Statistical methods in Atomistic Computer Simulations

4. Biased sampling

Michele Ceriotti

MSE 639 - EPFL - EDMX



Outline

1. Sampling the canonical ensemble in atomistic simulations: Monte Carlo, correlation functions, ergodicity
2. Thermostatting MD efficiently: white and colored-noise Langevin dynamics
3. Rare events: transition state theory and the transition state ensemble
4. Statistical re-weighting, biased sampling, metadynamics
5. Linear and non-linear dimensionality reduction: determining automatically order parameters

Re-weighting to get a different ensemble

- Remember: Monte Carlo and MD are all about computing integrals by computing sequences of samples

$$\lim_{M\to\infty} \frac{1}{M} \sum_i A(\mathbf{q}_i) = \int \mathrm{d}\mathbf{q}\, P(\mathbf{q})\, A(\mathbf{q}) = \langle A \rangle_P$$

- What if we have $\{\mathbf{q}_i\}$ distributed according to $\tilde{P}$, but we want an integral relative to P? Re-weight!

$$\langle A \rangle_P = \int \mathrm{d}\mathbf{q}\, P(\mathbf{q})\, A(\mathbf{q}) = \int \mathrm{d}\mathbf{q}\, \tilde{P}(\mathbf{q})\, A(\mathbf{q})\, \frac{P(\mathbf{q})}{\tilde{P}(\mathbf{q})}$$

  - The denominator is there because typically we don't know the normalization of P and $\tilde{P}$

Torrie & Valleau, J. Comput. Phys. (1977)

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$$\langle A \rangle_P = \lim_{M\to\infty} \frac{\sum_i A(\mathbf{q}_i) \frac{P(\mathbf{q}_i)}{\tilde{P}(\mathbf{q}_i)}}{\sum_i \frac{P(\mathbf{q}_i)}{\tilde{P}(\mathbf{q}_i)}} = \frac{\left\langle A\, P/\tilde{P} \right\rangle_{\tilde{P}}}{\left\langle P/\tilde{P} \right\rangle_{\tilde{P}}}$$

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You can get everything... or not?

- Simulate at inverse temperature $\tilde{\beta}$ and evaluate at inverse temperature β: as simple as

$$\langle A \rangle_\beta = \left\langle A\, e^{-(\beta-\tilde{\beta})V} \right\rangle_{\tilde{\beta}} / \left\langle e^{-(\beta-\tilde{\beta})V} \right\rangle_{\tilde{\beta}}$$

- Simulate with a cheap potential $\tilde{V}$ and evaluate with an expensive potential V

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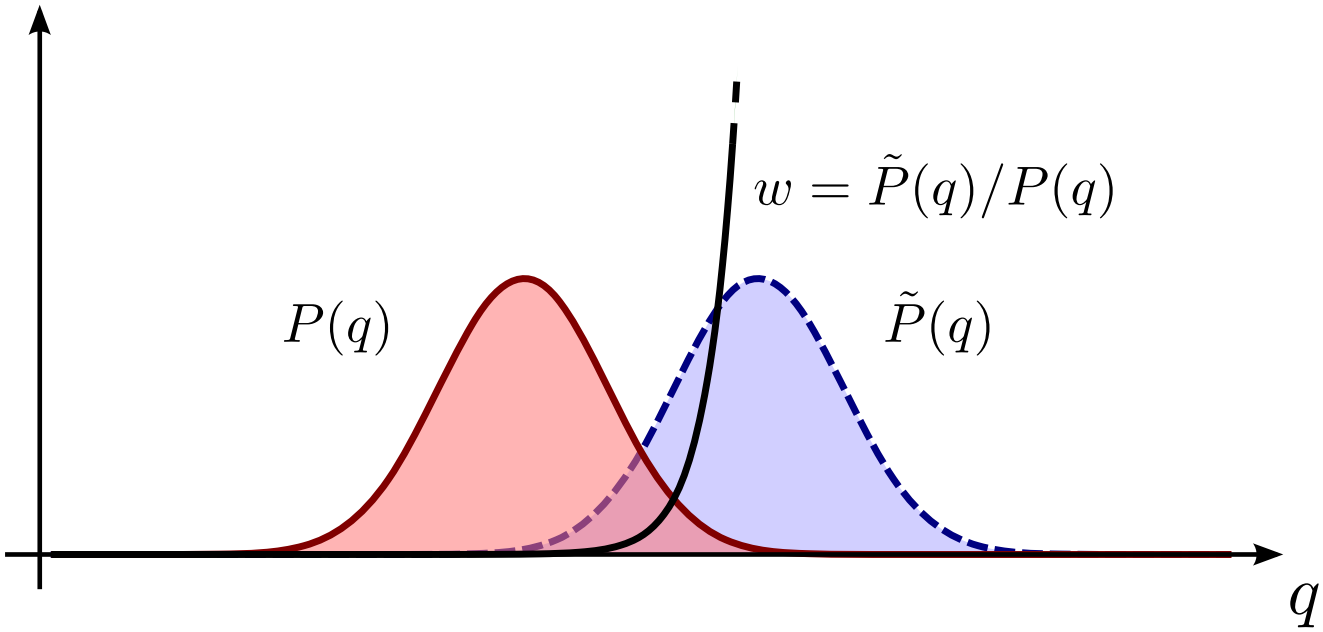
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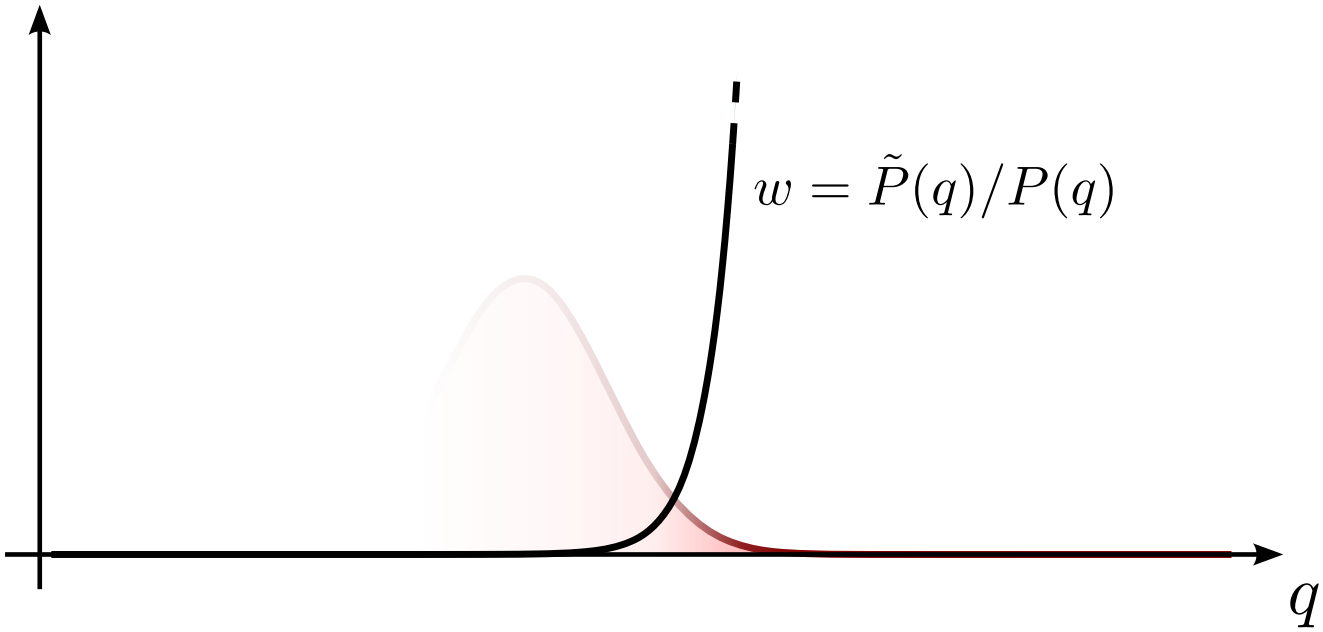
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Statistics of re-weighting

- Let a be our observable and $w = e^h$ the weight. Then everything is controlled by $p(a, w)$

$$p(a, w) = \int \mathrm{d}\mathbf{q}\, P(\mathbf{q})\, \delta(a - a(\mathbf{q}))\, \delta(w - w(\mathbf{q}))$$

- We want to get the error in the mean with n **independent** samples $\bar{a}_n$ (time correlation is a separate problem)

$$\bar{a}_n = \frac{\sum_{i=1}^{n} a_i w_i}{\sum_{i=1}^{n} w_i}$$

- Asymptotic expansion for $n \to \infty$
  - $\bar{a}_n$ is a biased estimator (easy to see: $\langle \bar{a}_1 \rangle = \langle a \rangle \neq \langle aw \rangle / \langle w \rangle$)
  - the error term is as hard to compute as $\langle aw \rangle$!

Ceriotti, Brain, Riordan, Manolopoulos, Proc. Royal Soc. A (2011)

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$$\langle \bar{a}_n \rangle = \left\langle \frac{\sum_{i=1}^n a_i w_i}{\sum_{i=1}^n w_i} \right\rangle = n \left\langle \frac{aw}{w + z_{n-1}} \right\rangle \qquad z_n = \sum_{i=1}^n w_i$$

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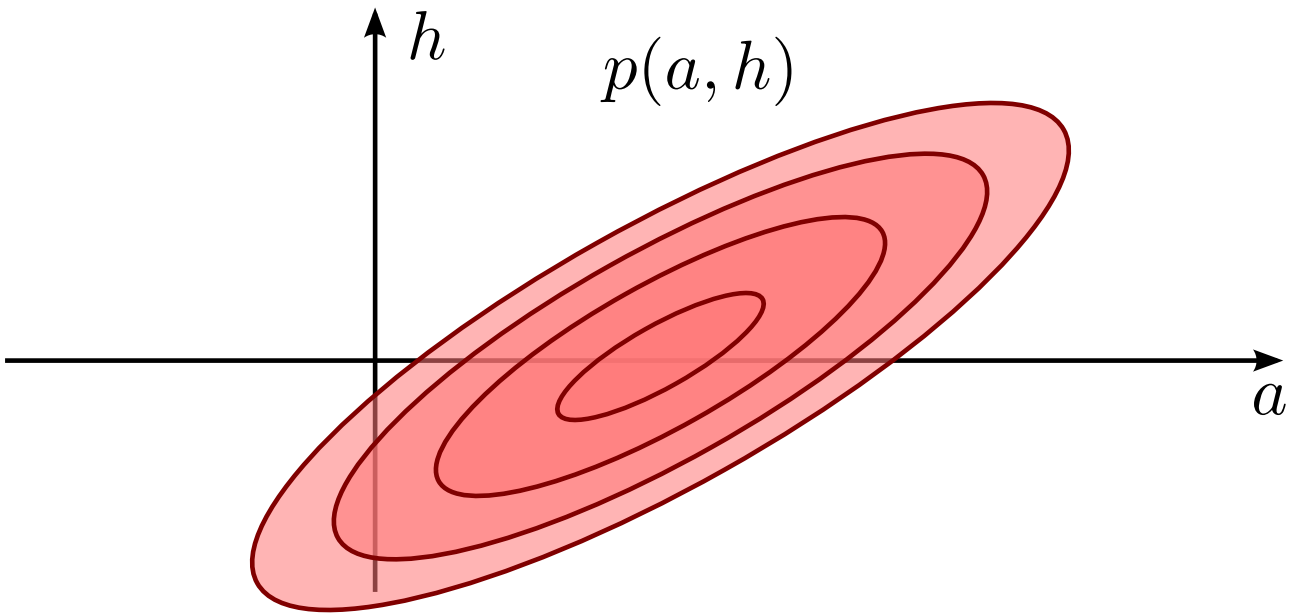
$$\langle \bar{a}_n \rangle \approx \frac{\langle aw \rangle}{\langle w \rangle} + \frac{1}{n} \frac{\langle aw \rangle \langle w^2 \rangle - \langle w \rangle \langle aw^2 \rangle}{\langle w \rangle^3}$$

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Gaussian statistics for the log-weight

