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A Unified Approach to Enhanced Sampling

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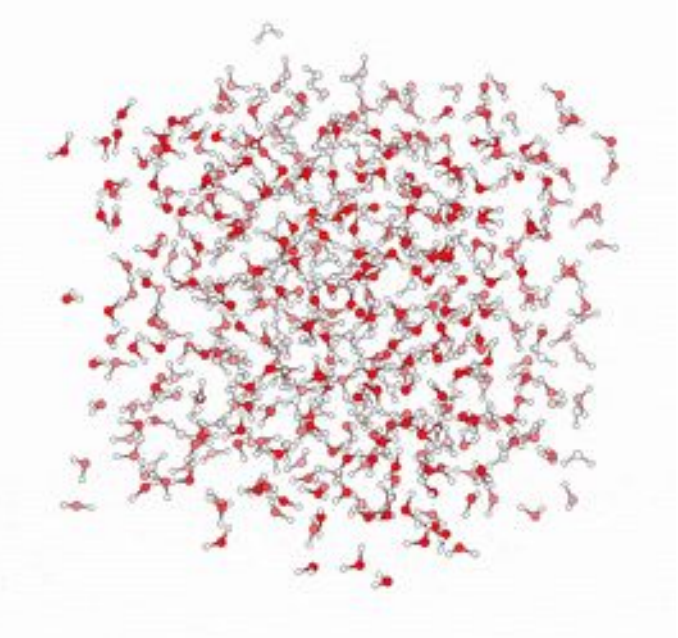
Topic

Computational methods for molecular simulations

Outline

1. Enhanced sampling
2. Unified perspective
3. The method in action



Invernizzi, Piaggi, and Parrinello. “A Unified Approach to Enhanced Sampling.” arXiv:2007.03055 (2020)

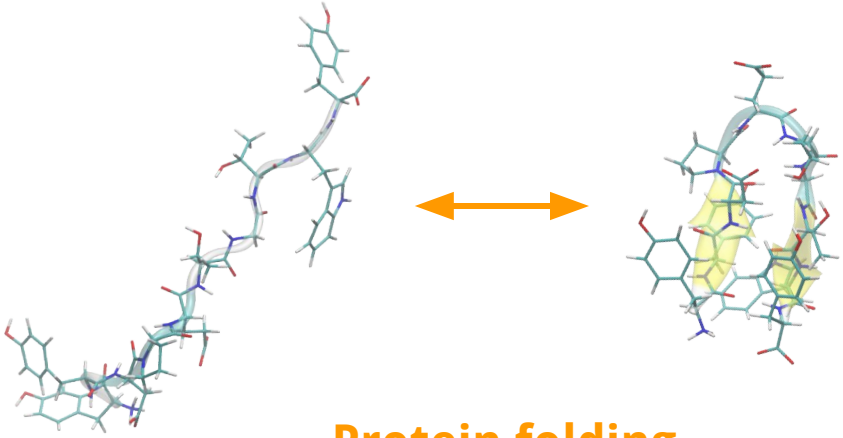
1. Enhanced sampling

tempering and collective variables approaches

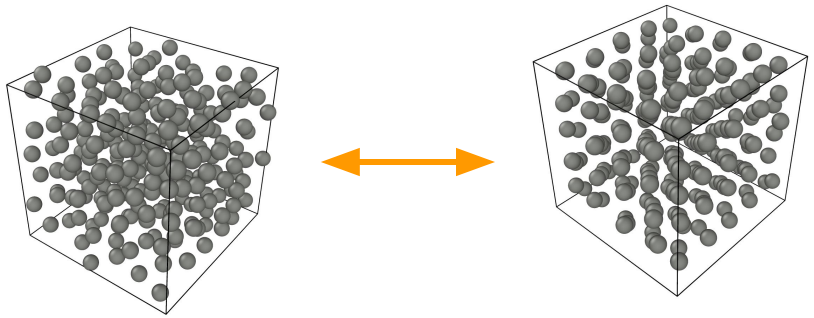
The sampling problem

Atomistic simulations are a great tool to **describe and predict** phenomena in physics, chemistry, biology, and material science. However, many phenomena are out of reach

