	JQ1	Hydrophobic contact	CD1 · C8	96%	88%	92%
A:LEU49	JQ1	Hydrophobic contact	CD1 · C6	99%	71%	85%
A:TYR54	JQ1	Hydrophobic contact	CE2 · C11	92%	70%	81%
A:PRO39	JQ1	Hydrophobic contact	CB · C12	73%	61%	67%
A:LEU51	JQ1	Hydrophobic contact	CD1 · C11	49%	81%	65%
A:TRP38	JQ1	Hydrophobic contact	CH2 · C13	89%	35%	62%

Residue	Partner	Interaction	Atoms	r1	r2	Share
A:VAL44	JQ1	Hydrophobic contact	CG1 · C11	49%	59%	54%
A:TYR96	JQ1	Hydrophobic contact	CE2 · C11	8%	54%	31%

Salt bridges inside the protein

Residue	Partner	Interaction	Atoms	r1	r2	Share
A:ARG70	A:ASP85	Salt bridge	NH1 · OD2	100%	100%	100%
A:LYS12	A:GLU81	Salt bridge	NZ · OE1	29%	82%	56%
A:LYS98	A:ASP101	Salt bridge	NZ · OD1	71%	33%	52%
A:ASN1	A:ASP45	Salt bridge	N · OD1	98%	0%	49%
A:ARG15	A:GLU124	Salt bridge	NH2 · OE1	77%	9%	43%

How each is measured: **salt bridge**, oppositely charged N and O $\leq 4.0 \text{ \AA}$; **hydrogen bond**, donor–acceptor $\leq 3.5 \text{ \AA}$, hydrogen within 30° of that line; **cation– π** , cation $\leq 6.0 \text{ \AA}$ from a ring centre, offset $\leq 2.0 \text{ \AA}$; **π -stacking**, aromatic ring centres $\leq 5.5 \text{ \AA}$, planes within 30° , offset $\leq 2.0 \text{ \AA}$; **π -stacking, t-shaped**, aromatic ring centres $\leq 5.5 \text{ \AA}$, planes $60\text{--}90^\circ$, offset $\leq 2.0 \text{ \AA}$; **metal coordination**, metal ion $\leq 3.0 \text{ \AA}$ from N, O or S; **water bridge**, one water oxygen $\leq 3.5 \text{ \AA}$ from a polar atom of each; **hydrophobic contact**, carbons bonded only to carbon $\leq 4.0 \text{ \AA}$.

Quality checks

- Temperature 300.3 K on average (sd 2.2 K): the thermostat held it.
- Box volume changed +0.02% from the first third to the last: the density had settled.
- 2 replicas ended at 1.30–1.57 $\text{\AA}$ backbone RMSD (mean $1.44 \pm 0.19 \text{ \AA}$).

METHODS

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.

DATA

Files and how long they are kept

The files below are kept until **13 November 2026**. They are deleted within 7 days after that (20 November 2026) unless you keep them longer from the results page, by the month, or download them first.

File	Size
analysis.json	237.1 kB
analysis/manifest.json	1.0 kB
bundle/CHECKSUMS.sha256	463 B
bundle/run_md.py	19.6 kB
bundle/solvated.pdb	1.9 MB
bundle/system.json	1.9 kB
bundle/system.xml	7.9 MB
r1/manifest.json	2.1 kB
r1/outputs/analysis.json	206.8 kB
r1/outputs/final.pdb	1.9 MB
r1/outputs/log.csv	186.2 kB
r1/outputs/md.log	6.3 kB
r1/outputs/progress.json	407 B
r1/outputs/trajectory.dcd	27.7 MB
r2/manifest.json	2.1 kB
r2/outputs/analysis_r2.json	206.7 kB
r2/outputs/final_r2.pdb	1.9 MB
r2/outputs/log_r2.csv	186.2 kB
r2/outputs/md_r2.log	6.3 kB
r2/outputs/progress_r2.json	410 B
r2/outputs/trajectory_r2.dcd	27.7 MB
setup/manifest.json	3.3 kB
setup/stages.json	2.1 kB
bundle/METHODS.docx	38.1 kB
bundle/METHODS.pdf	3.9 kB
bundle/README.txt	1.8 kB

Citing this run

Simulations were run with ConformerLab (conformerlab.com), run 0c53b82d-43fd-488b-aac7-795398bec64c, using OpenMM; the methods above give the force fields, water model and protocol. The input structure, system, run script and checksums are among the files listed.

Results page: <https://dev.conformerlab.com/lab#/runs/0c53b82d-43fd-488b-aac7-795398bec64c>