

Using a graph neural network for charge assignment and other updates at

Open Force Field

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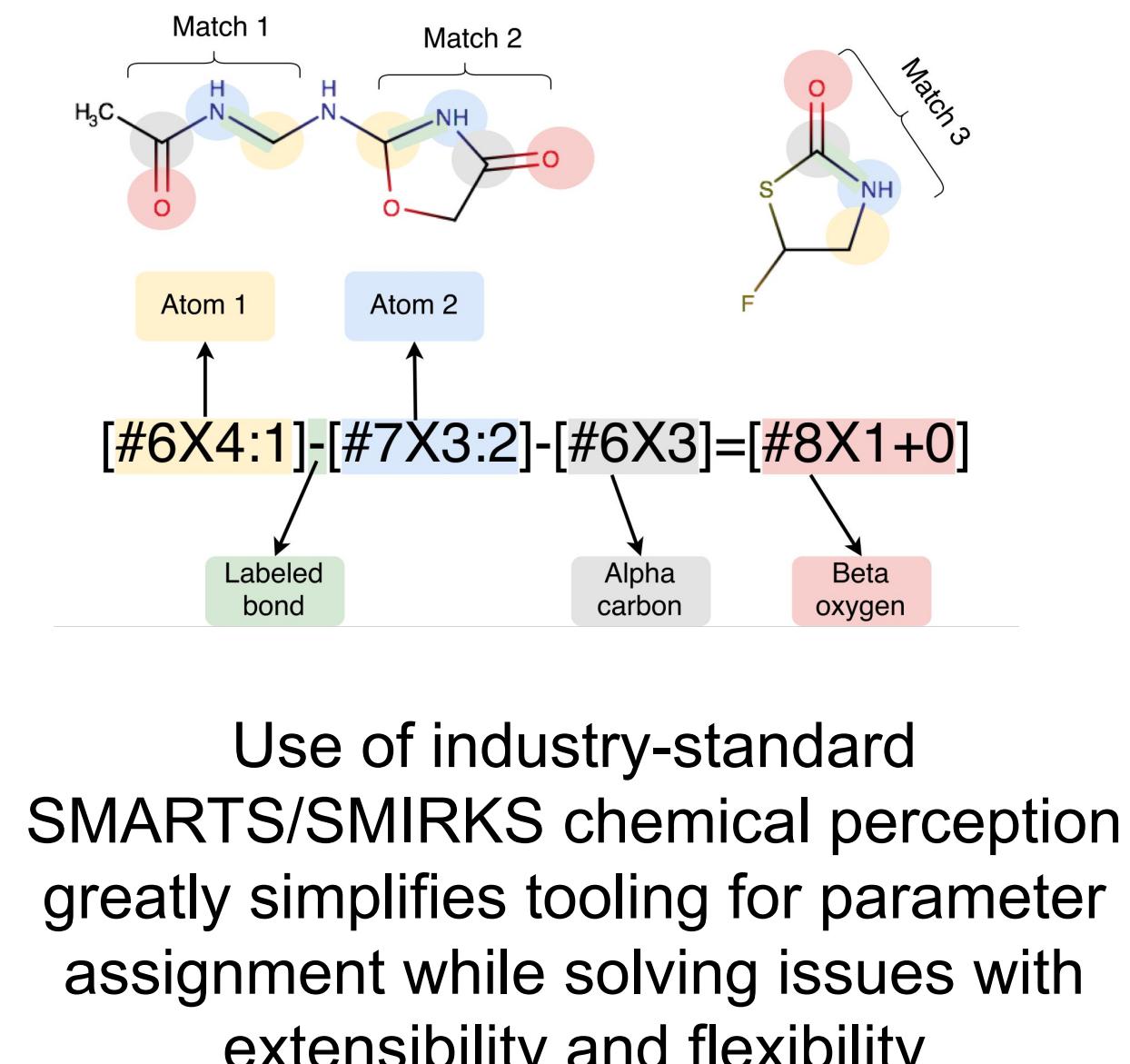


