Simulating Rare Events in Chemistry

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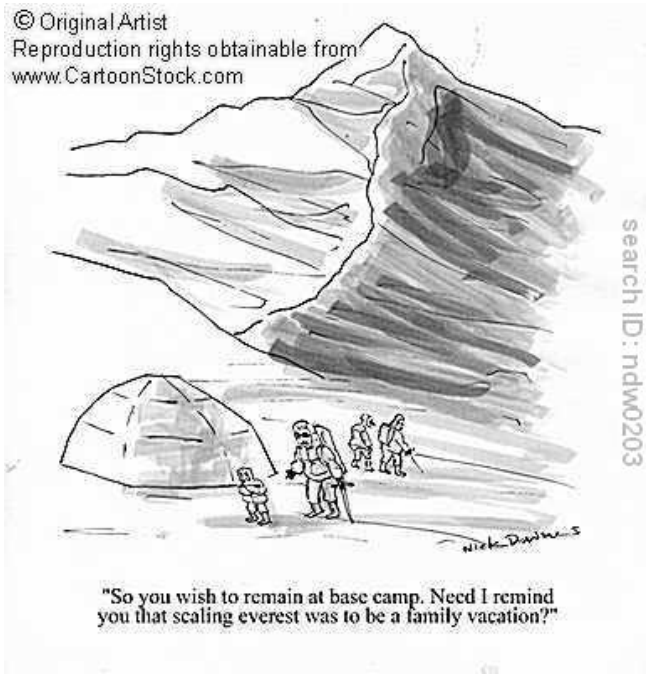
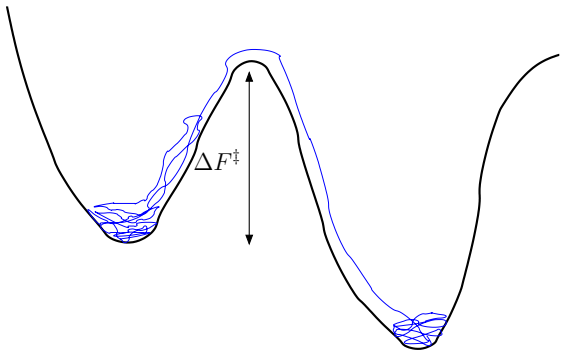
Rare Events (1)

Mountain climbing of molecular/extended systems!



- Climbing through the minimum energy pathway

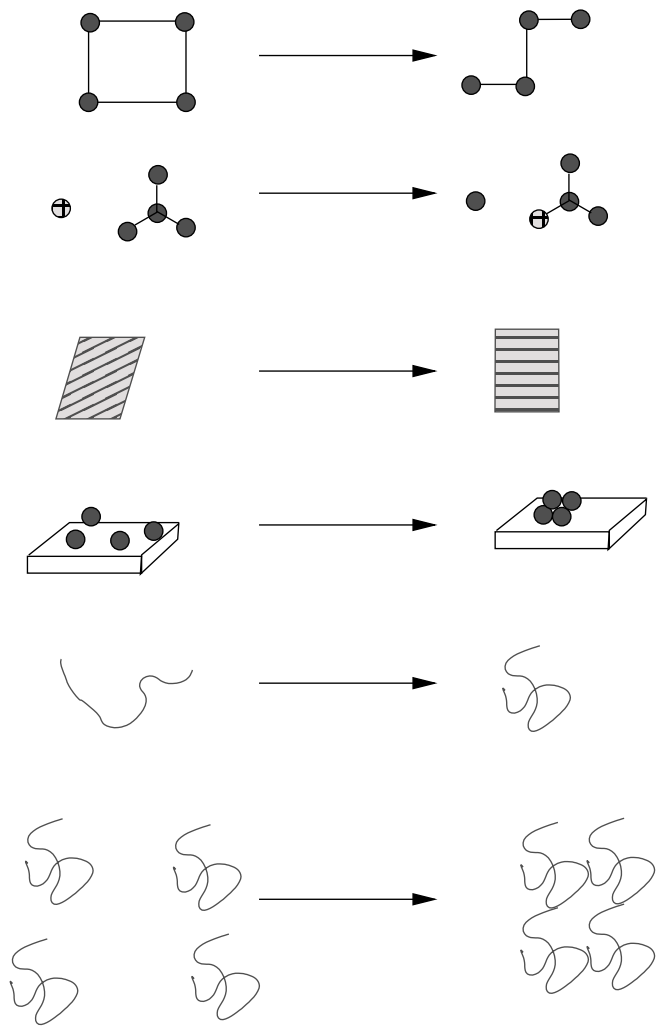


- Time scale to overcome depends on the height exponentially

Rare Events (2)

$$1/\tau \approx k \approx \frac{k_B T}{h} \exp\left(-\Delta F^{\ddagger}/k_B T\right)$$

At room temperature:	
$\Delta F^{\dagger}$ (kJ/mol)	τ (approx)
2.5	0.1 ps
10	1 ps
20	0.1 ns
60	1 ms
100	8 hr



Rare Events & Computer Simulations (1)

- Classical dynamics of nuclei

$$H(\mathbf{R}^N, \mathbf{P}^N) = \frac{1}{2}\sum_I^N M_I \dot{\mathbf{R}}_I^2 + U(\mathbf{R}^N)$$

- U from density functional theory
  Al_2O_3 ($Al_{48}O_{72}$) 1 MD step/1 fs$\rightarrow$ 2200 CPU s

$\Delta F^\dagger$ (kJ/mol)	τ	CPU time
2.5	0.1 ps	10 h
10	1 ps	1 month
20	0.1 ns	100 years
60	1 ms	1.9×10^6 years
100	8 hr	10^{17} years

Rare Events & Computer Simulations (2)

- Accelerating and sampling rare events

Thermodynamic Integration

Ciccotti et al. CPL (1989)

Umbrella Sampling

Valleau et al. JCP (1975)

Adaptive Force Bias

Rodriguez-Gomez et al. JCP (2004)

Conformational Flooding

H. Grubmüller, PRE (1995)

Transition Path Sampling

Chandler et al. JCP (1998)

Parallel Tempering

Wenzel et al. CPL (2002)

Metadynamics

Laio & Parrinello, PNAS (2002)

Minimum Free Energy Path

Ciccotti et al. JCP (2006)

Metadynamics (1)

- Dimensionality reduction: a set of collective coordinates is selected
  - Distance, angle, coordination number, cell vectors, RMSD, pathways etc.
- Biasing: history dependent replusive potential is slowly grown along the trajectory of the collective coordinates

