

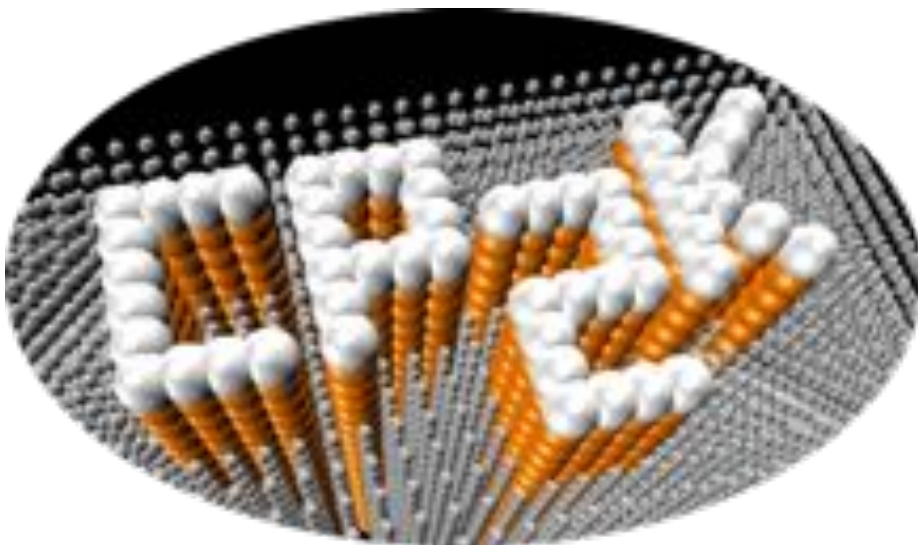
4th CP2K tutorial

August 31st -September 4th, Zurich

Sampling Free Energy Surfaces by MD

Marcella Iannuzzi

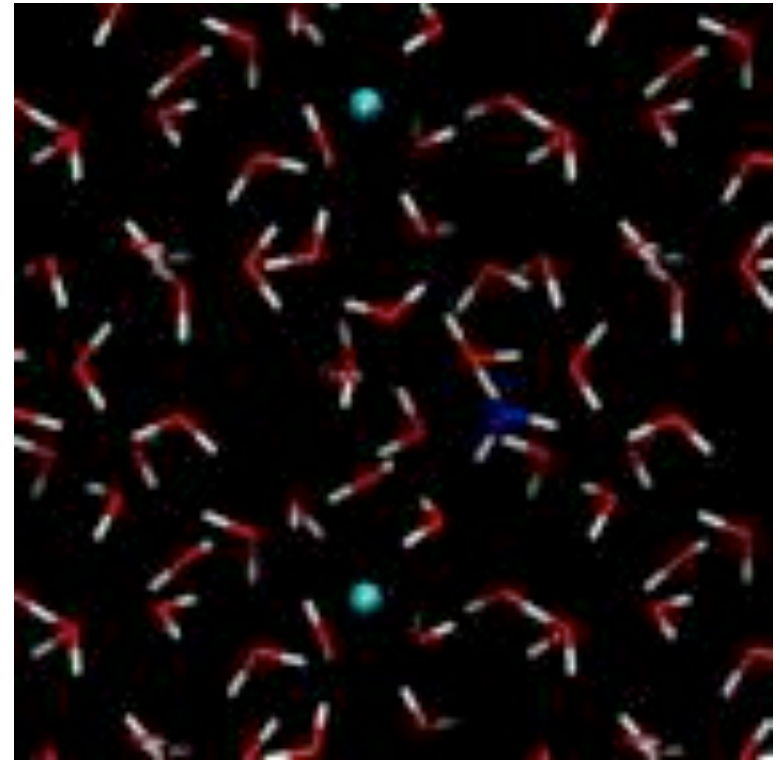
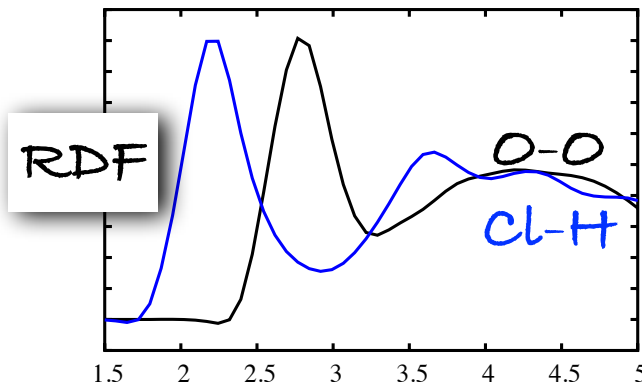
Department of Chemistry, University of Zurich



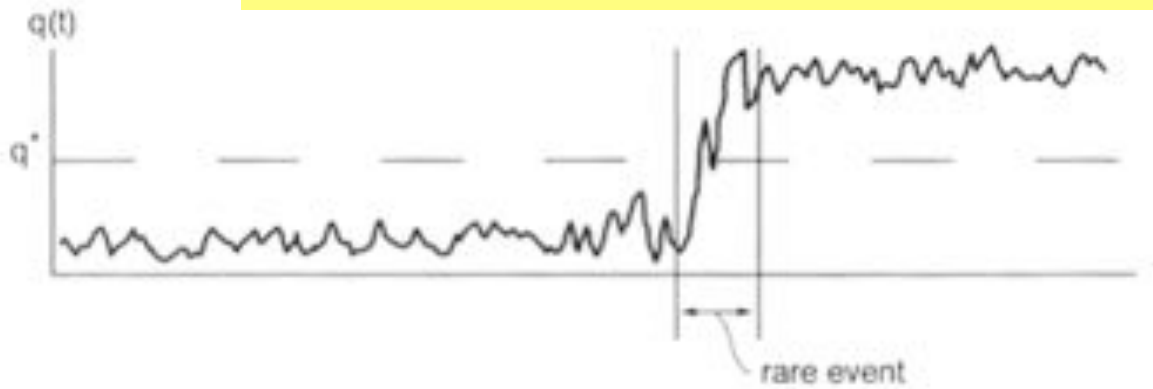
<http://www.cp2k.org>

Complex Processes by MD

- * Choose a suitable model of the system
- * Determine the thermodynamic conditions \Rightarrow Ensemble averages
- * Equilibrium sampling of physical quantities



Predictive power frustrated by sampling fast degrees of freedom with time-steps from < 0.1 fs (CPMD) up to 1 fs (MM)

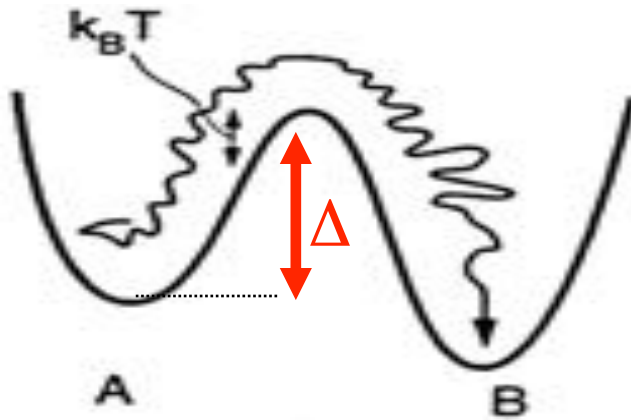


\sim few ns

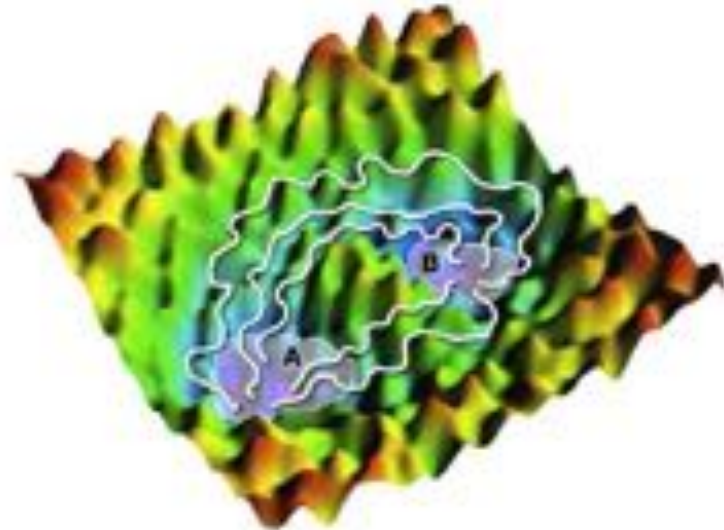
Rare Events

Phase Transitions, Conformational Rearrangements,
Chemical Reactions, Nucleation, Diffusion, Growth, etc.