=> **rare events**, that happen on **macroscopic timescales**



Protein folding

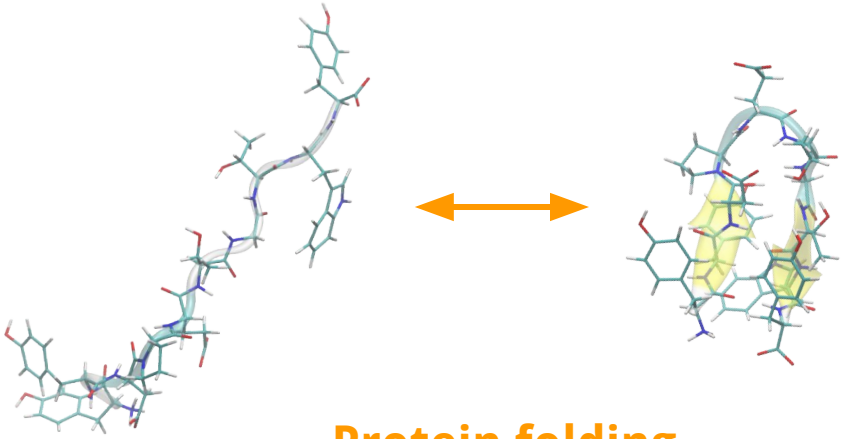


Phase transitions

The sampling problem

The simulations remains stuck in one of the **metastable** states

Might take years of computation to observe just one **transition** event!



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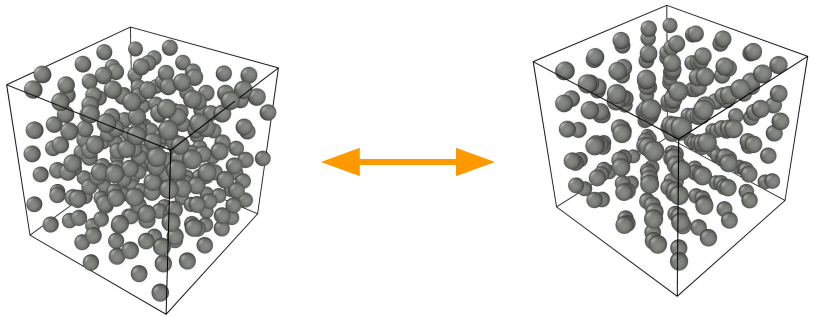


Phase transitions

The sampling problem

Many **enhanced sampling** methods have been proposed to overcome this problem

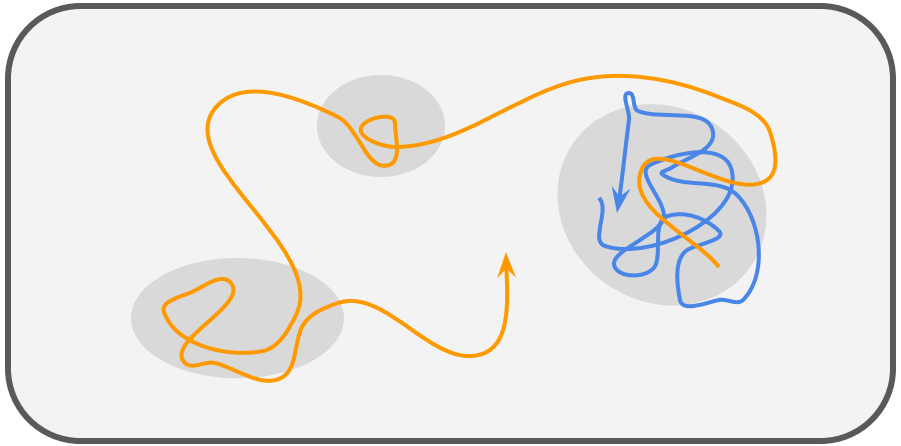
Two main families, with complementary approaches:

- Tempering methods
- Collective variables methods

We propose a unifying perspective **and a novel** general method **that allows to combine them and opens up to new possibilities**

Tempering methods

At higher temperature the system explores a larger portion of phase space, and escapes metastable basins **=>** combine **different temperatures** to enhance the sampling



- *Parallel tempering*
- *Simulated tempering*
- *Replica exchange*
- *Multicanonical methods*
- *...*

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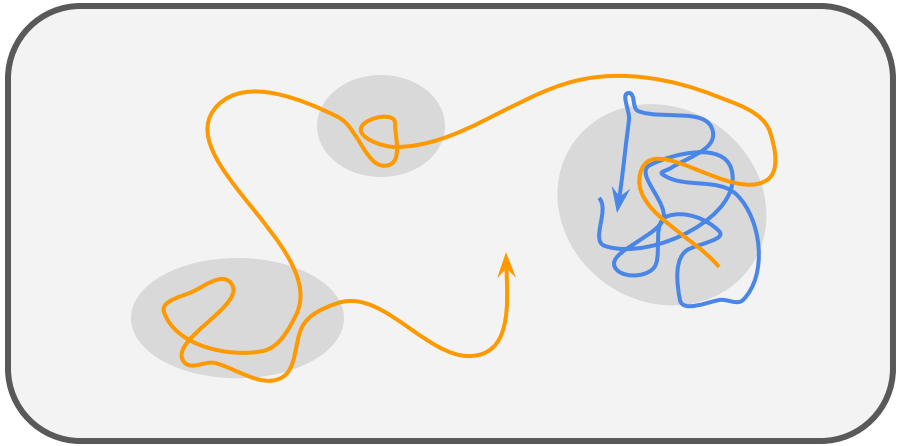