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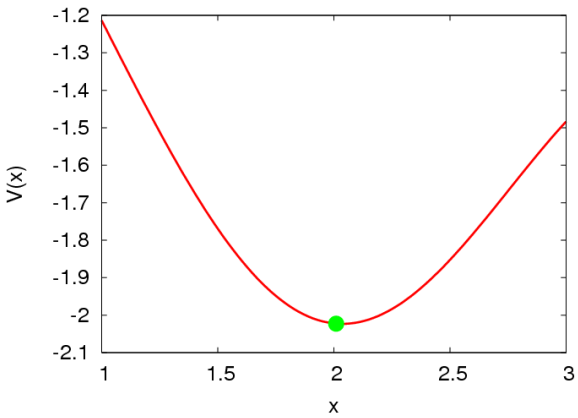

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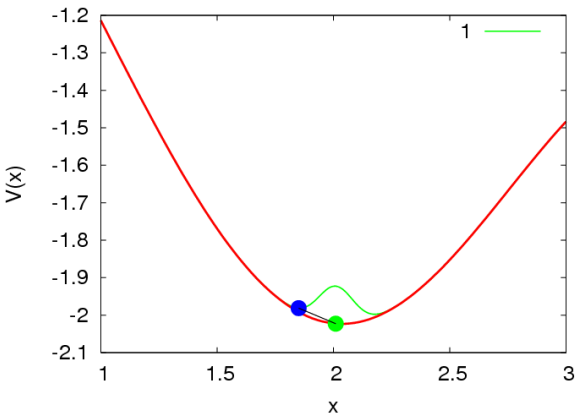

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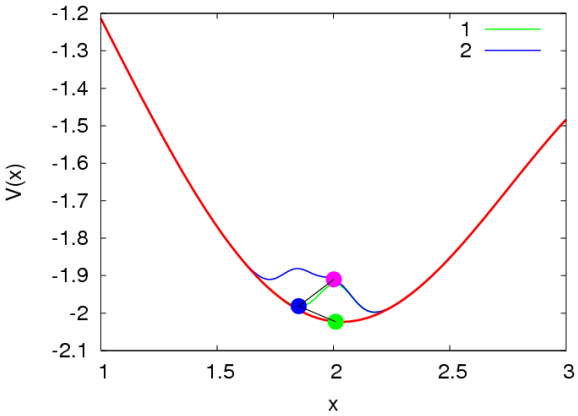

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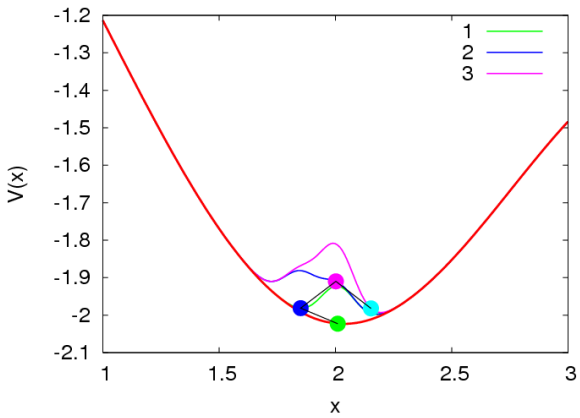
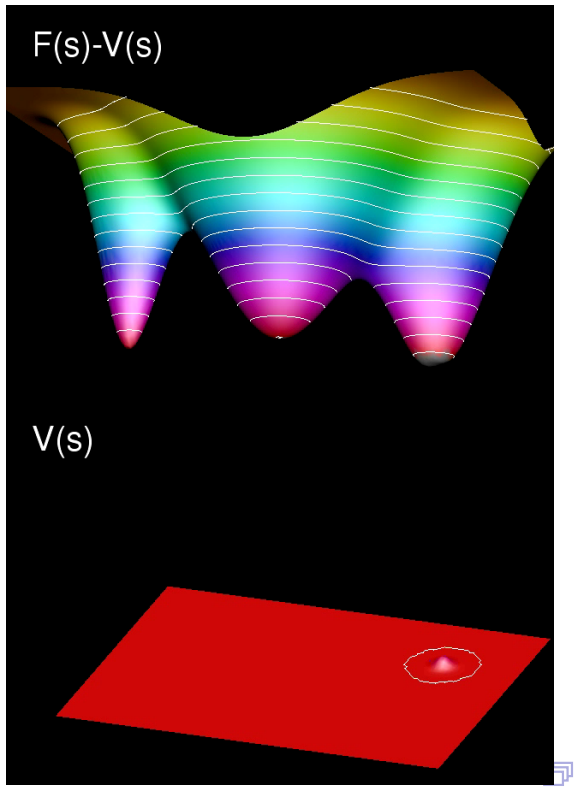


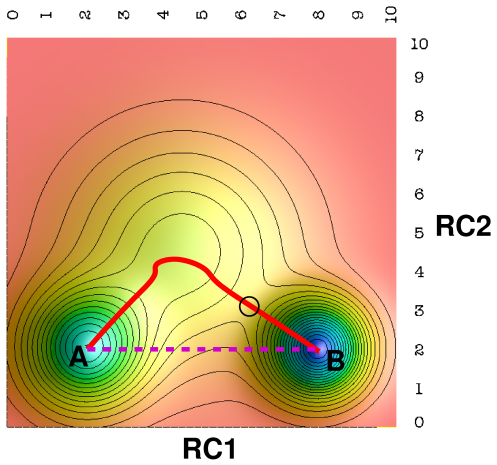


Metadynamics (2)

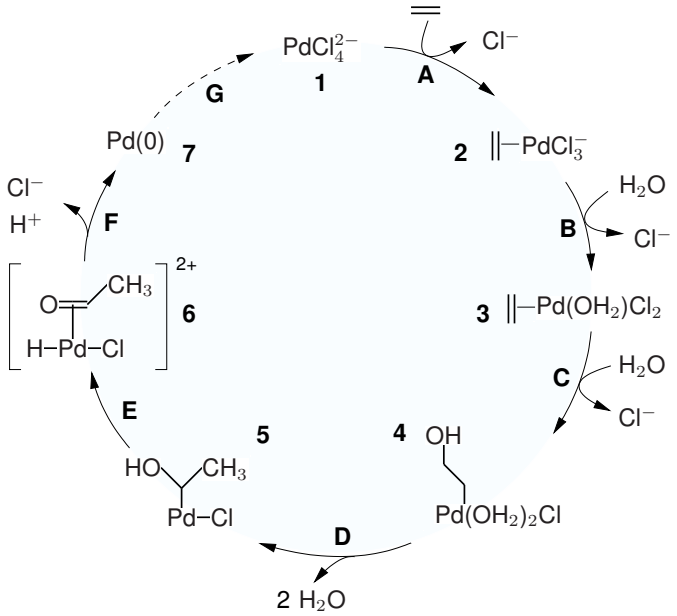
- Configurational sampling (no guess for minima)
- No guess of "true" reaction coordinate
- System moves along minimum free energy path
- System explores new and unpredicted minima
- Underlying free energy surface can be constructed

$$F(S) = -\lim_{t\to\infty} V^{\text{bias}}(S,t) + \text{constant}$$

- Need a set of n collective coordinates
- Have to fill the volume using Gaussians
- Practically n is less than 4