Activation Energies



Minimum energy pathways



Exploration of configurational space

- * Complex and high dimensional configurational space
- * Intrinsically multidimensional order parameter
- * Multitude of unknown intermediates and products
- * Entropic bottlenecks
- * Unforeseen processes, many irrelevant transition states
- * Diffusive trajectories

Canonical Partition Function

The Laplace transform of the density of state

$$Q(N, V, T) = \int \exp(-\beta E) \Omega(N, V, E) dE$$

Probability of the macrostate at a given T

$$Q(N, V, T) = \frac{1}{N! h^{3N}} \int \exp[-\beta \mathcal{H}(\mathbf{r}^N, \mathbf{p}^N)] d\mathbf{r}^N d\mathbf{p}^N = \frac{1}{\Lambda(\beta)^{3N} N!} Z(N, V, T)$$

one dimensional integral over E replaced by configurational integral
analytic kinetic part is integrated out

$$Z(N, V, T) = \int e^{-\beta U(\mathbf{r})} d\mathbf{r}$$

**configurational partition
function**

Free Energy

Helmholtz free energy or thermodynamic potential

$$A = -\frac{1}{\beta} \ln Q(N, V, T)$$

Thermodynamics

Statistical Mechanics

$$\Delta A = -\frac{1}{\beta} \ln \left(\frac{Z_1}{Z_0} \right)$$

entropic and enthalpic contributions

$$Q_0 \propto \int_{\Gamma_0} e^{-\beta \mathcal{H}(\mathbf{r}, \mathbf{p})} d\mathbf{r} d\mathbf{p}$$

Macroscopic state 0 corresponds to a portion of the phase space : Γ_0

$$Q_0 \propto \int_{\Gamma} e^{-\beta \mathcal{H}_0(\mathbf{r}, \mathbf{p})} d\mathbf{r} d\mathbf{p}$$

Macroscopic state 0 corresponds to H_0

$$Q_0 \propto \int_{\Gamma} e^{-\beta_0 \mathcal{H}(\mathbf{r}, \mathbf{p})} d\mathbf{r} d\mathbf{p}$$

Macroscopic state 0 corresponds to a value of a macroscopic parameter, e.g T

Perturbation formalism

Reference (0) and target system (1)

$$\mathcal{H}_1(\mathbf{r}, \mathbf{p}) = \mathcal{H}_0(\mathbf{r}, \mathbf{p}) + \Delta\mathcal{H}(\mathbf{r}, \mathbf{p})$$

Probability of finding (0) in configuration (\mathbf{r}, \mathbf{p})

$$\mathcal{P}_0(\mathbf{r}, \mathbf{p}) = \frac{e^{-\beta\mathcal{H}_0(\mathbf{r}, \mathbf{p})}}{\int e^{\mathcal{H}(\mathbf{r}, \mathbf{p})} d\mathbf{r}d\mathbf{p}}$$

Free energy difference

$$\Delta A = -\frac{1}{\beta} \ln \frac{\int e^{-\beta\mathcal{H}_1} d\mathbf{r}^N d\mathbf{p}^N}{\int e^{-\beta\mathcal{H}_0} d\mathbf{r}^N d\mathbf{p}^N} = -\frac{1}{\beta} \ln \frac{\int e^{-\beta\mathcal{H}_0} e^{-\beta\Delta\mathcal{H}} d\mathbf{r}^N d\mathbf{p}^N}{\int e^{-\beta\mathcal{H}_0} d\mathbf{r}^N d\mathbf{p}^N}$$

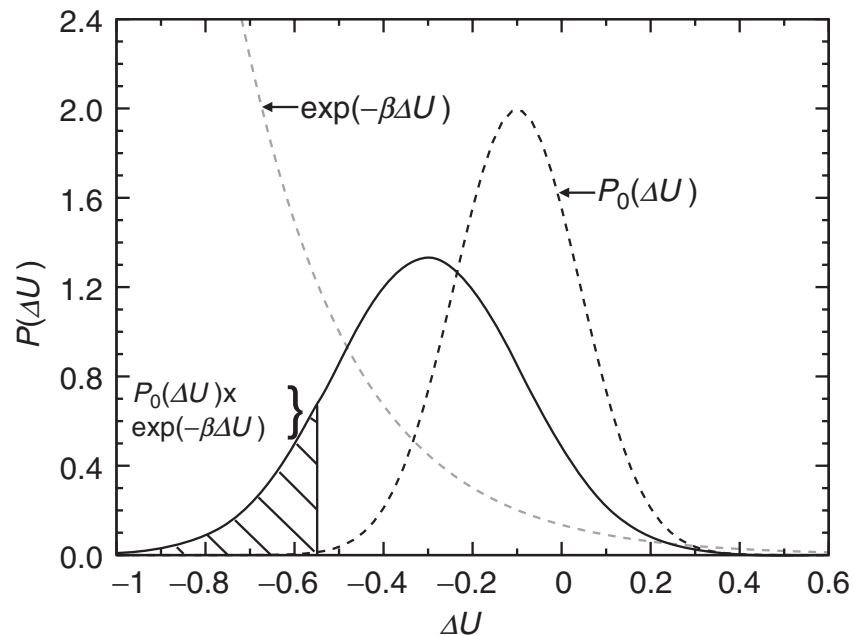
$$\Delta A = -\frac{1}{\beta} \ln \langle \exp [-\beta\Delta\mathcal{H}(\mathbf{r}^N, \mathbf{p}^N)] \rangle_0$$

Integrating out the analytic kinetic part

$$\Delta A_{0,1} = -\frac{1}{\beta} \ln \langle e^{-\beta\Delta U} \rangle_0 \quad \langle \mathcal{F}(\mathbf{r}, \mathbf{p}) \rangle_1 = \frac{\langle \mathcal{F} e^{-\beta\Delta U} \rangle_0}{\langle e^{-\beta\Delta U} \rangle_0}$$

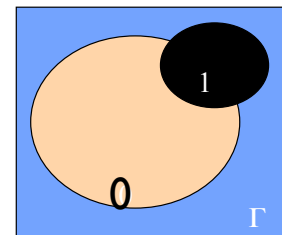
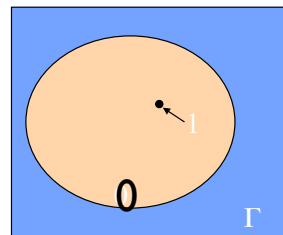
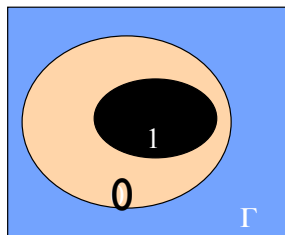
Limitations

$$\Delta A = -\frac{1}{\beta} \ln \int \exp[-\beta \Delta U] \mathcal{P}_0(\Delta U) d\Delta U$$



Shifted function
 Low- ΔU tail is poorly sampled
 low statistical accuracy
 but important contribution to ΔA

Accuracy \Rightarrow target and reference systems are similar \Rightarrow overlapping regions

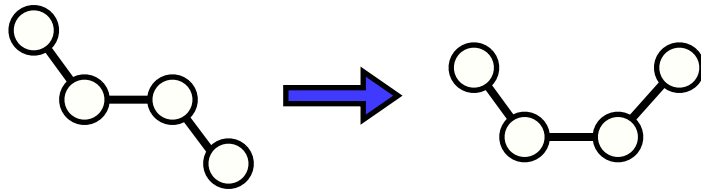


insufficient statistics or incomplete overlap \Rightarrow enhanced sampling

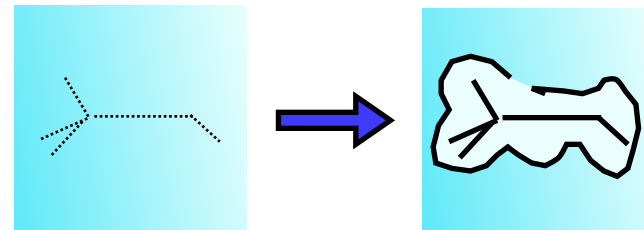
Order Parameters

Variables chosen to describe changes in the system

- **Reaction coordinate** : the order parameter corresponds to the pathway along which the transformation occur in nature
- **Collective variable** : fully represented as function of coordinates
- Indicating intermediate stages of the transformation: **mutation point**



torsion angle



annihilation non-bonded

- Different possible definitions of OP
- Effects on accuracy and efficiency of ΔA calculations
- Set up of system with desired values of OP
- Smoothness of the simulated path

Extended Ensemble

Select parameters, continuous functions of coordinates $\hat{\xi}_i(\mathbf{r}^N)$