AshGC working paper

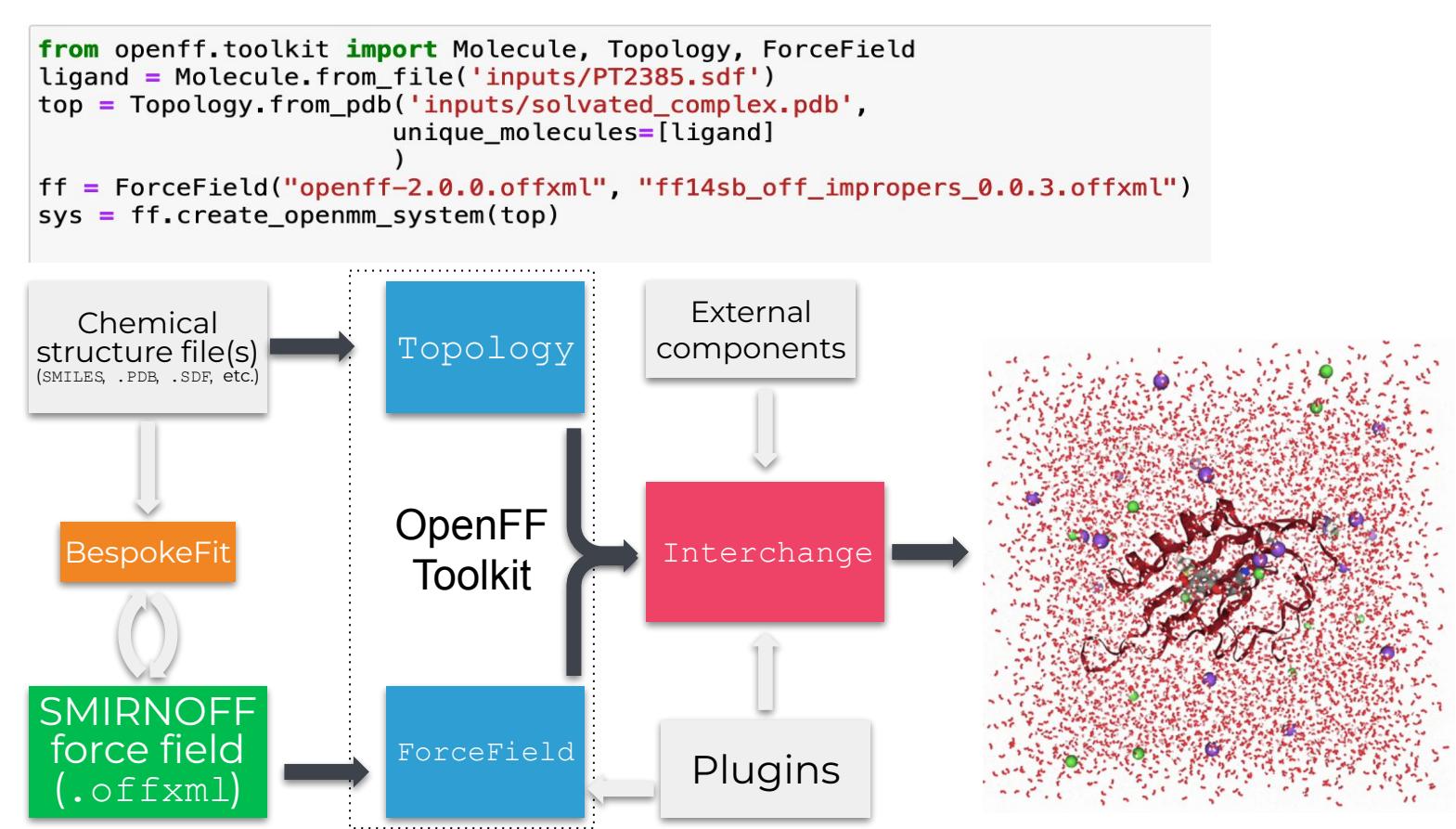
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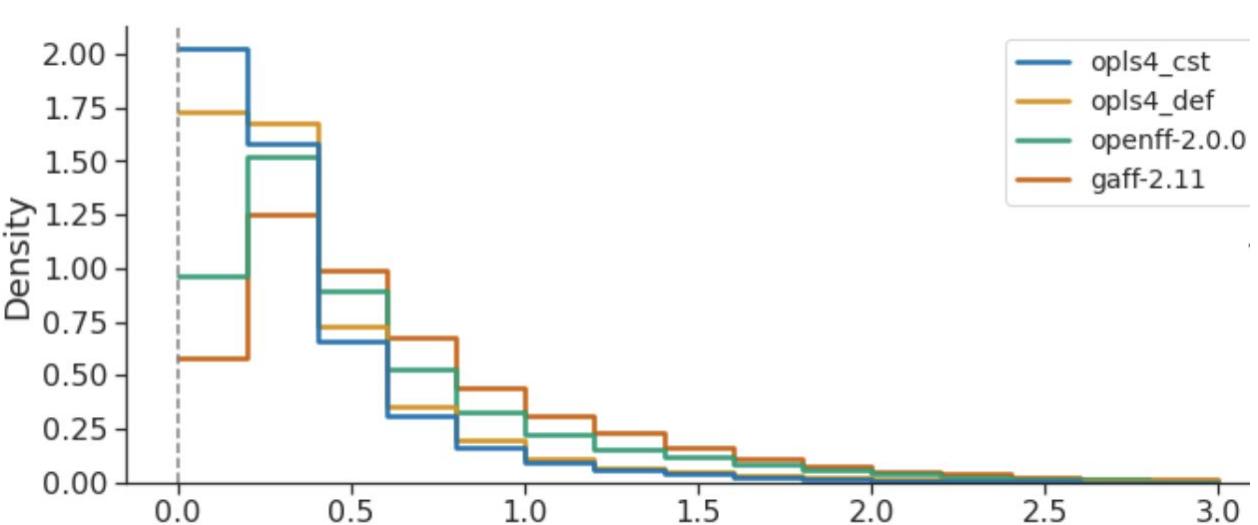