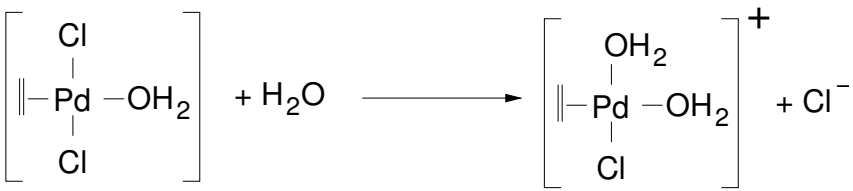


Wacker Reaction: Mechanistic investigations (1)

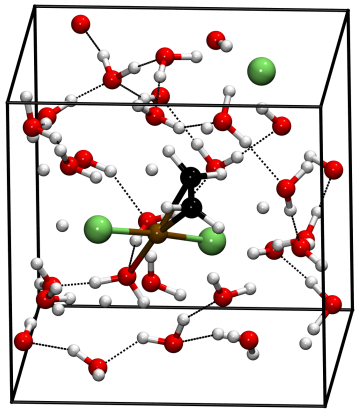


Let us focus on step **C**

Wacker Reaction: Mechanistic investigations (2)



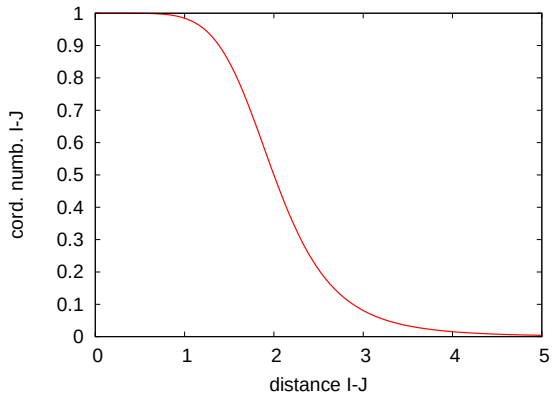
CPMD, Planewave–DFT, USPP, 30 Ry Cutoff, $10\times10\times10$ Å^3 box



Collective coordinates:

$$c(\mathrm{A}-\mathrm{B}) = \sum_{I}^{N_\mathrm{A}} \sum_{J}^{N_\mathrm{B}} \frac{1-\left(R_{IJ}/R^0_{\mathrm{A}-\mathrm{B}}\right)^p}{1-\left(R_{IJ}/R^0_{\mathrm{A}-\mathrm{B}}\right)^{p+q}}$$

1. Pd to all water oxygen *coordination number*
2. Pd to all Cl atom *coordination number*



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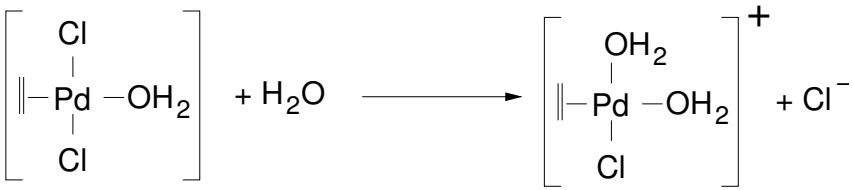

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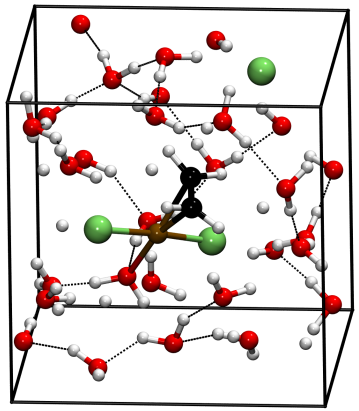
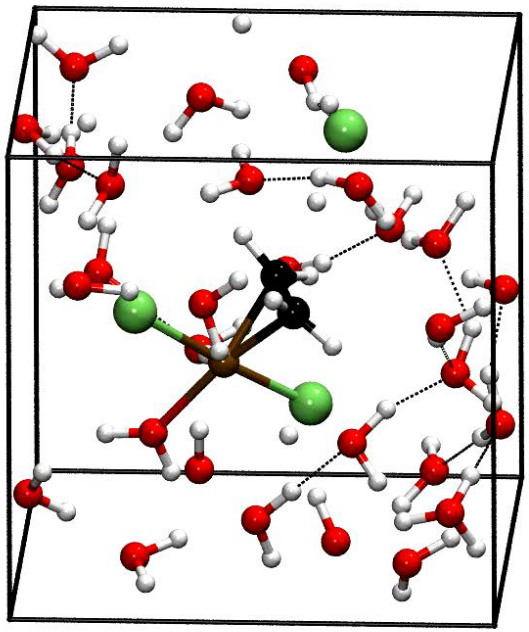
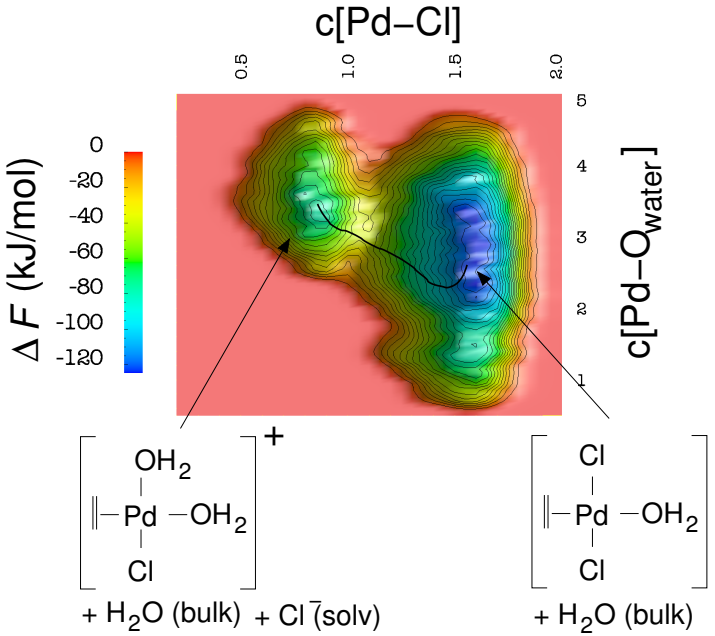
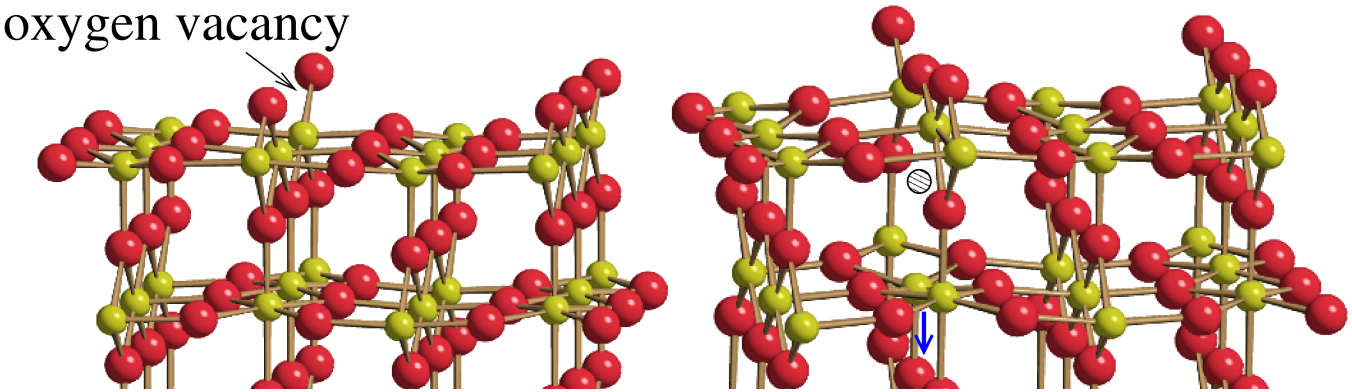




