

Modélisation de l'environnement et de son impact sur les propriétés des systèmes chimiques

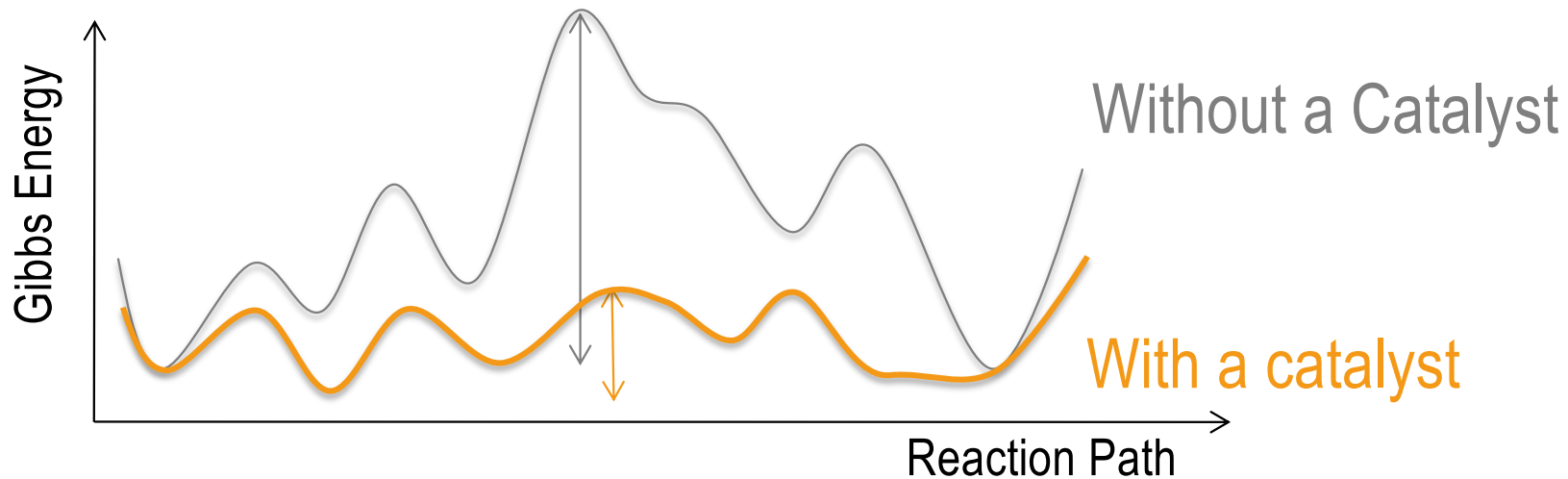
Réactivité/processus catalytiques par des approches DFT/MM et DM

Carine MICHEL

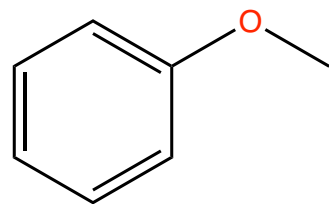
Looking at reactions

A FIRST EXAMPLE

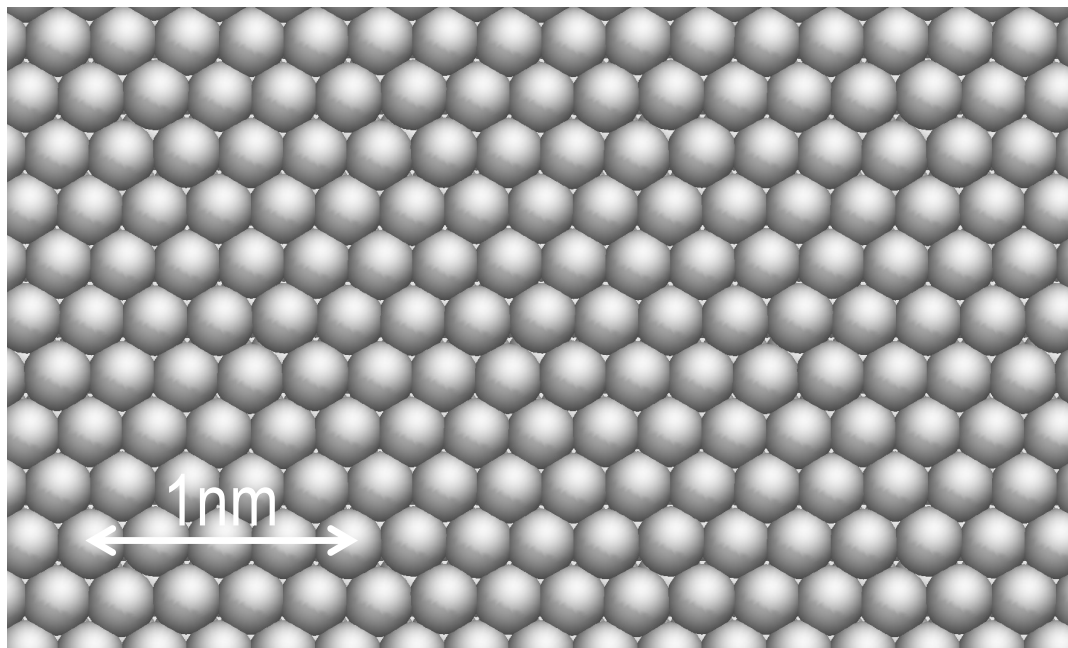
A catalyst lowers the energetic barriers to be overcome



An exemple



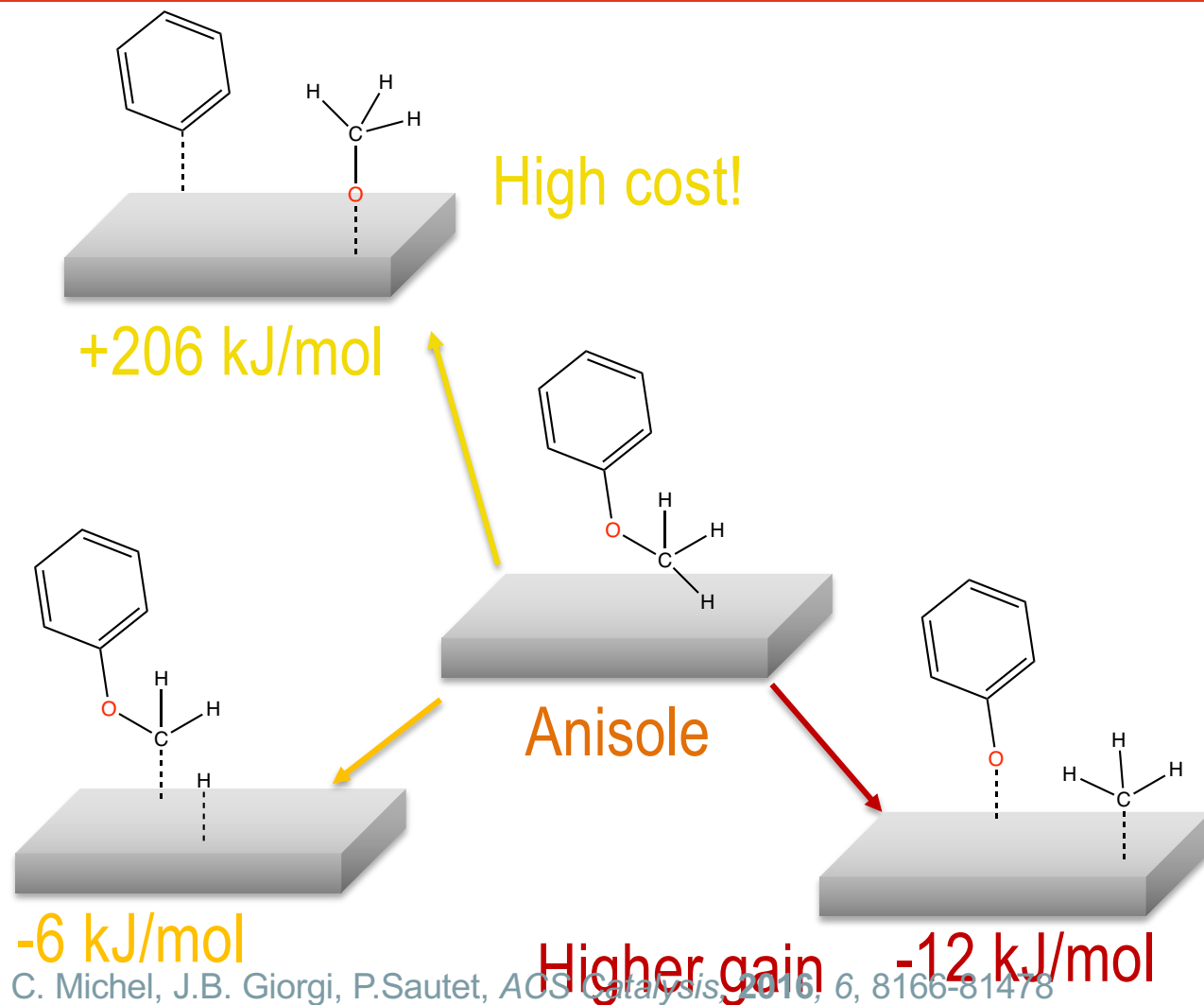
Anisole



Pt(111)

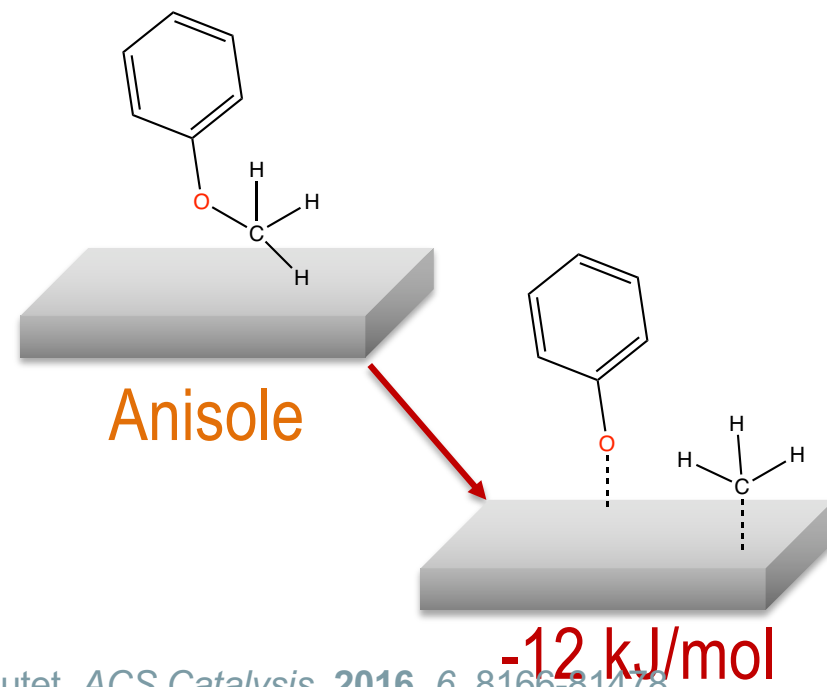
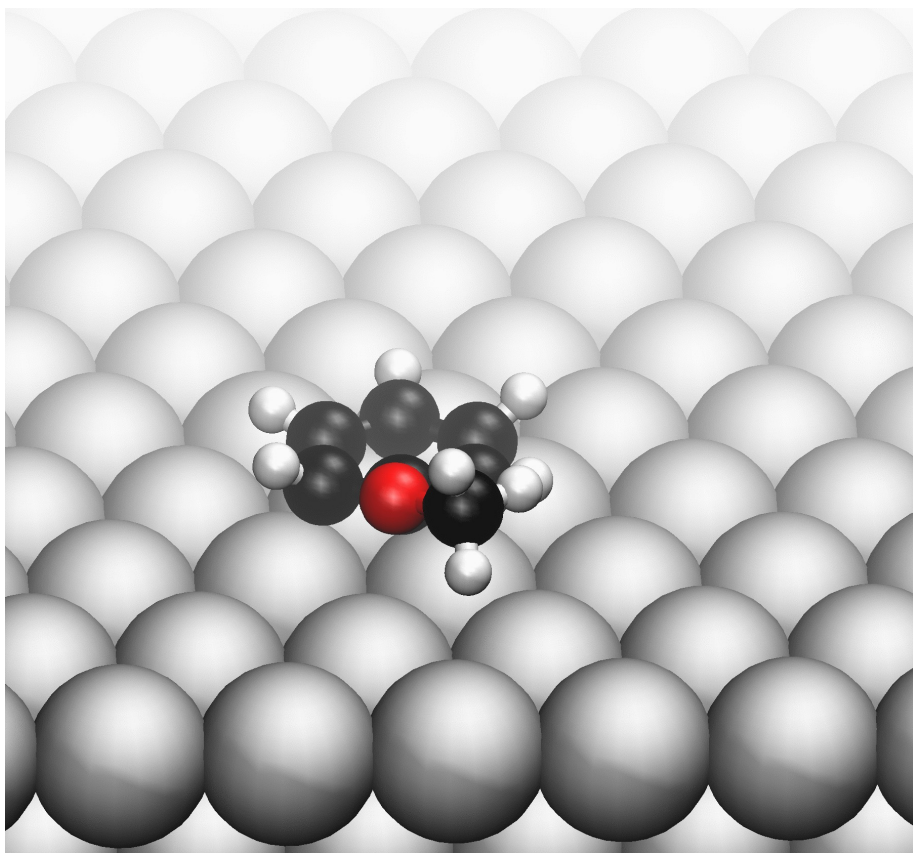
Evaluating thermo

Using periodic DFT we can explore the energetic gain and loss to break a given bond in anisole on Pt(111).