- *Parallel tempering*
- *Simulated tempering*
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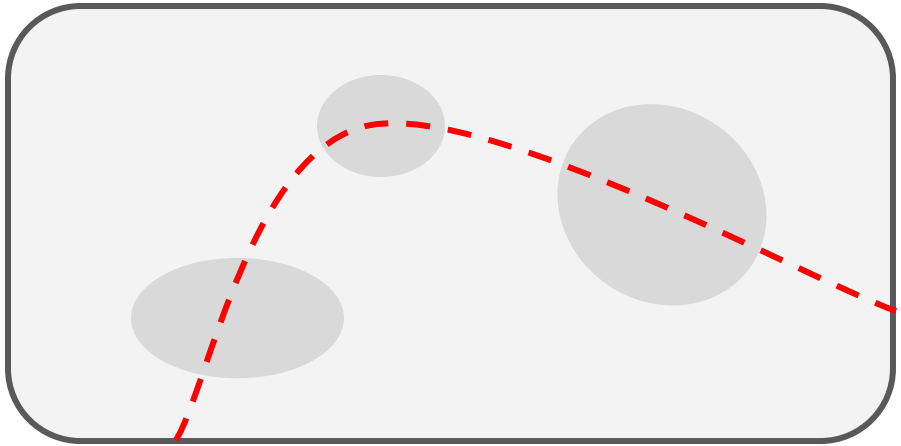
Expanded ensembles not only in temperature

Collective variables methods

Identify an order parameter or **collective variable (CV)** that describes the process

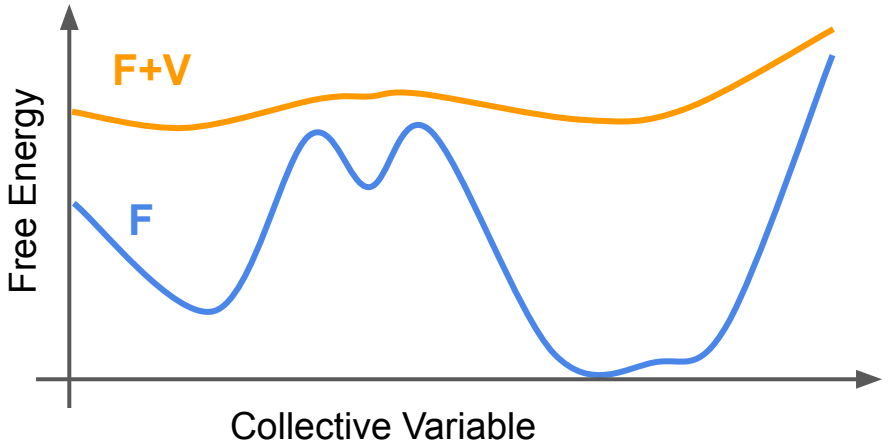


- *Umbrella sampling*
- *Metadynamics*
- *Variationally enhanced sampling*
- *...*

Collective variables methods

Identify an order parameter or **collective variable (CV)** that describes the process

Add a **bias potential V** that flatters the **free energy F**



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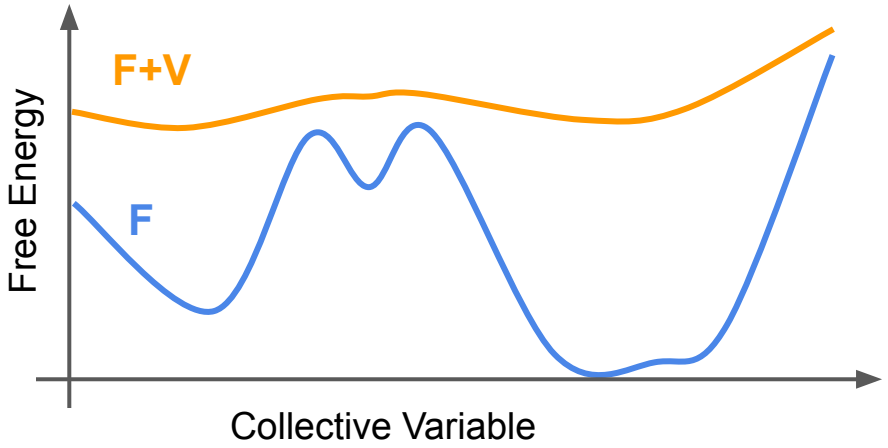

- *Umbrella sampling*
- *Metadynamics*
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- *...*

More efficient than tempering, but CV might be hard to find!

