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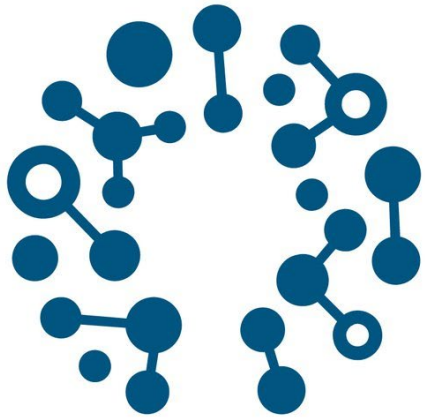
# Open Force Field Consortium

Dr Mark Mackey

CSO, Cresset

# Open Force Field

- Academic-industry consortium to develop open biomolecular force fields
- Academia
  - David Mobley
  - John Chodera
  - Lee-Ping Wang
  - Michael Gilson
  - Michael Shirts
- Industry
  - Bayer, BASF, Boehringer-Ingelheim, Bristol-Myers Squibb, Cresset, GlaxoSmithKline, Janssen, Merck KGaA, OpenEye, Pfizer, Qulab, Roche, Vertex Pharmaceuticals, XtalPi



open forcefield

# What's different about it?

## Open source science

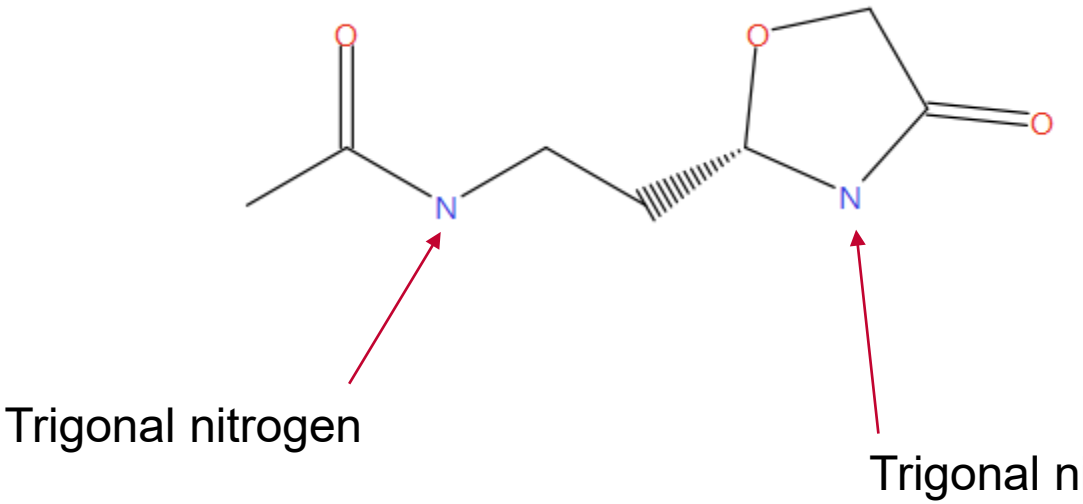
All code and materials released as open source

## Rapid turnaround

As improved versions of the force field are developed they are released to all to use

# Ligand force fields

- Initial focus is AMBER-compatible small molecule force field
- Based on SMIRNOFF (SMIRKS Native Open Force Field)
- Does away with atom typing!
  - Hugely simplifies the number of parameters needed