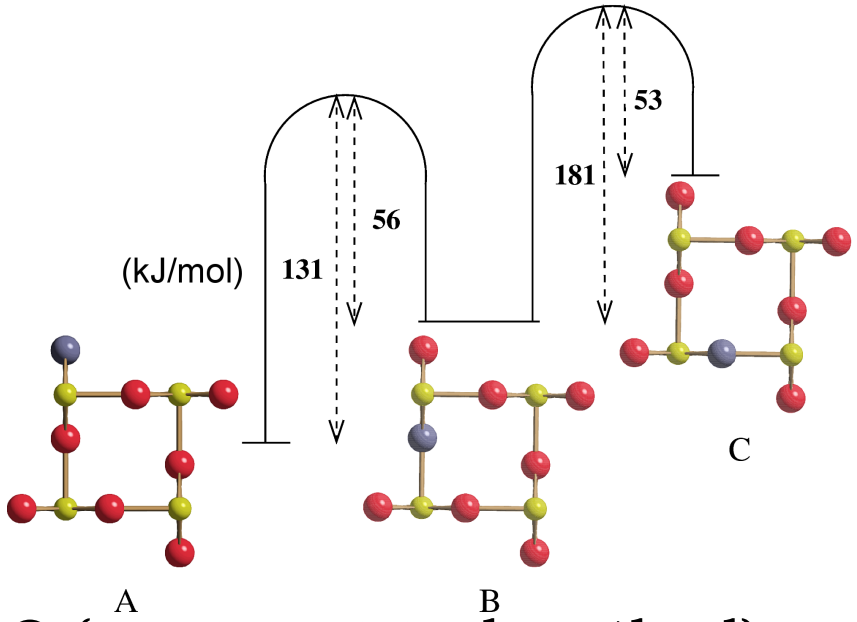


Diffusion of Vacancies in TiO_2 Rutile



Collective coordinates:

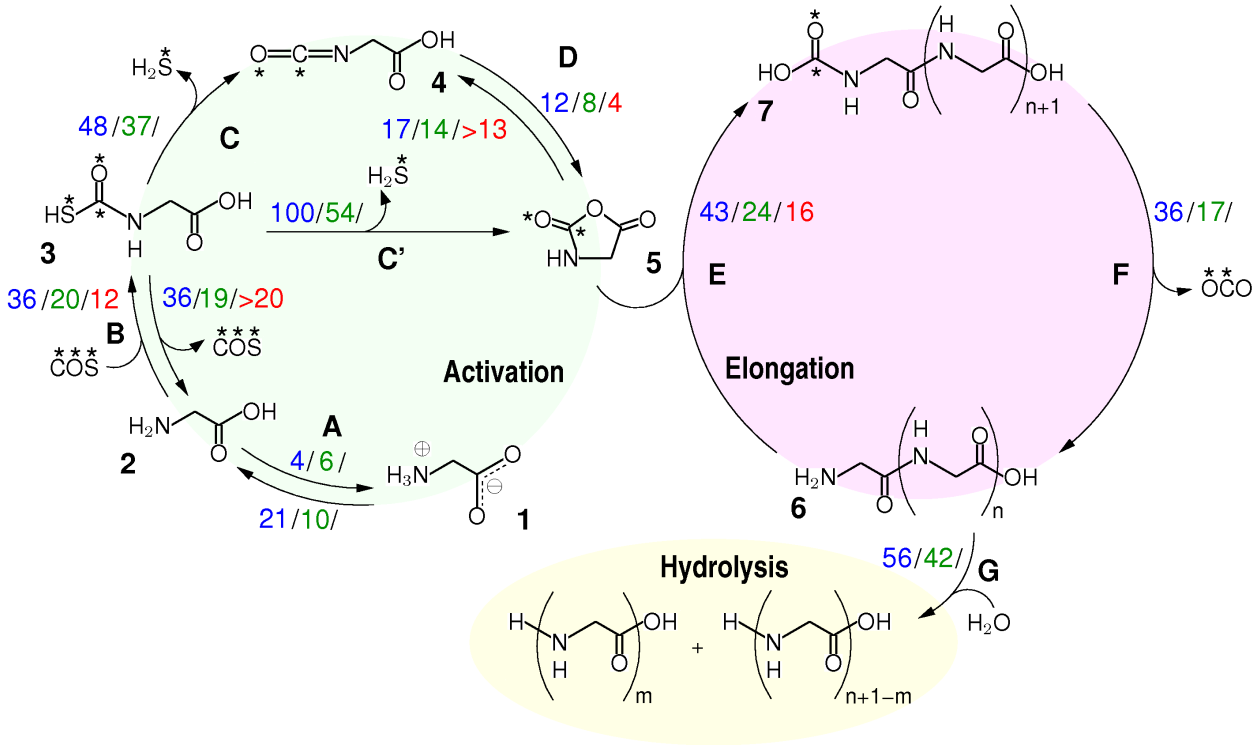
1. Ti–O distance
2. O–vacancy distance
3. Ti-O-Ti angle