2. Unified perspective

reaching a target distribution

The target distribution

- The **equilibrium Boltzmann distribution** is hard to sample
- Enhanced sampling methods explicitly or implicitly aim at sampling a different **target distribution**
- Via some **reweighting** technique it is then possible to retrieve statistics on $P(\mathbf{x})$

$$P(\mathbf{x}) = \frac{e^{-u(\mathbf{x})}}{Z}$$

$$p^{tg}(\mathbf{x})$$

We develop a biasing scheme that can be used to sample the target distributions of both tempering and collective variables methos

The OPES method

On-the-fly Probability Enhanced Sampling (OPES):

- We can sample any $p^{tg}(\mathbf{x})$ by adding the proper bias potential

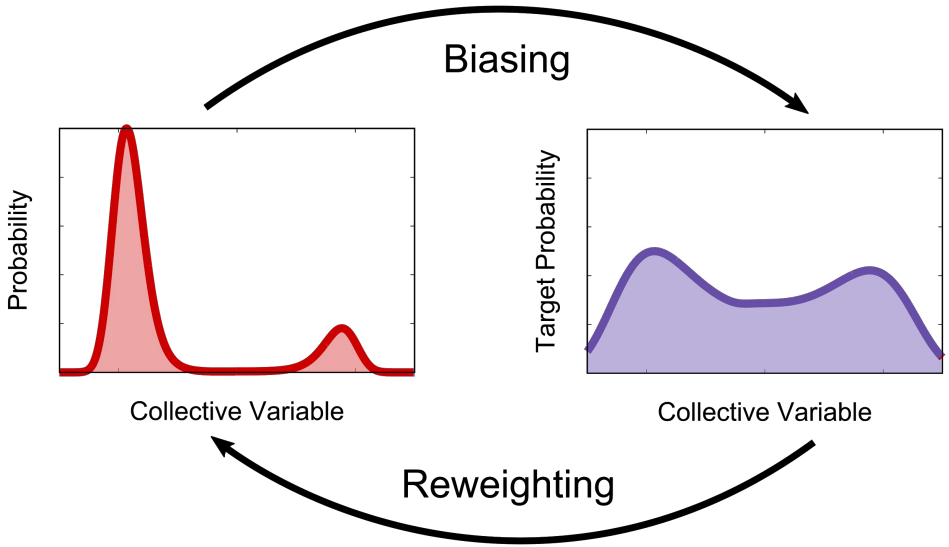
$$v(\mathbf{x}) = -\log \frac{p^{tg}(\mathbf{x})}{P(\mathbf{x})}$$

- Since $P(\mathbf{x})$ is unknown we set up an iterative scheme based on on-the-fly reweighting and adiabatic evolution of the bias

Let's first see the case of collective variables enhanced sampling using OPES

The OPES method: CVs

$$v(s) = -\log \frac{p^{tg}(s)}{P(s)}$$



$$P(s) = \frac{\sum_k^n w_k G(s,s_k)}{\sum_k^n w_k}$$

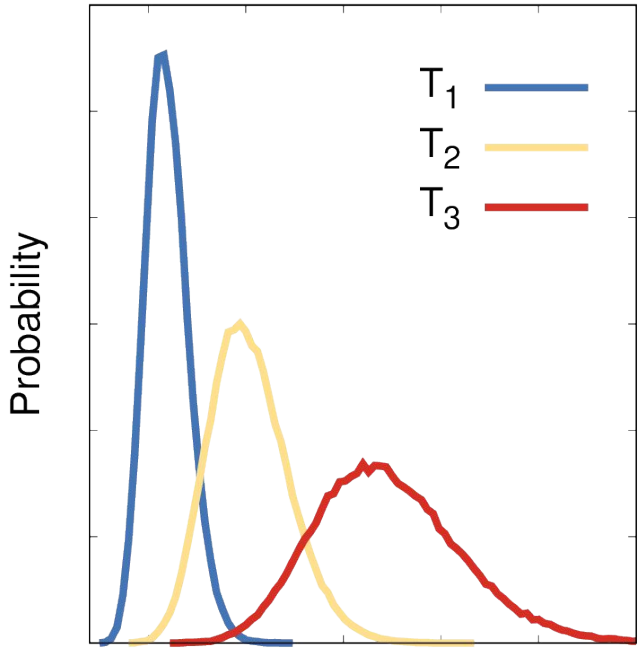
- Collective variable $s = s(\mathbf{x})$
- Target distribution is chosen by requiring its **marginal** $p^{tg}(s)$ to be easy-to-sample
- We only need to reconstruct the probability along the CV, we use a weighted kernel density estimation

