Ensemble simulations with experimental restraints: Running at Scale -or- a designed interface for MD simulations

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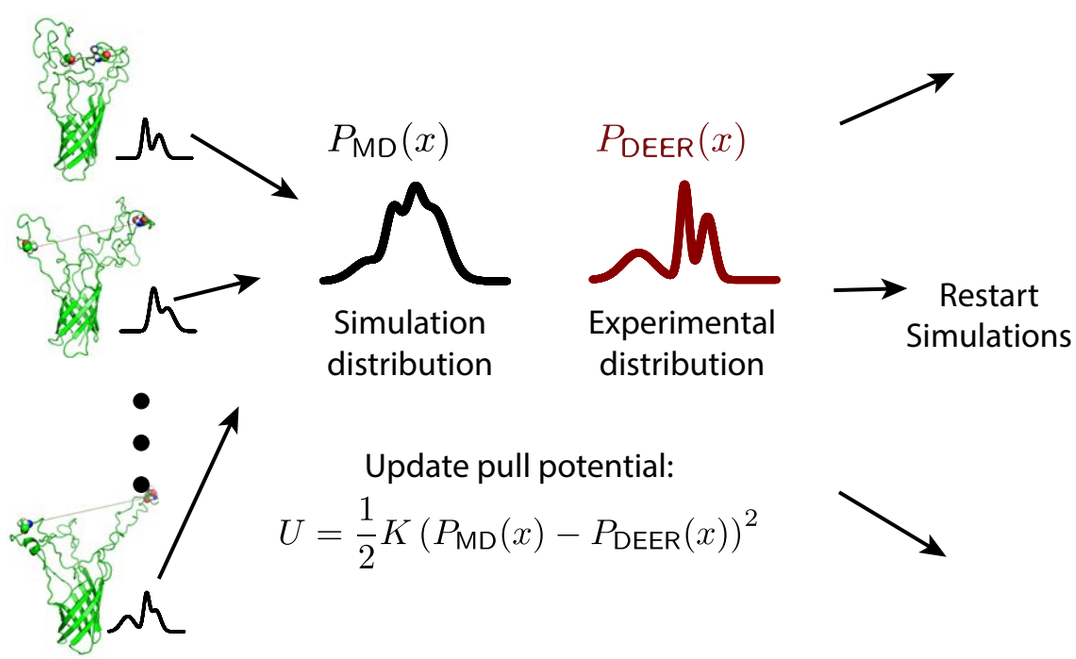


Motivation:

- Most molecular dynamics simulation packages are monolithic
- Most applications are not
- How can we enable flexible, performative use of large-scale MD simulations?

Motivation II

- Custom modifications of MD code are common, e.g. to implement additional potentials for experimental data
- Having open code that can be modified is great
- Having everyone modify it is a Bad Idea for barrier-to-entry, performance, reproducibility, maintainability
- Goal: <u>custom modifications with no changes to core MD code</u>.

Motivation III

- Not just another Python API
- Design inspiration from TensorFlow (API compatible)
- Procedural commands set up a computational graph
- Enables user-transparent performance optimizations