Calculations using MSINDO (semiempirical method)

K. Jug, N. N. Nair, and T. Bredow, PCCP, 7, 2616-2621 (2005).

Peptide Synthesis on Pyrite Surface at Extreme Conditions (1)



free energy barriers in $k_B T$ (ABW,HPW,PIW)

- Schreiner, Nair, Marx, JACS (2009)
- Nair, Schreiner, Marx, JACS (2008)
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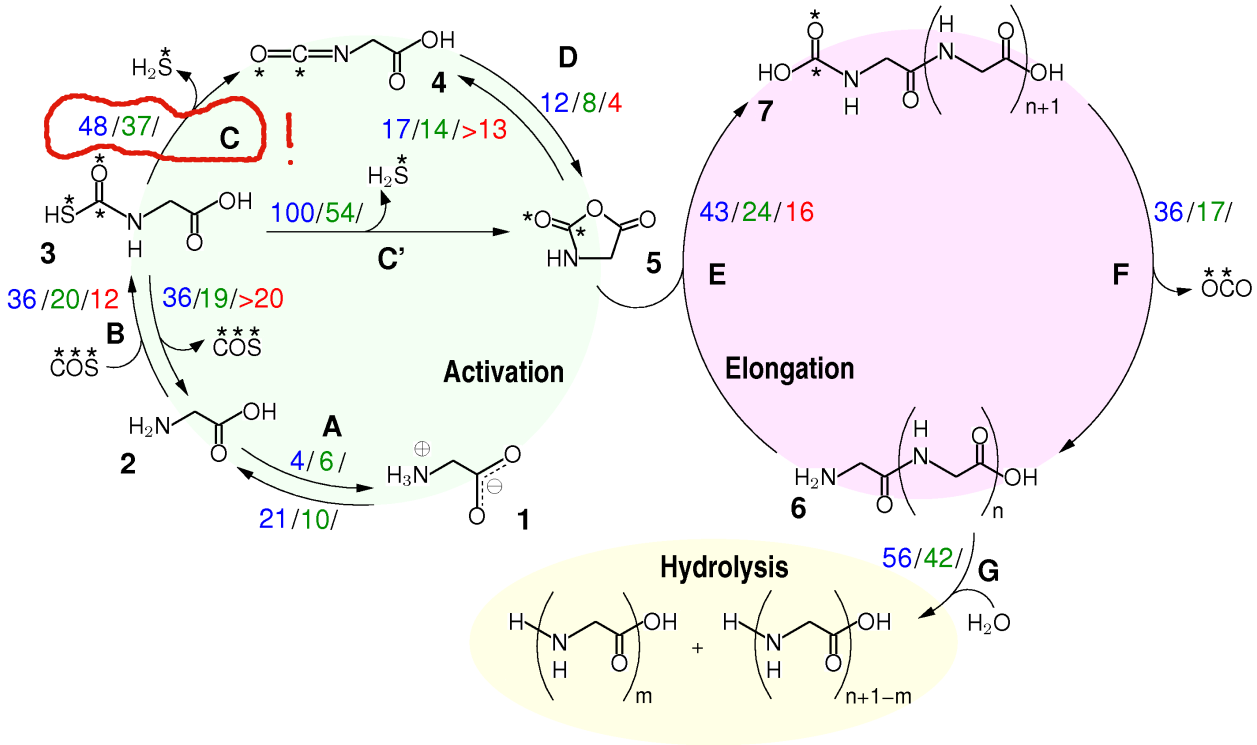

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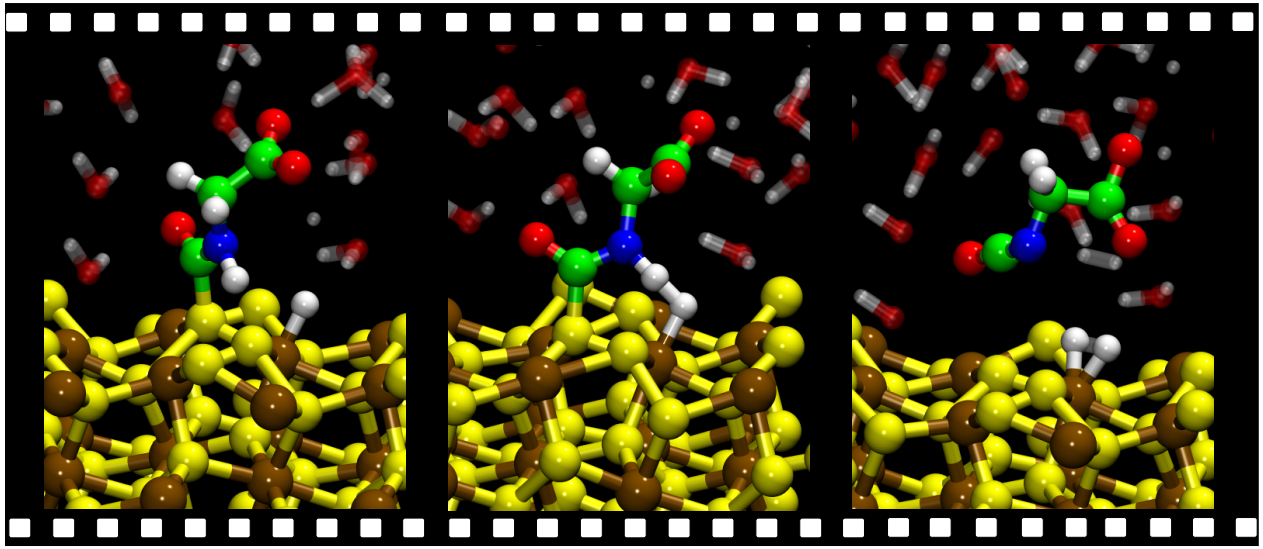
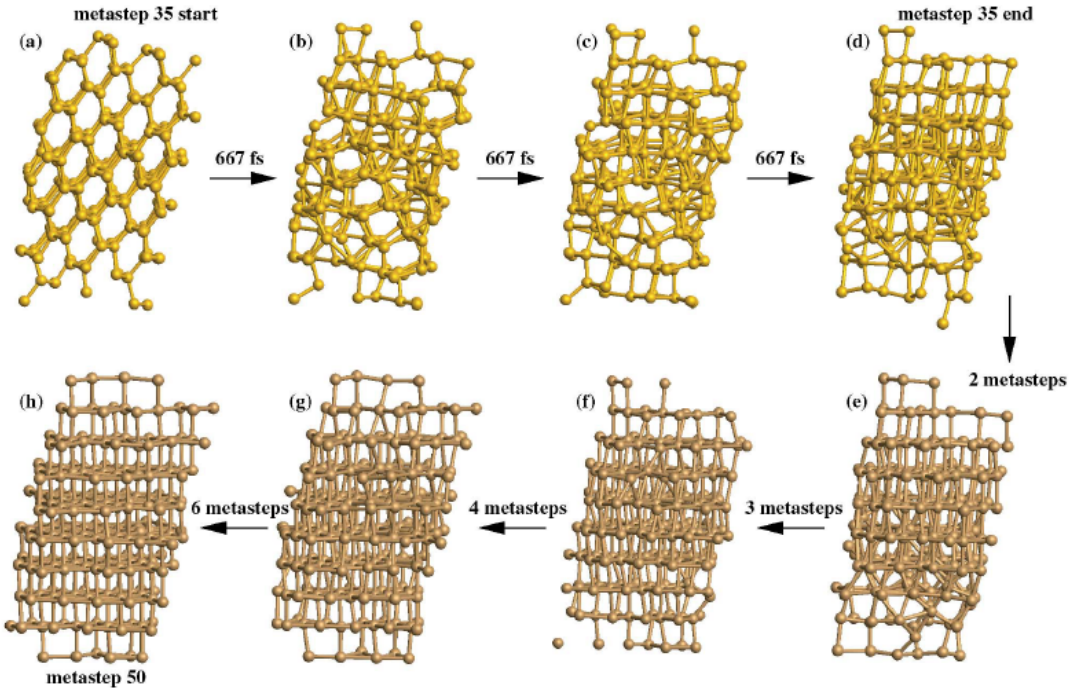