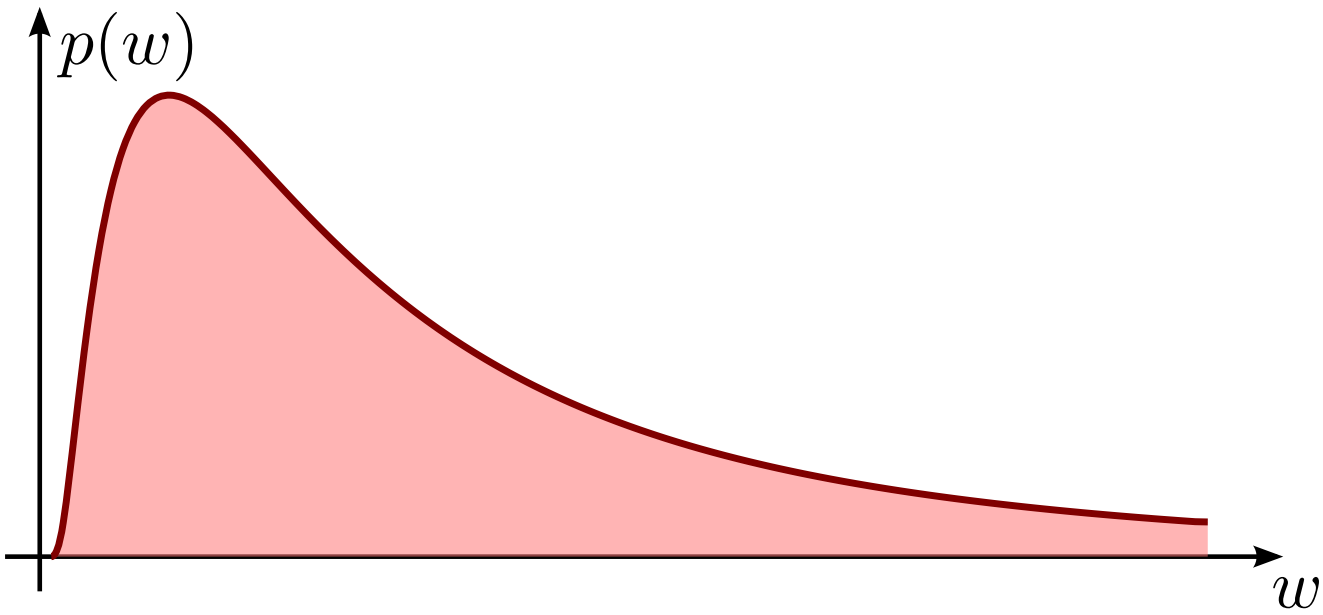
- Often a and $h = \ln w$ are sums of many weakly correlated terms $\rightarrow$ central limit theorem, Gaussian statistics is a reasonable ansatz.
  - $p(a, w)$ is fully determined by $\langle a \rangle$, $\sigma^2(a)$, $\sigma^2(h)$, $\langle ah \rangle$
  - The whole problem is that $w = e^h$ has **log-normal** statistics, with pathological tail behavior: $\langle w^n \rangle / \langle w \rangle^n = \exp n^2 \sigma^2(h)/2$



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- Simple & stable estimate of systematic and statistical error on $\bar{a}_n$:

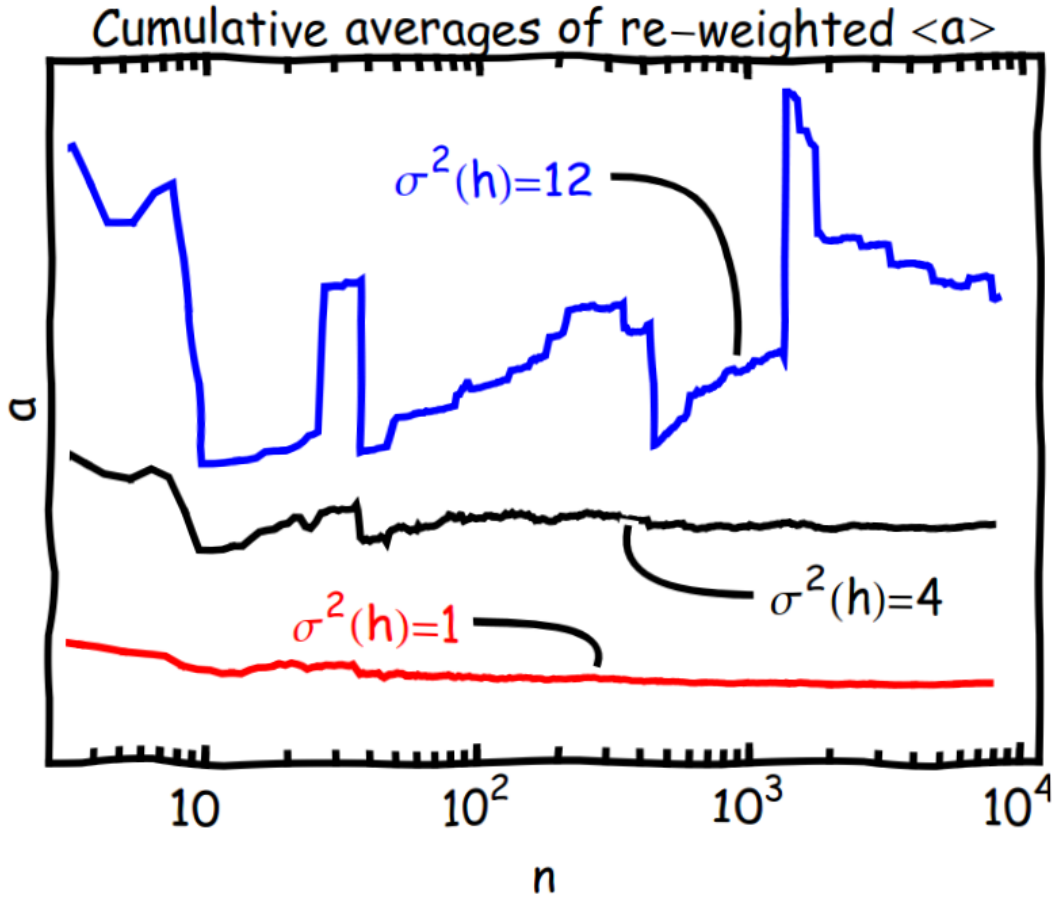
$$\langle \bar{a}_n \rangle \approx \langle a \rangle - \langle ah \rangle + \frac{1}{n} \langle ah \rangle e^{\sigma^2(h)} \qquad \sigma^2(\bar{a}_n) \approx \frac{1}{n} \left[\sigma^2(a) + \langle ah \rangle^2 \right] e^{\sigma^2(h)}$$

  - re-weighting is dangerous whenever $\sigma^2(\log w) \gg 1$.
  - these are asymptotic estimates. For $n < e^{\sigma^2(h)}$, the error is smaller *but decreases more slowly than* $1/\sqrt{n}$
  - pathological behavior depends on large-h tail. Things work *much* better if the statistics is not Gaussian

Ceriotti, Brain, Riordan, Manolopoulos, Proc. Royal Soc. A (2011)

A simple check of re-weighting problems

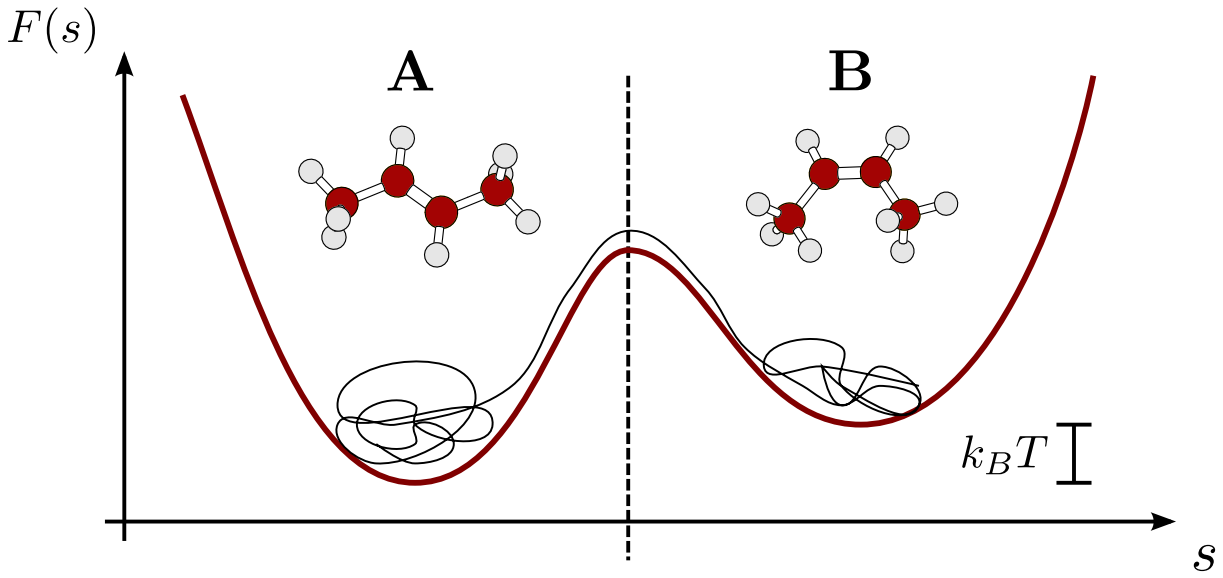
- When $\sigma^2(h) \gg 1$, the statistics are dominated by outliers. This is made apparent by looking at the cumulative average of observables
  - The cumulative average has large jumps even for large n
  - The problem is already evident with $\sigma^2(h) \approx 4$



Ceriotti & Markland, J. Chem. Phys. (2013)

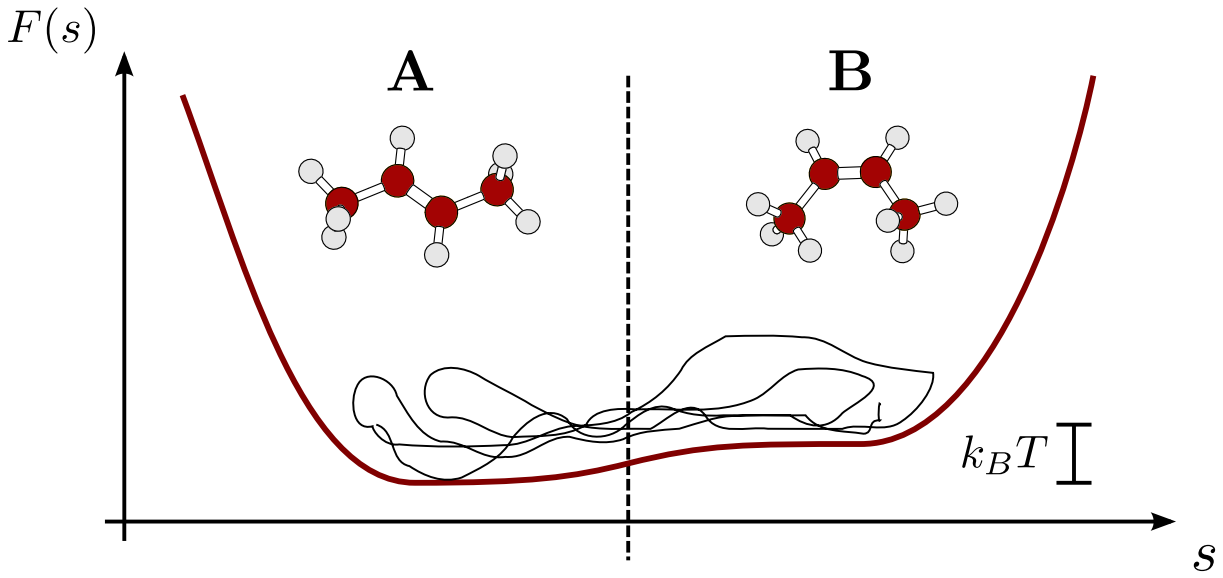
Umbrella sampling

- Returning to rare events – the problem is the free-energy barrier
  - The system would be diffusing freely if the barrier was not there
  - What happens if one adds a s-dependent bias term to the potential?
  - Bias can be un-done by re-weighting!