Density of States

$$\Omega_{\xi}(N, V, E, \xi) = \int \delta[\mathcal{U}(\mathbf{r}^N) - E] \left(\prod_i \delta[\hat{\xi}_i(\mathbf{r}^N) - \xi_i] \right) d\mathbf{r}^N$$

$$\xi = \{\xi_i\}$$

Canonical Partition Function

$$Q_{\xi}(N, V, T, \xi) = \int e^{-\beta \mathcal{U}(\mathbf{r}^N)} \left(\prod_i \delta[\hat{\xi}_i(\mathbf{r}^N) - \xi_i] \right) d\mathbf{r}^N$$

Free Energy

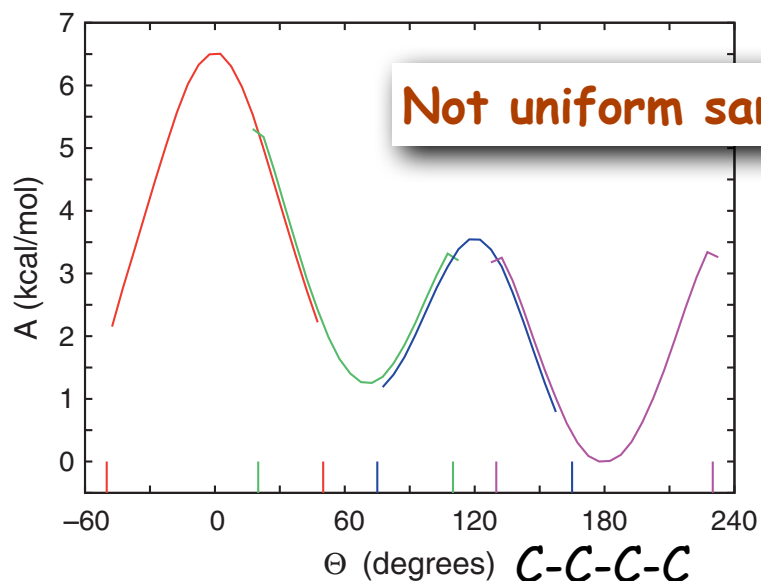
$$A_{\xi} = -\frac{1}{\beta} \ln Q_{\xi}$$

$\hat{\xi}_i(\mathbf{r}^N)$ must distinguish among metastable states

select specific configurations in the partition function

Stratification Scheme

Free energy butane isomerisation



Probability distribution of the order parameter

$$\Delta A(\xi) = A(\xi_1) - A(\xi_0) = -\beta^{-1} \ln \frac{\mathcal{P}(\xi_1)}{\mathcal{P}(\xi_0)}$$

Histogram of M bins $\delta\xi = (\xi_1 - \xi_0)/M$

$$\mathcal{P}(\xi_0 + (i - 0.5)\delta\xi) = \frac{f_i}{\sum_j f_j}$$

Restrain the system within a window by harmonic potential

Overlapping windows

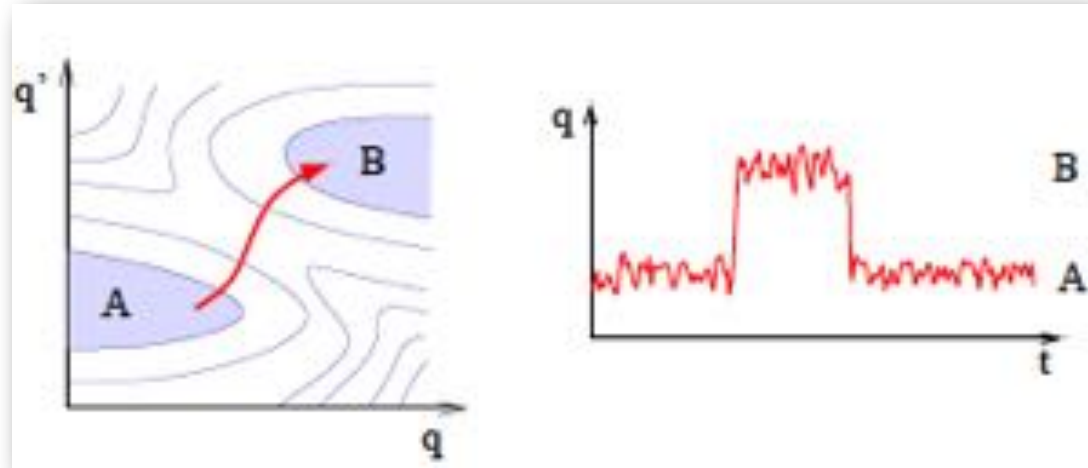
Efficient sampling

$$\tau = L\tau_w \propto \frac{(\xi_1 - \xi_0)^2}{LD_\xi}$$

Reconstruct the full probability by matching

Good Coordinates for Pathways

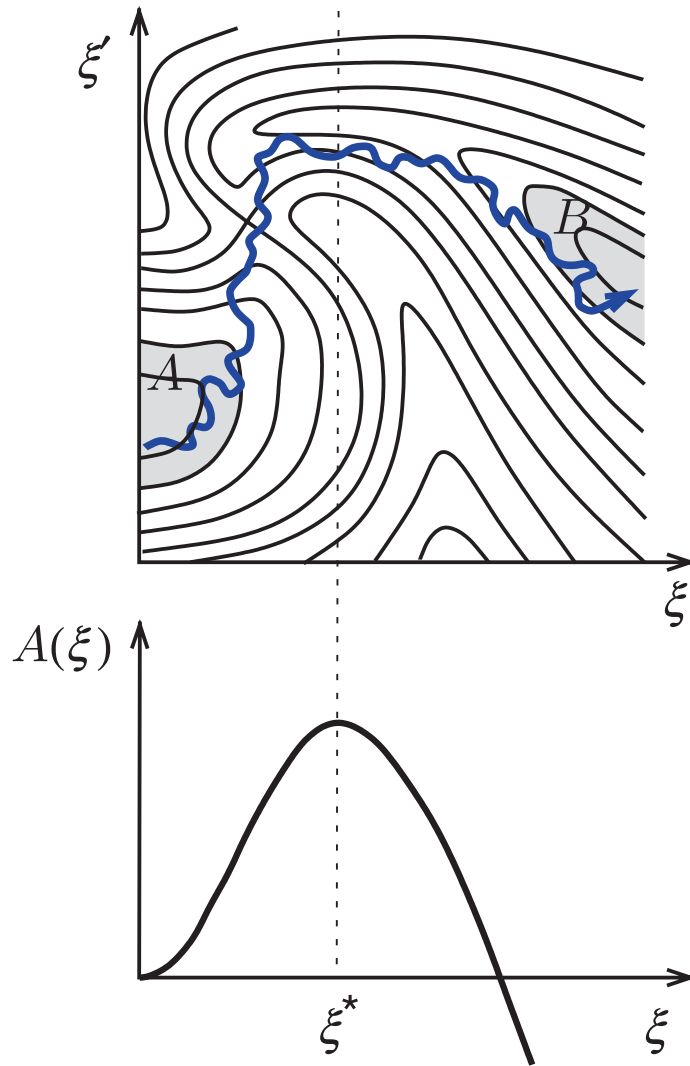
Capture the essential physics include all relevant DoF and properly describes the dynamics



q distinguishes between A and B but might fail in describing essential aspects of the transition

- Discriminate configurations of reactants and products and intermediates
- Characterisation of the mechanisms of transition
- Reversibility
- Fast equilibration of orthogonal DoF (no relevant bottlenecks)

Hypothetical 2D Free Energy Landscape



Not including
important DoF leads
to wrong
interpretation

Some simple collective variables

Derivable function of the degrees of freedom to which a given value can be assigned

● Distance

$$|\mathbf{R}_I - \mathbf{R}_J|$$

● Angle

$$\theta(\mathbf{R}_I, \mathbf{R}_J, \mathbf{R}_k)$$

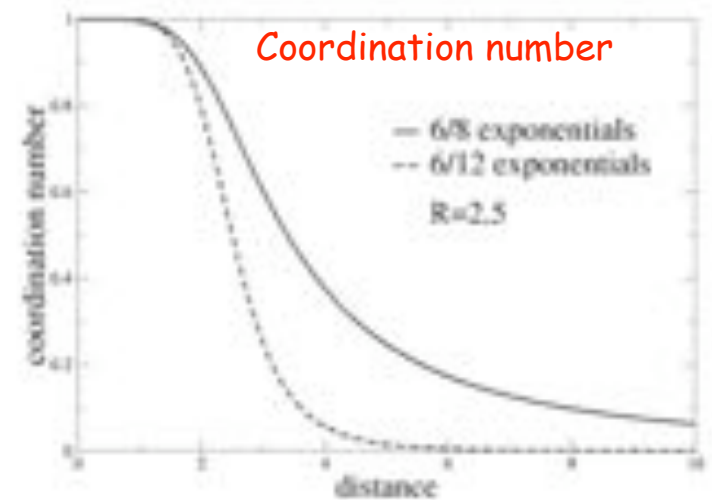
● Dihedral

$$\Theta(\mathbf{R}_I, \mathbf{R}_J, \mathbf{R}_k, \mathbf{R}_L)$$

● Difference of distances $|\mathbf{R}_I - \mathbf{R}_J| - |\mathbf{R}_J - \mathbf{R}_K|$