Free energy barrier decreases from $37k_BT$ (HPW) to $20k_BT$ (ABW)
Calculations using CPMD

N. N. Nair, E. Schreiner, D. Marx, *in preparation*

Phase transition in Silicon

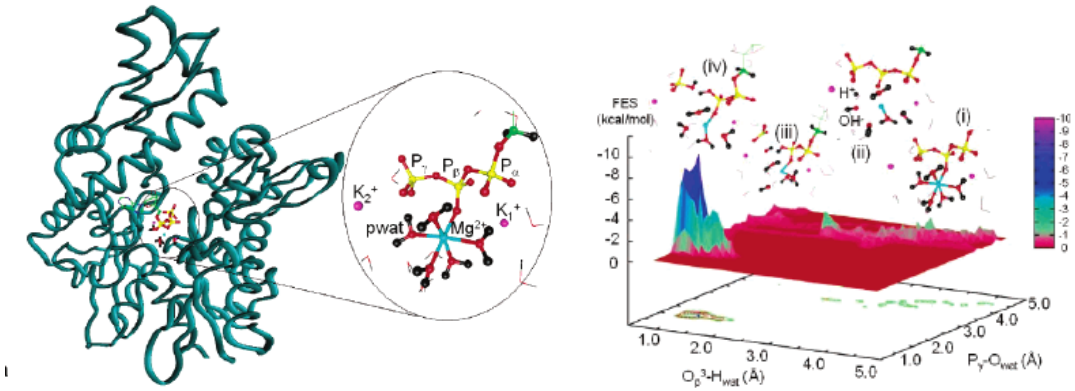


Tight binding calculations, *NPT* (Parrinello–Rahman) collective coordinates: cell vectors, thus sampling G(**h**)

Matrŏnák, Laio, Parrinello, PRL (2003)

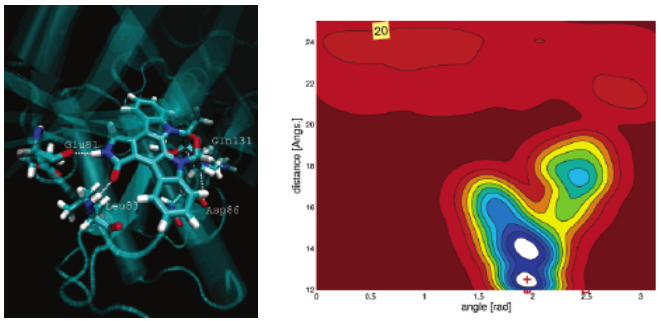
Applications in Biomolecular Systems

In combination with QM/MM techniques:



ATP hydrolysis reaction in ATP synthase (• Boero et al. JACS, 2006)

Docking



(• Parrinello et al. JACS, 2005)

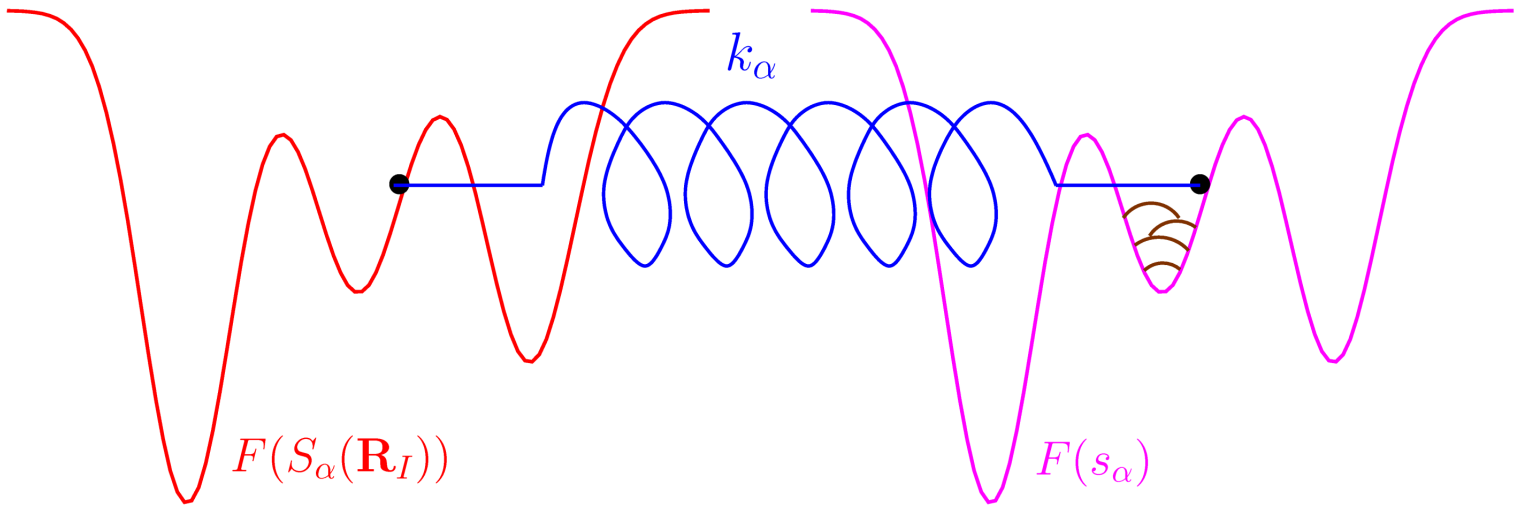
Collective coordiantes

- Geometry based
- Coordination number based
- Cell parameters
- Energy
- Spin density
- Reaction paths
- Normal modes
- Protein–specific: helicity of backbone, dihedral correlation etc.