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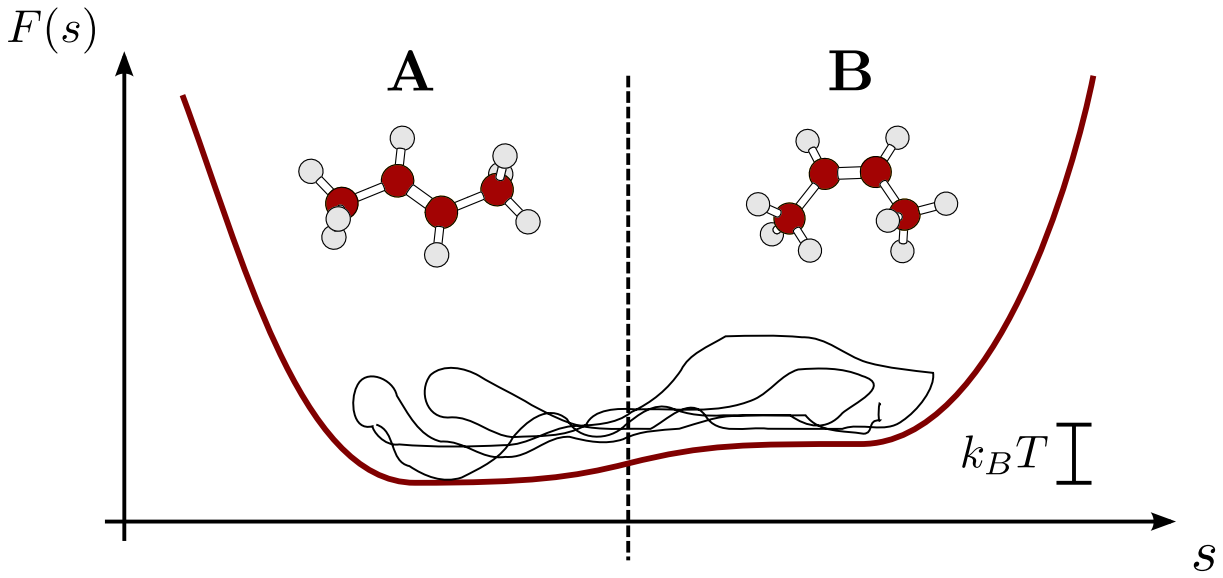
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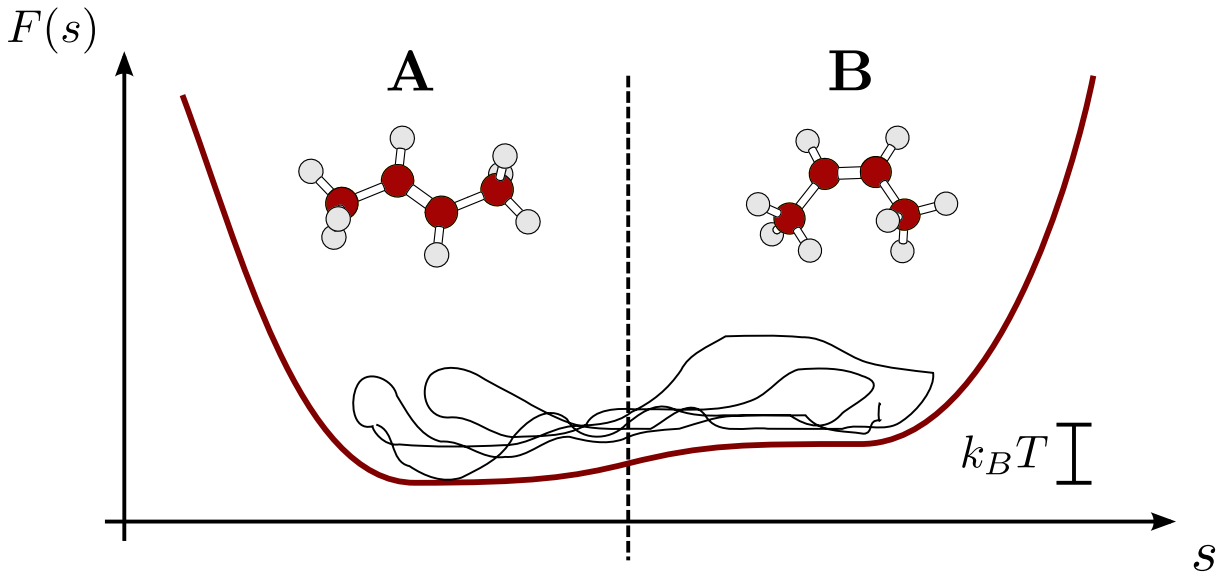
$$e^{-\beta \tilde{F}(s)} = \int \mathrm{d}\mathbf{q}\, \delta\left(s - s\left(\mathbf{q}\right)\right)\, e^{-\beta[V(\mathbf{q}) + v(s(\mathbf{q}))]}$$



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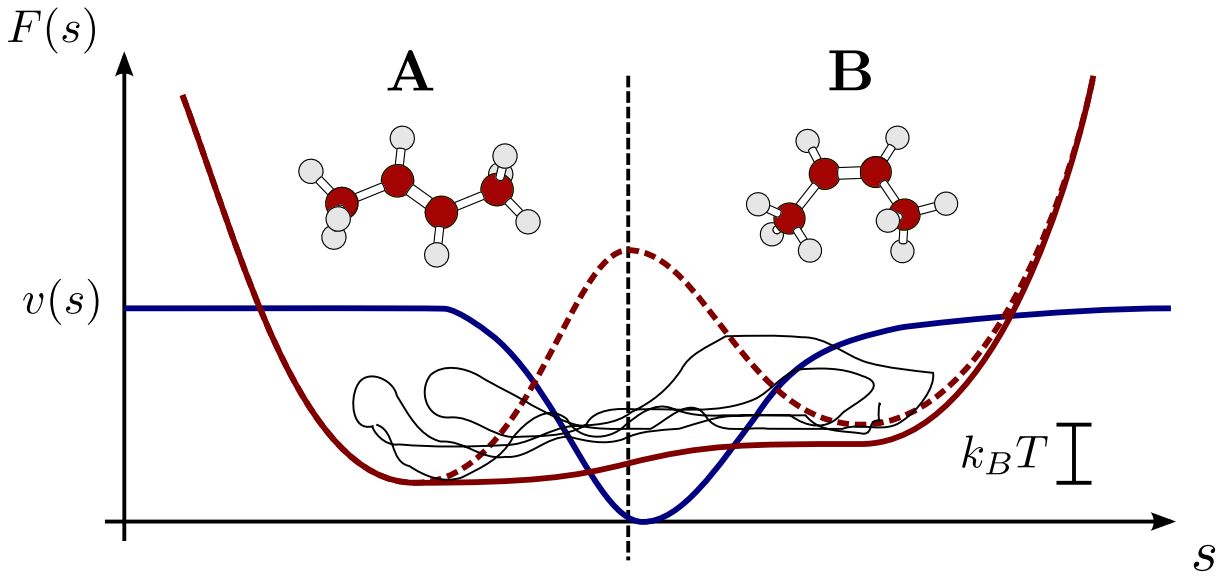
$$e^{-\beta \tilde{F}(s)} = e^{-\beta v(s)} \int \mathrm{d}\mathbf{q}\, \delta\left(s - s\left(\mathbf{q}\right)\right)\, e^{-\beta [V(\mathbf{q})]} = e^{-\beta v(s)} e^{-\beta F(s)}$$



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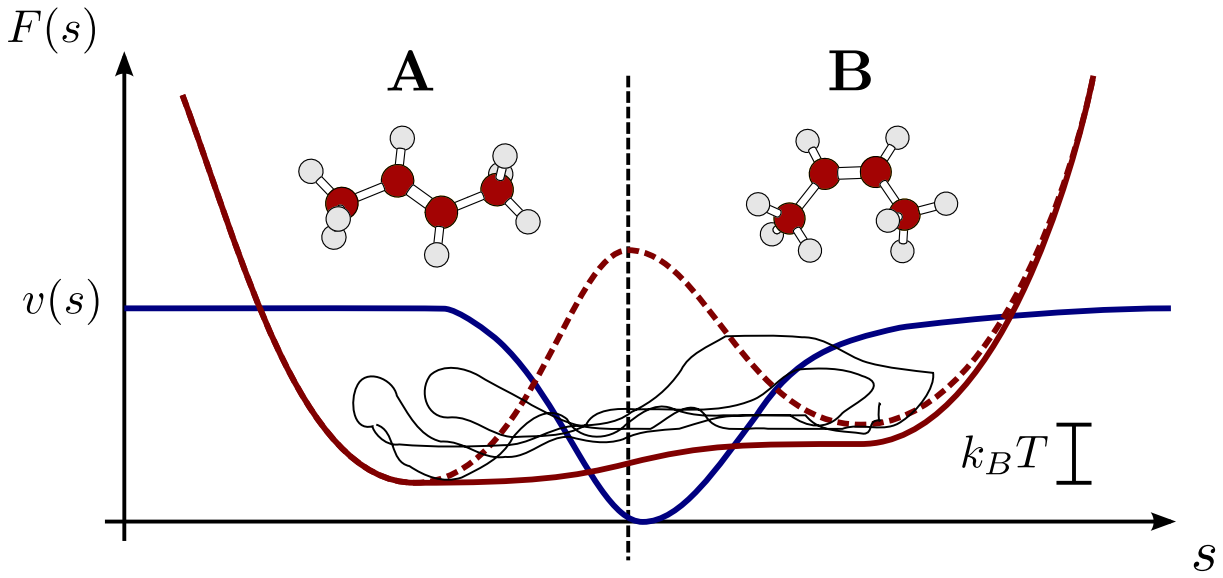
$$\tilde{F}(s) = F(s) + v(s)$$



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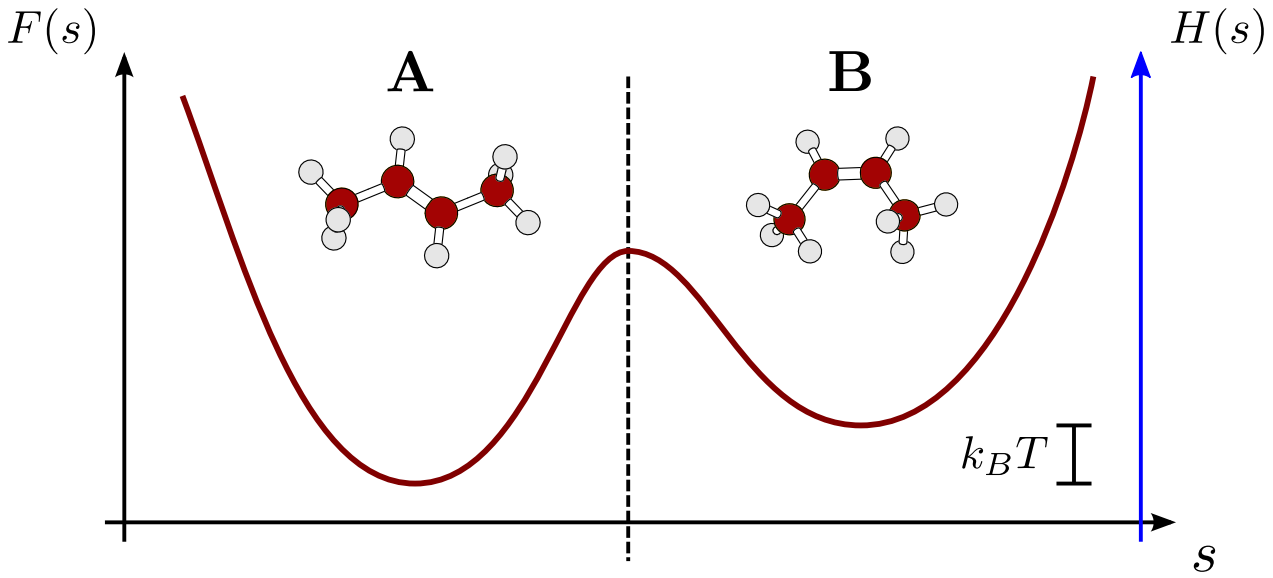
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$$\langle A \rangle_{\text{unbiased}} = \left\langle A\, e^{\beta v(s(\mathbf{q}))} \right\rangle_{\text{biased}}$$



Adaptive bias sampling

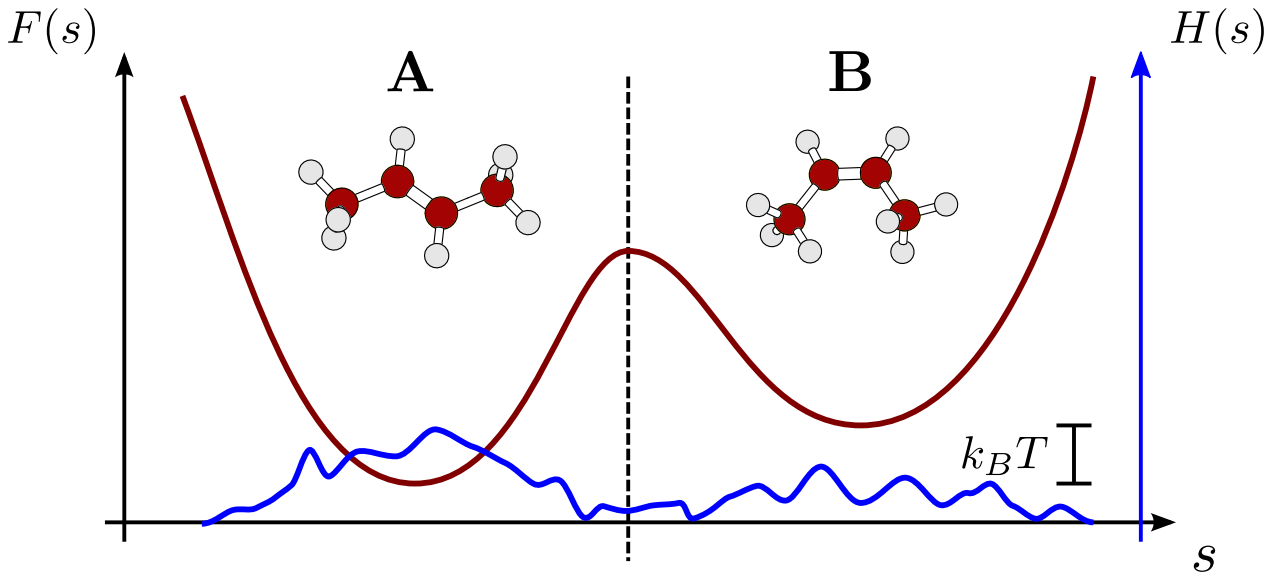
- Ideally, one would like to have $\beta v(s) = -\beta F(s) = \log H(s)$. How to generate this bias?
  1. Start with a flat histogram $\rightarrow v_0(s) = \text{const}$
  2. Run for a while, accumulate histogram $v_1(s) = k_B T \log e^{\beta v_0(s)} \langle \delta(s - s(\mathbf{q})) \rangle_{v_0}$
  3. Run with bias $v_1(s)$. Update the bias, and repeat.