Invernizzi, and Parrinello. "Rethinking Metadynamics: from bias potentials to probability distributions." **J. Phys. Chem. Lett. 11.7 (2020)**

The OPES method: Tempering

The target distribution is a combination of different temperatures

$$p^{tg}(\mathbf{x}) = \frac{1}{N} \sum_{T} P_T(\mathbf{x})$$



The OPES method: Tempering

The target distribution is a combination of different temperatures

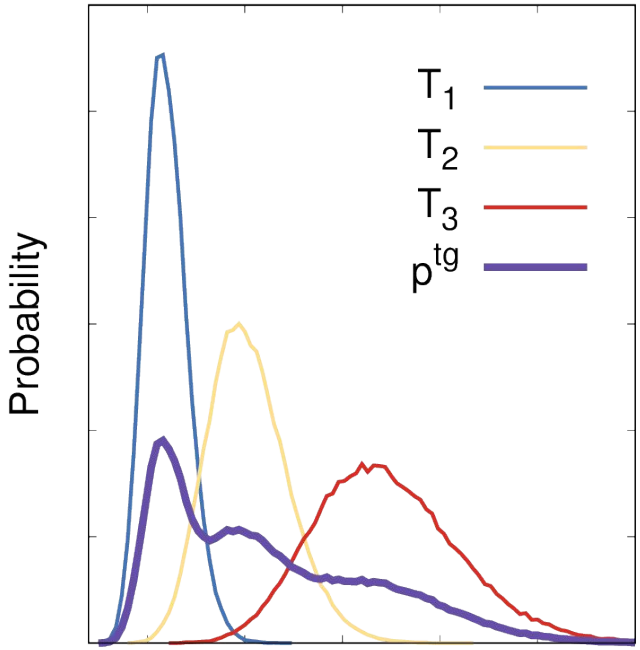
$$p^{tg}(\mathbf{x}) = \frac{1}{N} \sum_T P_T(\mathbf{x})$$

The bias can be written as

$$v(\mathbf{x}) = -\log \left[\frac{1}{N} \sum_T e^{-\Delta u_T(\mathbf{x}) + \Delta F(T)} \right]$$

Where the free energy difference as a function of temperature is iteratively estimated via reweighting

$$\Delta F(T) = -\log \left[\frac{\left\langle e^{-\Delta u_T + v} \right\rangle_{p^{tg}}}{\left\langle e^{v} \right\rangle_{p^{tg}}} \right]$$