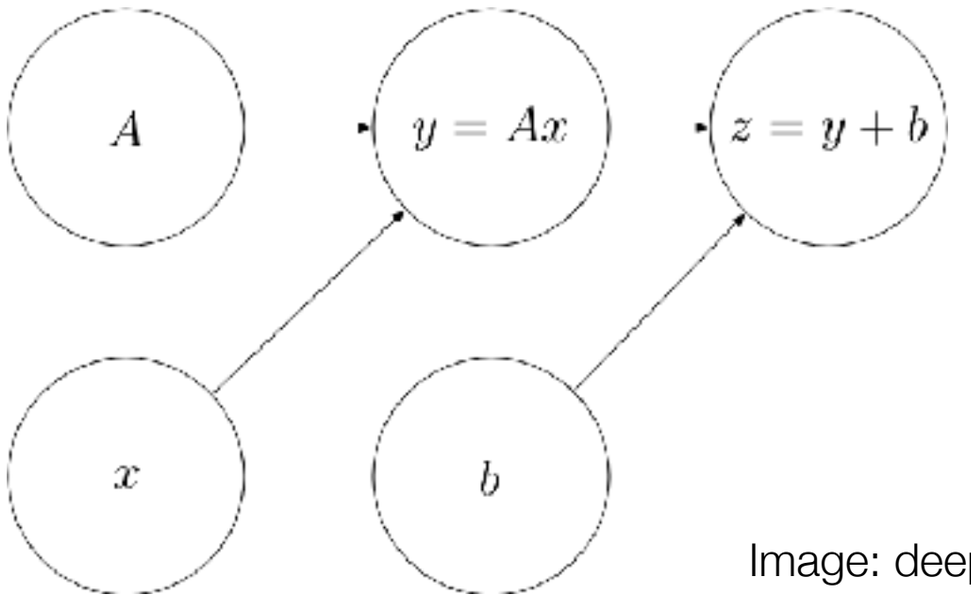
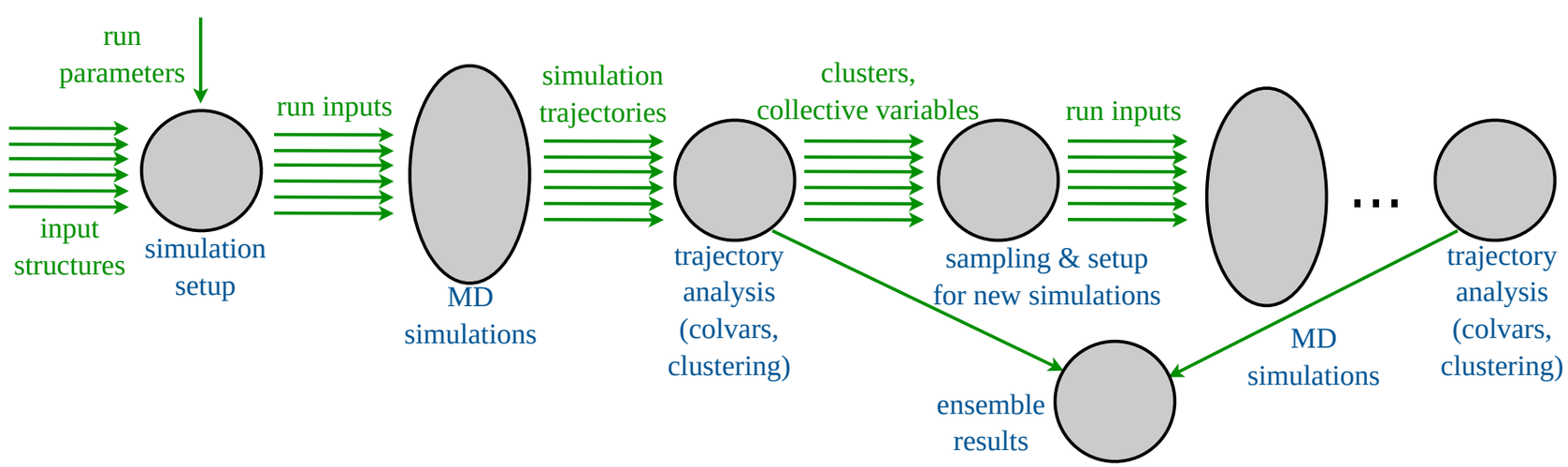


Image: deepideas.net

Motivation IV

- Ensembles as first-class entities, computational context abstracted
- Description of what to execute should be distinct from specification of where to execute.



gmxapi: Python (and more) API for Gromacs

- Running molecular dynamics simulations
- Clean interface that permits scalable, optimized execution with standard or custom code
- Build and execute a computational graph

What does this mean in practice?

```
import gmx
import myplugin

md = gmx.workflow.from_tpr(tpr_list)
potential = gmx.workflow.WorkElement(
    namespace="myplugin",
    operation="ensemble_restraint",
    depends=[],
    params=params)
potential.name = "ensemble_restraint_1"
md.add_dependency(potential)

context = gmx.context.ParallelArrayContext(md)
with context as session:
    session.run()
```