Wang & Landau, Phys. Rev. Lett. (2001)

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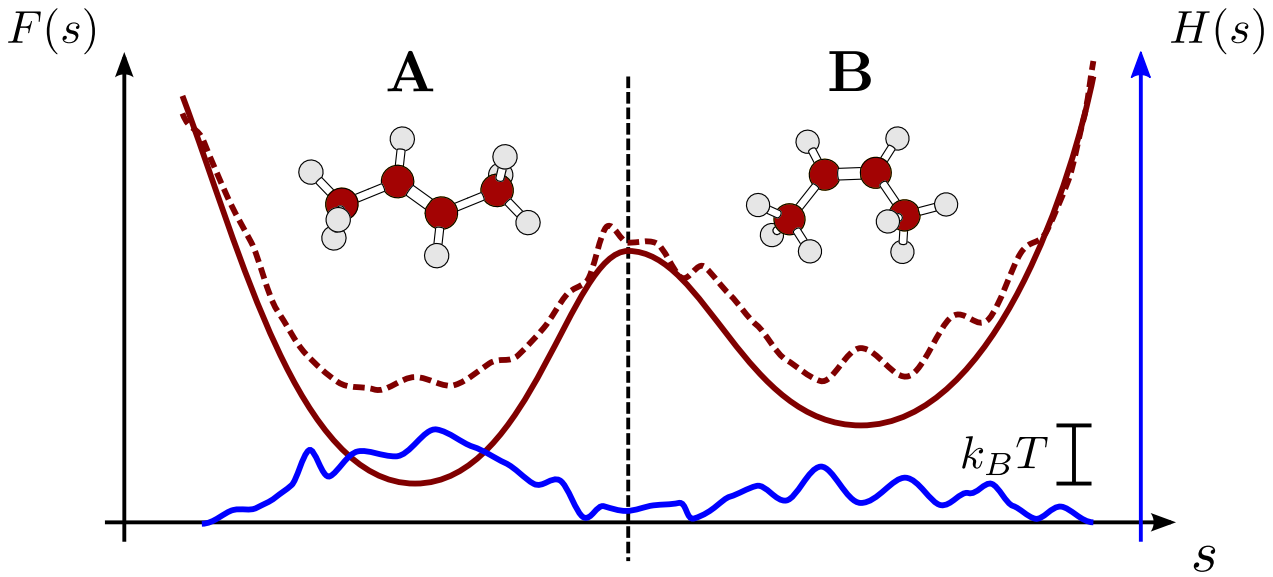
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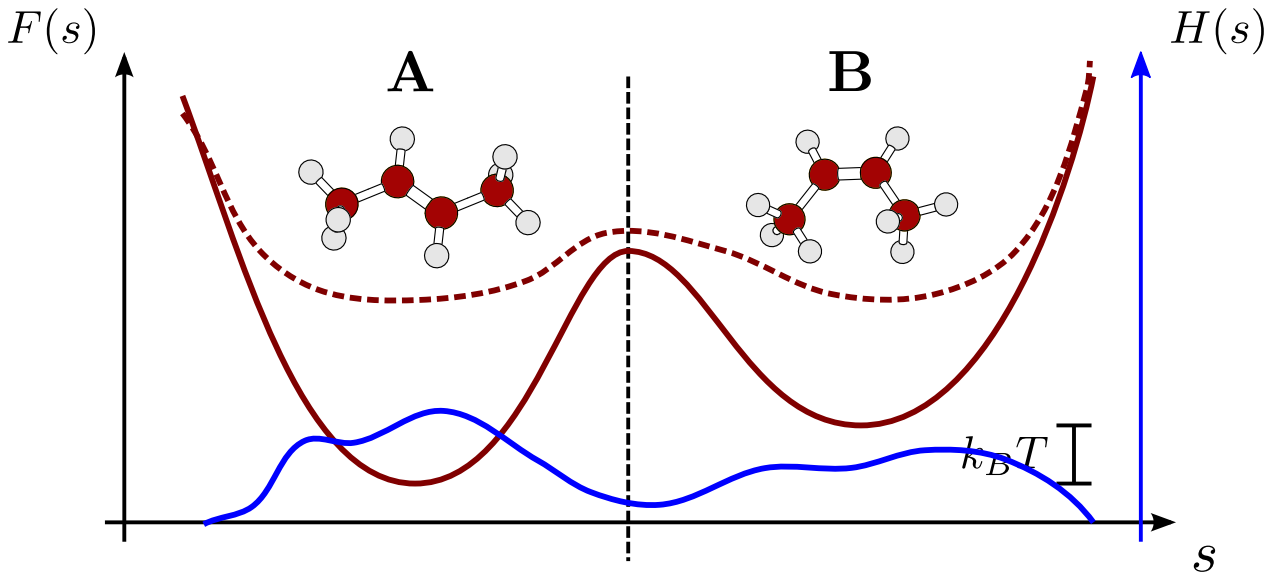
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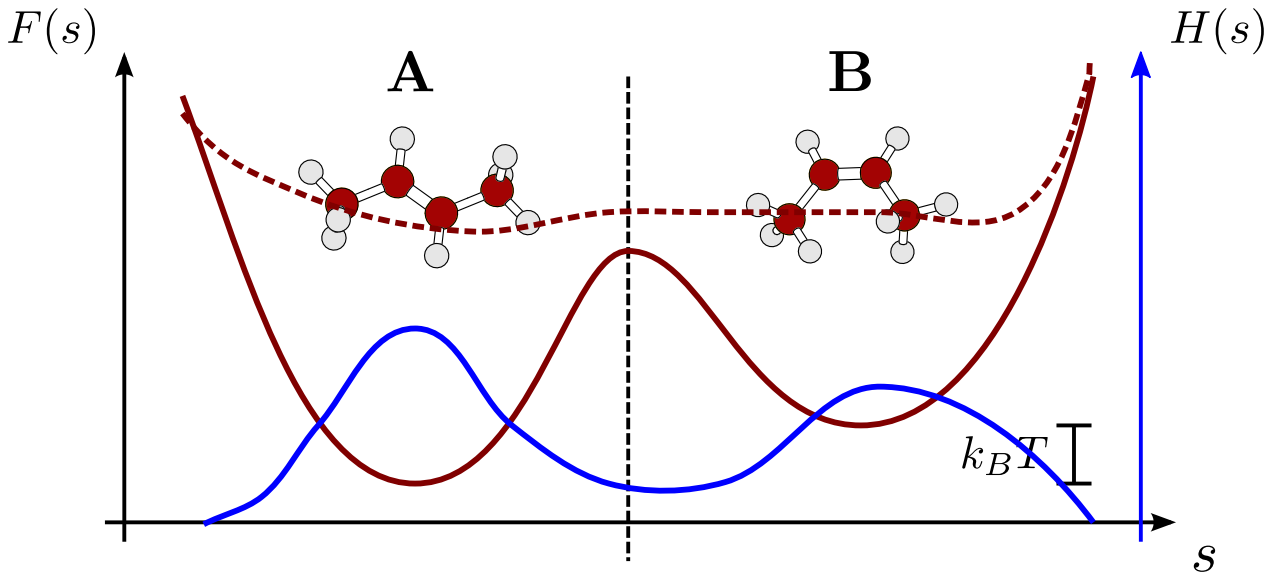
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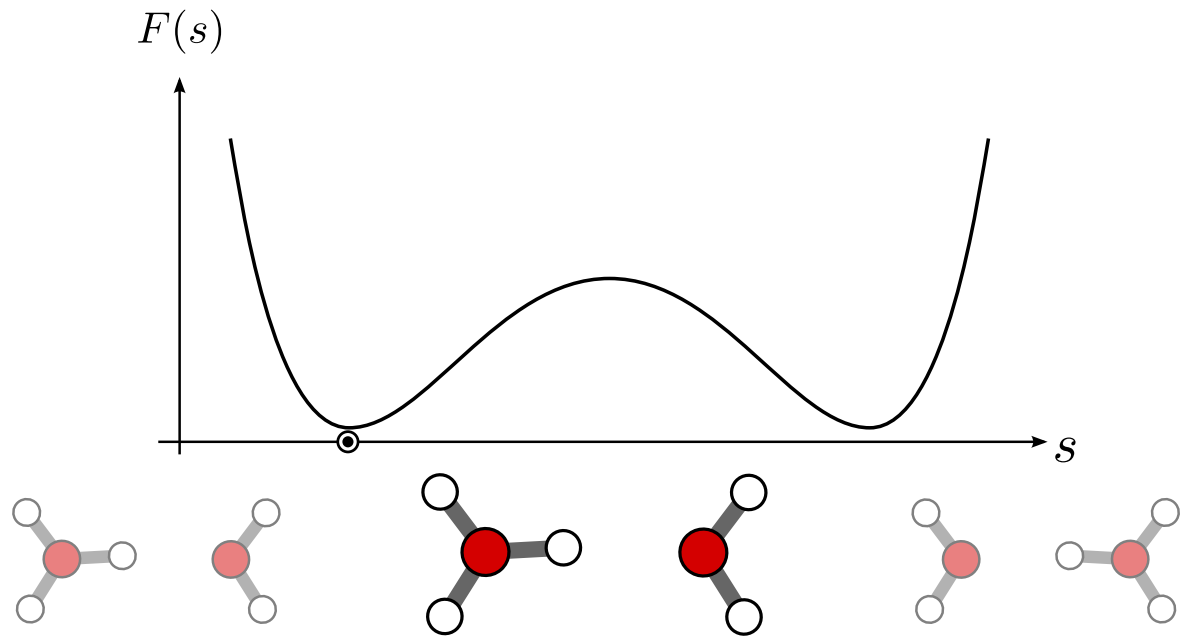
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Metadynamics

- Build-up of the optimal bias by history-dependent dynamics
- Repulsive Gaussians accumulate in locations visited by the system, pushing it to visit all values of the collective variables

$$v(\mathbf{q},t) = v(s(\mathbf{q}),t) = w \sum_{t'<t} \exp -\frac{(s(\mathbf{q}) - s(\mathbf{q}(t')))^2}{2\sigma^2}$$

- At convergence, the bias is the negative of the free energy, $v(s, t \to \infty) \to -F(s)$... however it never *really* converges