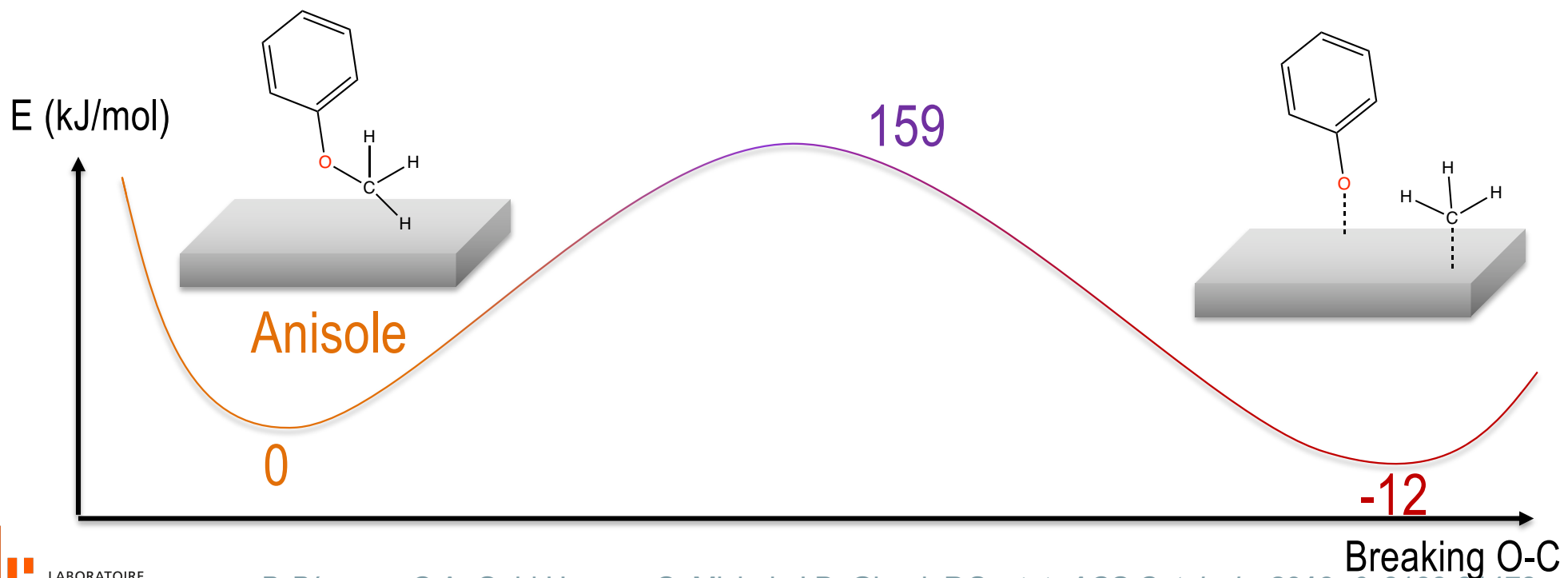
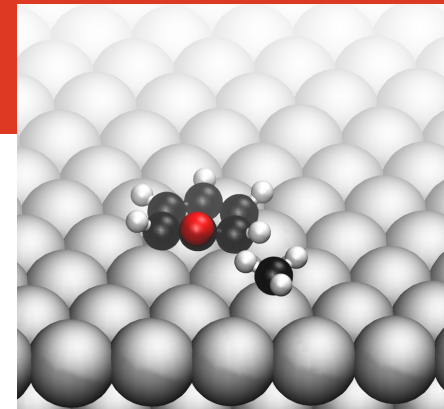
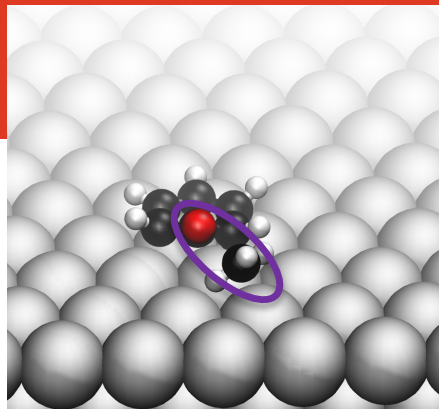
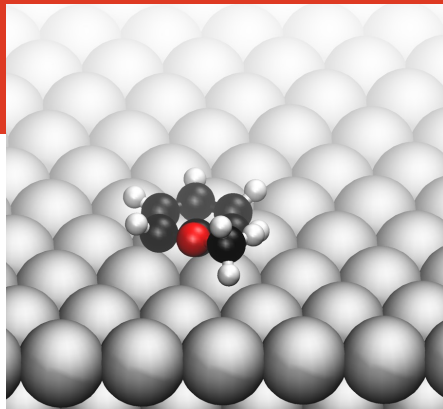


R. Réocreux, C.A. Ould Hamou, C. Michel, J.B. Giorgi, P.Sautet, *ACS Catalysis*, 2016, 6, 8166-81478

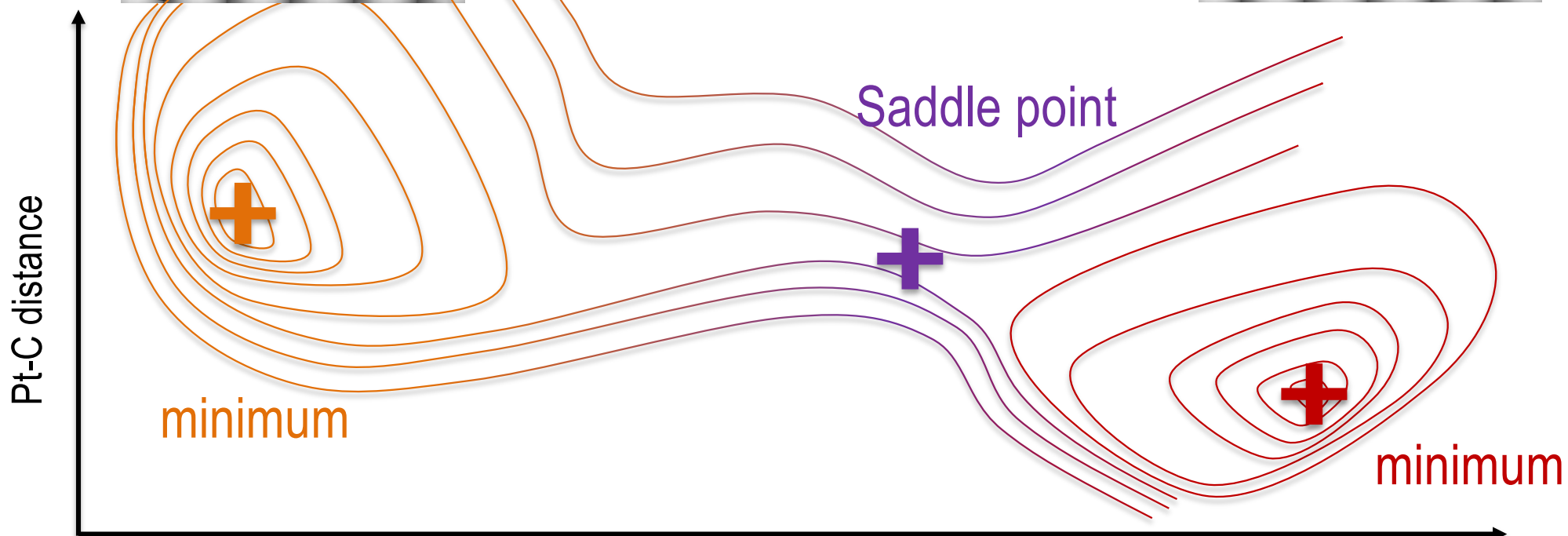
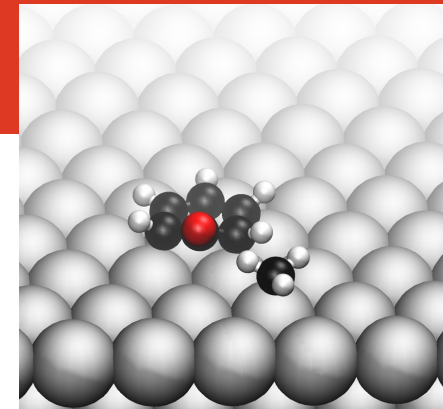
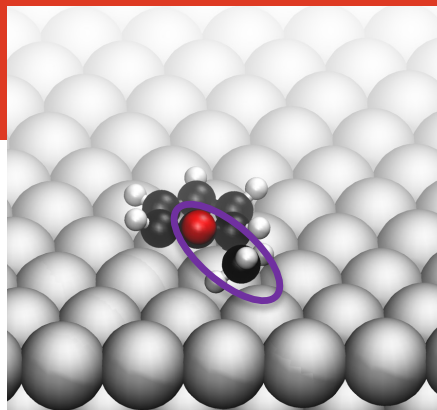
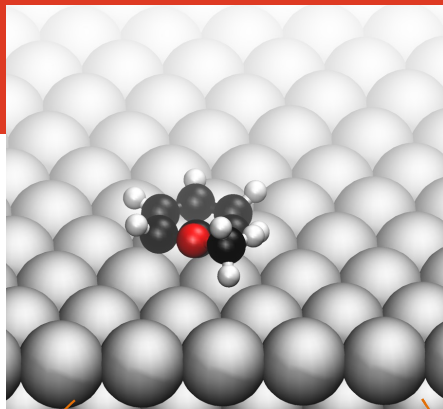
A "movie"



R. Réocreux, C.A. Ould Hamou, C. Michel, J.B. Giorgi, P.Sautet, *ACS Catalysis*, 2016, 6, 8166-81478

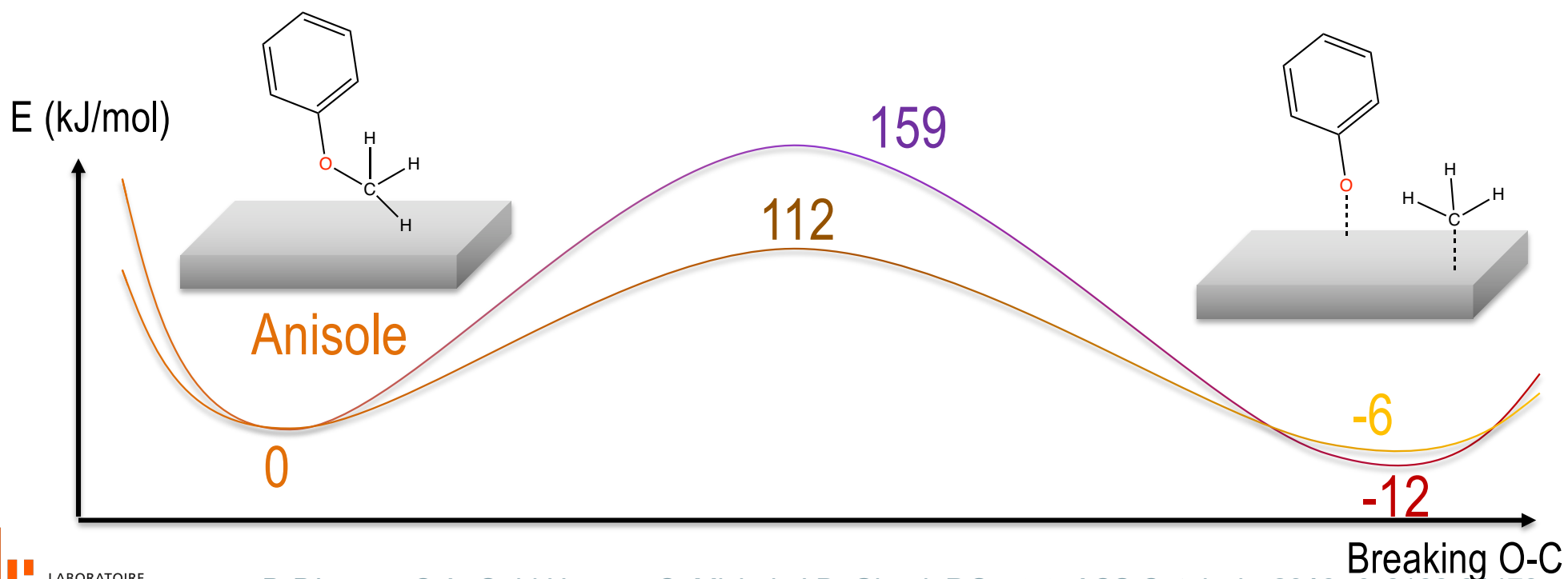


R. Réocreux, C.A. Ould Hamou, C. Michel, J.B. Giorgi, P.Sautet, *ACS Catalysis*, 2016, 6, 8166-81478



Comparing pathways

Faster to go through the lower saddle point...
...even if the product is not the most stable one



CONCEPTS AND TOOLS

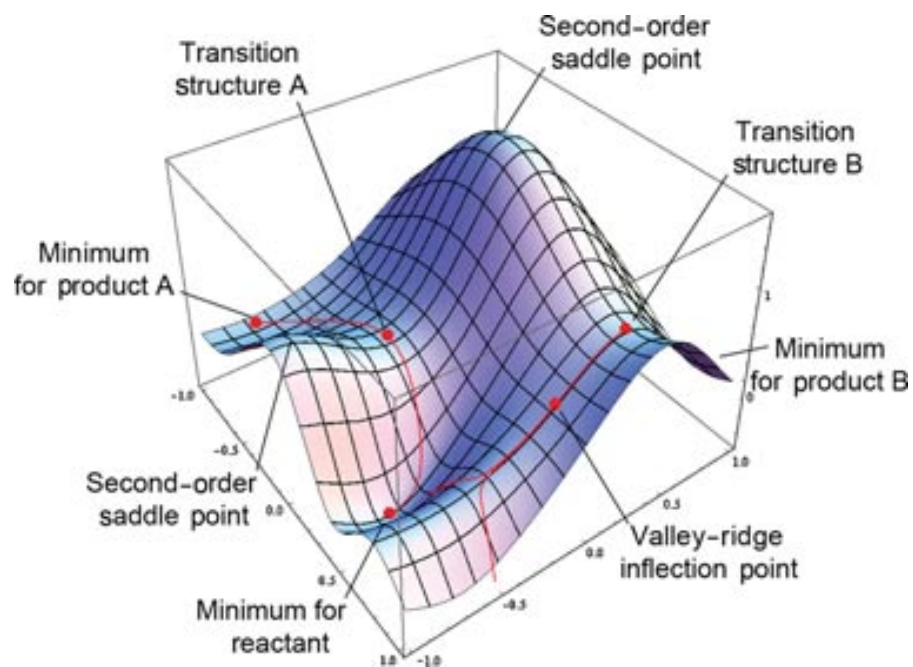
Few assumptions

We are working in the context of the Born-Oppenheimer approximation.

We are considering only the ground state.

We are working in the harmonic transition state theory context.

Key points of the potential energy surface

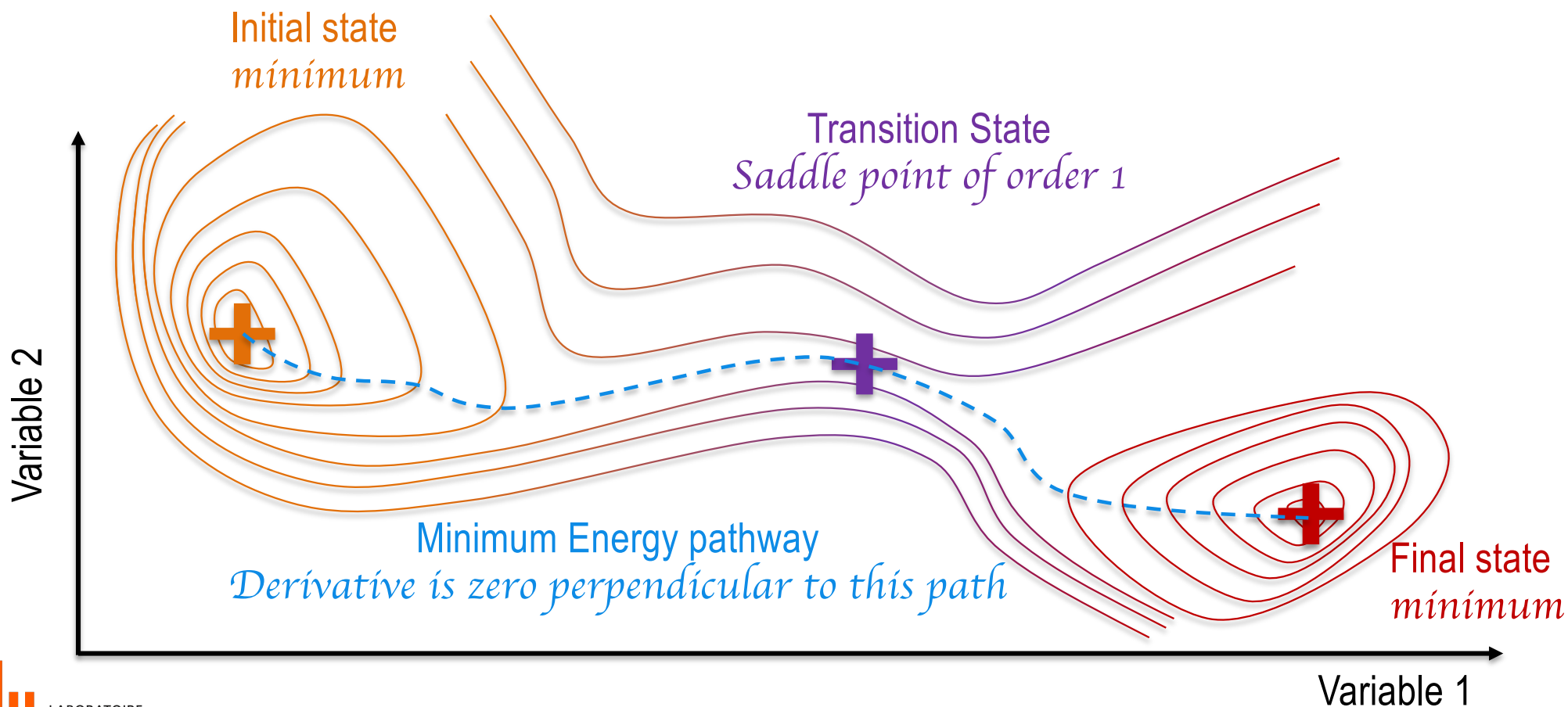


Locally quadratic:

$$E(\mathbf{R}) = E(\mathbf{R}_0) + \mathbf{g}_0^T (\mathbf{R} - \mathbf{R}_0) + \frac{1}{2} (\mathbf{R} - \mathbf{R}_0)^T H_0 (\mathbf{R} - \mathbf{R}_0)$$