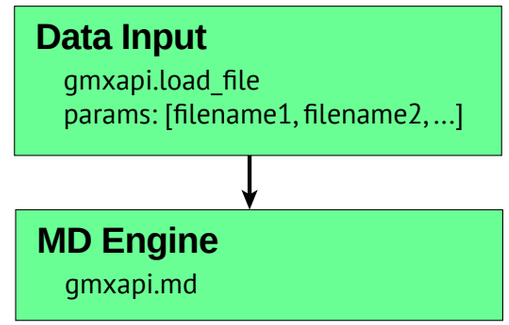
Simple, clean code.

This runs an ensemble of simulations using a custom potential.

A peek under the hood

a

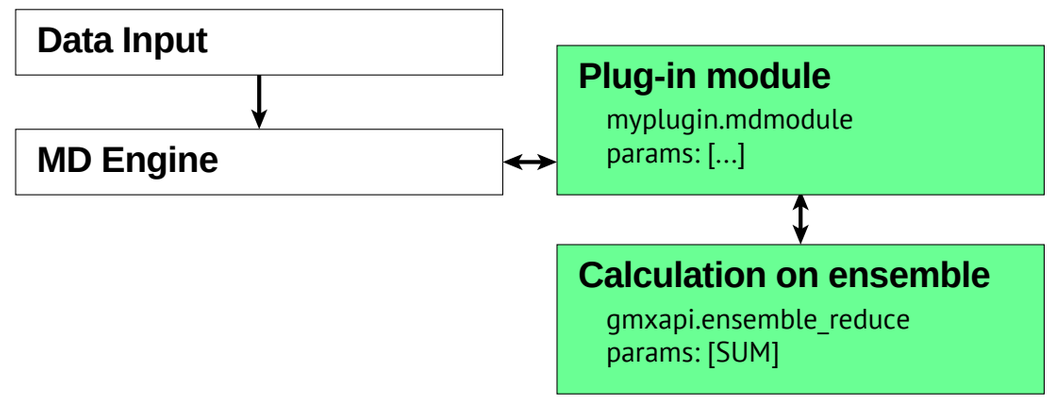
```
>>> md = gmx.from_file([filename1, filename2, filename3, ...])
```



b

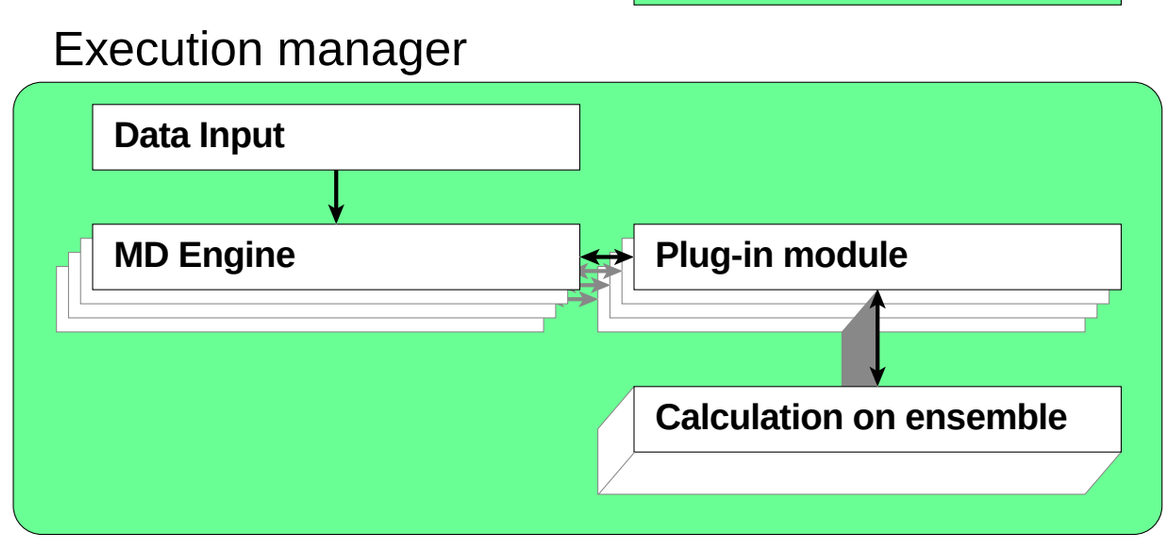
```
>>> potential = myplugin.EnsembleRestraint(sites, *args, **kwargs)
```

```
>>> md.add_dependancy(potential)
```



c

```
>>> gmx.run()
```



Custom potentials are easy(ish)