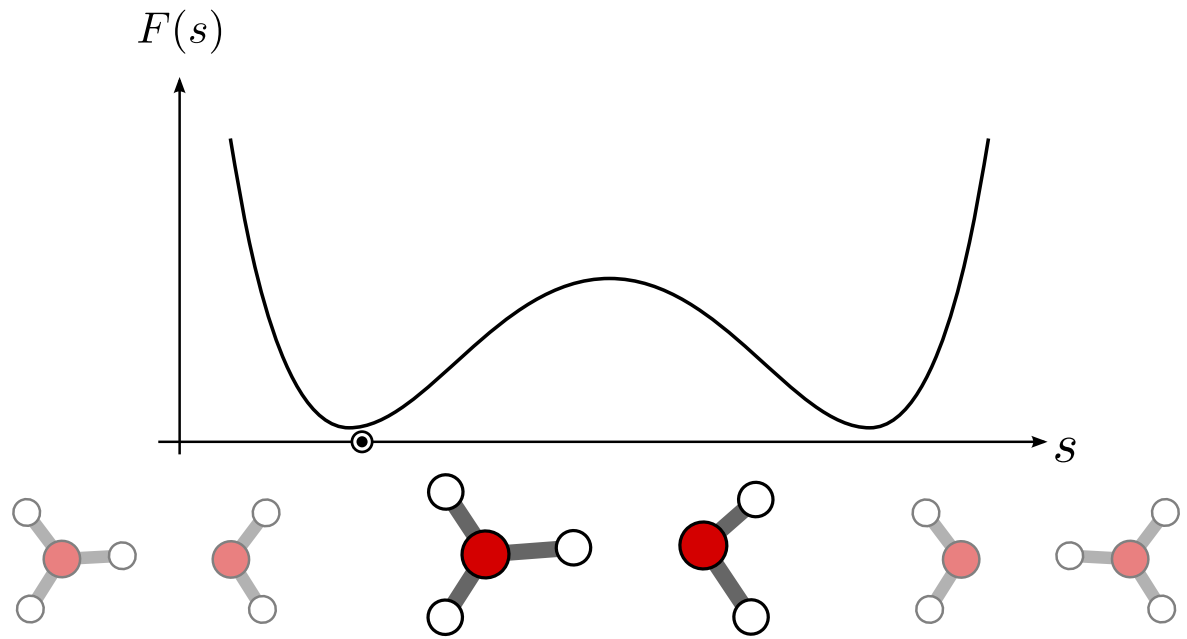
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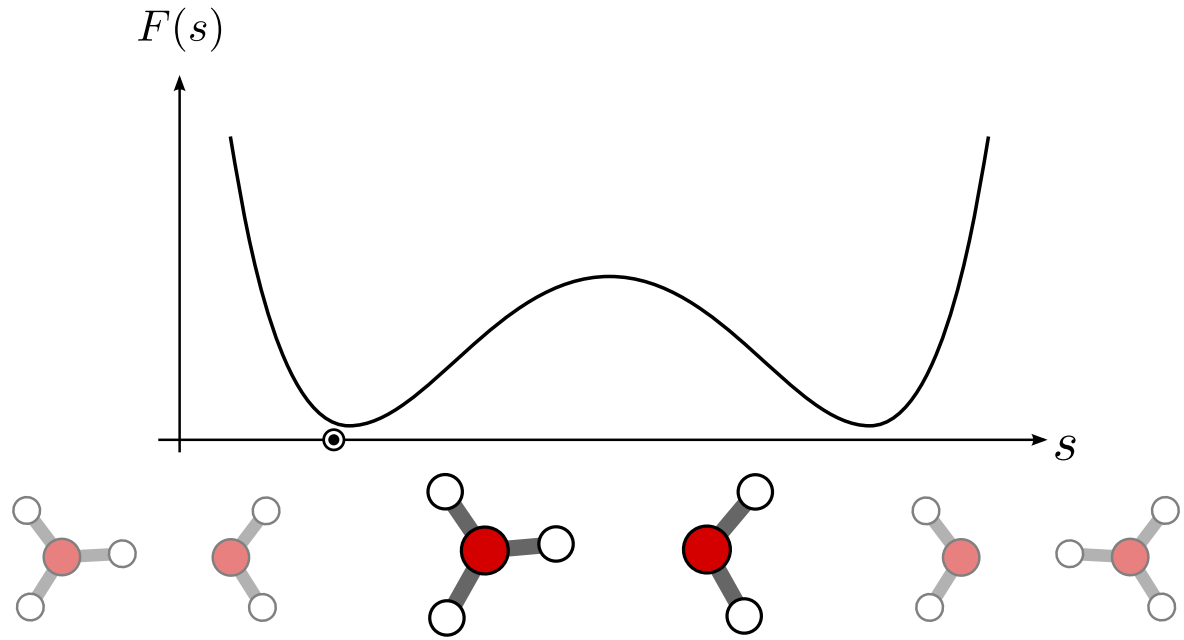
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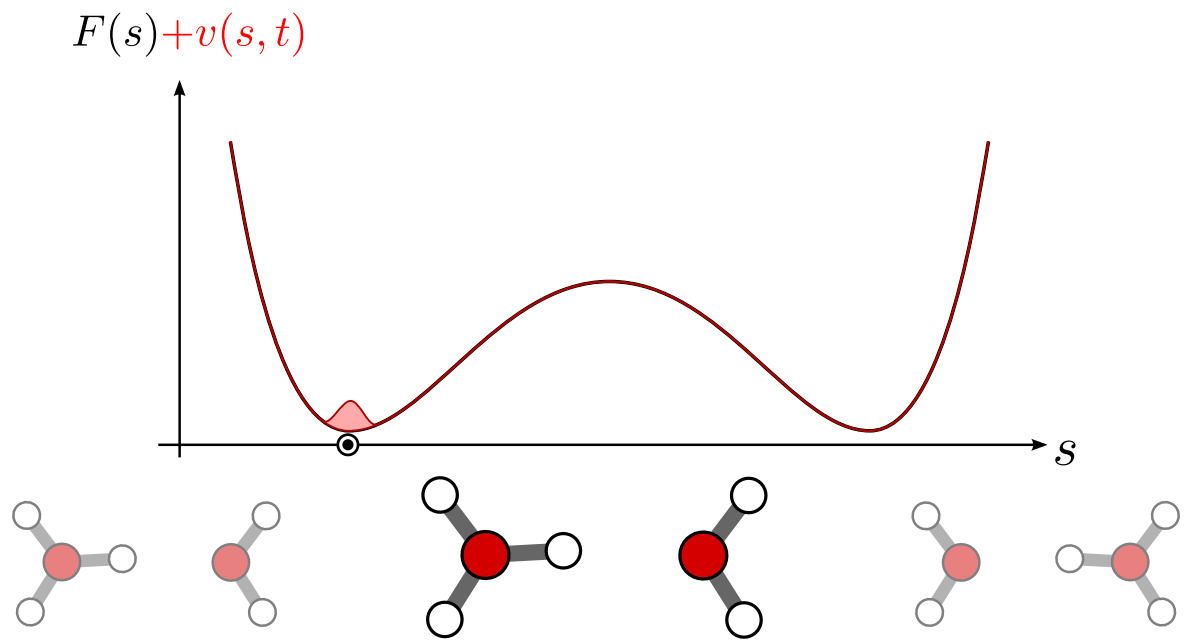
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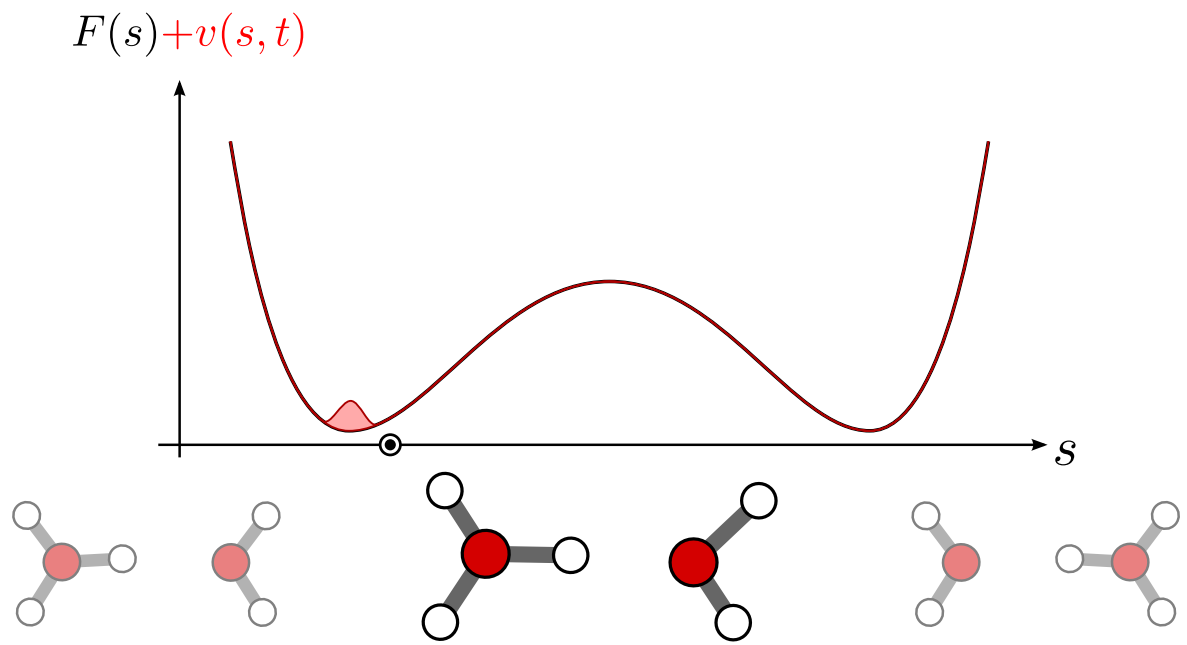
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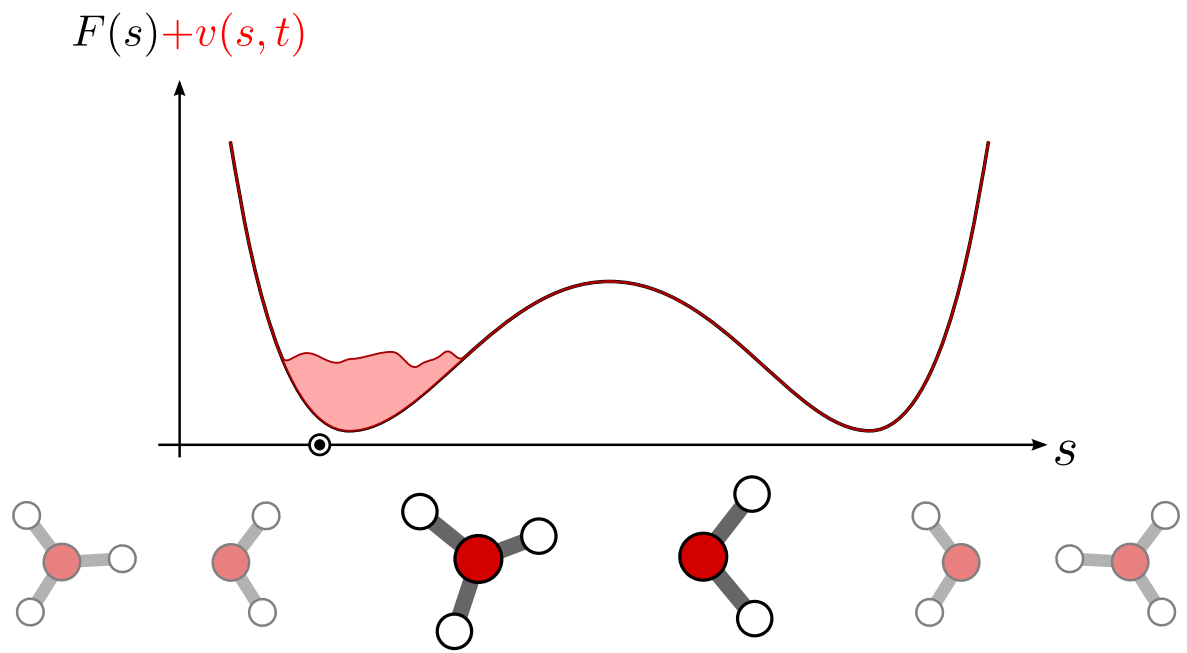
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- Build-up of the optimal bias by history-dependent dynamics
- Repulsive Gaussians accumulate in locations visited by the system, pushing it to visit all values of the collective variables

$$v(\mathbf{q},t) = v(s(\mathbf{q}),t) = w \sum_{t'<t} \exp -\frac{(s(\mathbf{q}) - s(\mathbf{q}(t')))^2}{2\sigma^2}$$

- At convergence, the bias is the negative of the free energy, $v(s, t \to \infty) \to -F(s)$... however it never *really* converges