● Generalised coordination number

$$C_{L_1 L_2} = \frac{1}{N_{L_1}} \sum_{j=1}^{N_{L_1}} \left\{ \sum_{i=1}^{N_{L_2}} \frac{1 - \left(\frac{r_{ij}}{r_0}\right)^n}{1 - \left(\frac{r_{ij}}{r_0}\right)^m} \right\}$$



● Generalised displacement

$$D_{L_1 L_2}^{[klm]} = \frac{1}{N_{L_1}} \sum_{i \in L_1} \mathbf{d}_i \cdot \hat{\mathbf{v}}_{[klm]} - \frac{1}{N_{L_2}} \sum_{j \in L_2} \mathbf{d}_j \cdot \hat{\mathbf{v}}_{[klm]}$$

CP2K input for CV

In SUBSYS add one section per CV

```
&COLVAR
  &DISTANCE
    AXIS X
    ATOMS 1 4
  &END DISTANCE
&END COLVAR
```

```
&COLVAR
  &DISTANCE_FUNCTION
    ATOMS 4 6 6 1
    COEFFICIENT -1.00000
    # distance 1 = ( 4 - 6 )
    # distance 2 = ( 6 - 1 )
  &END DISTANCE_FUNCTION
&END COLVAR
```

```
&COLVAR
  &COORDINATION
    KINDS_FROM N
    KINDS_TO O
    R_0 [angstrom] 1.8
    NN 8
    ND 14
  &END COORDINATION
&END COLVAR
```

```
&COLVAR
  &RMSD
    &FRAME
      COORD_FILE_NAME planar.xyz
    &END
    &FRAME
      COORD_FILE_NAME cage.xyz
    &END
    SUBSET_TYPE LIST
    ATOMS 1 3 5 6 8 9
    ALIGN_FRAMES T
  &END
&END
```

Constraints and Restraints

In MOTION add one section per constraint

```
&CONSTRAINT
&COLLECTIVE
  COLVAR 1
  INTERMOLECULAR
  TARGET 5.
  TARGET_GROWTH 1.1
  TARGET_LIMIT 10.
&END COLLECTIVE
&END CONSTRAINT
```

```
&COLLECTIVE
  TARGET [deg] 0.0
  MOLECULE 1
  COLVAR 1
  &RESTRAINT
    K [kcalmol] 4.90
  &END
&END COLLECTIVE
```

Geometrical Constraints

Implicit functions of the degrees of freedom of the system

$$\sigma(\{\mathbf{R}_I\}, \mathbf{h}, \Psi) = 0 \quad \dot{\sigma}(\{\mathbf{R}_I\}, \mathbf{h}, \Psi) = 0$$

- ☀ To freeze fast degrees of freedom and increase the time step: e.g., intra-molecular bonds by distance constraints
- ☀ To explore only a sub-region of the conformational space
- ☀ As reaction coordinates : constrained dynamics and thermodynamic integration
- ☀ To prevent specific events or reactions

Lagrange formulation for simple constraints, functions of \mathbf{R}_I

$$\mathcal{L}'(\{\mathbf{R}_I\}, \{\mathbf{P}_I\}) = \mathcal{L}(\{\mathbf{R}_I\}, \{\mathbf{P}_I\}) - \sum_{\alpha} \lambda_{\alpha} \sigma(\{\mathbf{R}_I\})$$

The Lagrange multipliers ensure that positions and velocities satisfy the constraints

Shake-Rattle algorithm

Modified velocity Verlet scheme by additional **constraint forces**

- First update of velocities (first half step) and positions

$$V'_I = V_I(t) + \frac{\delta t}{2M_I} F_I(t) \quad R'_I = R_I(t) + \delta t V'_I$$

- Positions' correction by **constraint forces**

$$R_I(t + \delta t) = R'_I + \frac{\delta t^2}{2M_I} g_I^{(p)}(t)$$

- Calculation of the new forces $F_I(t+\delta t)$

- Update of velocity (second half step)

$$V_I(t + \delta t) = V'_I + \frac{\delta t}{2M_I} [F_I(t + \delta t) + g_I^{(v)}(t + \delta t)]$$

- Correction by the constraint forces

Constraint Forces

$$g_I^{(p)}(t) = - \sum_{\alpha} \lambda_{\alpha}^{(p)} \frac{\partial \sigma_{\alpha}(\{R_I\})}{\partial R_I}$$

$$e_{\alpha}(\{\lambda_{\gamma}\}) = - \sum_{\beta} \mathbf{J}_{\alpha\beta}^{-1} \sigma_{\beta}(\{\lambda_{\gamma}\}) \quad \mathbf{J}_{\alpha\beta} = \frac{\partial \sigma_{\alpha}(\{\lambda_{\gamma}\})}{\partial \lambda_{\beta}}$$

Set of non-linear equations **solved iteratively**

$$g_I^{(v)}(t) = - \sum_{\alpha} \lambda_{\alpha}^{(v)} \frac{\partial \sigma_{\alpha}(\{R_I\})}{\partial R_I}$$

$$\sum_I \frac{\partial \sigma_{\alpha}}{\partial \mathbf{R}_I} \mathbf{v}_I = \sum_I \frac{\partial \sigma_{\alpha}}{\partial \mathbf{R}_I} \cdot \mathbf{v}'_I + \sum_{\beta} \left(\sum_I \frac{\delta t^2}{2M_I} \frac{\partial \sigma_{\alpha}}{\partial \mathbf{R}_I} \frac{\partial \sigma_{\beta}}{\partial \mathbf{R}_I} \right) \lambda_{\beta}^v = 0$$

Thermodynamic Integration

$$A(\xi_1) - A(\xi_0) = \int_{\xi_0}^{\xi_1} \frac{dA}{d\xi} d\xi$$

along a one dimensional
generalized coordinate $\xi(\mathbf{x})$
Path-independent

Potential of Mean Force exerted on ξ

$$(\mathbf{x}, \mathbf{p}) \Rightarrow (\xi, q_1 \dots q_{N-1}, p^\xi \dots p_{N-1}^q)$$

generalized coordinate to simplify derivative

$$\frac{dA}{d\xi} = \frac{\int \frac{\partial \mathcal{H}}{\partial \xi} e^{-\beta \mathcal{H}} dq_1 \dots dq_{N-1} dp^\xi \dots dp_{N-1}^q}{\int e^{-\beta \mathcal{H}} dq_1 \dots dq_{N-1} dp^\xi \dots dp_{N-1}^q} = \left\langle \frac{\partial \mathcal{H}}{\partial \xi} \right\rangle_\xi$$

instantaneous force on ξ

force at ξ , averaged over
fluctuations of other DoF

$$\left\langle \frac{\partial \mathcal{H}}{\partial \xi} \right\rangle_\xi = \left\langle \frac{\partial U}{\partial \xi} - \frac{1}{\beta} \frac{\partial \ln |\mathbf{J}|}{\partial \xi} \right\rangle$$