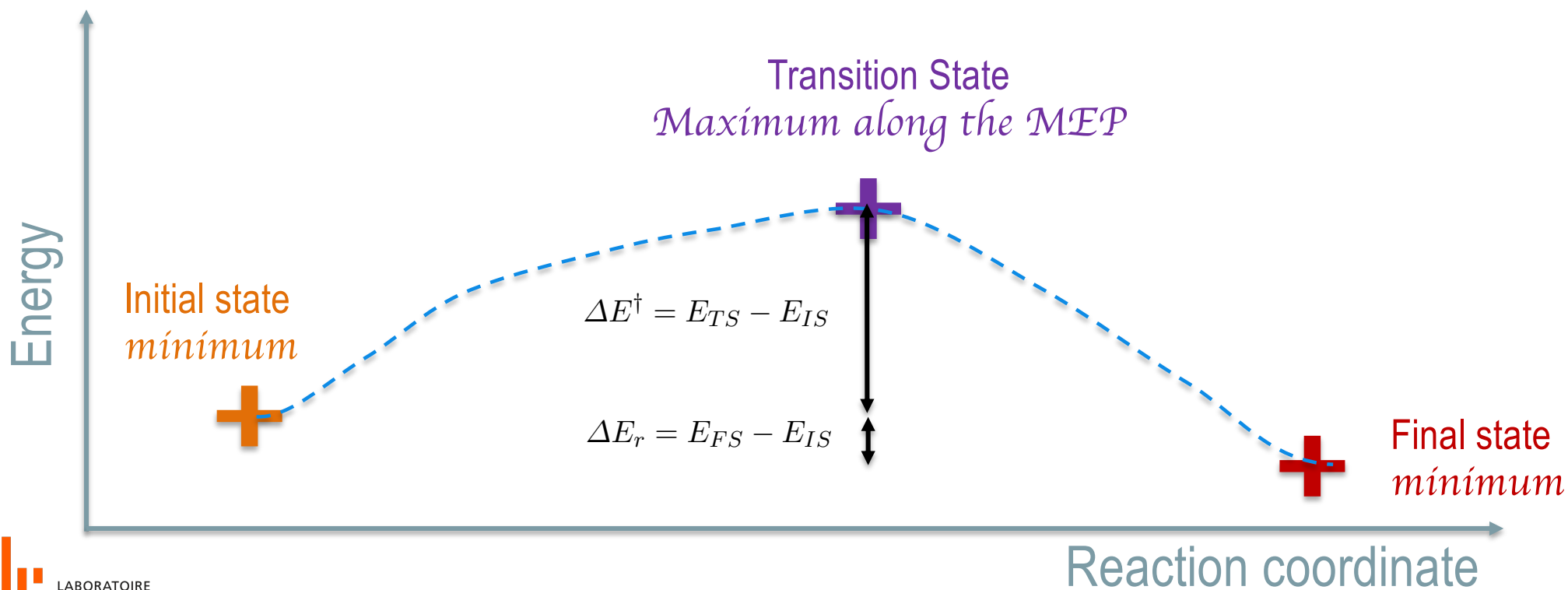
Schlegel HB. Geometry optimization. In: Schleyer PvR, Allinger NL, Kollman PA, Clark T, Schaefer HF III, Gasteiger J, Schreiner PR, eds. Encyclopedia of Computational Chemistry. Vol 2. Chichester: John Wiley & Sons; 1998, 1136–1142.

Key points of the potential energy surface



The rate of an elementary step

$$k^{hTST} = \frac{\prod_i^{N_{DOF}} \nu_i^{IS}}{\prod_i^{N_{DOF}-1} \nu_i^{TS}} \exp\left(\frac{E^{TS} - E^{IS}}{k_B T}\right)$$



Exploring the potential energy surface

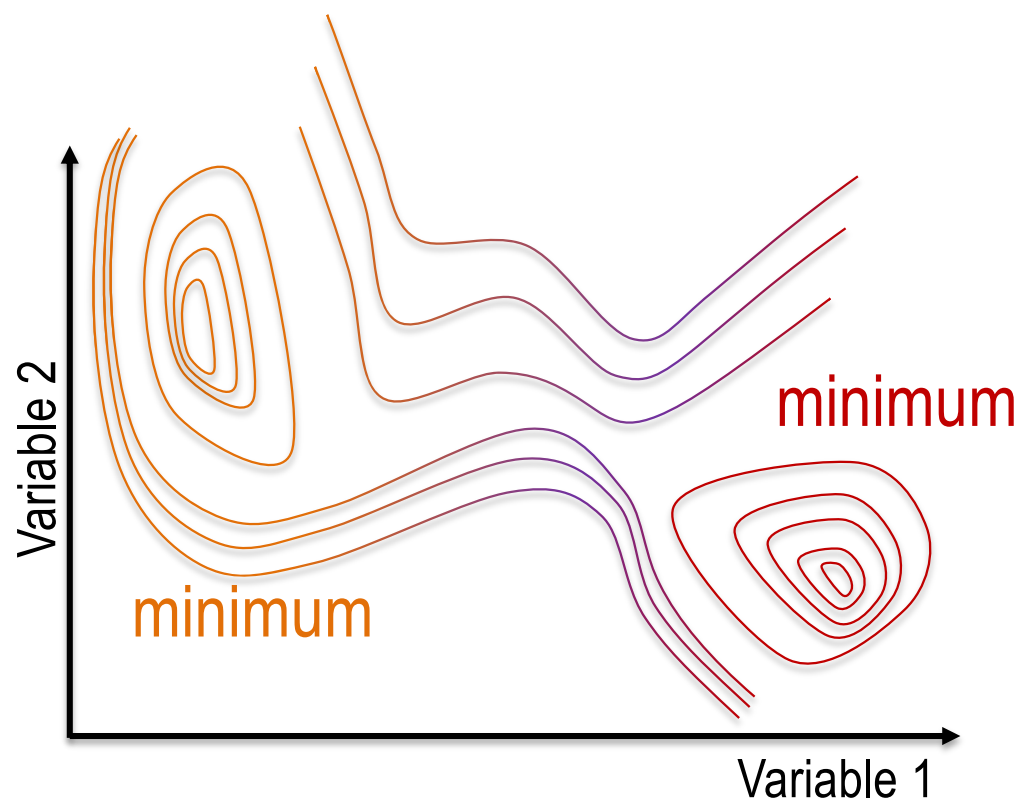
A minimum is defined by:

$$\forall i, \left(\frac{\partial E}{\partial R_i} \right)_i = 0$$

Eigenvalue of the mass-weighted
Hessian k_i

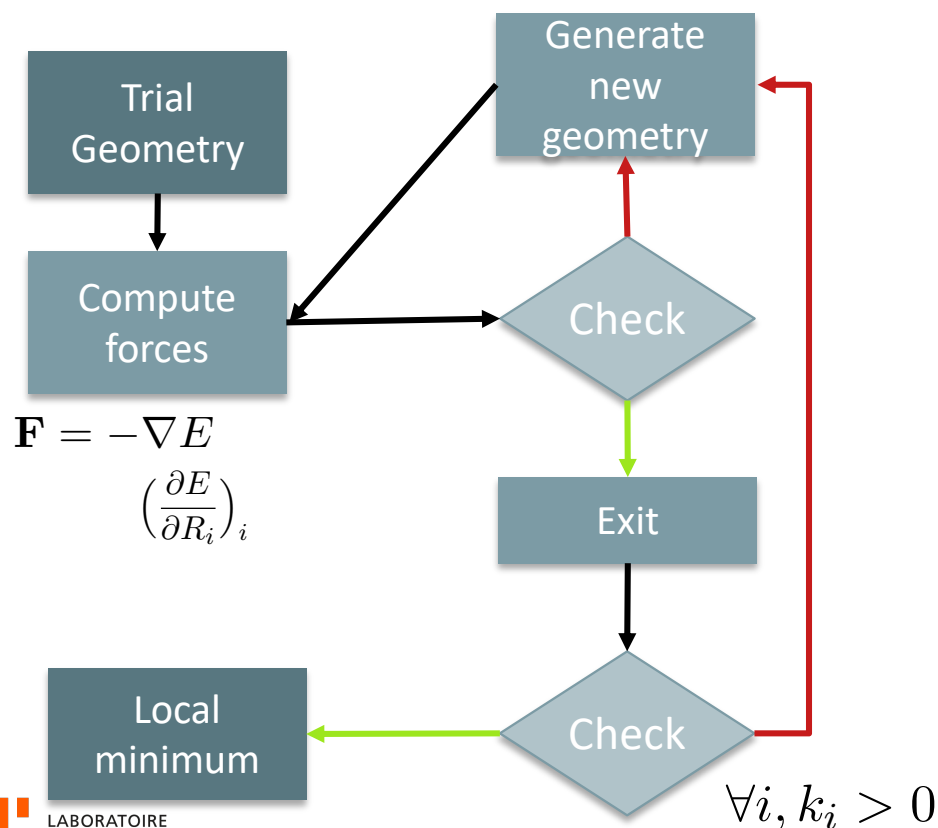
$$\forall i, k_i > 0$$

Harmonic frequencies: $\nu_i = \frac{1}{2\pi} \sqrt{\frac{k_i}{\mu}}$

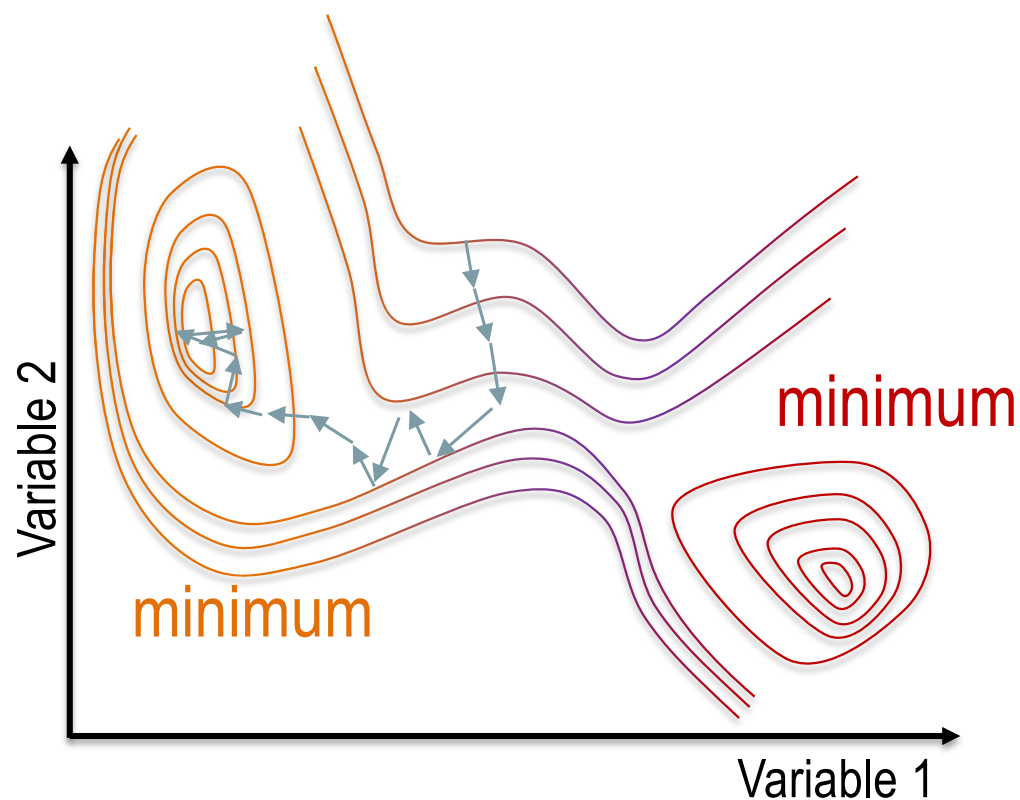


Exploring the potential energy surface

Geometry optimisation loop



Typical criteria:
variation of E, force, max displacement,
average displacement



Exploring the potential energy surface

Geometry optimisation algorithms

Newton-Raphson

searching for zero gradient

Few steps, costly

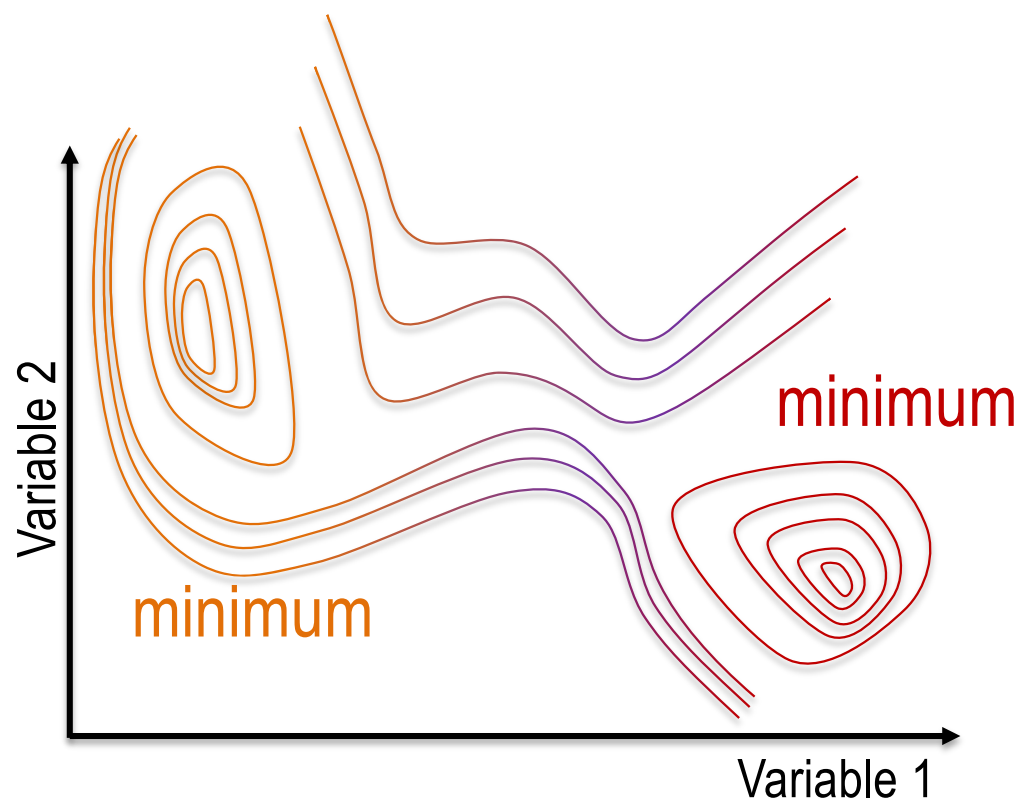
Quasi-Newton methods

Approximate the Hessian

e.g. BFGS algorithm

Conjugated gradient

Follow the gradient corrected
thanks to the previous steps



Exploring the potential energy surface

Choice of the coordinates, not to be neglected

TABLE II.
Comparison of the Number of Steps Required to Optimize Equilibrium Geometries Using Various Coordinate Systems.