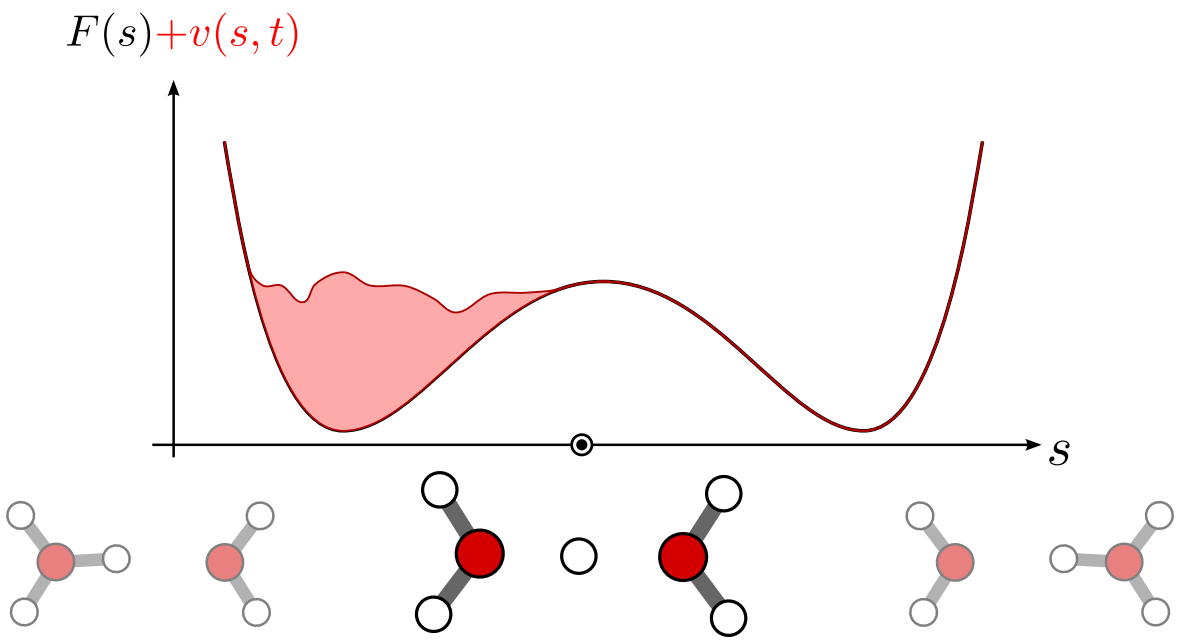
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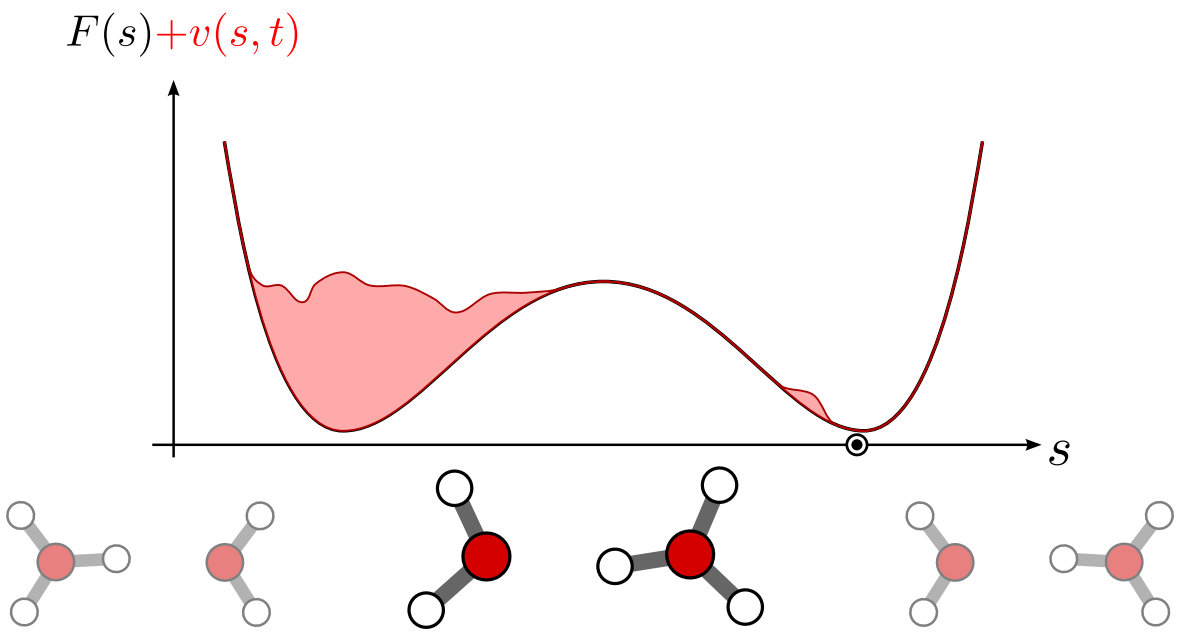
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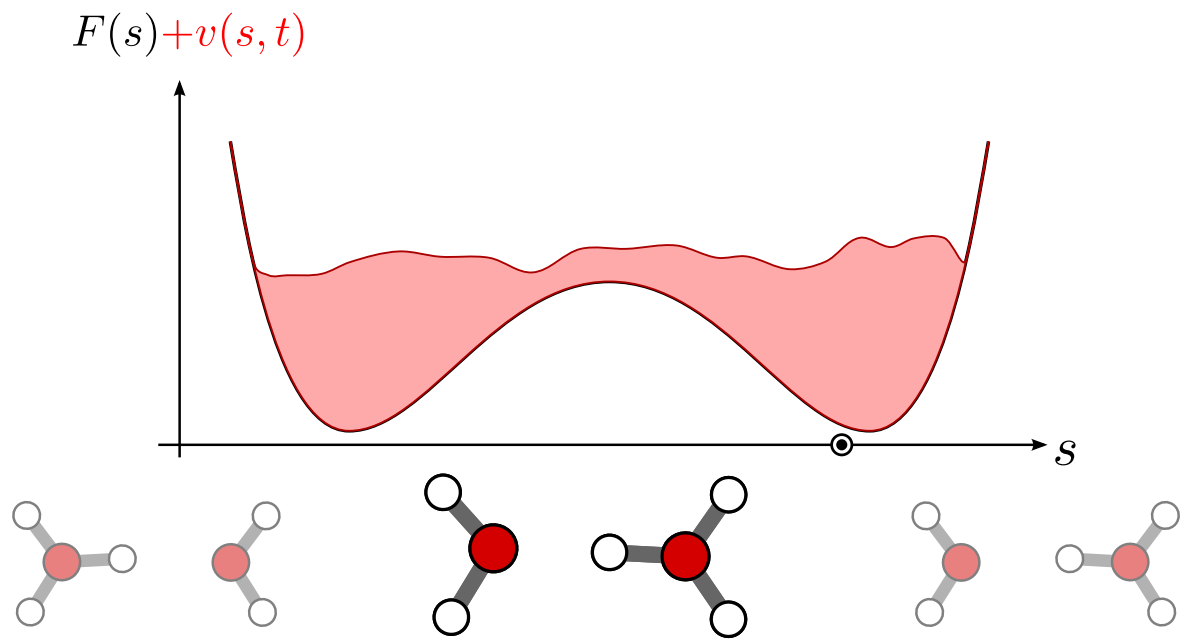
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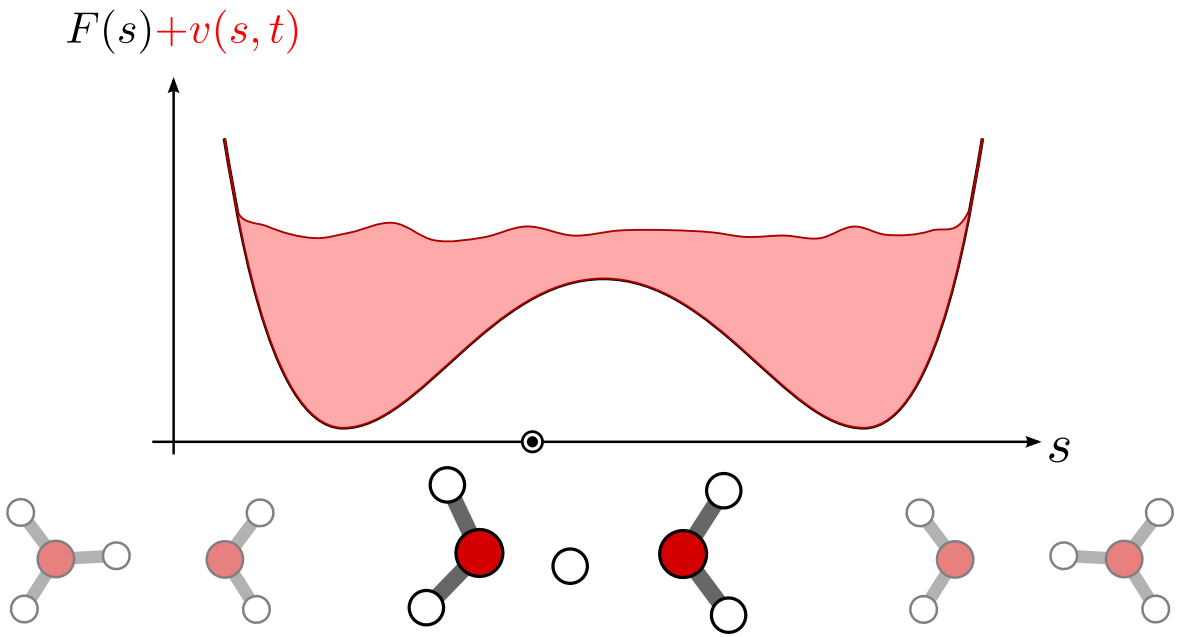
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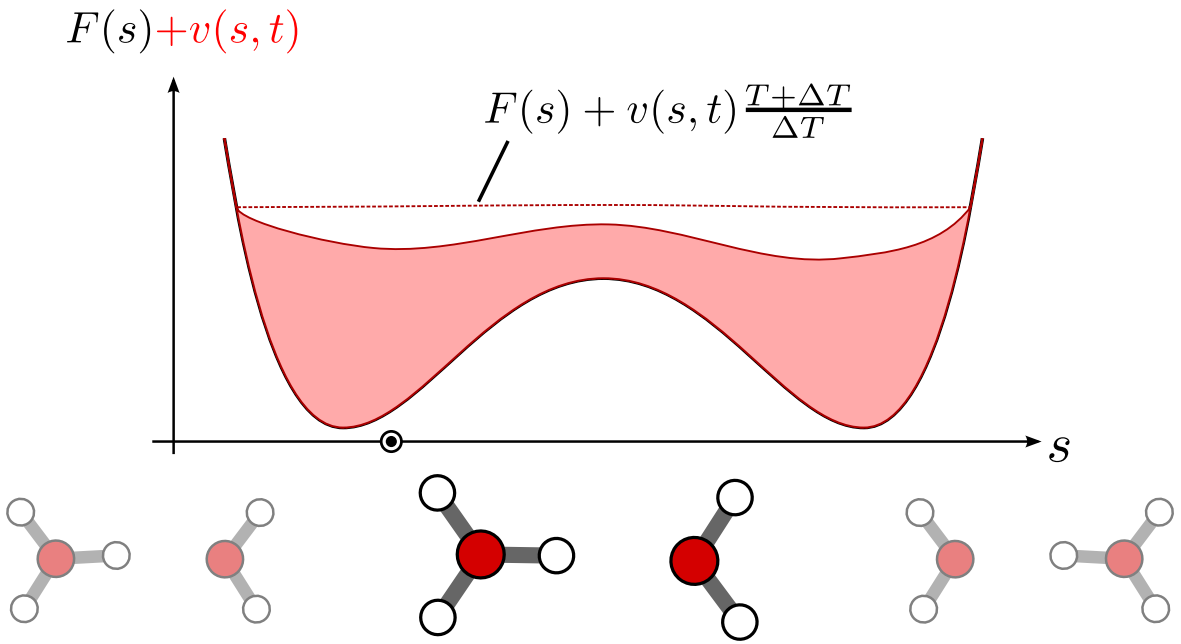
Well-tempered metadynamics

- Reduce the hills height as the simulations goes - use lower hills where there is already a large bias

$$v(\mathbf{q}, t) = w \sum_{t'<t} e^{-v(s(\mathbf{q}(t')),t')/k_B \Delta T} \exp -\frac{(s(\mathbf{q}) - s(\mathbf{q}(t')))^2}{2\sigma^2}$$

- The bias does *not* converge to $-F(s)$, but to

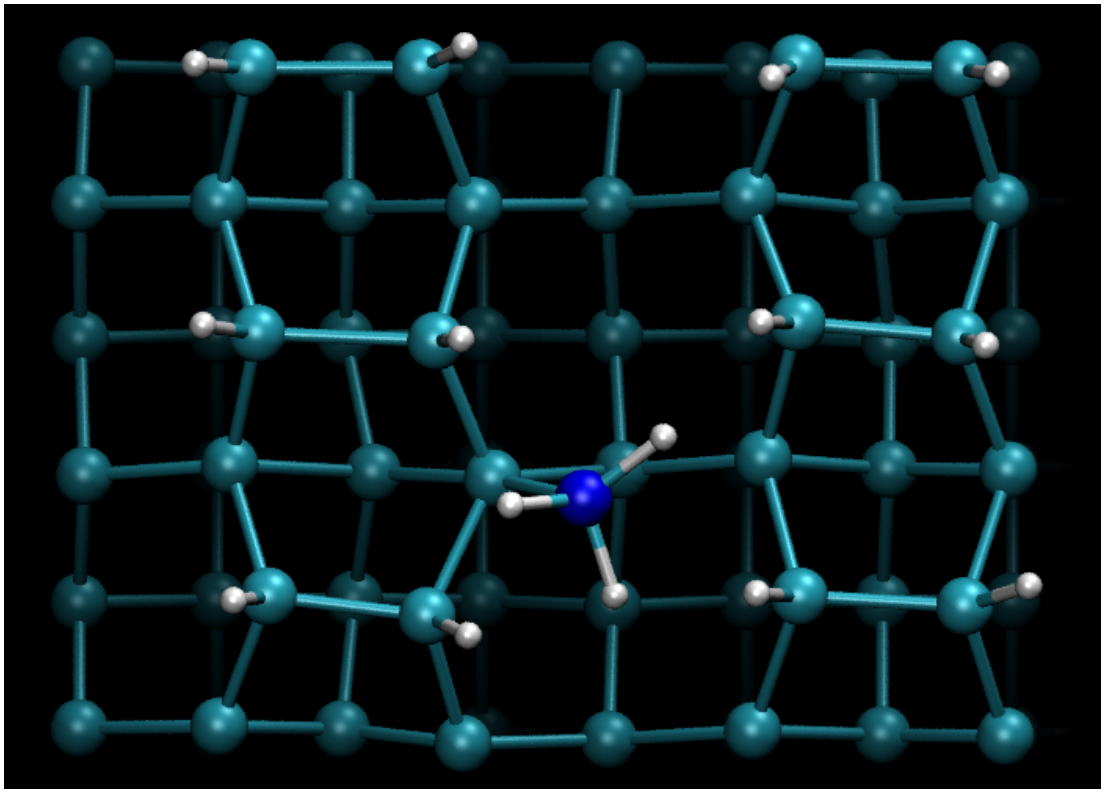
$$v(s, t \to \infty) \to -\frac{\Delta T}{T + \Delta T} F(s)$$