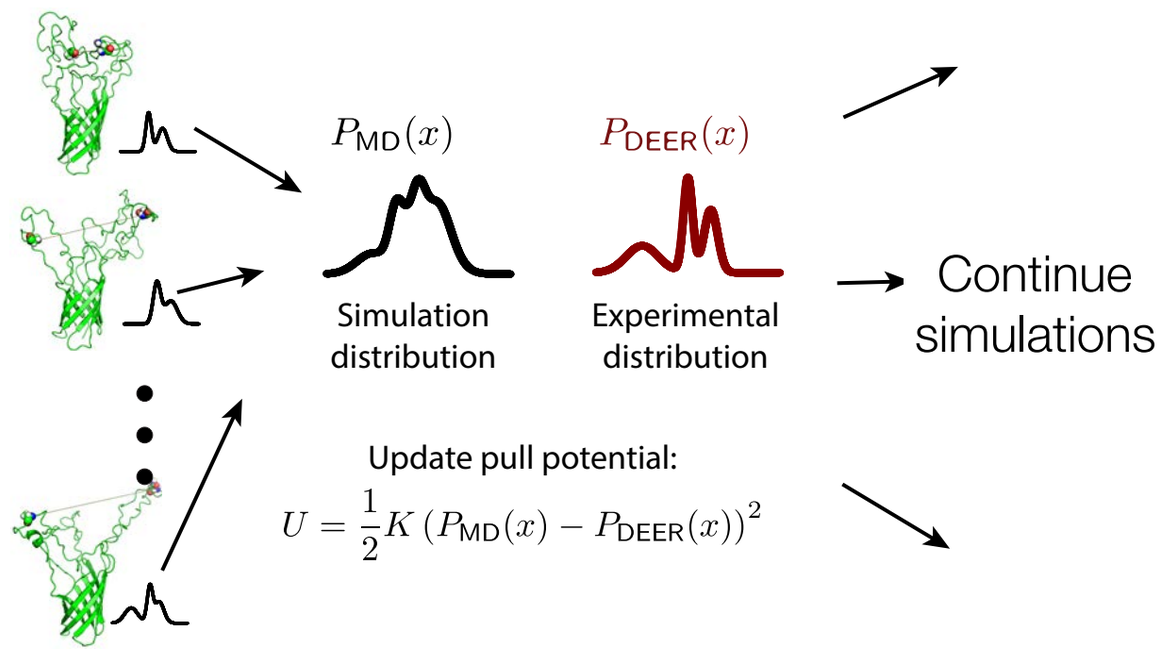
- Boilerplate C++ code, en route to templated classes
- essentially implement a calculate() method and then an update callback to update potentials for adaptive approaches.

What this enables

- Implementation of restrained-ensemble simulation (Roux, 2013)
- Simple, scalable execution within 5% of native code performance.
- Can either execute multiple iterations with independent ensemble members or update potentials with a (blocking) reduce