Laio and Gervasio, Rep. Prog. Phys. (2008)

Extended Lagrangian Metadynamics

$$H^{\text{MTD}} = H^0 + \frac{1}{2}\sum_{\alpha=1}^{d} \mu_\alpha \dot{s_\alpha}^2 + V^{\text{bias}}(s,t) + \frac{1}{2}\sum_{\alpha=1}^{d} k_\alpha \left[S_\alpha(\mathbf{R}_I) - s_\alpha\right]^2$$

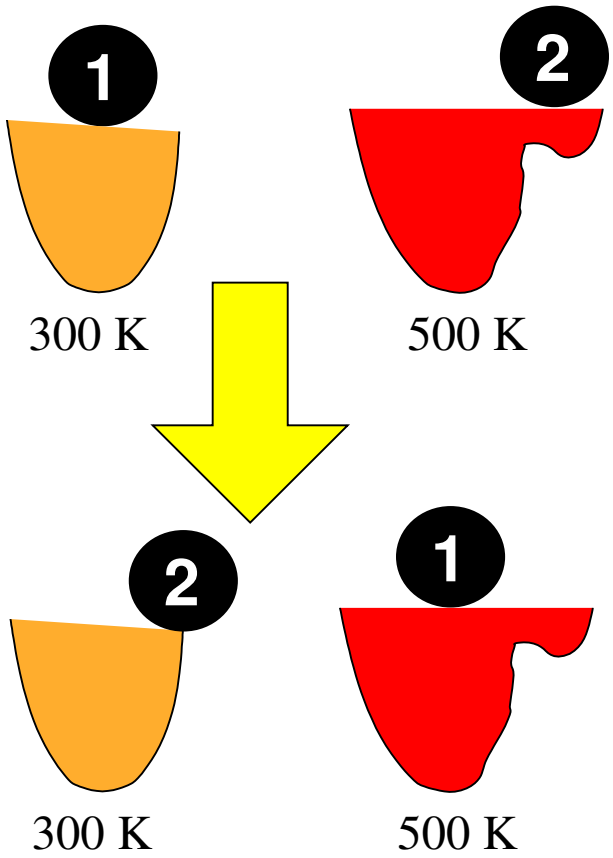


Iannuzzi, Laio & Parrinello, *Phys. Rev. Lett.*, **90**, 238302, 2003.

Parallel Tempering Metadynamics

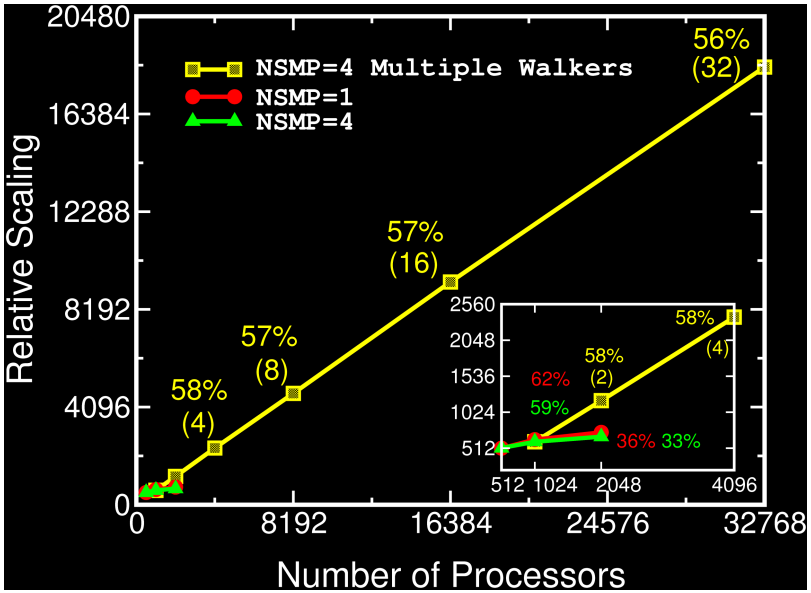
- If missed any slow coordinate?
- Combining parallel tempering with metadynamics
- Multiple replicas at different temperature
- Attempt exchange of replicas with nearest temperature
- Acceptance ratio accounts for different biasing potentials

Parrinello et al. JACS (2006)



Multiple Walker Metadynamics

- What if large number of CVs?
- Many walkers/replicas fill the same free energy surface
- N_w walkers reduces the total simulation time by $1/N_w$



- Raiteri et al. *J. Phys. Chem. B* **110**, 3533 (2006)
- N. N. Nair, E. Schreiner, D. Marx, *inSiDE* **6**, 30 (2008)
- N. N. Nair, E. Schreiner, D. Marx, *in preparation*