Barducci, Bussi, Parrinello, Phys. Rev. Lett. (2008)

Make things happen in *ab initio* MD

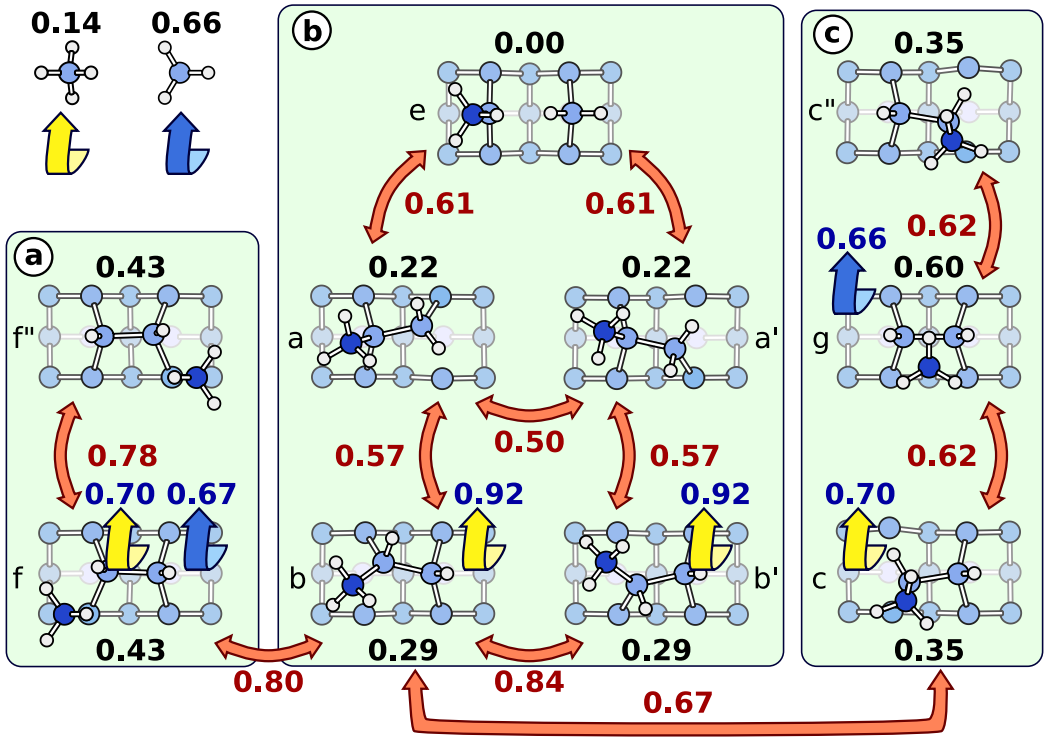
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  - Deposition rate is too large to evaluate a free energy surface
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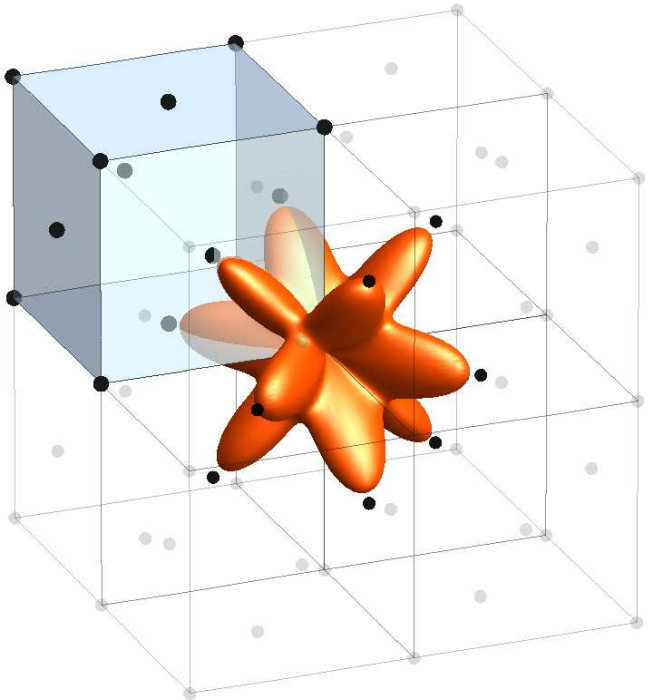
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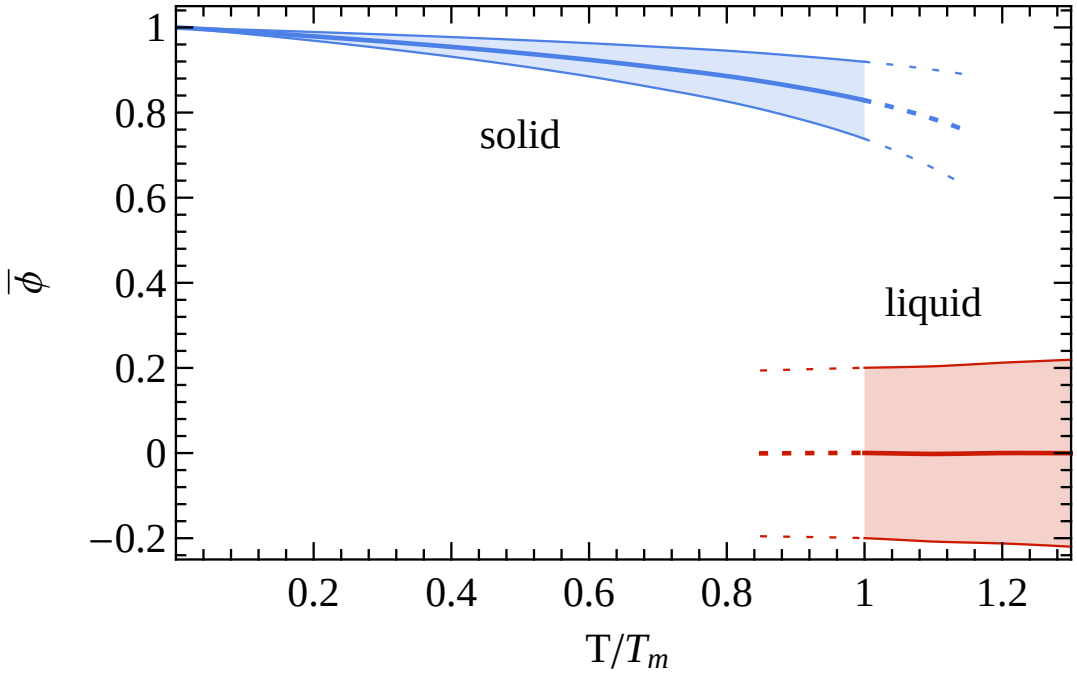


Ceriotti, Bernasconi, Phys. Rev. B. (2007)

Computing the solid-liquid surface tension

1. Choose an order parameter that can discriminate solid and liquid
2. Integrate over two different regions in the simulation box
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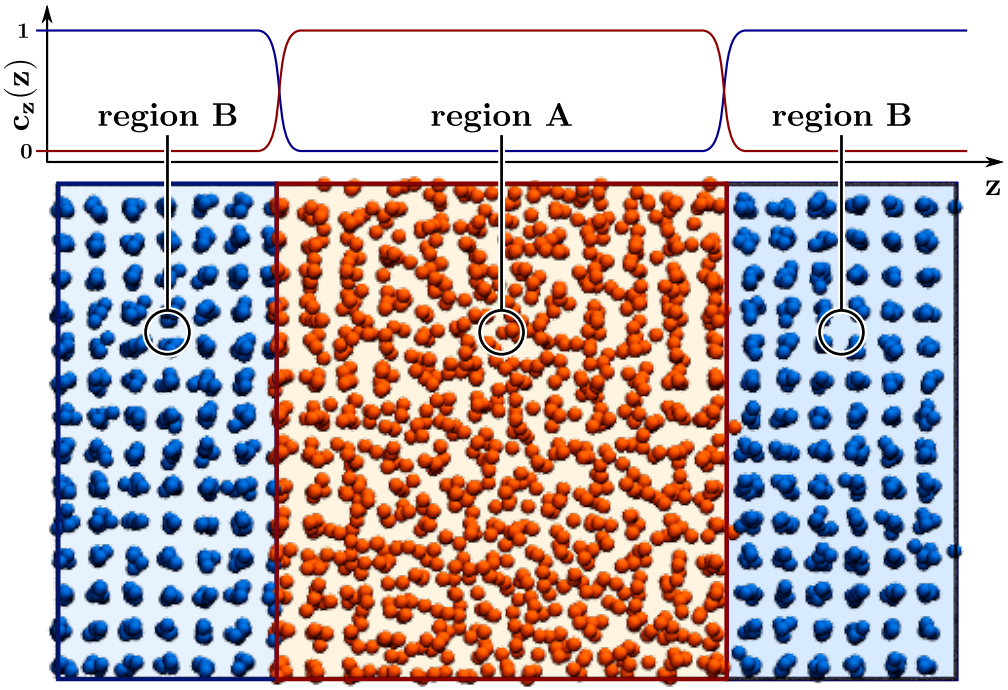




Angioletti, Ceriotti, Lee, Finnis, Phys. Rev. B (2010)

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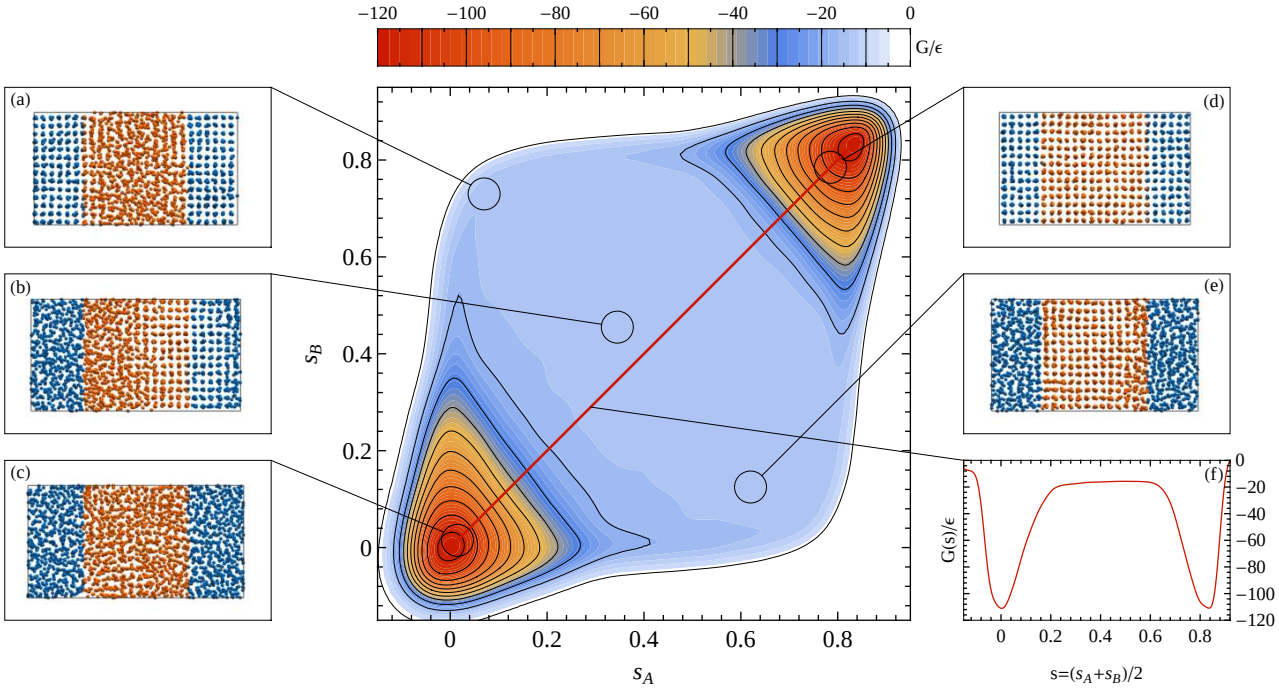
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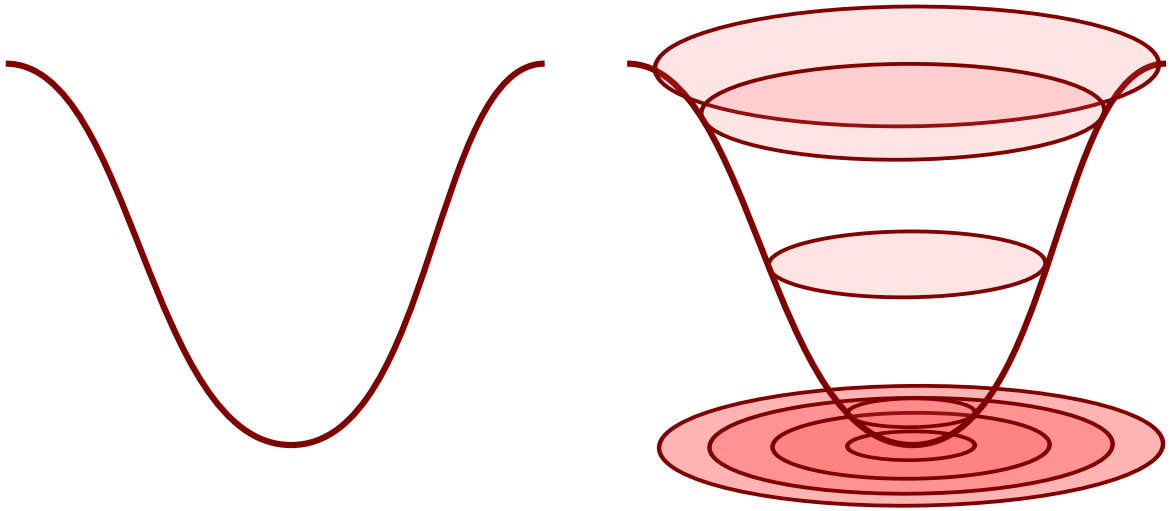
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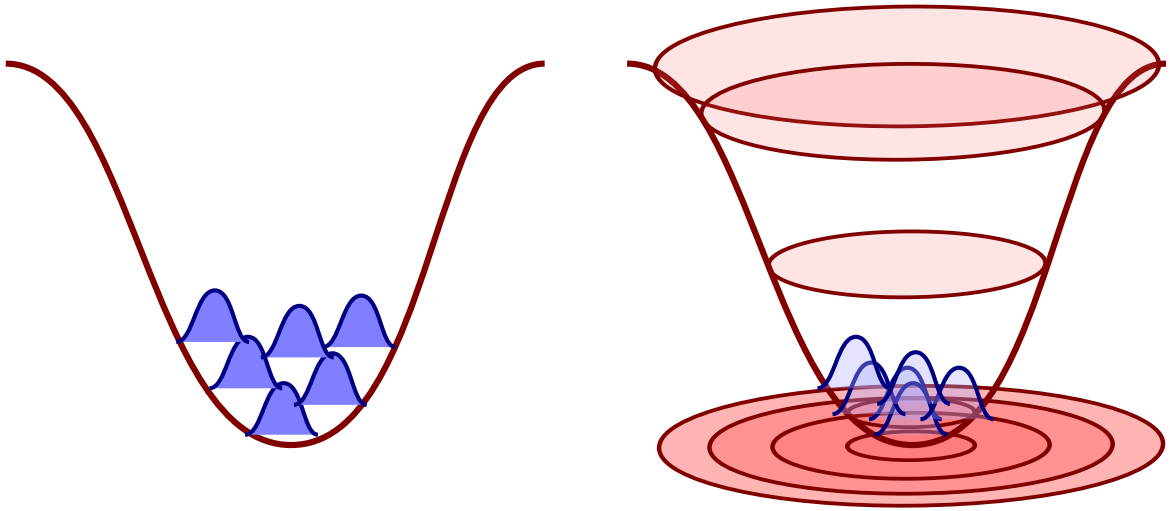
Dimensionality of CV space