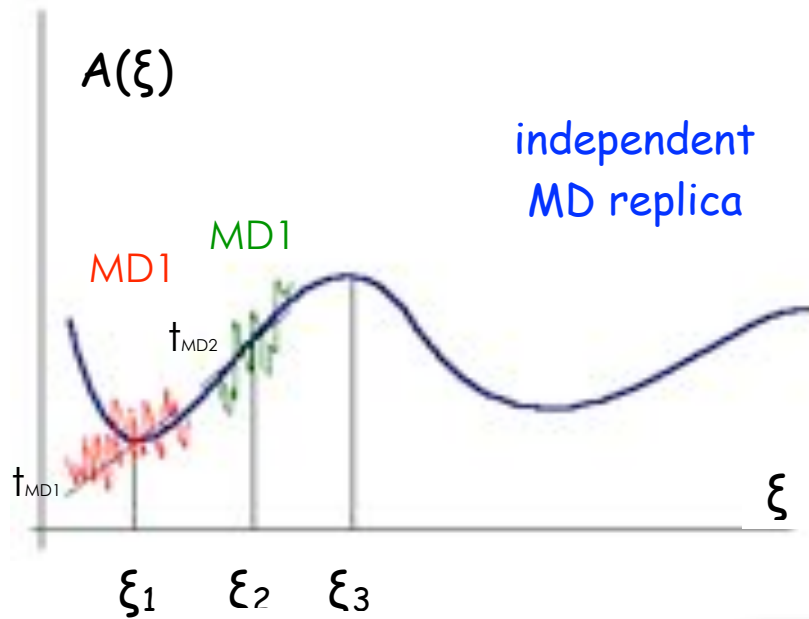
$$[\mathbf{J}]_{ij} = \frac{\partial x_i}{\partial q_j}$$

mechanical + entropic

Blue Moon Ensemble

Series of constrained MD simulations

$$\mathcal{H}^\lambda = \mathcal{H} + \lambda(\xi - \xi(\mathbf{r}))$$



$$-\lambda \nabla(\xi - \xi(\mathbf{r})) \quad \text{mean force acting on the system to hold } \xi \text{ constant}$$

$$\dot{\xi} = 0 \quad : \quad p^\xi(\mathbf{q}, \mathbf{p}^q)$$

un-constrained $\langle \dots \rangle =$ constrained corrected $\langle \dots \rangle^F$

Fixman Potential

$$\mathcal{H}_F^\lambda = \mathcal{H}^\lambda + \frac{1}{2\beta} \ln Z_\xi$$

$$Z_\xi = \sum_i \frac{1}{m_i} \left(\frac{\partial \xi}{\partial x_i} \right)^2$$

$$\frac{dA}{d\xi} = \langle \lambda_F \rangle_{\xi\xi}^F$$

mean force acting on ξ related to external force to hold ξ constant

...some difficulties

MD performed at fixed ξ , collecting statistics of the force acting on $\xi \Rightarrow \lambda \nabla \xi$, **constraint force**

- Many estimates at ξ to reduce statistical errors
- Many windows to get accurate integrals
- May not be easy to prepare by hand the system at given ξ
- Different possible pathways: the starting configuration selects one path, but crossing is rare, $\xi(r)=\xi$ partially sampled or rate limiting
- Multidimensionality (more coordinates) too expensive

Metadynamics

- ☀ Canonical equilibrium distribution under potential $V(\mathbf{r})$
- ☀ Choose a set of relevant **Collective Variables** $\mathbf{S}(\mathbf{r}):\{S_a(\mathbf{r})\}$, such that the process is well defined in the reduced space $\Sigma(\mathbf{S})$

$$P(\mathbf{S}) = \frac{e^{-\beta A(\mathbf{S})}}{\int d\mathbf{S} e^{-\beta A(\mathbf{S})}} \quad A(\mathbf{S}) = -\frac{1}{\beta} \ln \left(\int d\mathbf{r} e^{-\beta V(\mathbf{r})} \delta(\mathbf{S} - \mathbf{S}(\mathbf{r})) \right)$$

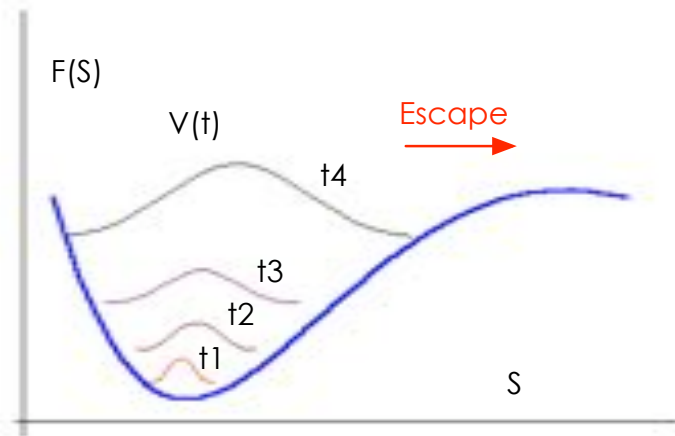
- ☀ Perform MD and re-map each micro-state by projecting the trajectory into the configuration space $\Sigma(\mathbf{S})$: **meta-trajectory** $\mathbf{S}(\mathbf{r}(t))$
- ☀ Enhance the exploration by adding a **penalty potential** that discourages the system to visit already explored macro-states

$$V_{\text{MTD}}(\mathbf{S}(\mathbf{r}), t) = \sum_{t'=\tau_G, 2\tau_G, \dots} W_{t'} e^{-\frac{[\mathbf{S}(\mathbf{r}) - \mathbf{S}(\mathbf{r}_G(t'))]^2}{2\Delta\mathbf{S}^2}}$$

- ☀ New probability distribution generated under the action of $V+V_{\text{MTD}}$

History Dependent Potential

Non Markovian Coarse-grained MD



Fill-up by successive contributions
Keeping track of the explored space
Direct estimate of FES topology

Eliminate metastability and reconstruct $A(\mathbf{S})$ within $\Sigma(\mathbf{S})$

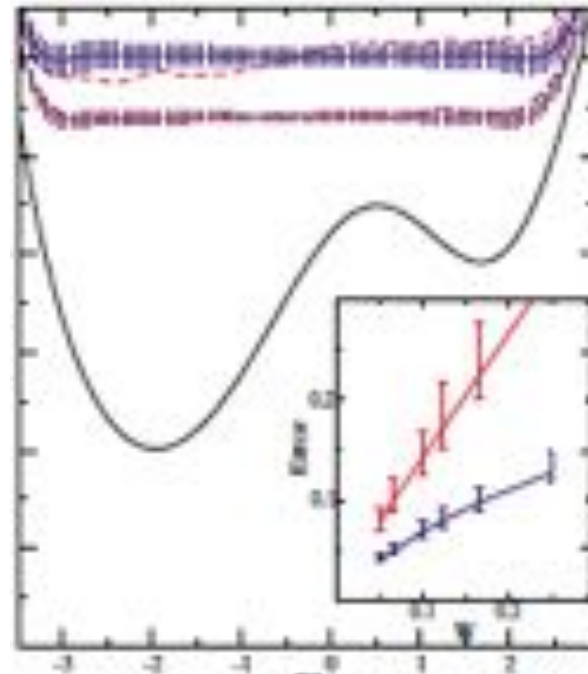
$$A_G(\mathbf{S}, t) = -V_{\text{MTD}}(\mathbf{S}(\mathbf{r}), t)$$