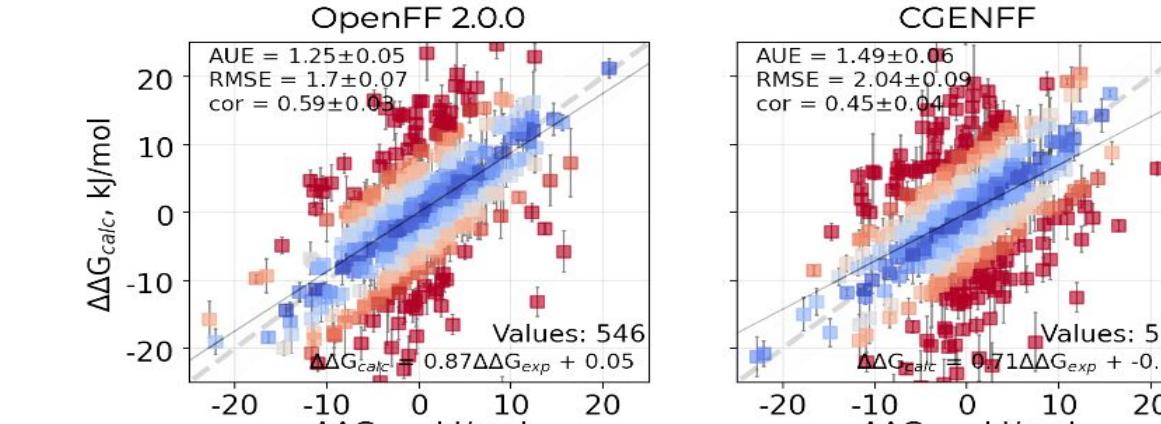
The OpenFF mission: building next-gen force fields with open software, open science, open data



