Open Free Energy

An Open Source Ecosystem for Alchemical Free Energy Calculations

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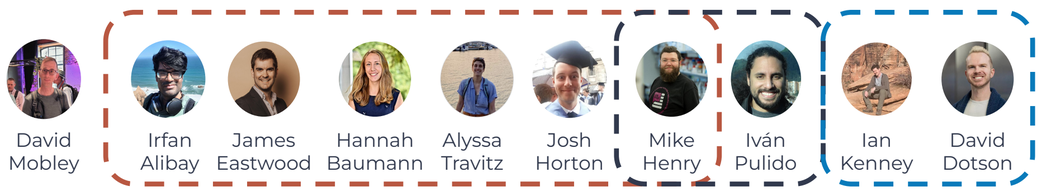
openfree.energy

Open Molecular Software Foundation

A precompetitive consortium of industry & academic partners

- Developing reusable and extensible open-source tools for alchemical calculations
- Maintaining existing open-source tools and datasets
- Simplifying free energy calculations with a modular Python-based toolkit, openfe, as a single entry point for system definition, execution, and analysis.



The OpenFE Ecosystem

The simplicity and customizability of the **openfe** interface is made possible by a robust ecosystem of sub-projects (as well as the broader open-source community!)

Learn more at **openfree.energy/projects**

System Definition:

`gufe`: OpenFE's custom data models for memory-efficient representation of alchemical systems

`konnektor`: framework for constructing free energy network graphs

Atom Mapping:

`LOMAP`: widely-used atom mapping tool originating from the Mobley Lab

`kartograf`: atom mappings focused on 3D geometries

setup

Execution

`alchemiscale`: distributed execution across heterogeneous compute

ALCHEMISCALE

run

Analysis

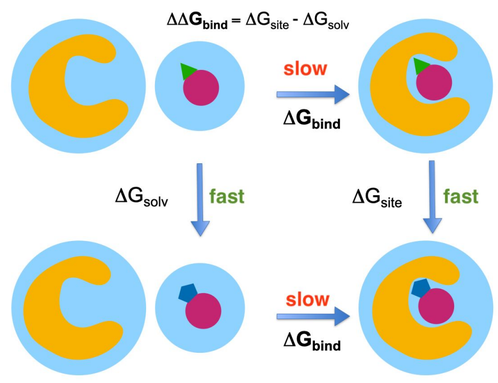
`cinnabar`: analysis back-end originating from the Chodera Lab

gather

Calculating RBFEs with the openfe CLI

The command-line interface is the easiest way to use openfe to calculate relative binding free energies.

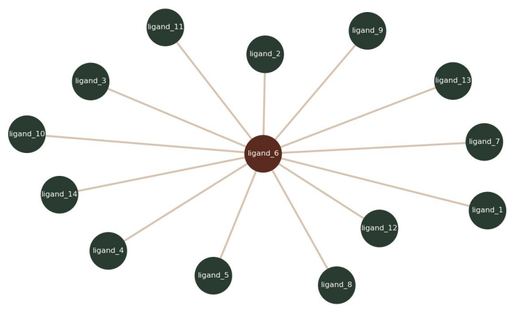
For even more advanced and customized functionality, see our Python API at **docs.openfree.energy**.



1. setup [generate an alchemical network, define simulations]

```
$ openfe plan-rbfe-network -M ligands.sdf -p protein.pdb
```

customize with `-s settings.yaml`:



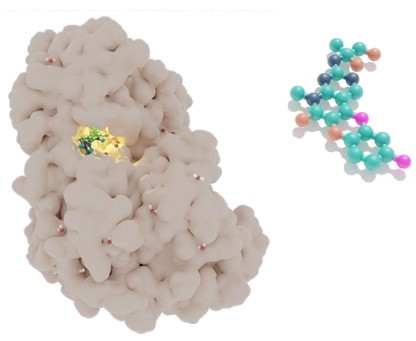

```
mapper:
  method: kartograf

network:
  method: generate_maximal_network

partial_charge:
  method: am1bccelf10
  settings:
    off_toolkit_backend: openeye
```

2. run [execute simulations]

```
$ openfe quickrun transform.json -o results/transform.json
```



Execute openfe quickrun individually for each unique transform.json, allowing for full control of simulation execution.

3. gather [collect and analyze results]

```
$ openfe gather results/*.json --report=ddg -o results.csv
```

ligand	DG(MLE) (kcal/mol)	uncertainty (kcal/mol)
lig_ejm_31	-0.09	0.05
lig_ejm_42	0.7	0.1
lig_ejm_46	-0.98	0.05
lig_ejm_47	-0.1	0.1
lig_ejm_48	0.53	0.09
lig_ejm_50	0.91	0.06
lig_ejm_43	2.0	0.2
lig_jmc_23	-0.68	0.09
lig_jmc_27	-1.1	0.1
lig_jmc_28	-1.25	0.08

- computes MLE-derived absolute free energies (ΔG) using **`cinnabar`**
- choose from ΔG, ΔΔG, or raw data output
- the `--allow-partial` flag allows for computing preliminary results on incomplete datasets

Project Road Map

Open Free Energy Fund founded

2022

OpenMM RBFEs
OpenFE v0.7
- GPU-powered workflow based on **perses**
- Full **OpenFF** support

2023

First Stable Release
openfe v1.0
- Improved validation
- Charge changes
- Automated trajectory analysis
- Absolute hydration free energies
- "Vanilla" MD simulations

RFE support
kartograf v1.0
- Kartograf
- LOMAP v2
- Cinnabar

2024

Improved Setup
- **Konnektor**
- **Gromacs MD Protocol**
- Custom ligand parameters
- Non-cubic solvation
- Improved CLI

2025

Advanced methods
openfe v2.0
- Separated Topologies and ABFEs
- Membrane support
- Improved large scale execution

Industry Benchmarks
- Large-scale benchmarking of OpenFE
- Collaboration with industry partners on private and public datasets

OpenFE Industry Partners

- Achira
- Amgen
- AstraZeneca
- Bayer
- Biogen
- Boehringer Ingelheim
- Bristol Myers Squibb
- Charm Therapeutics
- Confo Therapeutics
- Cresset
- Deep Origin
- Eli Lilly
- Genentech (Roche Group)
- GSK
- Janssen
- Merck KGaA
- Neomorph
- Pfizer

Technical Advisory Committee

- Oliver Beckstein
- Phil Biggin
- Stefan Boresch
- John Chodera
- Zoe Cournia
- Emilio Gallicchio
- Antonia Mey
- Julien Michel
- David Mobley
- Bharath Ramsundar
- Sereina Riniker
- Michael Shirts
- Sukrit Singh
- Jonah Vilseck

Collaborators & Emeriti

Perses development team (Chodera Lab), Matt Thompson, David Swenson, Richard Gowers

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