Molecule ^a	Z Matrix ^b	Cartesian ^b	Mixed ^b	Redundant ^c
2-Fluoro furan	7	7	7	6
Norbornane	7	5	5	5
Bicyclo[2.2.2]octane	11	19	14	7
Bicyclo[3.2.1]octane	6	6	7	5
Endo hydroxy bicylopentane	8	18	9	12
Exo hydroxy bicylopentane	10	20	11	11
ACTHCP	65	> 81	72	27
1,4,5-Trihydroxy anthroquinone	10	11	17	8
Histamine H ⁺	42	> 100	47	19

^aStarting geometries given in ref. 6; calculated by HF / STO-3G.

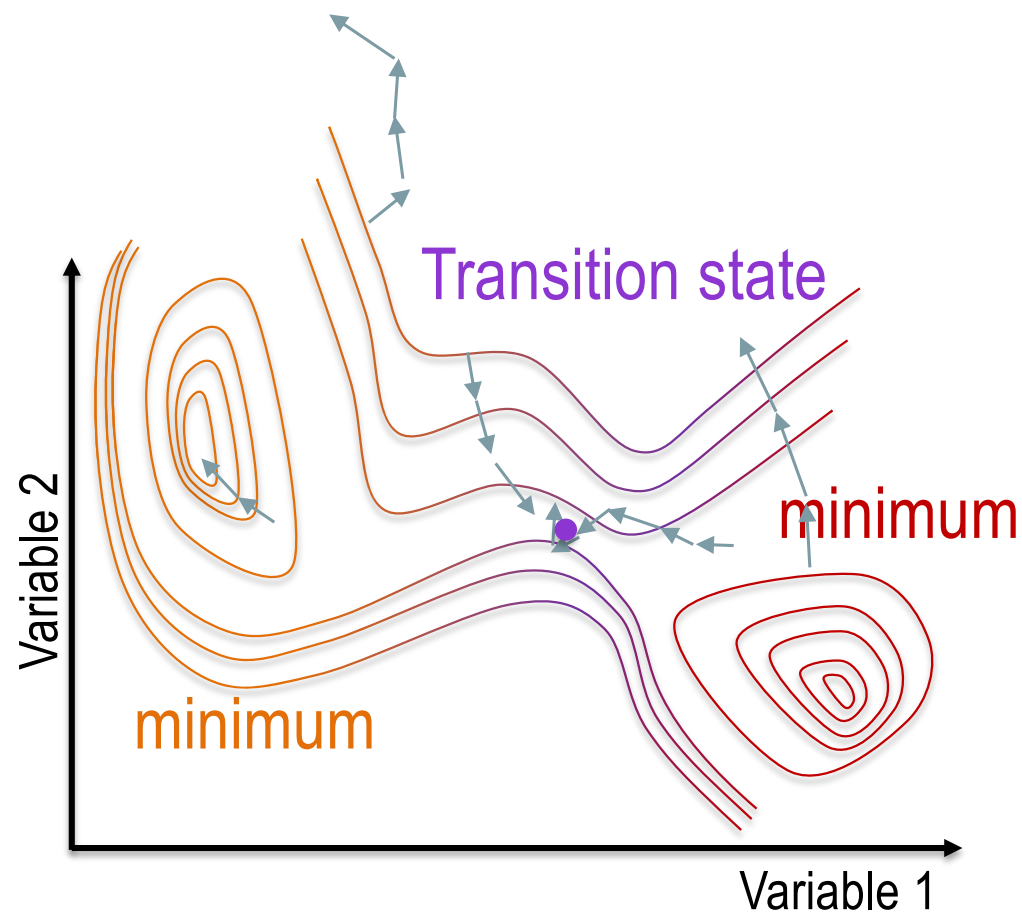
^bRef. 6.

^cPresent work

Exploring the potential energy surface

Transition states

Not easy to get!



Exploring the potential energy surface

Two major approaches:

Single-ended methods

Newton, Quasi-Newton, eigen-follow methods, dimer method

Chain-of-states and Double-ended methods

Nudge Elastic Band, String Method, Growing String Method, Linear Synchronous Transit, Quadratic Synchronous Transit

Exploring the potential energy surface

Newton and Quasi-Newton methods

The Hessian update must allow negative eigenvalues.

Starting structure must be in the quadratic region

- +50% rule of thumb for bond breaking

- Hammond postulate

- Constrained optimization

- Double-ended methods!

Good initial estimate of the Hessian is necessary

Exploring the potential energy surface

Eigen-Follow method

Divide the eigenvectors of \mathbf{H} into two groups:

- (i) Search a maximum along one eigenvector (even if the eigenvalue is not negative)
- (ii) Search a minimum in the remaining space.

Exploring the potential energy surface

Dimer method

Designed initially for periodic DFT calculations where computing the Hessian is prohibitive.

Based only on the energy and forces of two “images” that forms the dimer.

The dimer is pushed uphill and rotated to find the lowest curvature mode.

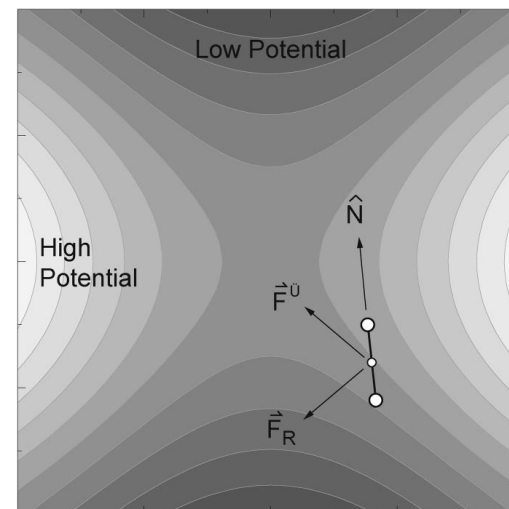


FIG. 4. The effective force \mathbf{F}^\dagger acting on the center of the dimer is the true force \mathbf{F}_R with the component along the lowest curvature mode $\hat{\mathbf{N}}$ inverted. In the neighborhood of a saddle point, the effective force points towards the saddle point.

Exploring the potential energy surface

Building a pathway

Constrained geometry optimization along a **selected** coordinate

→ *Choice of this coordinate is critical (e.g. distance, angle)*

Extrapolate and optimize a path from the reactant to the product

→ *The initial pathway is critical (e.g. cartesian vs. internal ;)*

→ *We will focus on the NEB method.*

Exploring the potential energy surface

Building a pathway

Image dependent pair potential (IDPP)

Interpolation of pairwise distances
at each discretization point along
the path

Opt'nPath: Mixing Cartesian and
redundant/internal coordinates

<http://pfleurat.free.fr/ReactionPath.php>

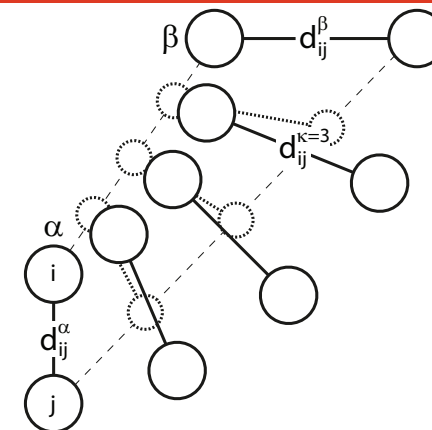


FIG. 1. An illustration of paths generated by linear interpolation of Cartesian coordinates, LI (dashed), and by interpolation of distances between atom pairs, IDPP (solid).

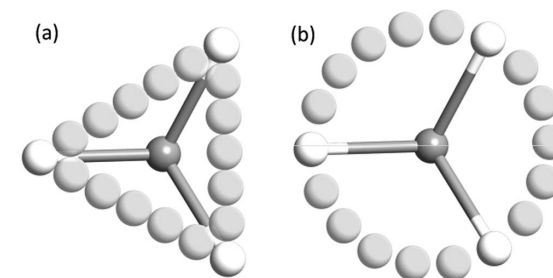


FIG. 2. Initial path for the rotation of a methyl group in ethane, (a) created by LI, a linear interpolation of Cartesian coordinates; (b) created using the IDPP method. The rotation is clearly better represented by the latter method. The NEB calculation starting from the IDPP path required about a third as many atomic iterations and SCF iterations to reach convergence as compared with a calculation starting with the LI path, see Table 1.

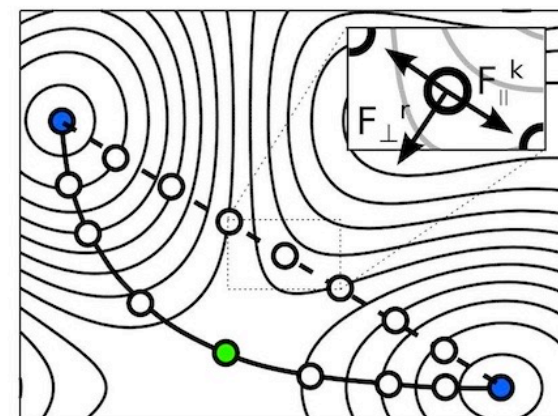
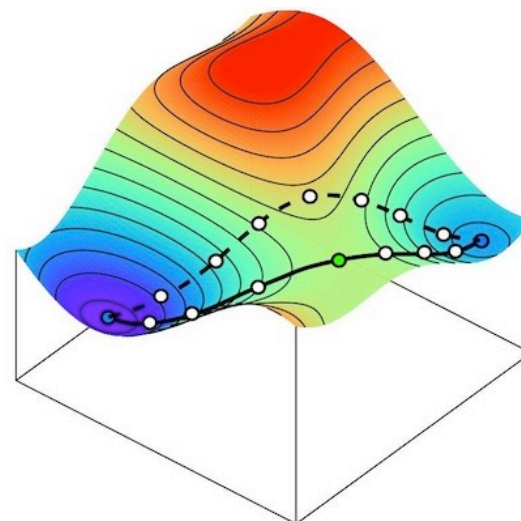
Exploring the potential energy surface

Nudge elastic band (NEB)

N images i , separated by a spring of constant k_i^{spring} which controls the spacing.

Force projection using the tangent $\hat{\tau}_i$ to avoid the sliding-down problem

$$\mathbf{F}_i = \mathbf{F}_i^\perp + \mathbf{F}_i^\parallel$$



<https://umet.univ-lille.fr/Projets/RheoMan/en/to-learn-more-about/nudged-elastic-band.php.html>

$$\mathbf{F}_i^\perp = \mathbf{F}_i - (\mathbf{F}_i \cdot \hat{\tau}_i) \hat{\tau}_i$$

$$\mathbf{F}_i^\parallel = (k_i^{spring} |\mathbf{R}_{i+1} - \mathbf{R}_i| - k_{i-1}^{spring} |\mathbf{R}_i - \mathbf{R}_{i-1}|) \hat{\tau}_i$$

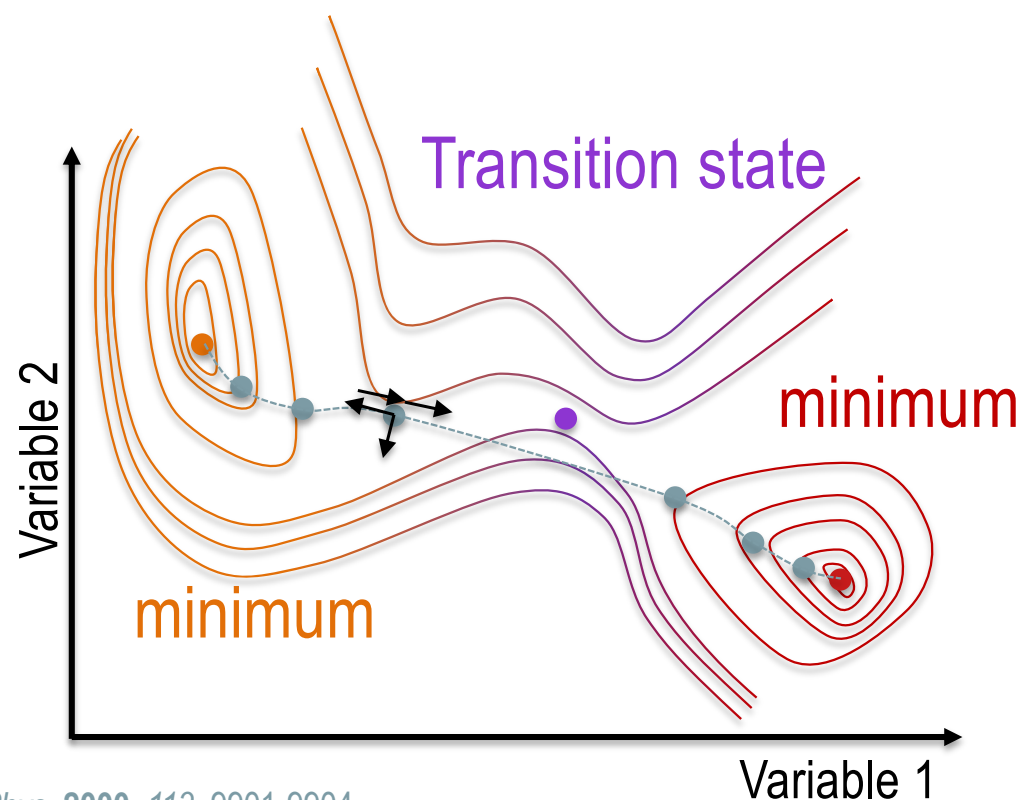
G. Mills, H. Jönsson, G.K. Schenter, *Surf. Sci.* **1995**, 324, 305
G. Henkelman, H. Jönsson, *J Chem Phys*, **2000**, 113, 9978-9985

Exploring the potential energy surface

Climbing-image NEB (CI-NEB)

To obtain a better convergence to the saddle point, the highest image climbs along the MEP and is not affected by the spring anymore:

$$\mathbf{F}_{i_{max}} = \mathbf{F}_i - 2(\mathbf{F}_i \cdot \hat{\boldsymbol{\tau}}_i)\hat{\boldsymbol{\tau}}_i$$



Exploring the potential energy surface

Variable Spring/energy weighted NEB

To improve the sampling close to the saddle point, stronger springs can be used for images higher in energy than a reference energy E_{ref} , in the range of spring constant $[k_l, k_u]$

$$k_i^{spring} = \begin{cases} (1 - \alpha_i)k_u + \alpha_i k_l, & \text{if } E_i > E_{ref} \\ k_l, & \text{otherwise} \end{cases}$$

$$\alpha_i = \frac{E_{max} - E_i}{E_{max} - E_{ref}}$$

Exploring the potential energy surface

Comparing NEB methods

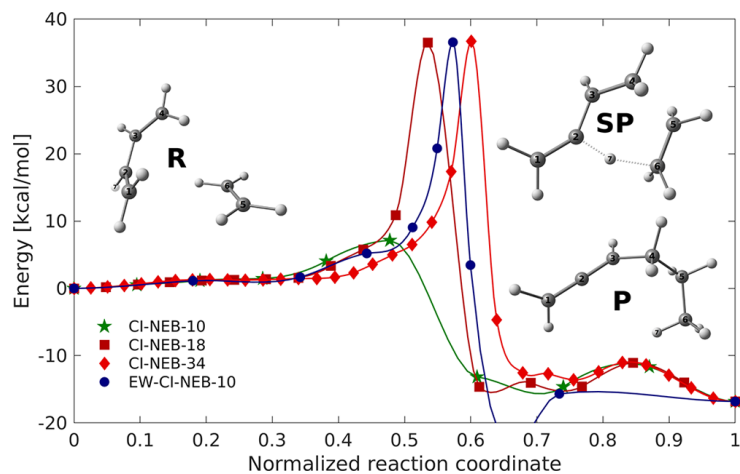


Figure 5. Energy curves (or profiles) for the reaction path of ethylene and 1,3-butadiene to form 1,2-hexadiene. The CI-NEB calculations use fixed spring constant of $k^{\text{SP}} = 0.1 E_{\text{H}}/a_0^2$ and the number of images is $N_{\text{im}} = 10, 18, \text{ or } 34$. For comparison, the energy weighted CI-NEB calculations use k^{SP} scaled from 0.01 to $0.1 E_{\text{H}}/a_0^2$ and $N_{\text{im}} = 10$.