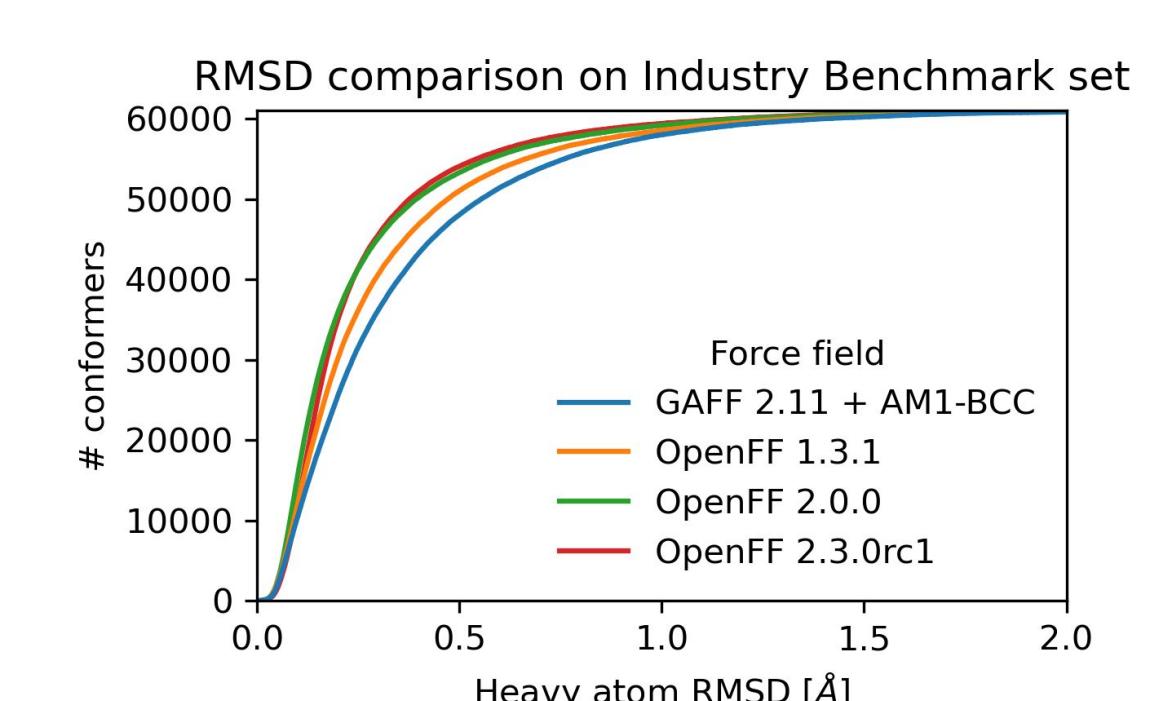
Our software stack enables the easy **creation** and **combination** of arbitrary OpenMM systems, and export to OpenMM, GROMACS, AMBER*, LAMMPS*