- Coarse-graining of config. space is an essential feature of biased MD
- The time it takes to "fill" a FES basin of depth ΔF scales **exponentially** with the dimensionality of CV space



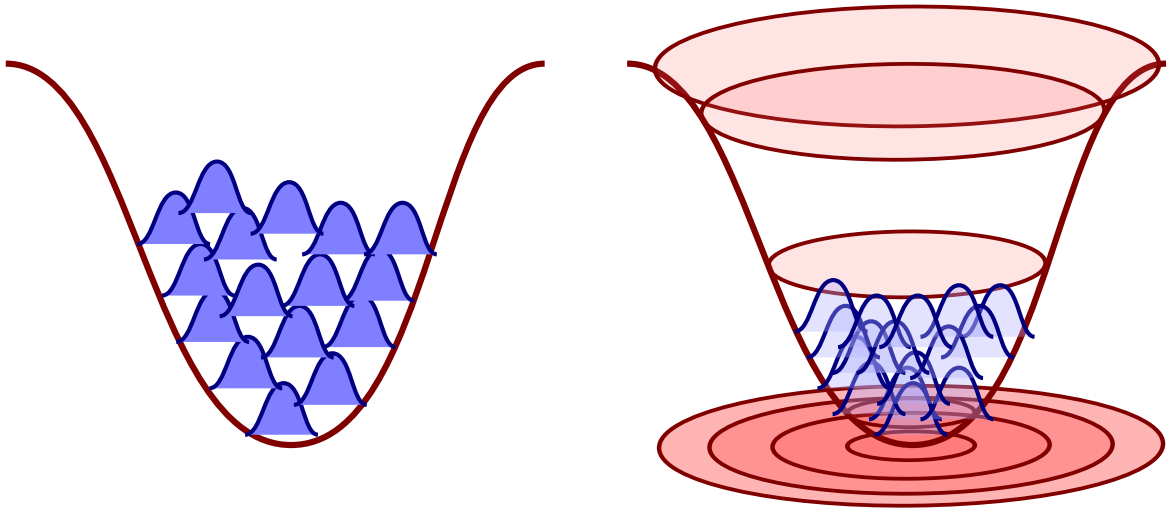
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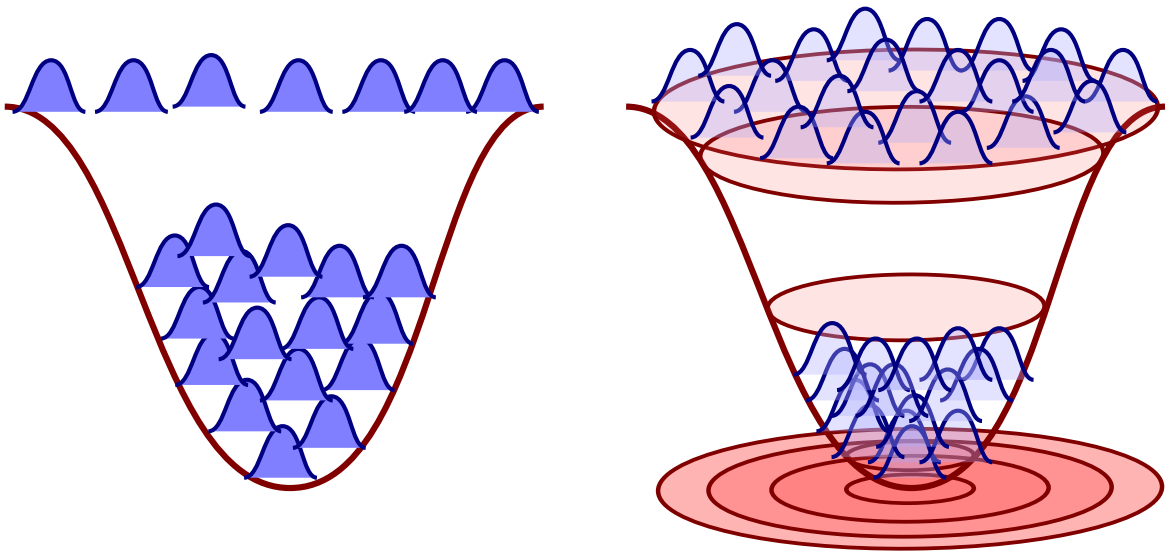
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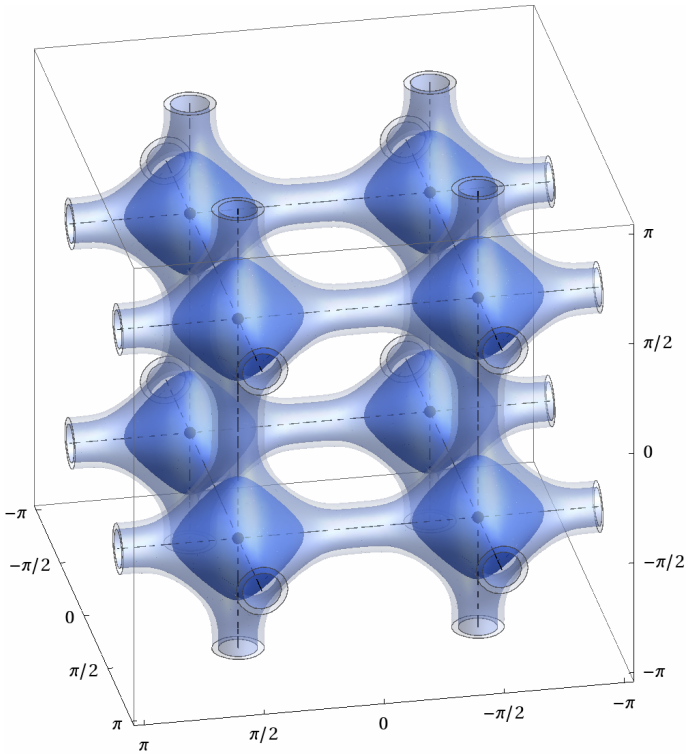


Orthogonal degrees of freedom

- A model PES in three dimensions – *periodic in all directions*

$$V(\theta, \phi, \psi) = \exp\left[3\left(3 - \sin^4\theta - \sin^4\phi - \sin^4\psi\right)\right] - 1$$

  - Barriers are much higher than $k_B T$ – sampling would be very slow
  - MetaD biassing only θ and $\phi \rightarrow$ slow sampling along ψ!

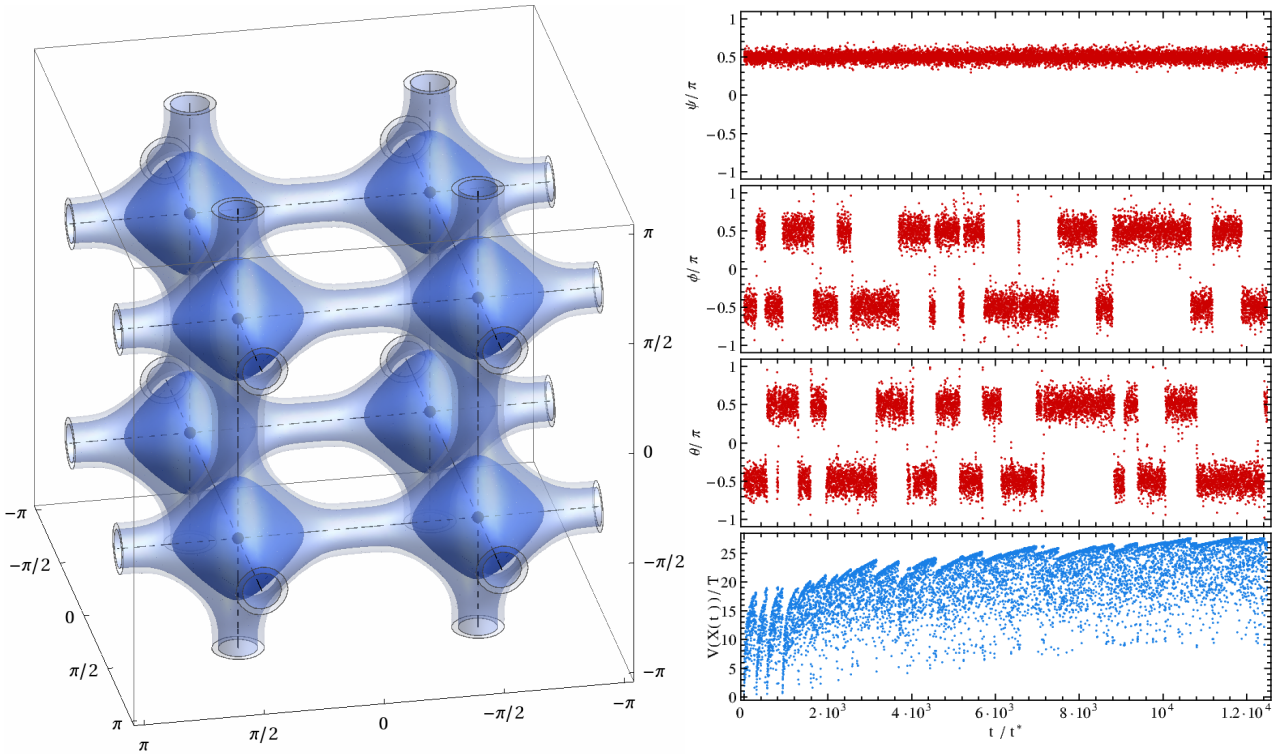


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Wrap up and take home

- It is possible to recover statistics from a different ensemble by **re-weighting** a trajectory
  - This is a powerful but dangerous technique – monitor the fluctuations of the log-weights and make sure they are not $\gg 1$
- Biased sampling can be used to overcome free energy barriers
  - umbrella sampling introduces a bias in CV space
  - **metadynamics** is an option to construct the optimal bias by history-dependent dynamics
- Finding optimal collective variables for the system is the key problem
  - MetaD gets exponentially slower as the number of CVs increases
  - MetaD cannot work if there are barriers orthogonal to CV space

Bibliography

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Bussi, Laio, Parrinello, Phys. Rev. Lett. (2006)

Barducci, Bonomi, Parrinello, *Metadynamics*. Wiley Interd. Reviews (2011)