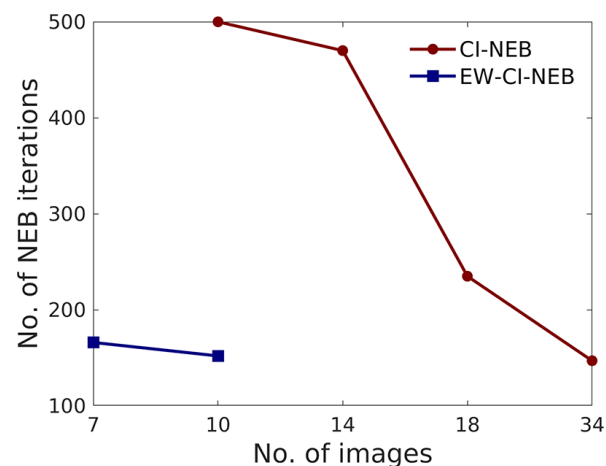


Figure 6. Efficiency of CI-NEB and EW-CI-NEB calculations of the reaction of ethylene and 1,3-butadiene to form 1,2-hexadiene. The efficiency is measured in terms of NEB iterations (or optimization steps) required to reach convergence. The CI-NEB calculations are carried out with a fixed spring constant of $k^{\text{SP}} = 0.1 E_{\text{H}}/a_0^2$ and $N_{\text{im}} = 10, 14, 18, \text{ or } 34$. The energy-weighted CI-NEB calculations scale the k^{SP} from 0.01 to $0.1 E_{\text{H}}/a_0^2$ and are carried out using $N_{\text{im}} = 7$ and 10. Note that CI-NEB-10 with $k^{\text{SP}} = 0.1 E_{\text{H}}/a_0^2$ failed to converge within 500 iterations.

Exploring the potential energy surface

Combining the best of two worlds

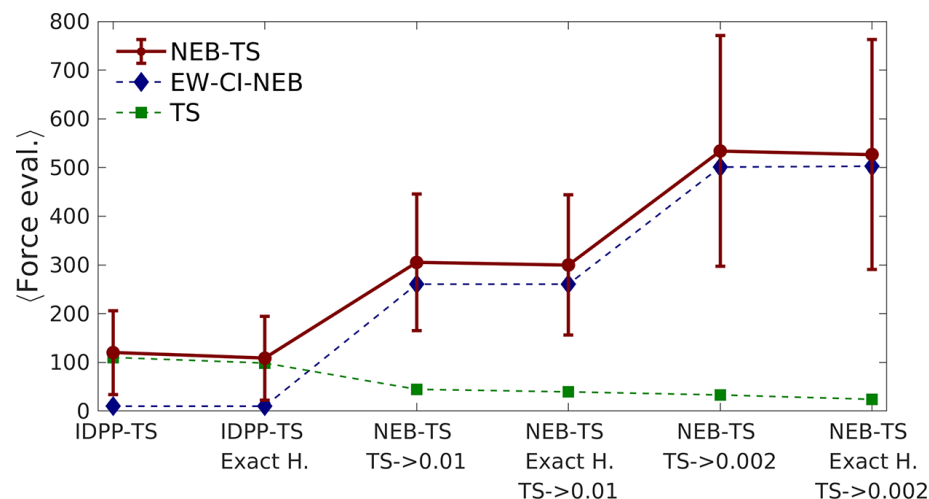


Figure 8. Computational efficiency of NEB-TS and IDPP-TS calculations of the benchmark set of 121 molecular reactions. The NEB-TS calculations differ in the degree to which the climbing image of the initial EW-CI-NEB calculation is converged before the TS search is started, i.e., $\epsilon_{\max}^{\text{TS}}$ is 0.01 or 0.002 E_{H}/a_0 . In IDPP-TS, the initial EW-CI-NEB phase is skipped. The calculations also use either an initial Hessian matrix that is constructed using the empirical Almlöf scheme or computed analytically (labeled on the x -axis). All calculations use 10 images. The average number of energy/force evaluations required by convergent NEB-TS (and IDPP-TS) calculations to locate saddle points is shown with red solid line along with the standard deviation shown as an error bar. The dashed blue and green dashed lines show how the computational effort of the NEB-TS calculations is divided into the initial EW-CI-NEB phase and the subsequent TS search. Nonconvergent calculations are omitted from the calculation of the averages.

Exploring the potential energy surface

Success depends on the topology of the surface.

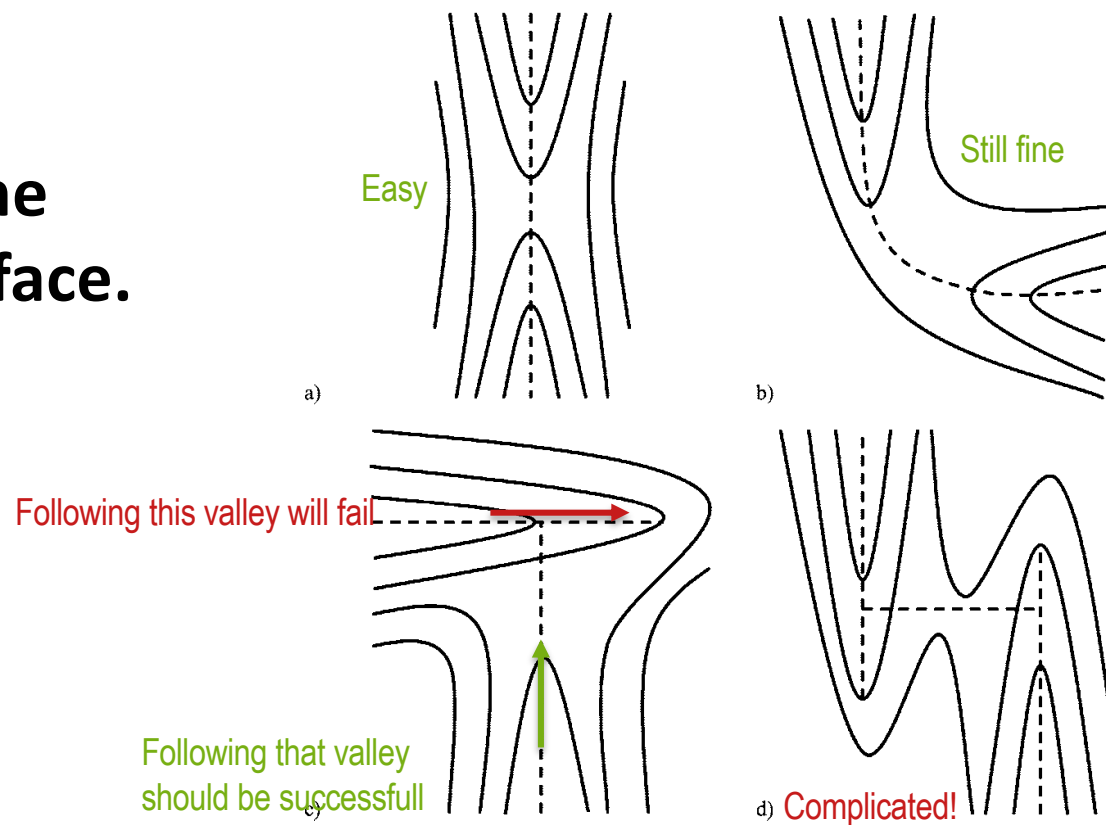
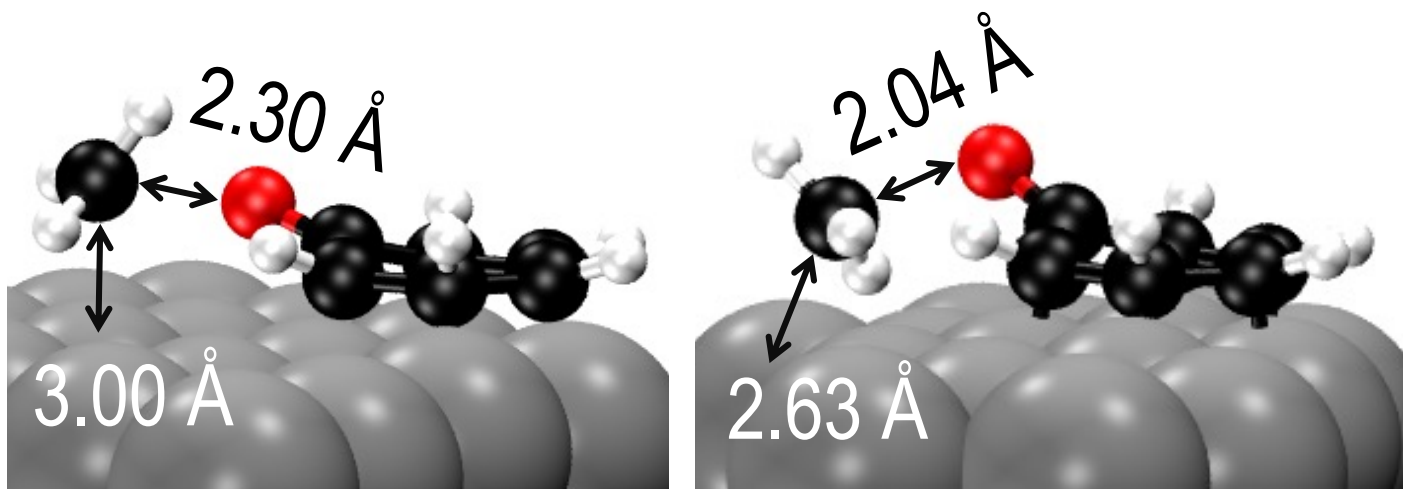


Figure 5. Various classes of reaction channels near the TS on reactive potential energy surfaces: (a) I-shaped valley, (b) L- or V-shaped valley, (c) T-shaped valley, (d) H- or X-shaped valley.

J. L. Sonnenberg, K. F. Wong, G. A. Voth, H. B. Schlegel *J. Chem. Theory Comput.*, **2009**, *5*, 949-961

A tricky example

Same IS and FS, two different TS...



-12 kJ.mol⁻¹
183 kJ.mol⁻¹

-12 kJ.mol⁻¹
159 kJ.mol⁻¹

The secret ingredient

Chemical intuition or educated guess.

The closer to the point you are searching, the better.

Your results are certainly **not** improved by starting from 'far'.

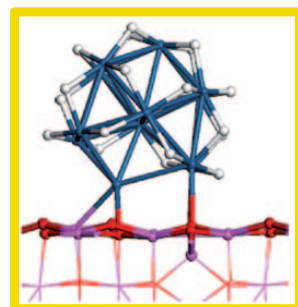
Including reaction conditions

CONCENTRATION & TEMP

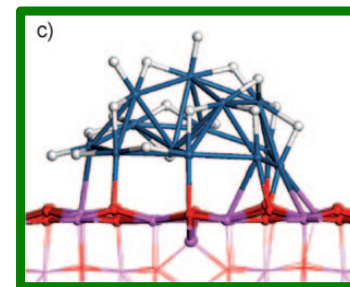
Moving to macroscopic quantities

Thanks to physical statistics we can turn ab initio data into kinetic constants k and equilibrium constants K (be careful with standard states etc.).

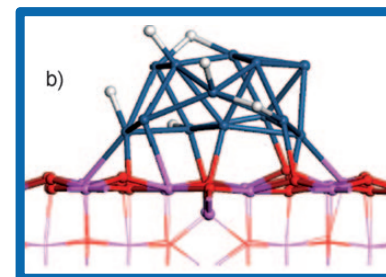
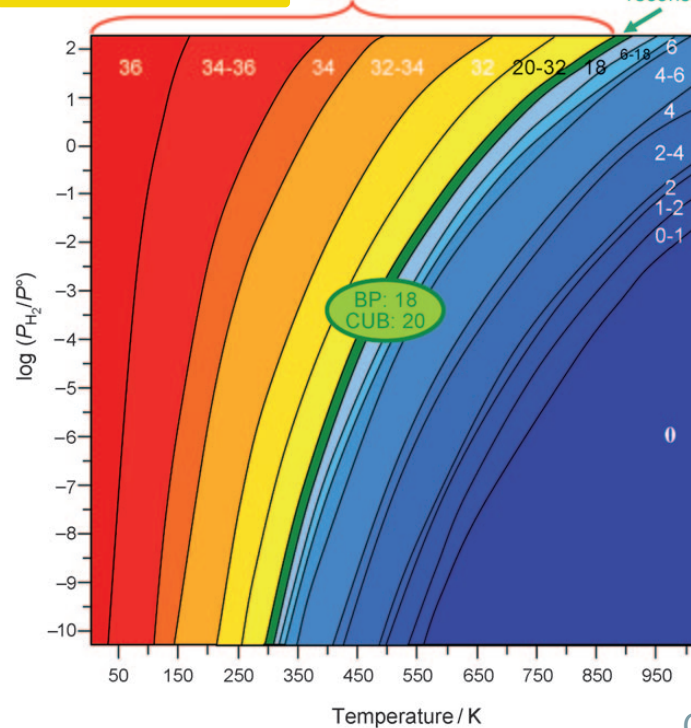
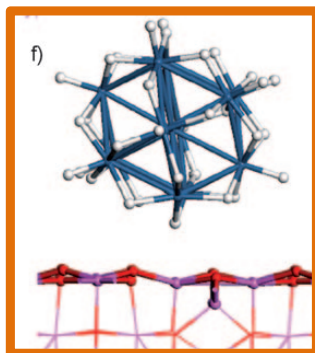
Determining a predominance diagram



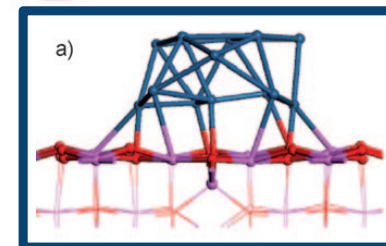
CUB



Cluster reconstruction



BP



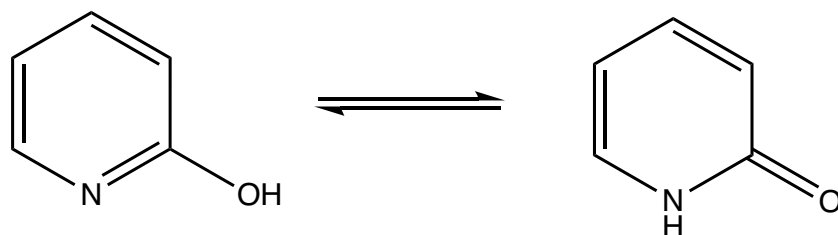
$$\Delta_r G = \frac{n}{2} \Delta_{\text{ads}} U - \frac{n}{2} \left(\mu_{\text{H}_2} - h_{\text{H}_2}^{\text{OK}} + RT \ln \frac{P_{\text{H}_2}}{P^0} \right)$$

$$\frac{n}{2} \Delta_{\text{ads}} U = U_{\text{Pt}_{13}\text{H}_n/\text{Al}_2\text{O}_3}^{\text{OK}} - U_{\text{Pt}_{13}/\text{Al}_2\text{O}_3}^{\text{OK}} - \frac{n}{2} E_{\text{H}_2}^{\text{OK}}$$

Including a water environment

MICRO-SOLVATION

A prototypic example in practical session.