Sage 2.0.0 is a leading public small molecule force field



... and we are improving

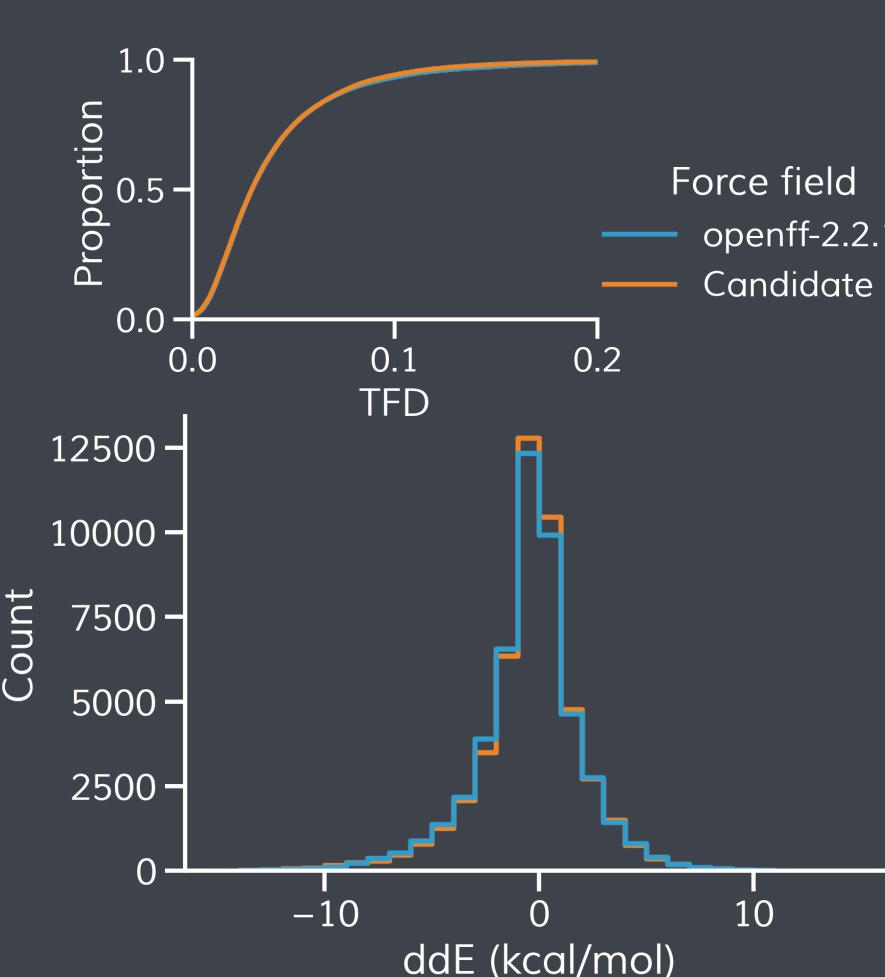


Towards Sage 2.3.0 + AshGC, a neural network charge model

Improving valence terms

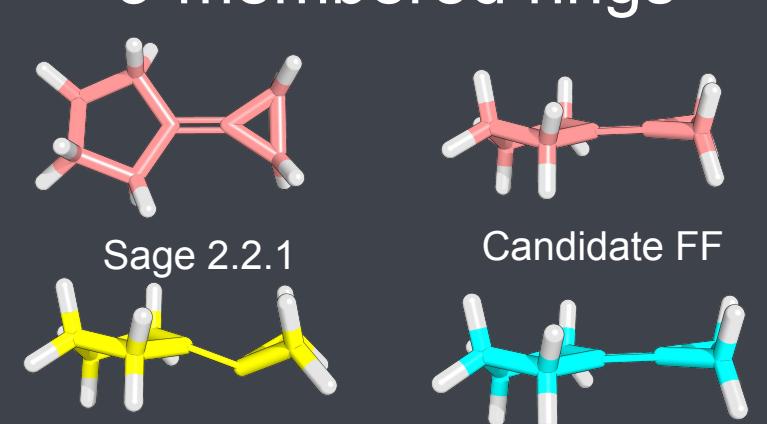
t58: [#6X4:1]-[#6X4:2]-[#7X4,#7X3:3]-[#6X4:4]

- Splitting out torsion multiplicities
 - improving 3-membered ring angles
- results in improved geometries and relative conformer energies



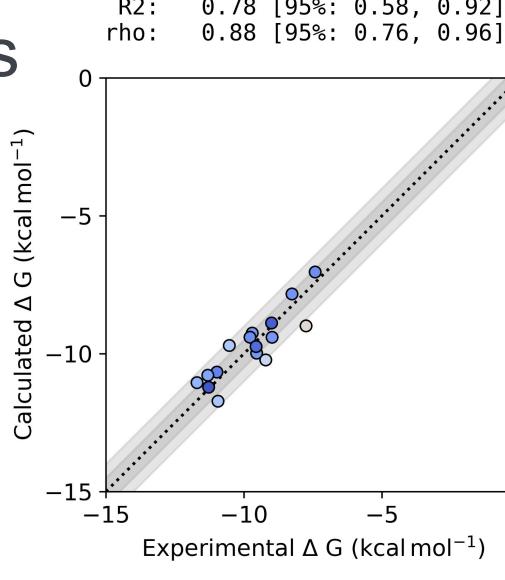
Strike team improvements

The candidate FF correctly keeps planar double bonds from 3-membered rings



Benchmarking on 4 tiers of properties

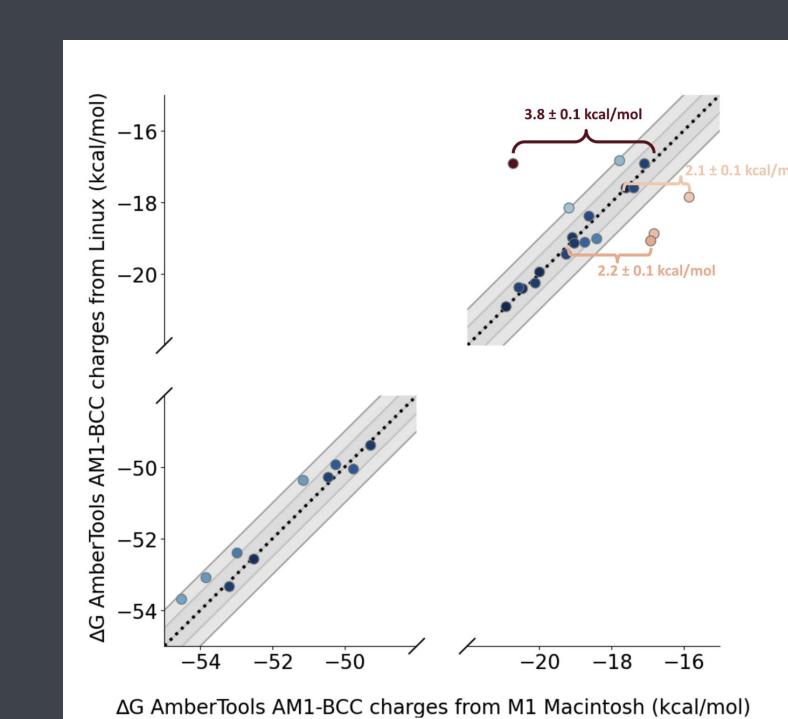
- QM benchmarks
- Physical properties
- Solvation free energies
- Protein-ligand binding free energies