Flattening of free energy surface

$$W/\tau_G \rightarrow 0$$

$$P(\mathbf{S}) \propto e^{-\beta[A(\mathbf{S}) - A_G(\mathbf{S}, t)]}$$

$$\delta t_{\text{MD}} \ll \tau_G \ll \tau_s$$

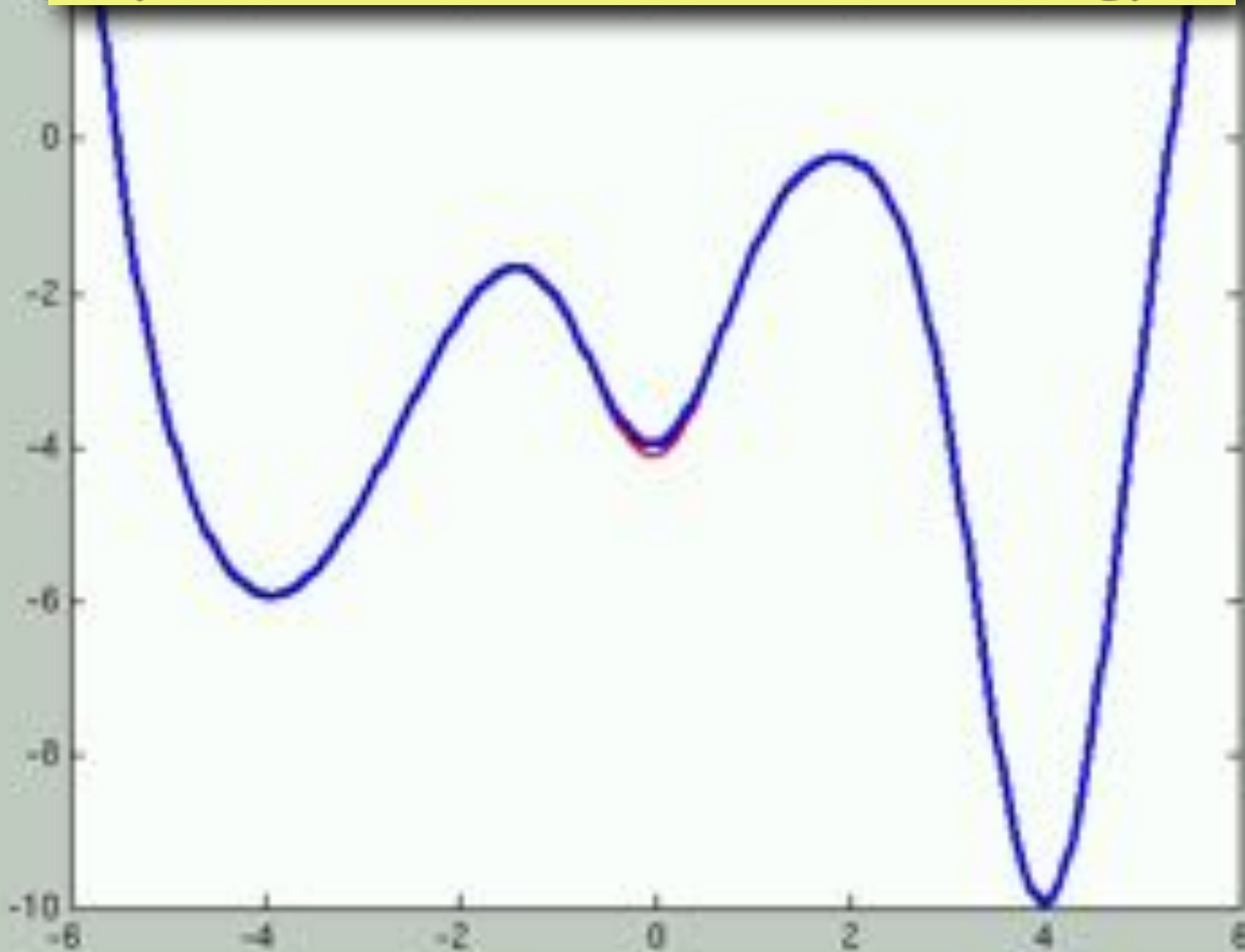


$$\delta A(\mathbf{S}) = A(\mathbf{S}) - A_G(\mathbf{S}, t)$$

$$\langle \delta A(\mathbf{S}) \rangle$$

2D FES

Histogram of a trajectory generated by $V+V_{\text{MTD}}$ provides a direct estimate of free energy



Extended Lagrangian MTD

Enforcing adiabatic separation, $\tau_s \gg$ other time scales and memory effects

Introduction of auxiliary variables $\mathbf{s} : \{s_\alpha\}$ one for each $S_\alpha(\mathbf{r})$
with large enough \mathbf{M}

$$\mathcal{L} = K - V(\mathbf{r}) + \sum_{\alpha} \frac{1}{2} M_{\alpha} \dot{s}_{\alpha} - \sum_{\alpha} \frac{1}{2} k_{\alpha} (s_{\alpha} - S_{\alpha}(\mathbf{r}))^2 - V_G(\mathbf{s}, t)$$

thermalization coupling to system DoF sampling enhancement

$$V_G(\mathbf{s}, t) = \sum_{t' < t} W_{t'} e^{-\frac{(\mathbf{s} - \mathbf{s}_G(t'))^2}{2\Delta s^2}}$$

For large t and slow deposition rate, V_G approximates the free energy and the meta-trajectory $\mathbf{s}(t)$ follows the MEP

$$A_{\mathbf{k}}(\mathbf{s}) = -\frac{1}{\beta} \ln \left(\int d\mathbf{r} e^{-\beta [V(\mathbf{r}) + \frac{1}{2} \sum_{\alpha} k_{\alpha} (s_{\alpha} - S_{\alpha}(\mathbf{r}))^2]} \right)$$

$$\lim_{\mathbf{k} \rightarrow \infty} A_{\mathbf{k}}(\mathbf{s}) = A(\mathbf{s})$$

Accuracy of FES profile

Dynamics generating the equilibrium distribution associated with $A(\mathbf{s}) - A_G(\mathbf{s}, t)$

Averaging over many independent trajectories

$$\epsilon(\mathbf{s}, t) = \sqrt{\langle (A_G(\mathbf{s}, t) - A(\mathbf{s}) - \langle A_G(\mathbf{s}, t) - A(\mathbf{s}) \rangle)^2 \rangle}$$

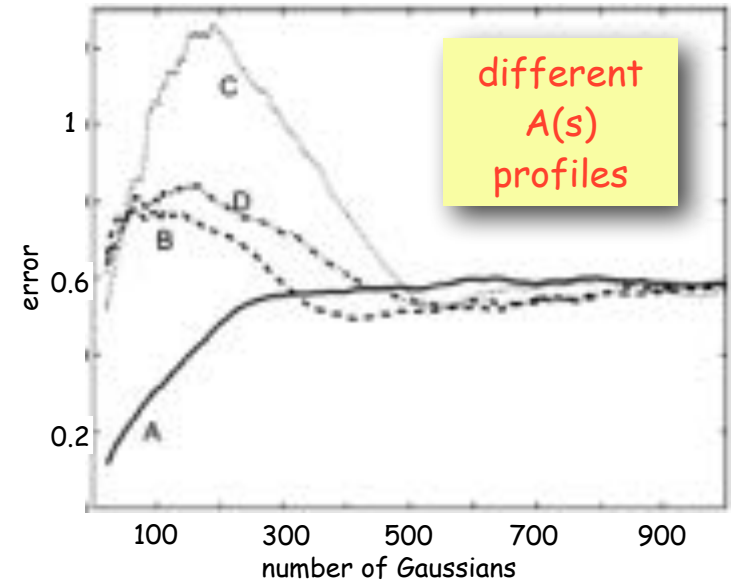
$$\bar{\epsilon}(t) = \frac{\int_{\Omega} ds \epsilon(\mathbf{s}, t)}{\int_{\Omega} ds}$$

Empirical error estimate

$$\bar{\epsilon} = C(d) \sqrt{\frac{\mathcal{V}_{\Omega} \|\Delta \mathbf{s}\| W}{\|\mathbf{D}\| \tau_G \beta}}$$

$$t_{\text{tot}} = \tau_G \frac{\int_{\Omega: A(\mathbf{s}) < A_{\text{max}}} ds (A_{\text{max}} - A(\mathbf{s}))}{(2\pi)^{d/2} W \prod_{\alpha} \Delta s_{\alpha}}$$

$$\bar{\epsilon} \propto \sqrt{\frac{\|\tau_{\mathbf{s}}\| \bar{A}}{t_{\text{tot}} \beta} \frac{\mathcal{V}_{\Omega}}{\prod_{\alpha} \Delta s_{\alpha}}}$$



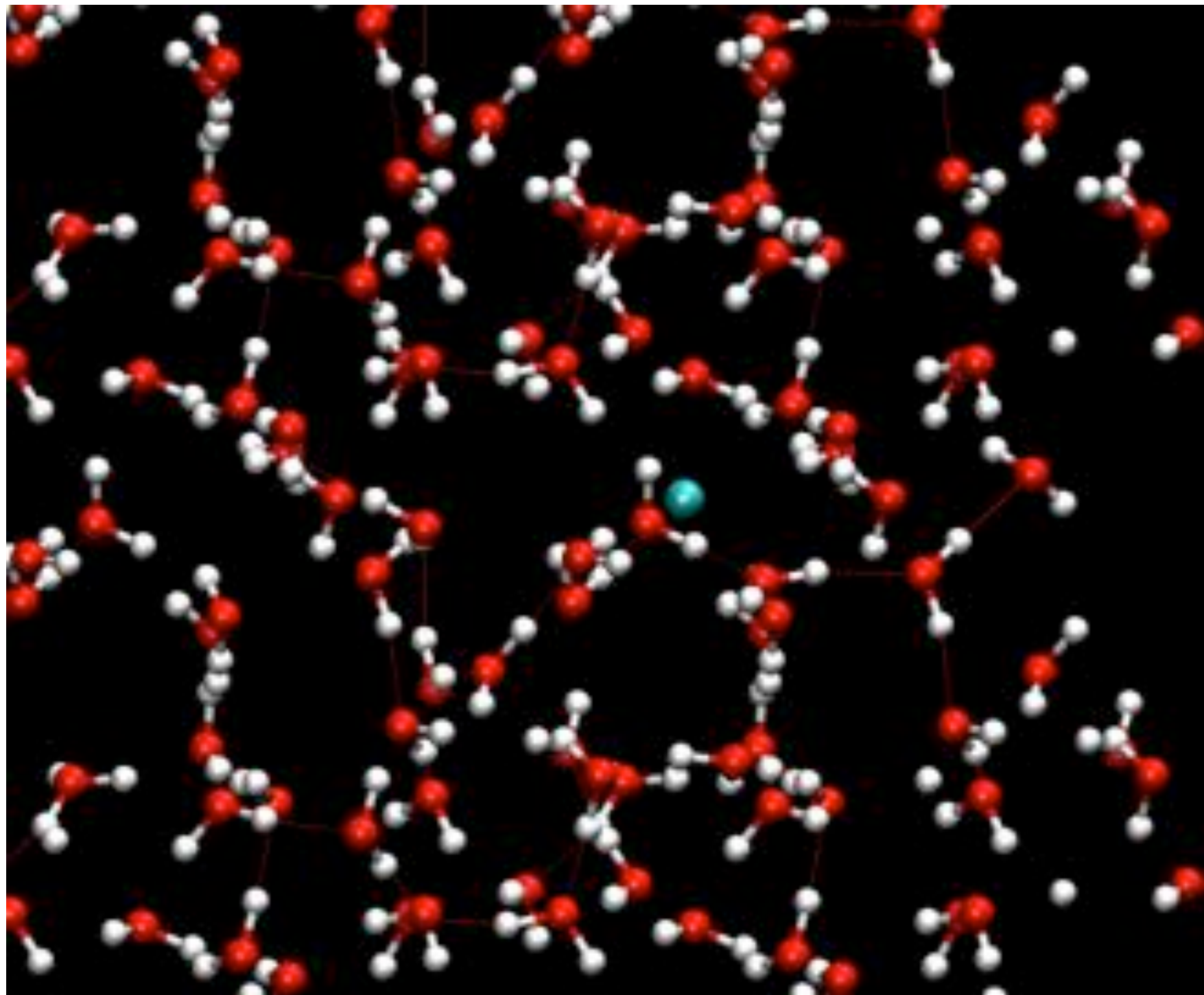
too large Δs would smear out $A(\mathbf{s})$ details : $\Delta s/L < 0.1$