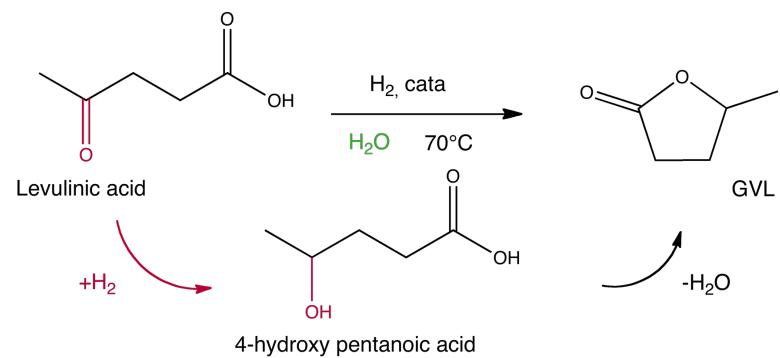


#H ₂ O	ΔE^\ddagger vac	ΔE^\ddagger PCM
0	149.3	161.8
1	61.3	63.9
2	69.8	71.3
3	94.1	82.4

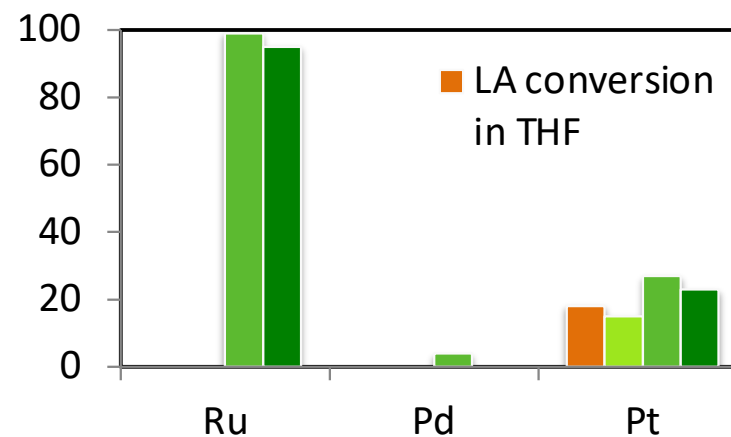
in kJ.mol⁻¹

MP2/6-311+G(d,p)/IEF-PCM

A less classic example



	THF	H ₂ O
Ru	X	✓
Pd	X	X
Pt	✓	✓



Modelling oxygenate hydrogenation at metals

Reactant/Product are simplified

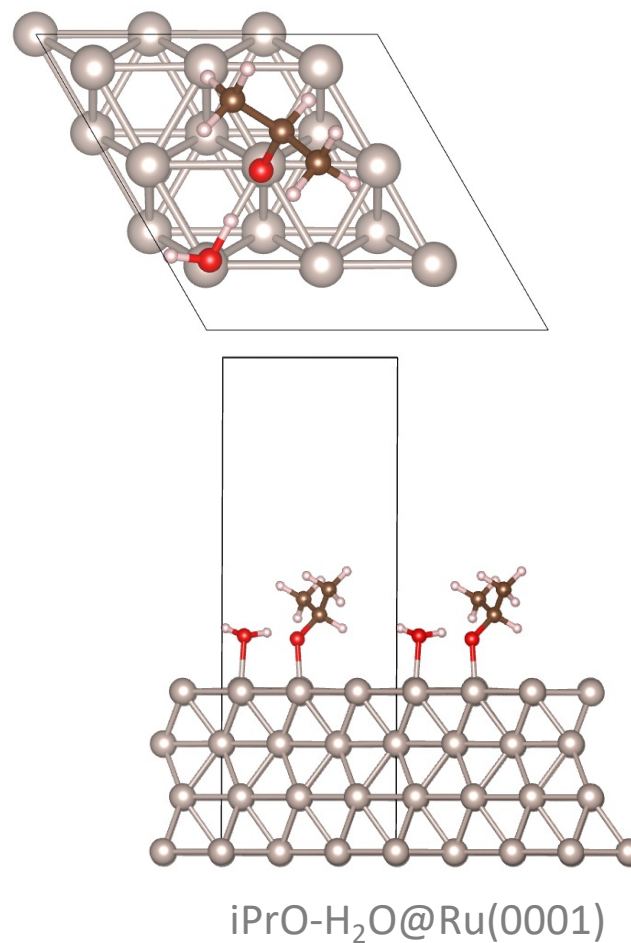
- Acetone/iPrOH

A periodic model of the Ru catalyst

- (0001) facet, 4 layers, p(3x3) cell
- Kpoints 3x3x1
- DFT GGA PW91
- PAW $E_{\text{cut}}=400\text{eV}$

TS search

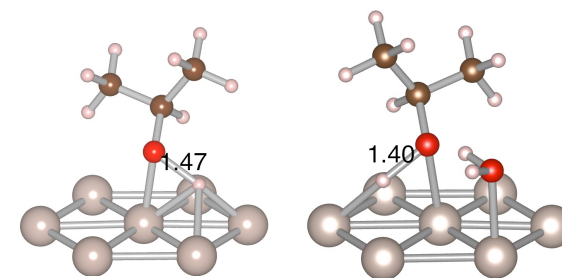
- Opt'n Path, NEB, Dimer and QN as implemented in the VTST package in VASP



Strategy

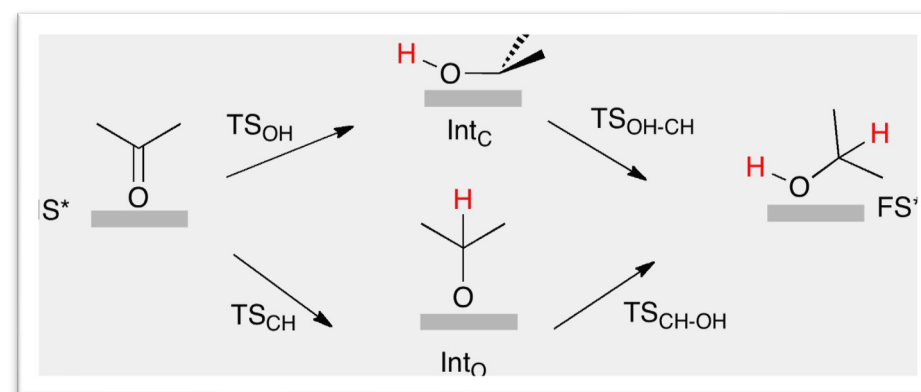
Comparison of model « catalysts » based on reaction paths

- Ru vs. H₂O@Ru
 - We expect an enhanced reactivity for H₂O@Ru
- Pt vs. H₂O@Pt
 - We expect similar reactivity

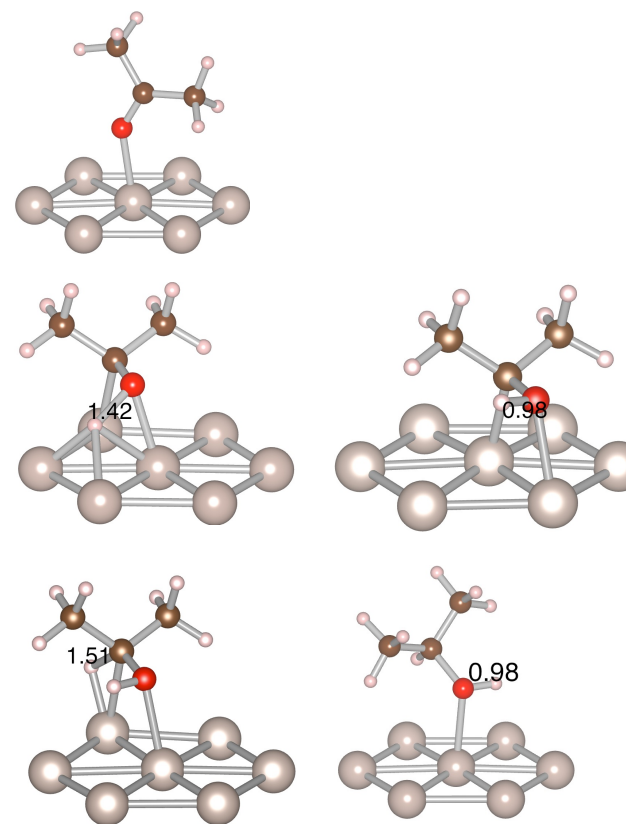
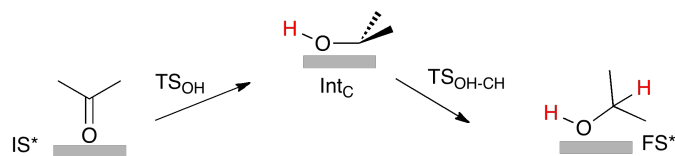
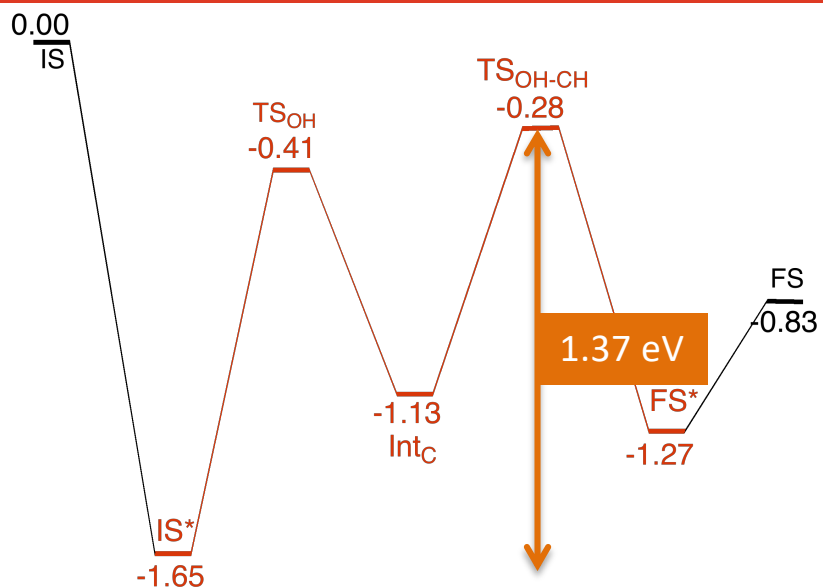


Two possible paths

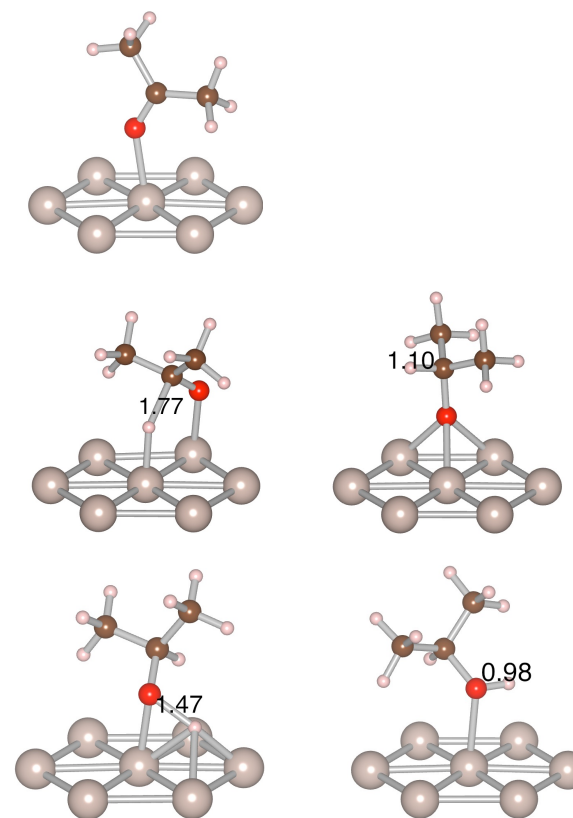
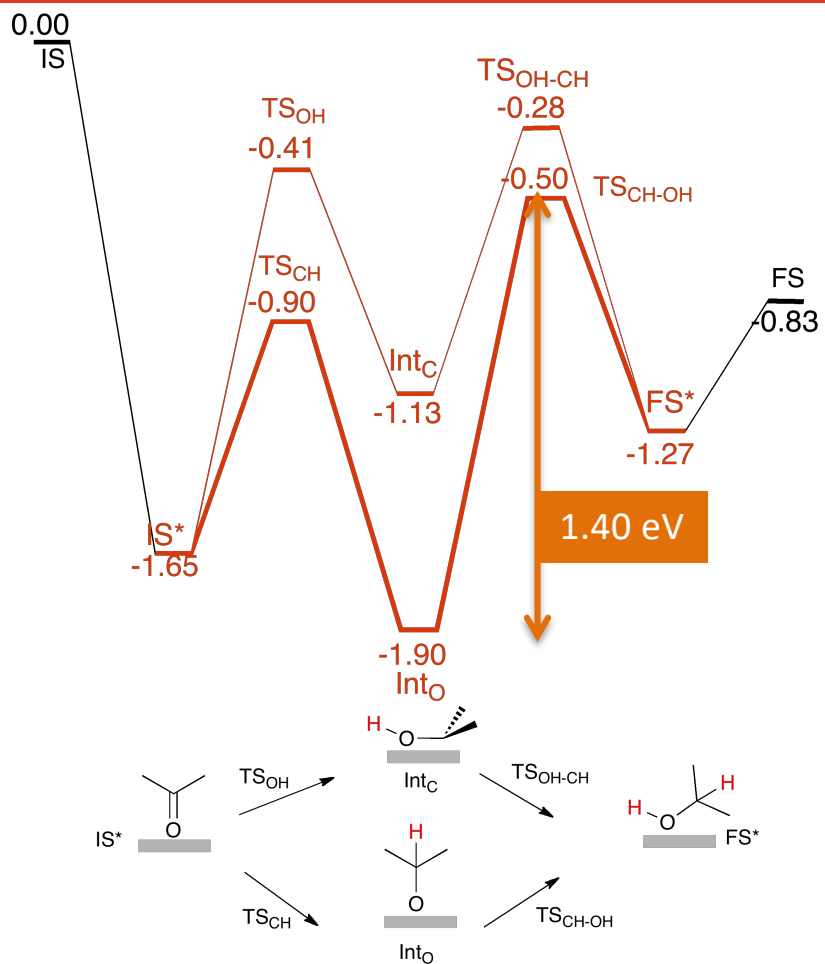
- Alkyl path
- Alkoxy path