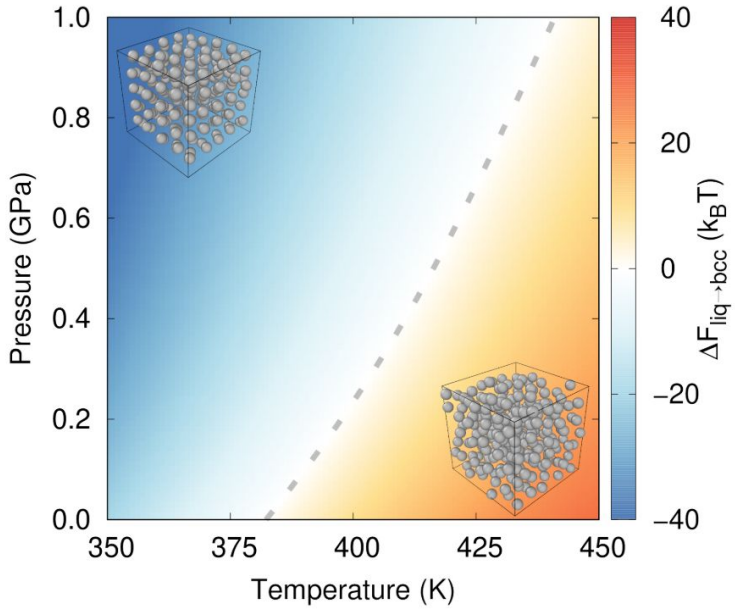


3. The method in action

a phase diagram from a single simulation

Sodium phase diagram

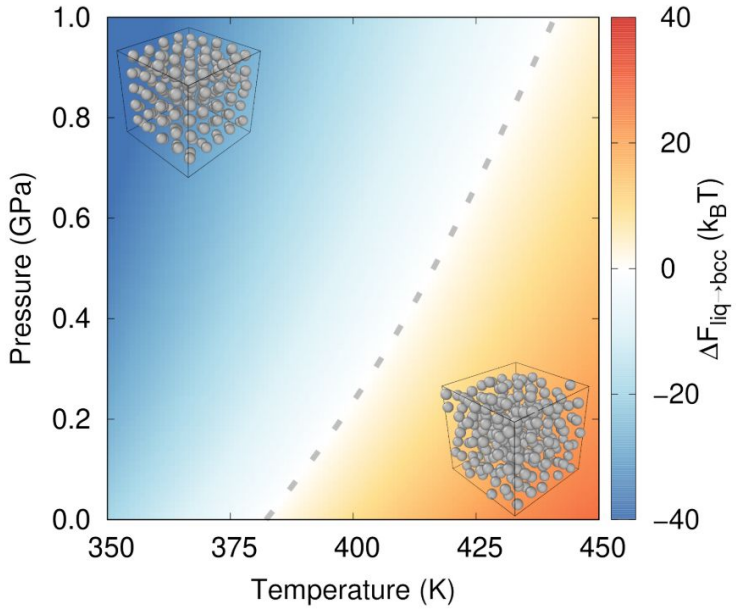
We want to calculate the phase diagram of sodium around its first order **solid-liquid** phase transition.



Sodium phase diagram

We want to calculate the phase diagram of sodium around its first order **solid-liquid** phase transition.

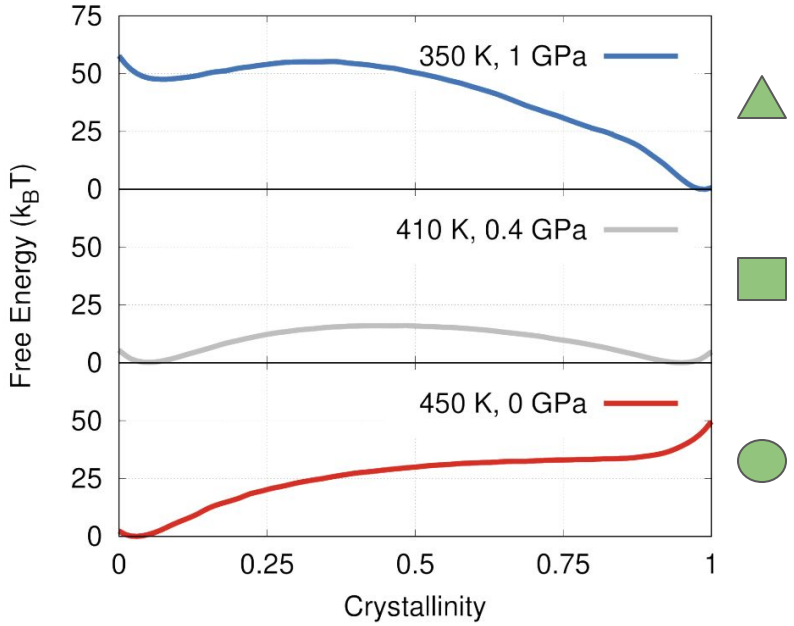
We combine tempering in **temperature** and **pressure** with the biasing of a **crystallization** collective variable[1].