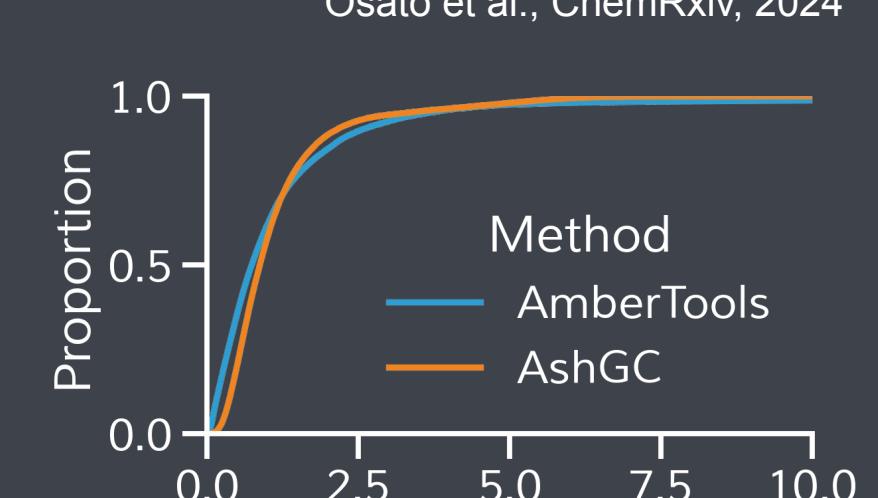
AshGC yields fast, conformer-independent charges

AM1-BCC charges assigned by OpenEye and AmberTools vary by conformer and even hardware

This can result in different free energies of solvation up to 3.8 kcal/mol



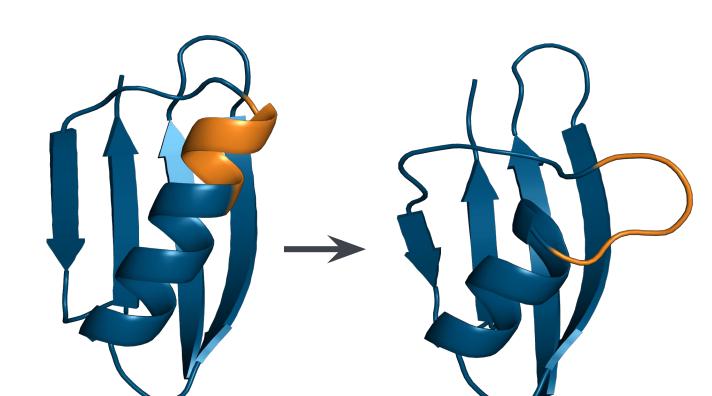
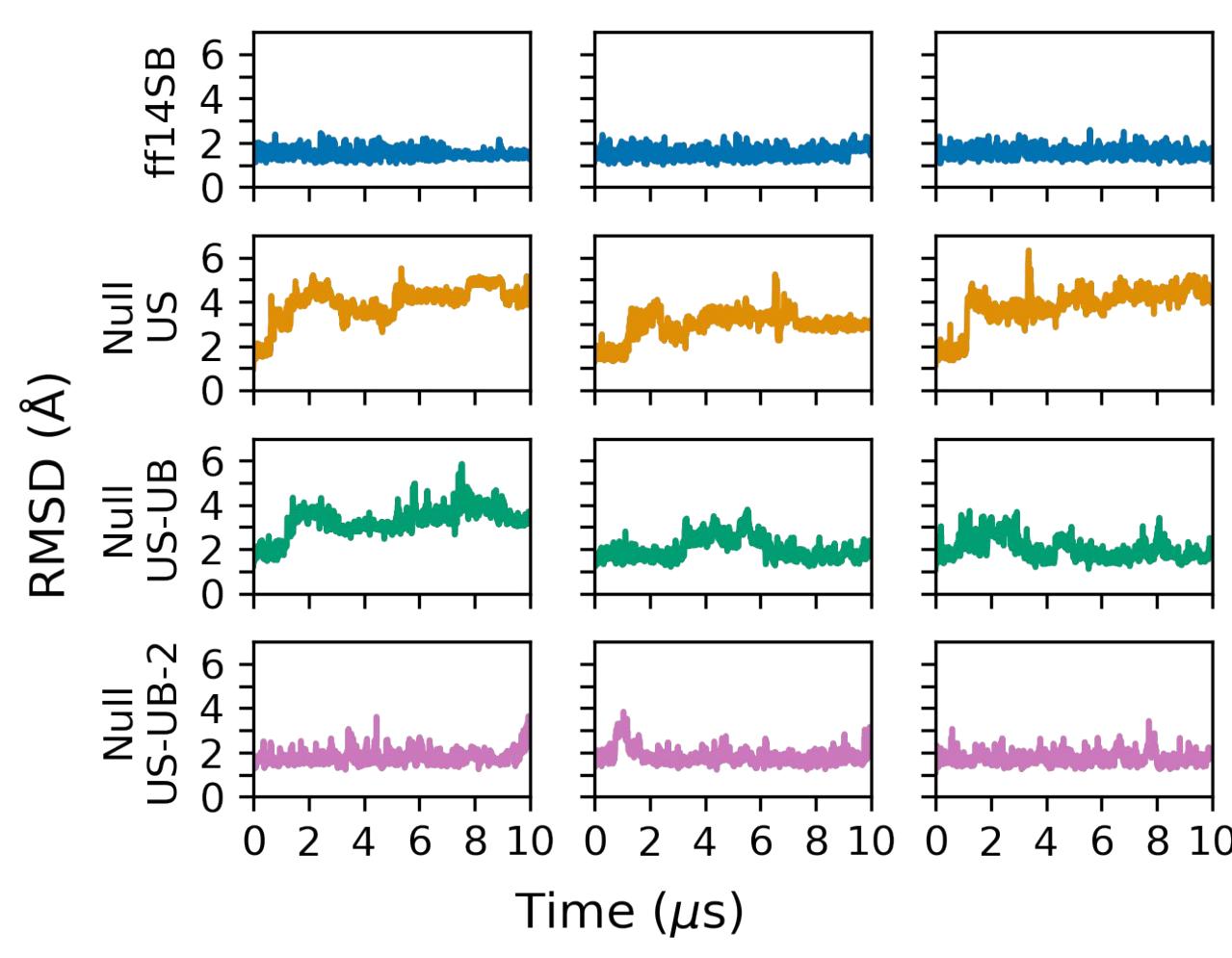
AshGC is a neural network charge model that produces **AM1-BCC-like** charges similar to OpenEye AM1-BCC ELF10