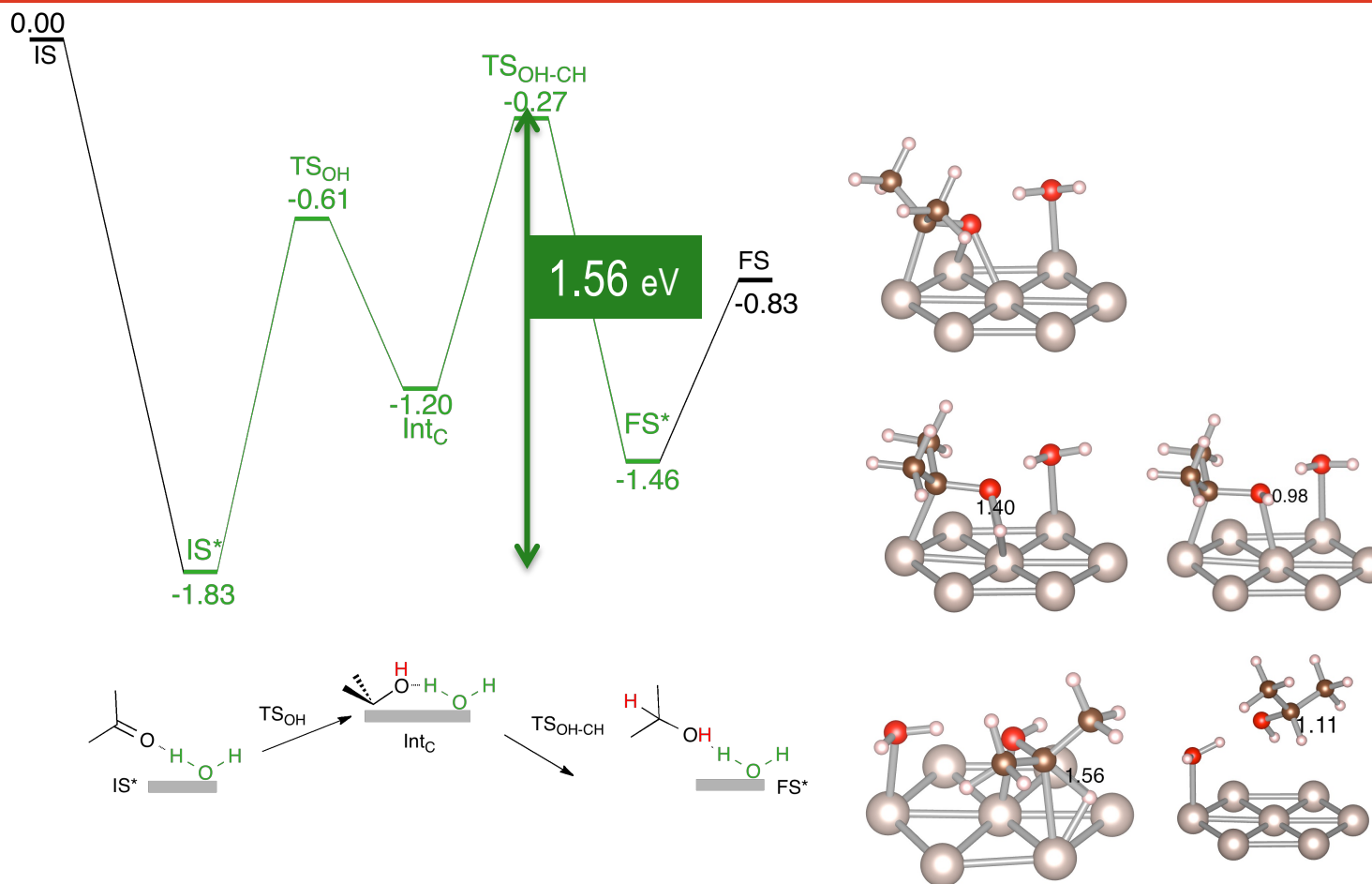
Ru(0001)



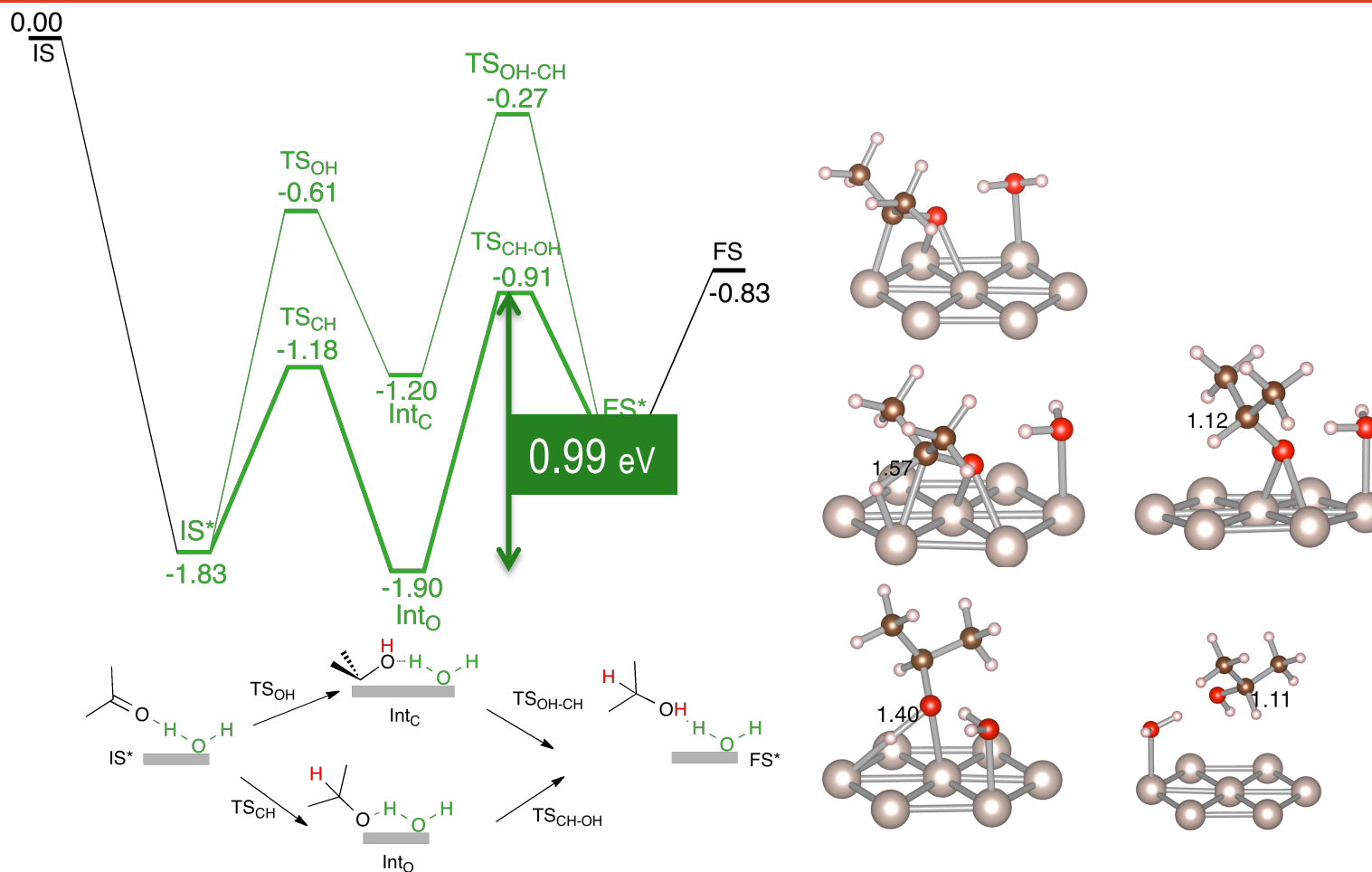
Ru(0001)



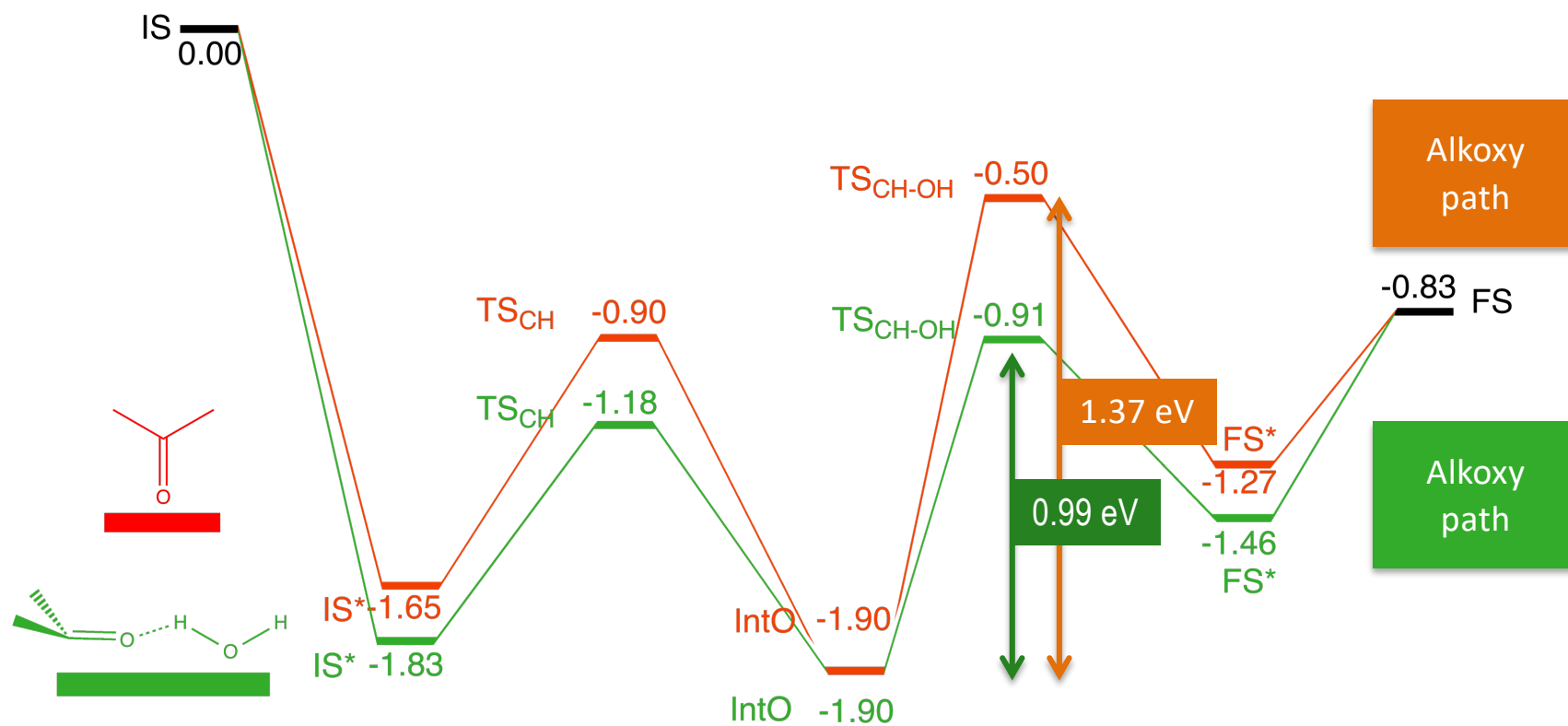
H₂O-Ru(0001)



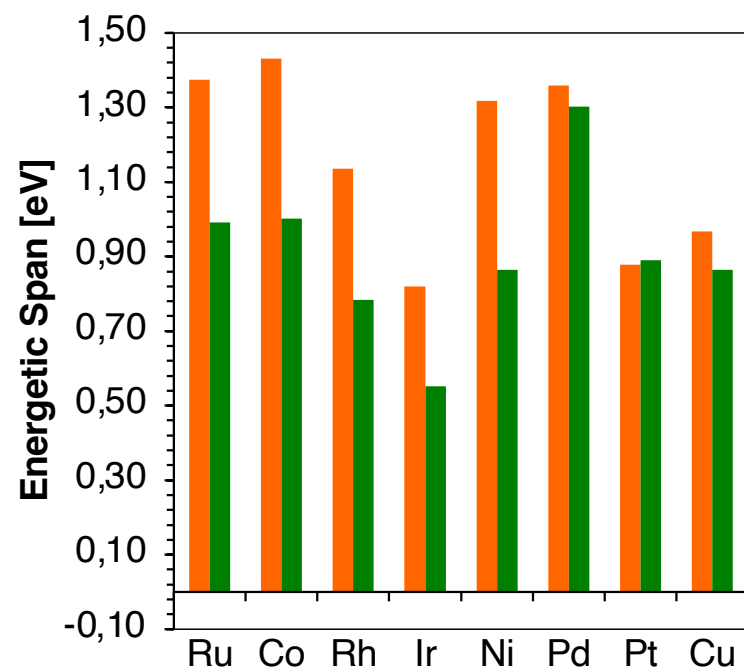
H₂O-Ru(0001)



Ru(0001) & H₂O@Ru(0001)

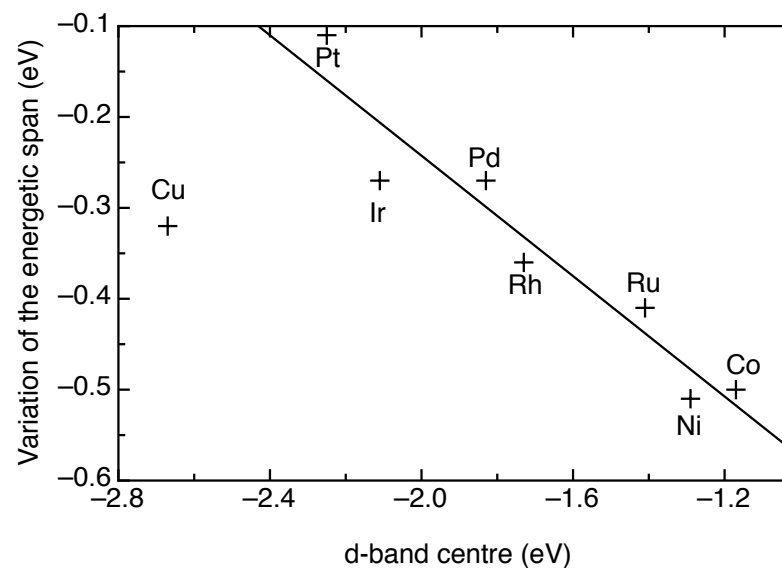
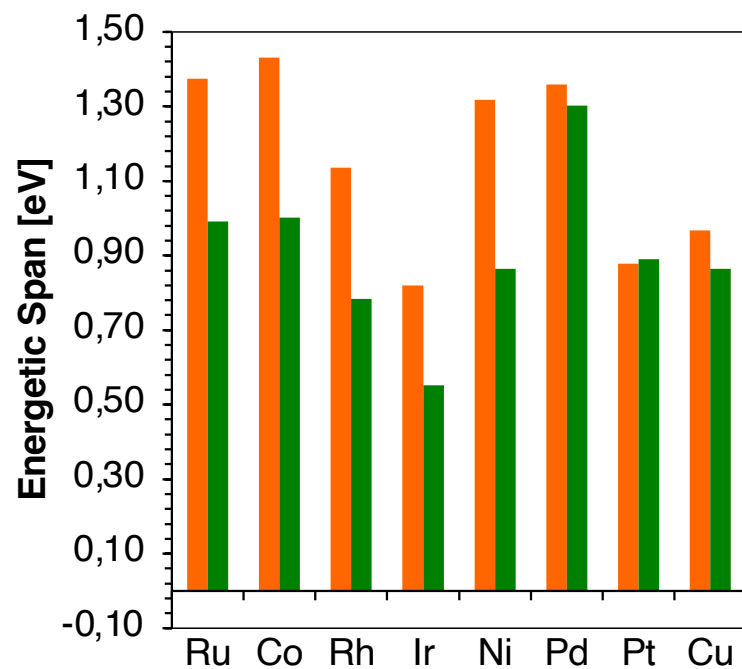