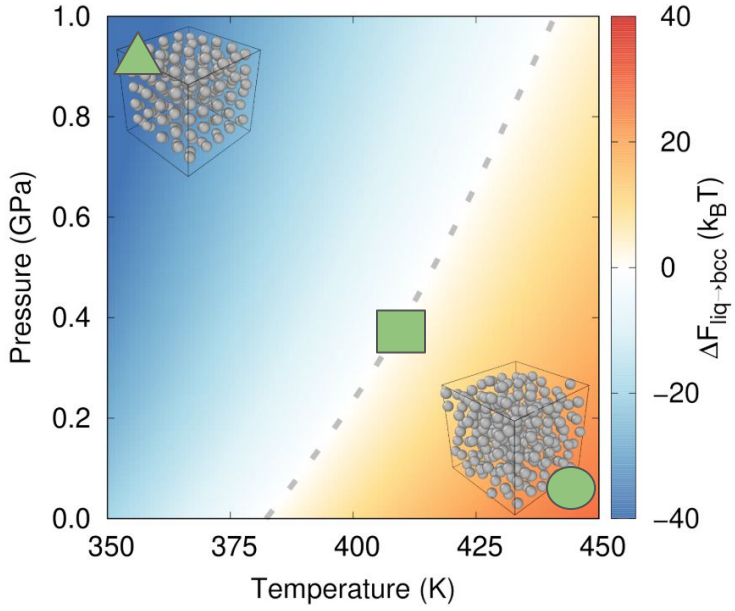


[1] Piaggi and Parrinello, J. Chem. Phys. 150, 244119 (2019)

Sodium phase diagram

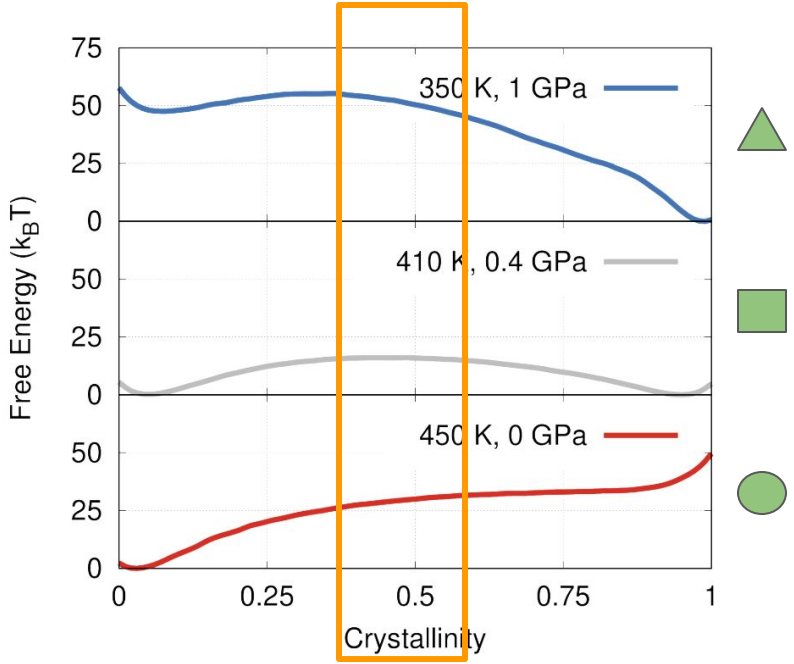
A multithermal-multibaric simulation alone would not be efficient