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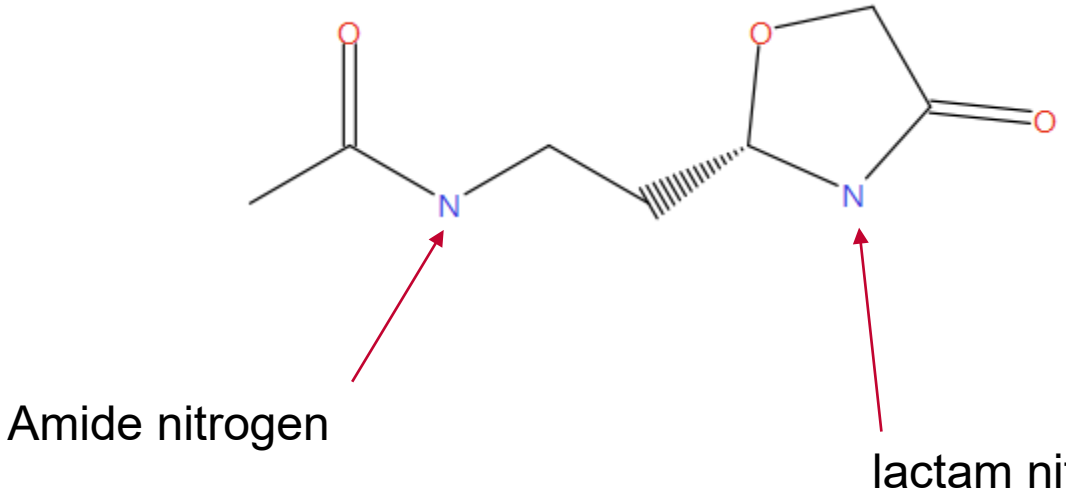

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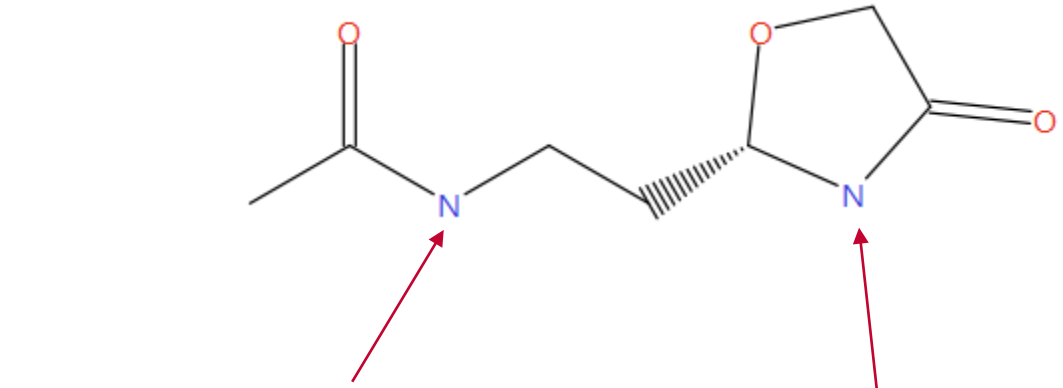


Amide nitrogen

5-membered lactam nitrogen

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- Initial release (v1.0 ‘Parsley’) in Oct 2019
- Currently on v1.2