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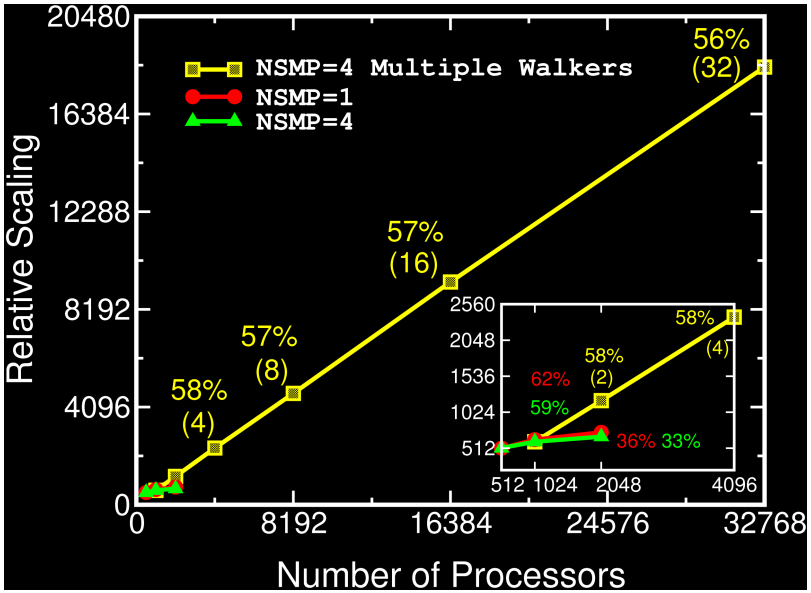
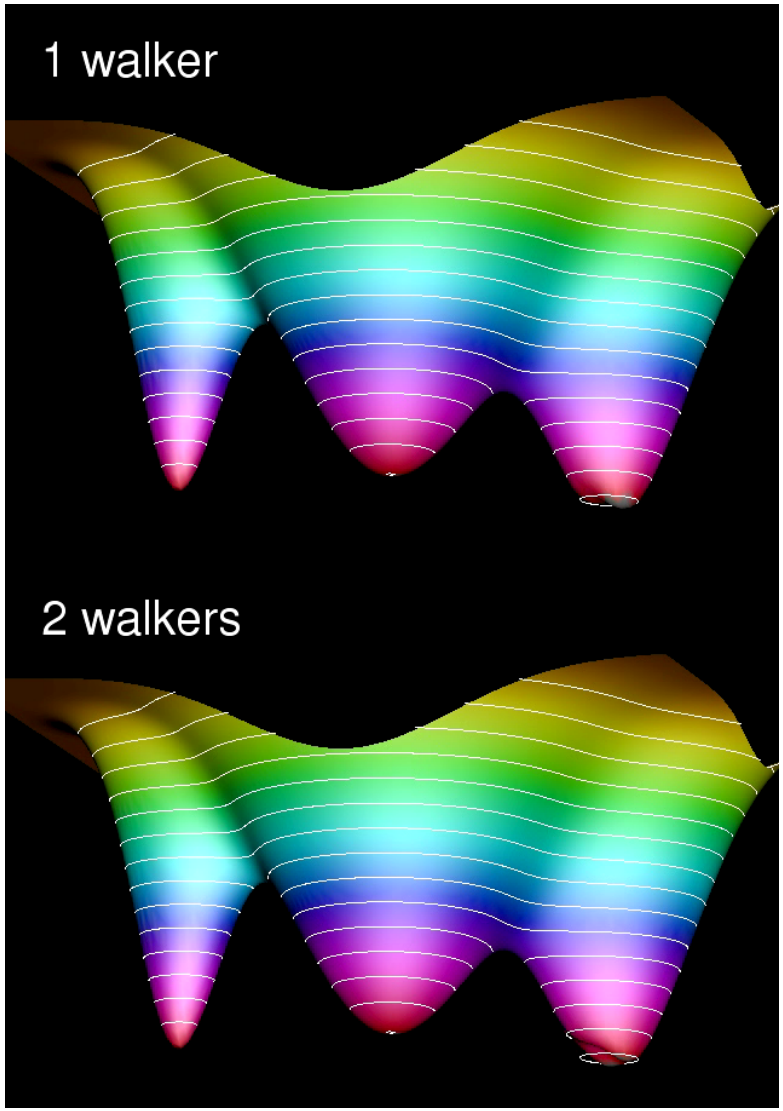
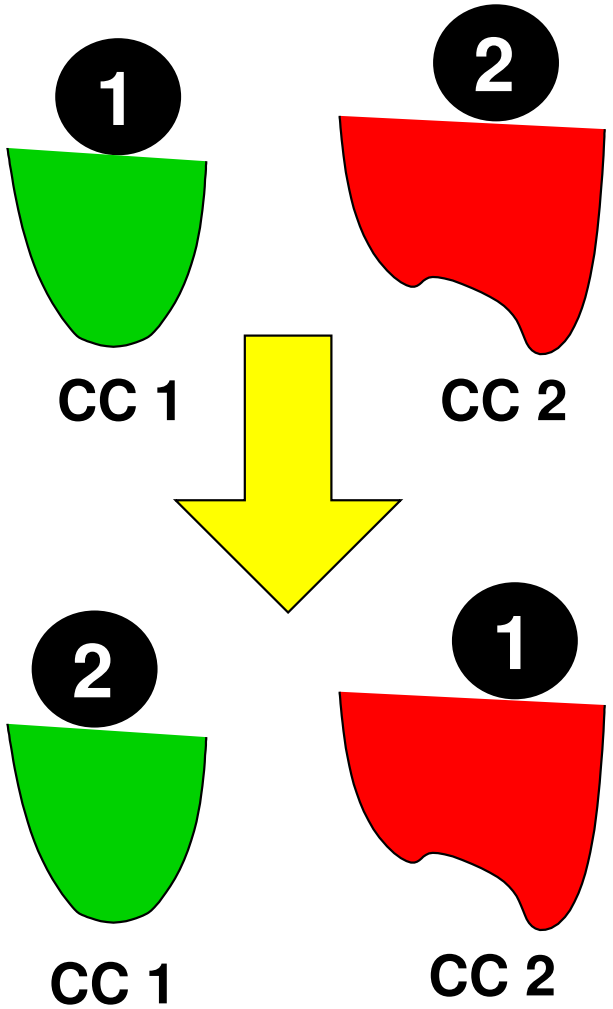




Bias Exchange Metadynamics

- How to deal with large number of coordinates?
- N_R replicas filling different but low dimensional CV space
- Biasing potentials are exchanged among N_R replicas
- Construction of N_R low–dimensional projection of free energy surface



Piana and Laio, JPCB (2007)

Conclusion & Outlook

- Advantages:
  - + Becoming popular method
  - + Easy implementation, usage and error control
  - + New pathways and structure prediction
  - + Reconstruction of free energy surface
- Disadvantages:
  - - Definition of CCs; chemical intuition!
  - - Affordable number CCs is limited 3–5
- Improved metadynamics procedures
- Dream of "virtual laboratory"
- *Powerful computational tool for material design and properties*

Acknowledgments

- Wacker Reaction:
  CHEMFIST
  computational lab
  Department of
  Chemistry, IIT Kanpur,
  India
  www.iitk.ac.in/chcm
- Oxygen Vacancy:
  Prof. Karl Jug
  University of Hannover,
  Germany
- Origin of Life:
  Prof. Dominik Marx
  Ruhr–Universität
  Bochum, Germany
  www.theochem.rub.de

  &

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- Alessandro Curioni
  (IBM Zürich)

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