AshGC is fast, assigning charges to proteins in seconds



Continuing work on protein parameters



Fitting to QM protein data yields force fields where the helix of GB3 unfolds in simulation.

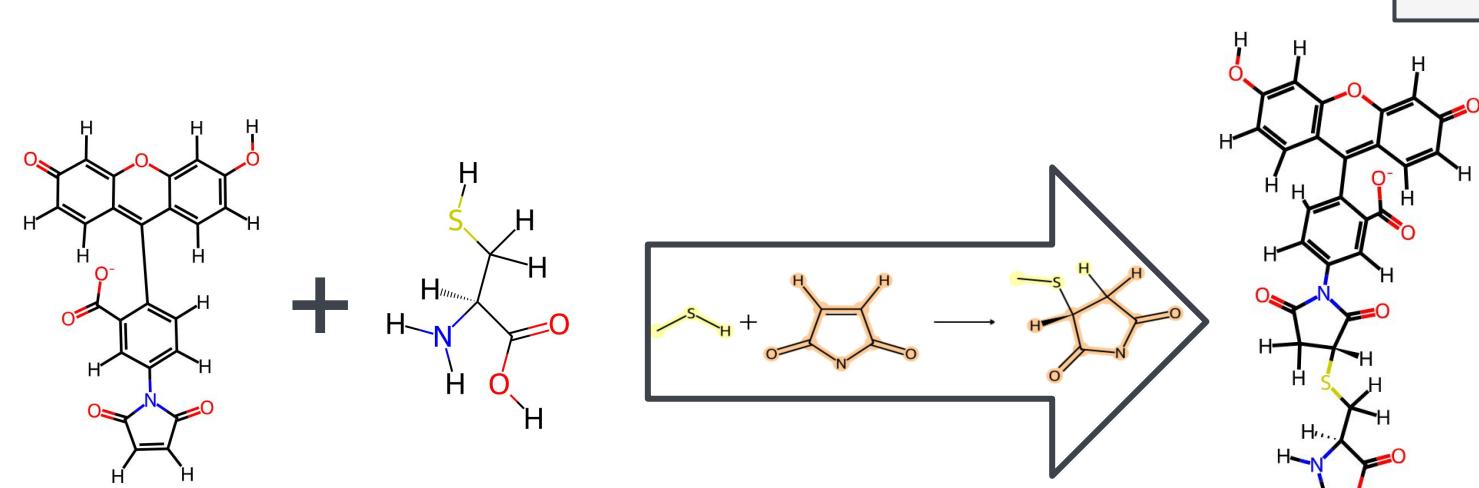
Fitting to NMR observables results in force fields where the helix of GB3 is more stabilized

and infrastructure for proteins and PTMs

Meanwhile, we have an easy workflow for patching Sage and AMBER 14sb force fields together with AshGC charges