Only relevant time scale is $\tau_{\mathbf{s}}$

the error depends on τ_G/W
small Gaussians more frequently
is better

To be considered ...

- The selected CV must **discriminate among the relevant states** (reactants, products, TS)
- The **number of hills** required to fill the well is proportional to $1/(\Delta)^{N_{CV}}$
- The sampling of large variations of the CV over almost **flat energy regions** is expensive: **diffusive behavior**
- **MTD is not the true dynamics**. Reaction rates are derived a posteriori from the estimated FES
- The analysis of the trajectory is needed to isolate the TS
- With proper choices of CV and parameters, the MTD trajectory describes the **most probable pathway** taking into account also possible kinetic effects (larger and shallower channels are preferred)
- The accuracy in the evaluation of the FES depends on hills' shape and size, and on the deposition rate. The **ideal coverage** $V_G(\{S\}) = -A(\{S\})$ (**flat surface**)



MTD input

&FREE_ENERGY

&METADYN

DO_HILLS T

LAGRANGE

NT_HILLS 40

SLOW_GROWTH

TEMPERATURE 300

TEMP_TOL 100

WW 0.0001

HILL_TAIL_CUTOFF 2

P_EXPONENT 8

Q_EXPONENT 20

&METAVAL

COLVAR 1 ! COORDINATION

SCALE 0.18

LAMBDA 0.8

MASS 20

&WALL

POSITION 2.0

TYPE QUADRATIC

&QUADRATIC

DIRECTION WALL_PLUS

K 1.0

&END QUADRATIC

&END WALL

&END METAVAL

&METAVAL

COLVAR 2 ! TORSION

SCALE 0.22

LAMBDA 0.8

MASS 30

&END METAVAL

&PRINT

&COLVAR

COMMON_ITERATION_LEVELS 3

&EACH

MD 1

&END

&END

&HILLS

COMMON_ITERATION_LEVELS 3

&EACH

MD 1

&END

&END

&END

&END METADYN

&END FREE_ENERGY

PLUMED in CP2K

External library with advanced MTD capabilities:

- Many different collective variables
- Well-tempered MTD
- Multiple walkers MTD
- Bias exchange MTD
- Reconnaissance MTD

2 versions work with cp2k: Plumed 1.3, Plumed 2.x

The logo for PLUMED is rendered in a bold, italicized, sans-serif font. The letters are a vibrant red color with a thick white outline, giving it a 3D, blocky appearance. The word is slanted to the right, consistent with the italicized font style.

Installation with PLUMED v1.3

- Need to separately compile Plumed with cp2k
- Different procedures for v 1.3 and 2.x

Compiling Plumed 1.3 with a current cp2k version:

1. Download a modified plumed 1.3 release from <http://www.cp2k.org/static/downloads/plumed/>
2. Extract the archive, run the provided script `plumedpatch_cp2k.sh`
3. Compile the plumed library
4. Compile cp2k with the flag `-D__PLUMED_CP2K`

Detailed instructions provided under: http://www.cp2k.org/howto:install_with_plumed

Issues:

- Need to recompile with this complicated 2-step procedure every time you want to update the code
- 1.3 is an outdated version of plumed

Installation with PLUMED v2.x

Compiling Plumed 2.x with a current cp2k version:

1. Download plumed from the official website
3. Modify cp2k ARCH file as specified under http://www.cp2k.org/howto:install_with_plumed
5. Compile cp2k

Much more straightforward procedure, giving you the most recent version of plumed, which is actively maintained.

Use CP2K v 2.7

Using Plumed

In the CP2K input file:

```
&FREE_ENERGY
...
  &METADYN
    USE_PLUMED .TRUE.
    PLUMED_INPUT_FILE ./filename.inp
  &END METADYN
&END FREE_ENERGY
```

Additional plumed input file (v2):

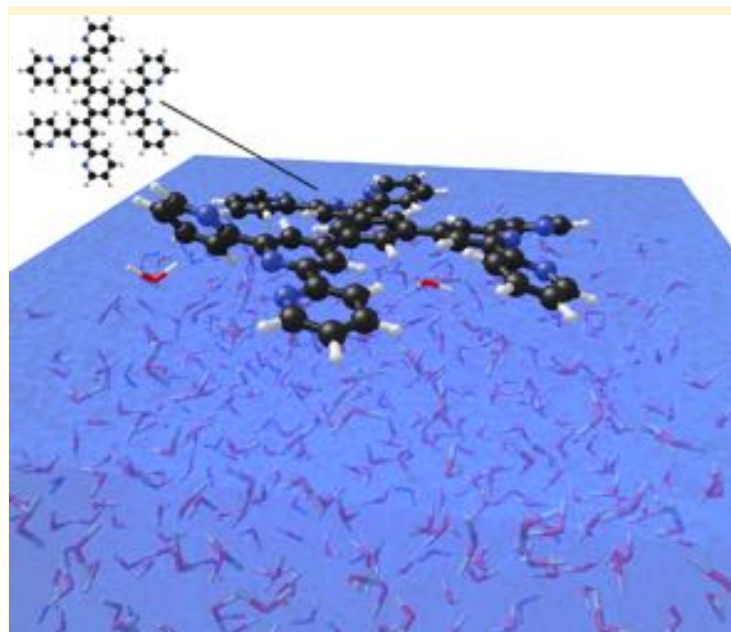
```
a: DISTANCE ATOMS=5,7
b: ANGLE ATOMS=7,9,15

metad: METAD ARG=a,b PACE=500 HEIGHT=1.2 SIGMA=0.35,0.35
FILE=HILLS

PRINT STRIDE=10 ARG=phi,psi,metad.bias FILE=COLVAR
```

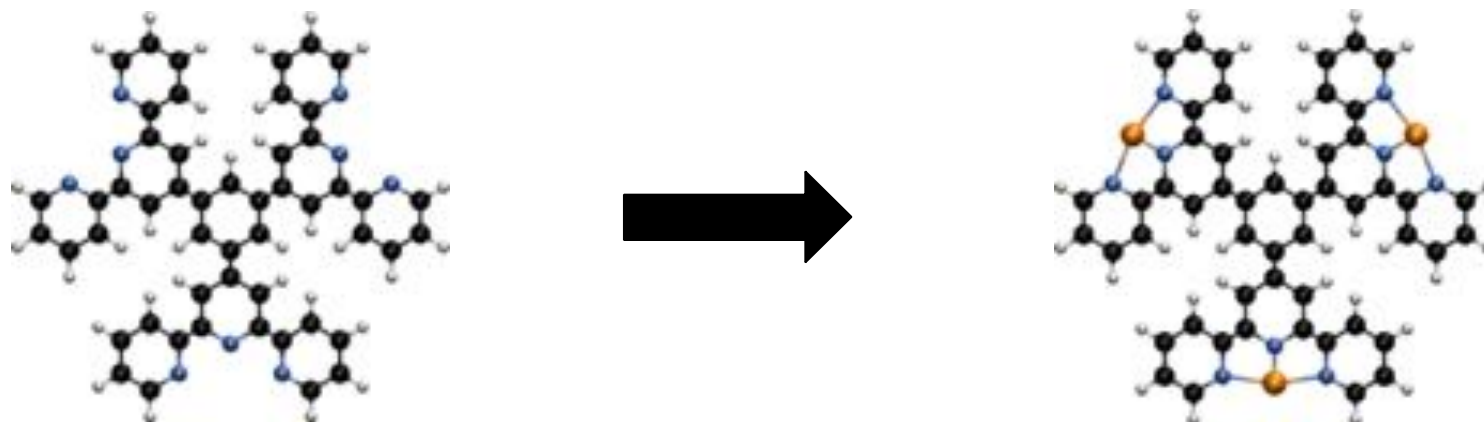
Colvar definition

Tris Terpyridine networks



TTPB is confined on a surface of liquid water, metal ion dissolved in the bulk coordinates to N-pockets