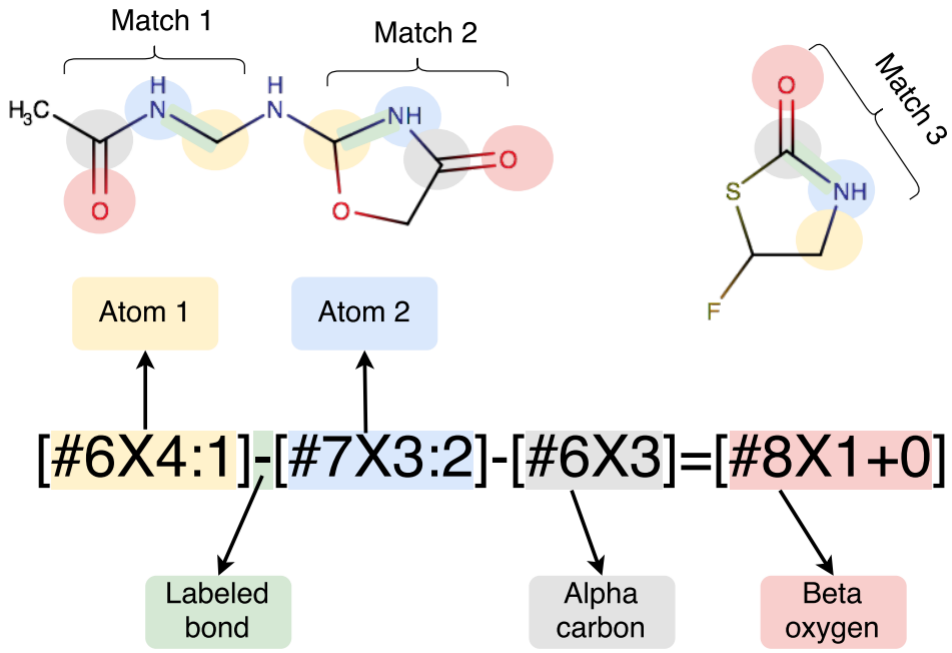
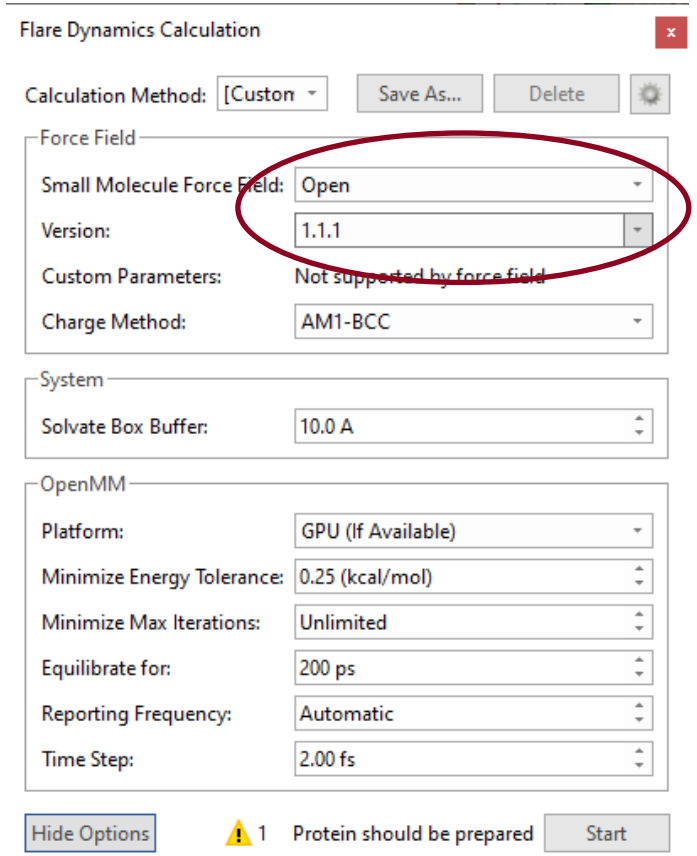



Image source: https://openforcefield.org/science/downloads/roadmap/open-forcefield-plan.pdf

# Flare implementation

- OpenFF support new in Flare™ V4
  - Ships with Parsley 1.0 and 1.1




- Easily extensible
  - OpenFF force fields are simple XML files
  - Drop a new file in the Flare folder and it will automatically be made available.
  - Parsley 1.2 released earlier this month

# FEP results with Parsley 1.0

| Dataset | GAFF 2.1 | | OpenFF 1.0 | |
|---|---|---|---|---|
| | R | MUE(I) | R | MUE(I) |
| Thrombin | 0.91 | 0.20 | 0.90 | 0.22 |
| TYK2 | 0.73 | 0.70 | 0.68 | 0.76 |
| JNK1 | 0.72 | 0.76 | 0.79 | 0.80 |
| CDK2 | 0.74 | 0.69 | 0.83 | 1.40 |
| MCL1 | 0.74 | 1.18 | 0.61 | 1.14 |
| p38 | 0.63 | 0.94 | 0.75 | 1.28 |
| BACE | 0.44 | 0.76 | 0.34 | 0.94 |
| PTP1B | 0.69 | 0.72 | 0.14 | 1.49 |

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Caveats: these are initial results and we know there are some problems with some data sets

# Outlook

- OpenFF is already comparable to GAFF in its performance
- Rapid pace of improvement
  - 3 releases in ~6 months
- Future goals are to co-develop a protein force field
  - Full compatibility between protein and ligand parameters
  - No more problems handling cofactors, modified proteins, covalent ligands etc.
- Available in Flare as a top-level option, and upgradeable as new versions come out


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Thanks to the OpenFF team, and to
Paolo Tosco, Giovanna Tedesco and Stuart Firth-Clark

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