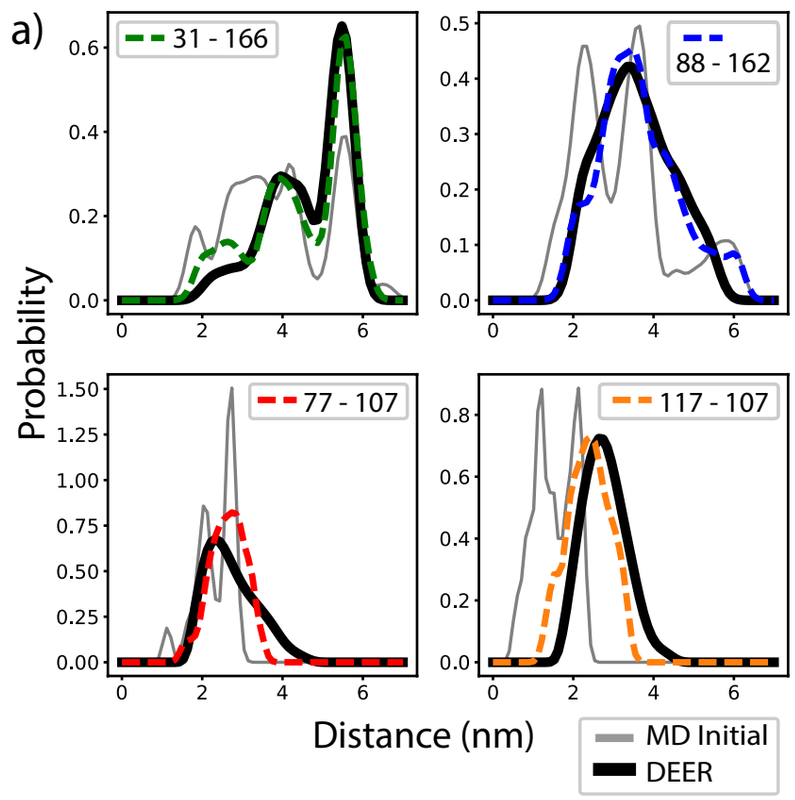
Example of restrained-ensemble simulation

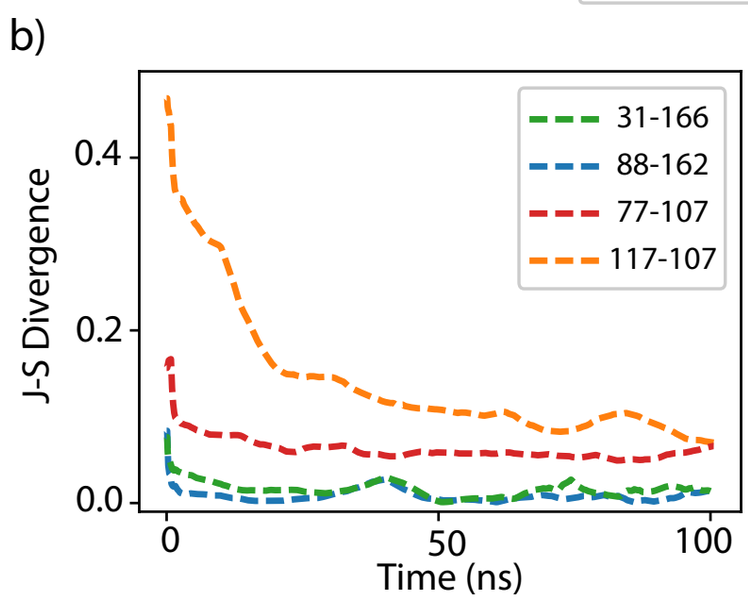
Ensemble of 20 simulations
ensemble reduce & potential update every 100 ps



Hays et al., 2018

Example of restrained-ensemble simulation and convergence





Convergence to experimental distributions (Assessed via histograms, Jensen-Shannon divergence)

Hays et al., 2018

Current status

- Functionality: Can run ensembles, enable custom force plugins, perform ensemble reduce as needed.
- Implementations: Two different ensemble-biasing algorithms implemented, working on automated umbrella sampling next.
- Alpha/beta code release github.com/kassonlab/gmxapi
- (almost) running on Blue Waters
- Next round of functionality in progress. Taking requests.

We want to hear from you!

- gmxapi manuscript: Irrgang et al., 2018 doi:10.1101/306043
- Restrained ensembles: Hays et al., 2018 doi:10.1101/319335
- Github: https://github.com/kassonlab/gmxapi
- Want to join as a scientist or developer? We're looking for students and postdocs!
- kasson@virginia.edu

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