Metal ion coordination leads to formation of 2D-MOFs



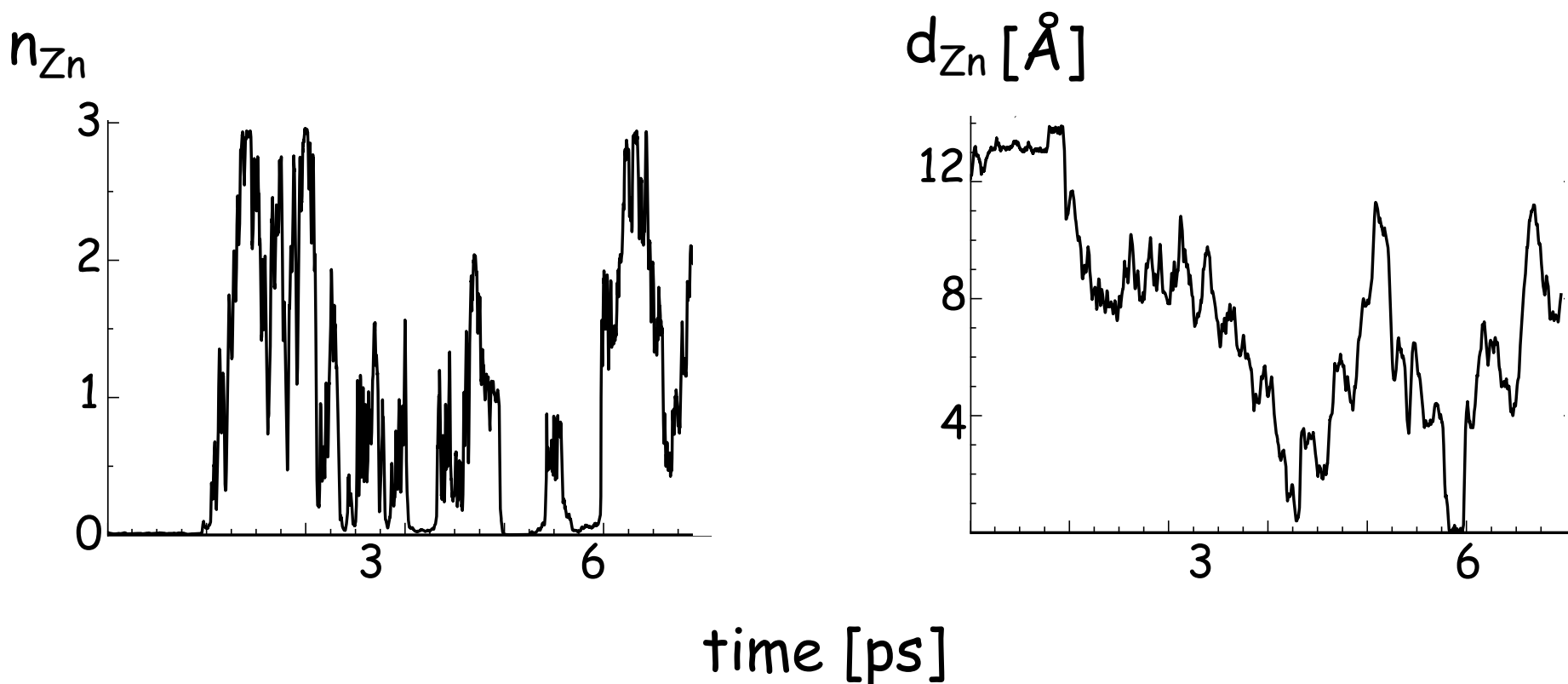
Zn ion migration and binding

mechanism and energetics of Zn binding by MTD

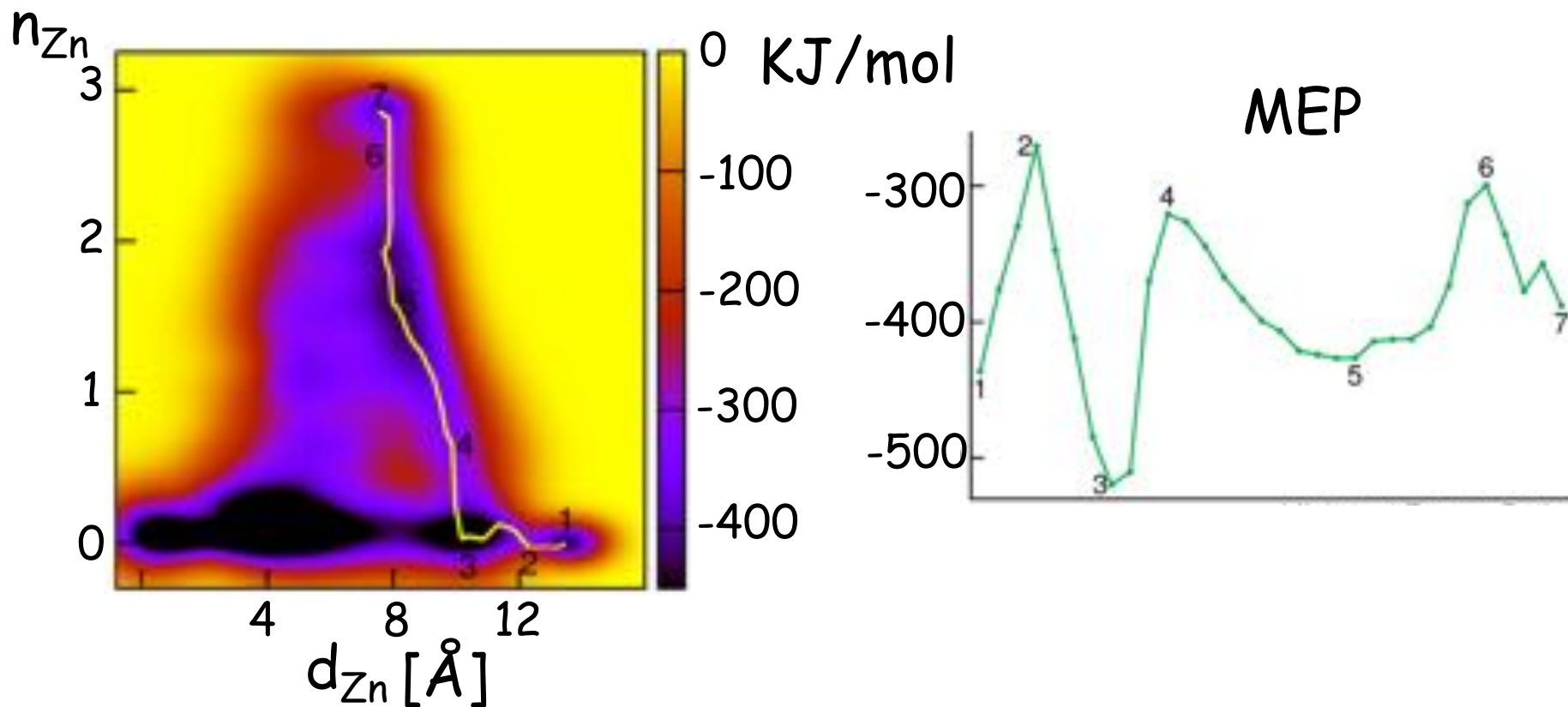
2 CVs

- Coordination number of Zn by TTPB (n_{Zn})
- Distance between Zn and centre of TTPB molecule (d_{Zn})

Hills spawned every 50 steps after 7.5ps of unbiased MD



FES of migration



Zn migrates towards the surface.

3-step binding process of the Zn ion, assisted by rotation of pyridyl groups.

Binding energy of Zn competes with the larger number of configurations in solution. More microstates for dissolved Zn lower in free energy.