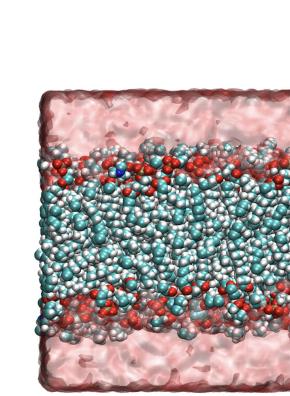
```

from ptm_prototype import parametrize_with_nagl
sage_ff14sb = ForceField("openff-2.2.1.offxml",
                         "ff14sb.off_impropers_0.0.4.offxml")
interchange = parametrize_with_nagl(force_field=sage_ff14sb,
                                    topology=topology)
    
```

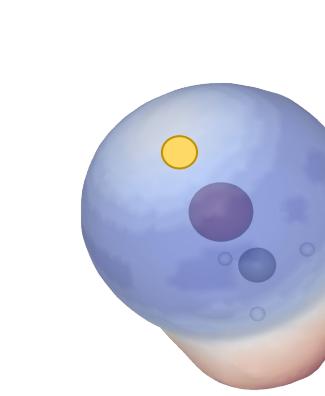


OpenFF Pablo allows working with canonical and custom residues, opening the path to post-translational modifications and covalently bound ligands

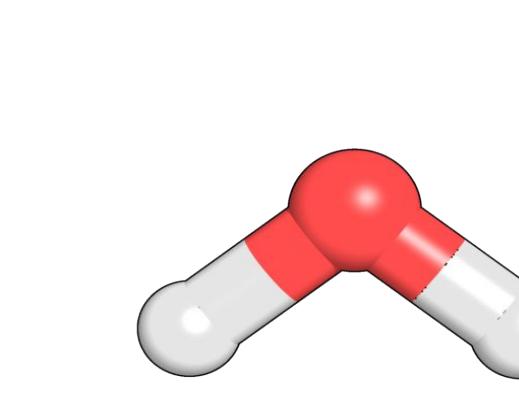
Ongoing and upcoming projects



Improving lipid parameters



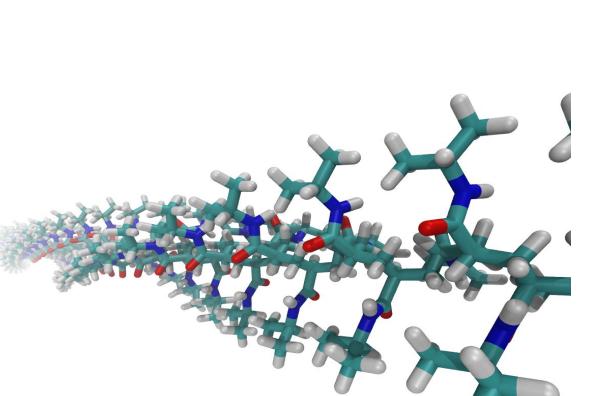
Adding virtual sites



Re-fitting self-consistent water model

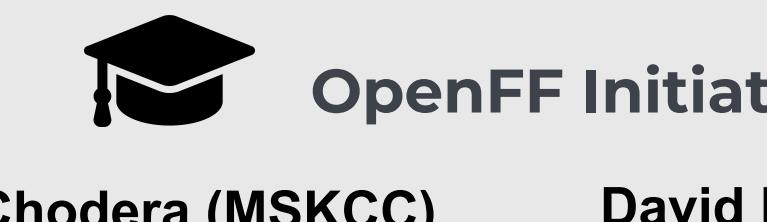


Expanding to nucleic acids



Improving polymer handling

OpenFF brings industry and academia together



Industry

- Achira
AstraZeneca
Bayer
Bristol Myers Squibb
Cresset
Johnson & Johnson
OpenEye
Pfizer
Roche
SandboxAQ
Ventus
Vertex
... and others

Open Molecular Software Foundation

- OpenFF Consortium**
- Project director: David Mobley
Tech lead: Jeff Wagner
Science lead: Lily Wang
Project manager: James Eastwood
Senior RSE: Matt Thompson
Staff scientist: Jennifer Clark
Science communicator: Josh Mitchell

John Chodera (MSKCC)

Ken Takaba

Daniel Cole (Newcastle)

Finlay Clark

Michael Gilson (UCSD)

Chapin Cavender
Tobias Hüfner
Jeffrey Setiadi
Willa Wang

Micaela Matta (KCL)

Charlie Adams
Hannah Turney

David Mobley (UCI)

Pavan Behara
Trevor Gokey
Meghan Osato

Michael Shirts (UC Boulder)

Tim Bernat
Patrick Frenkel
Anika Friedman
Julianne Hoeflich
Barbara Morales

Lee-Ping Wang (UCD)
David Dotson (Datryllic)
Dennis Della Corte (BYU)
... and more!

Contact us at info@openforcefield.org to know more!

Acknowledgements



References

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