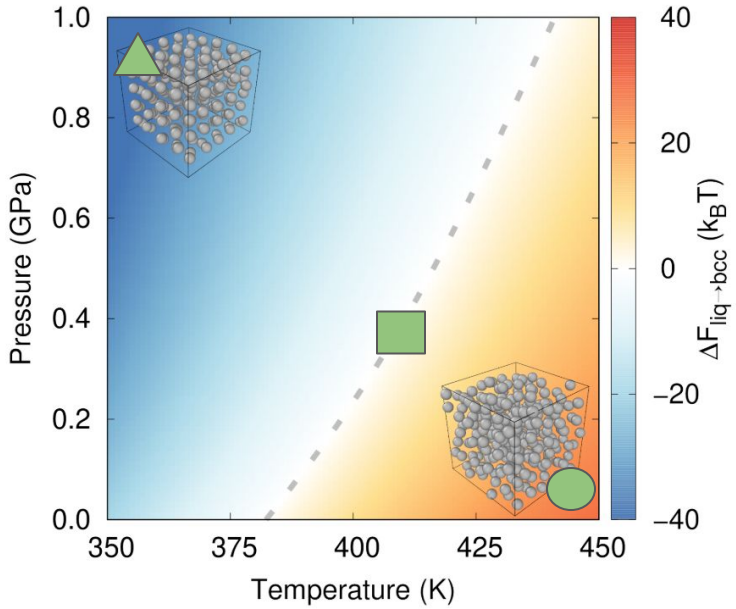




Sodium phase diagram

A multithermal-multibaric simulation alone would not be efficient

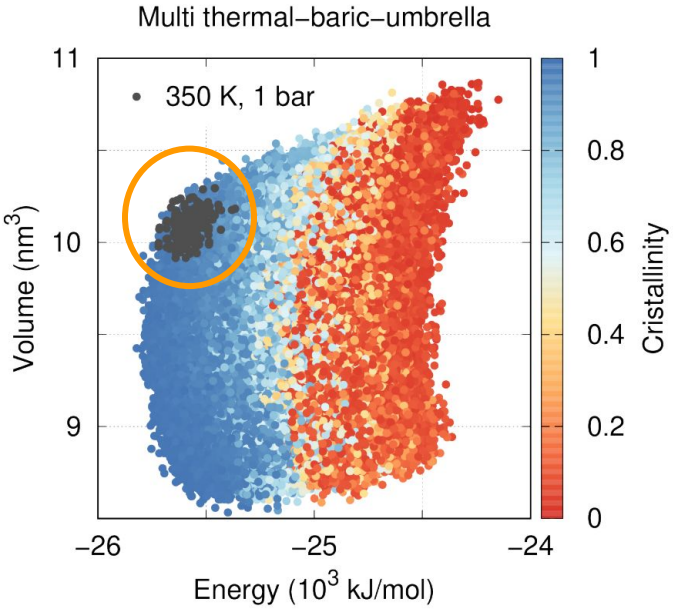




Sodium phase diagram

A standard simulation would sample only one phase and a narrow energy-volume region

Our method allows for a broad and efficient sampling



Summary

Using a target-distribution perspective we developed OPES method

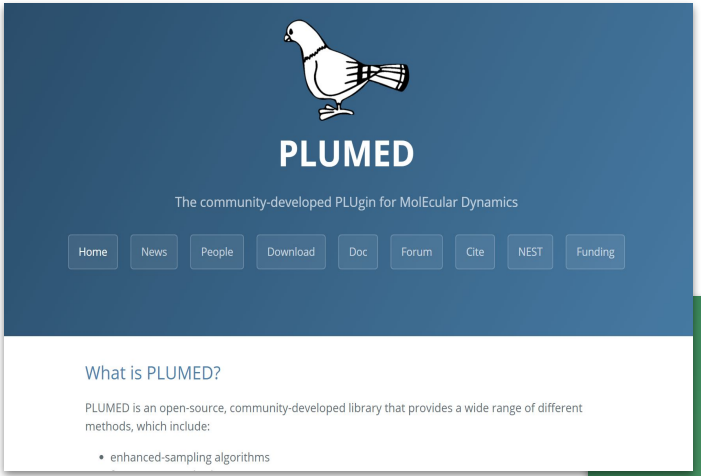
- General approach to various enhanced sampling strategies
- Efficient and robust
- Simple to use
- Scalable (no minimum number of replicas)
- Open source and portable

Available through PLUMED

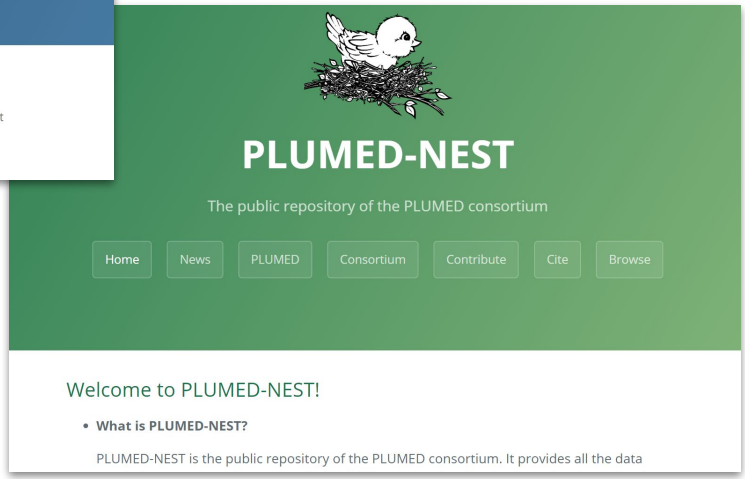
Implemented open source in PLUMED

www.plumed.org

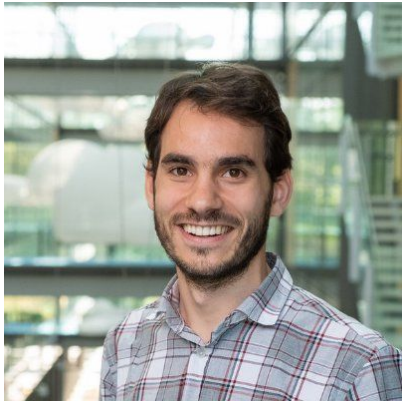
Can be used with LAMMPS, GROMACS, OpenMM, NAMD, QESPRESSO, CP2K, …



Examples on PLUMED-NEST



Acknowledgements



- Pablo M. Piaggi
- Parrinello Group