Levulinic acid to GVL conversion



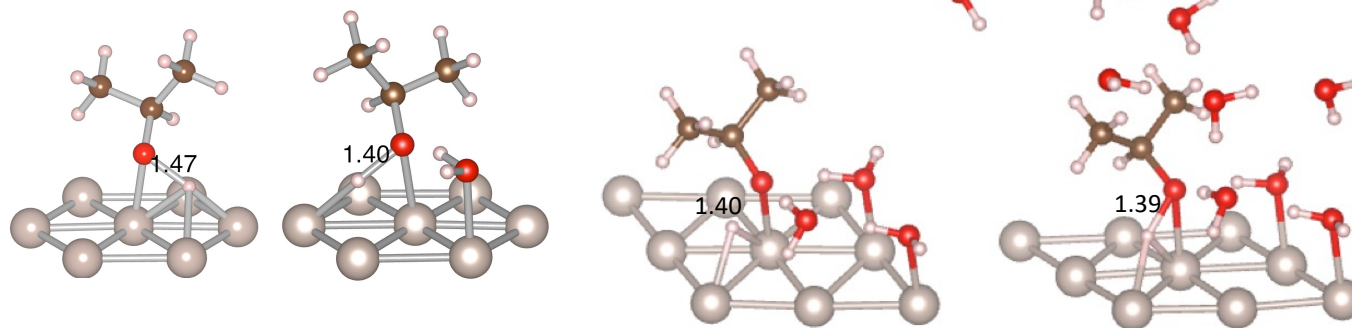
	THF	H ₂ O
Ru	X	✓
Pd	X	X
Pt	✓	✓

Water assists the hydrogenation by oxophilic metals



Improving the solvation model ?

Model	Energetic span on Ru (eV)
No solvent	1.37
Continuum model	1.39
1 water	0.99
3 waters	1.18
11 waters	1.03



Practical: perso.ens-lyon.fr/carine.michel

Carine Michel

Chargée de Recherche CNRS

Accueil

C.V.

Research

People

Publications

Contracts

Teaching & Dissemination

Teaching

Ecole d'été du GDR EMIE:

Part 1

Part 2.



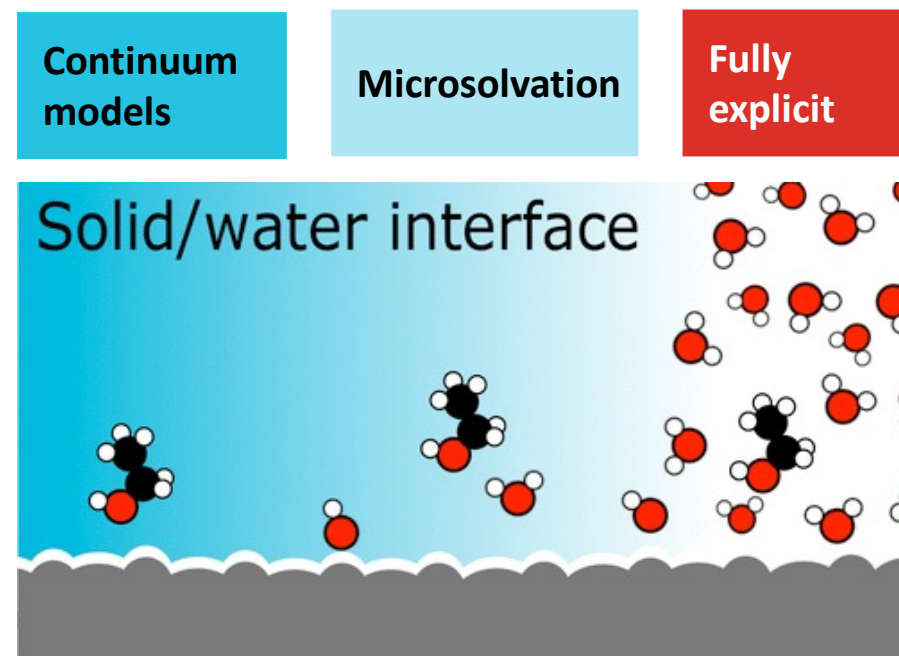
Carine Michel
M6 Building - Room M6.050

Improving the solvation model

Fully explicit

(QM)MM with free energy perturbation to compute solvation

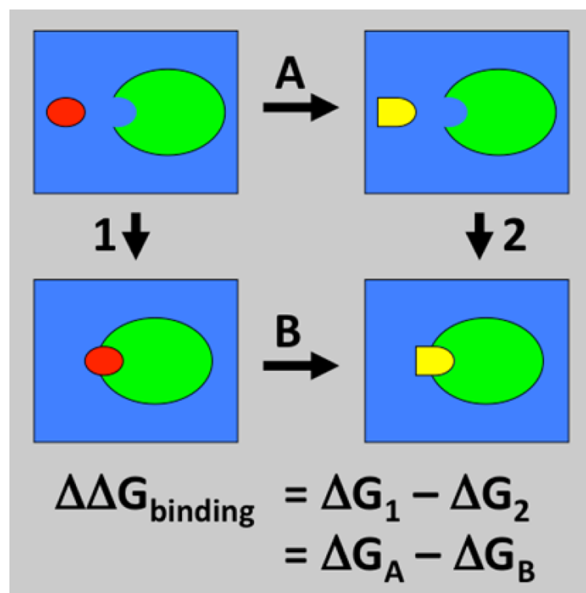
Biased AIMD to investigate reactions



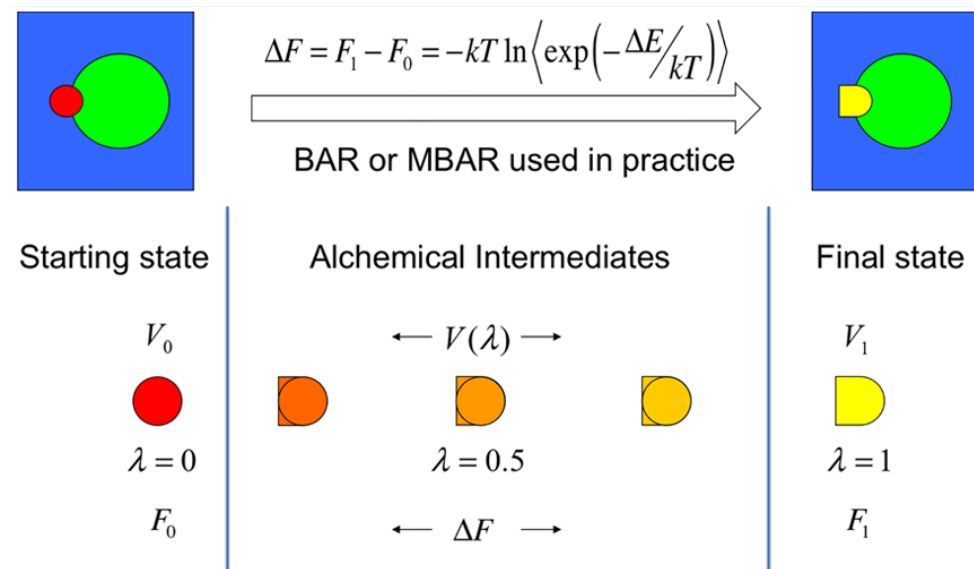
MOLECULAR DYNAMICS

Free energy perturbation

General principle illustrated on protein-ligand binding

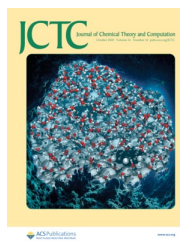
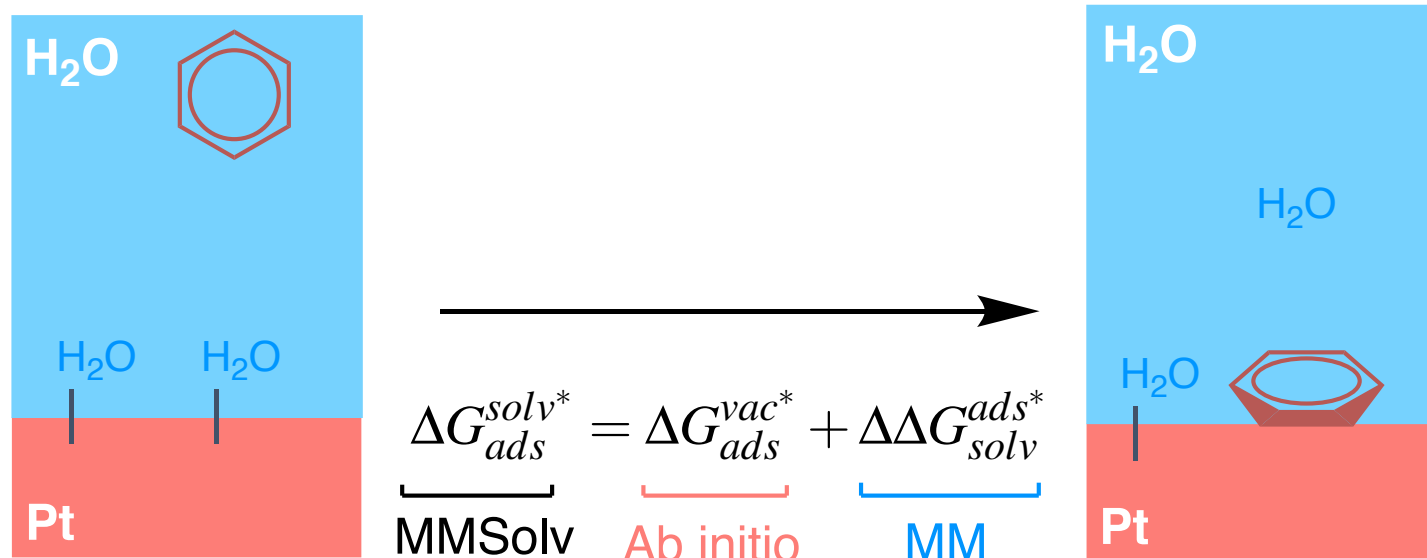


Large transformations
Small transformations



MMSolv combines DFT & MM

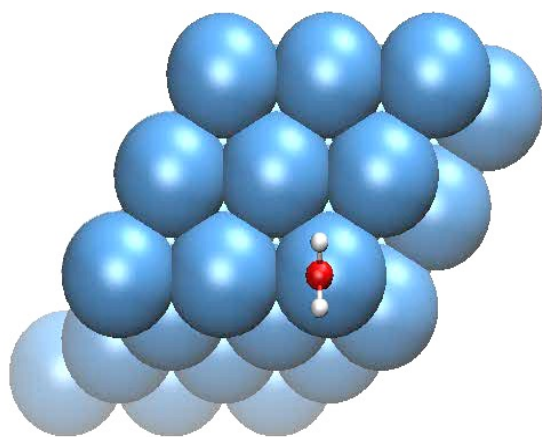
Adsorption of benzene at the Pt/water interface



MMSolv – SolvHybrid package

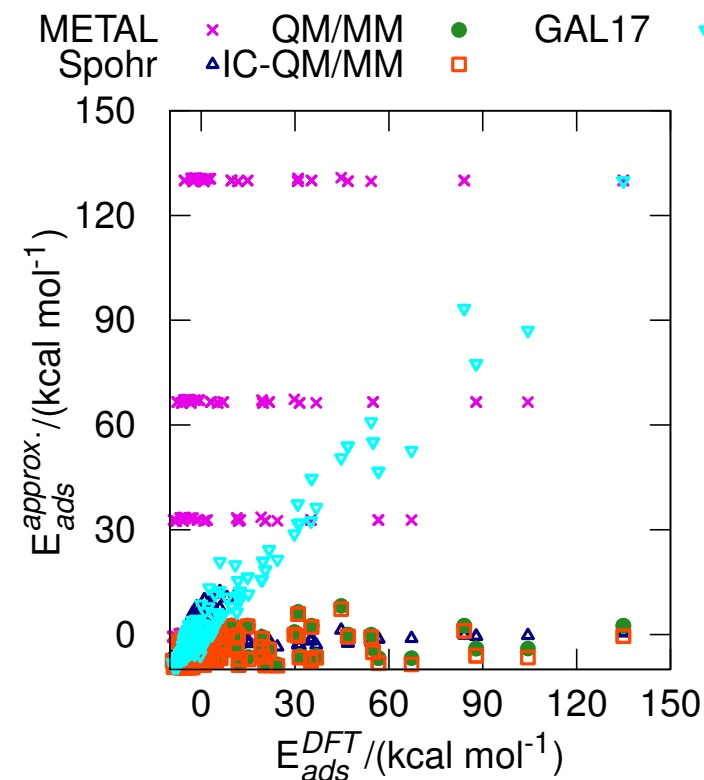
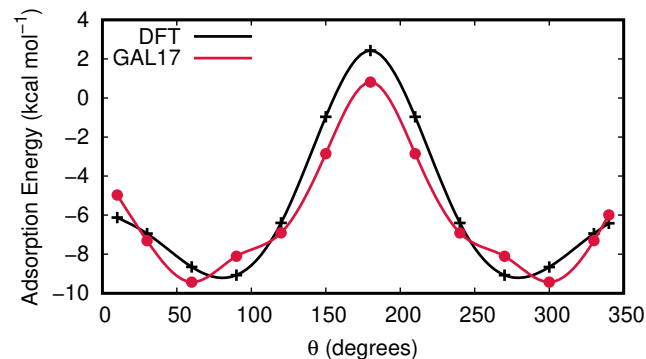
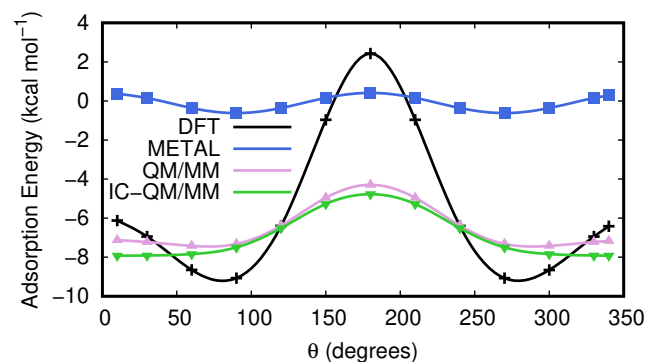
P. Clabaut et al. *J. Chem. Theo. Comp.* **2020**, *16*, 6539

We need a good Pt(111)/water force field



cartwheel
angle

GAL17: S. N. Steinmann, ..., C. Michel
J. Chem. Theo. Comp, **2018**, *14*, 3238-3251.

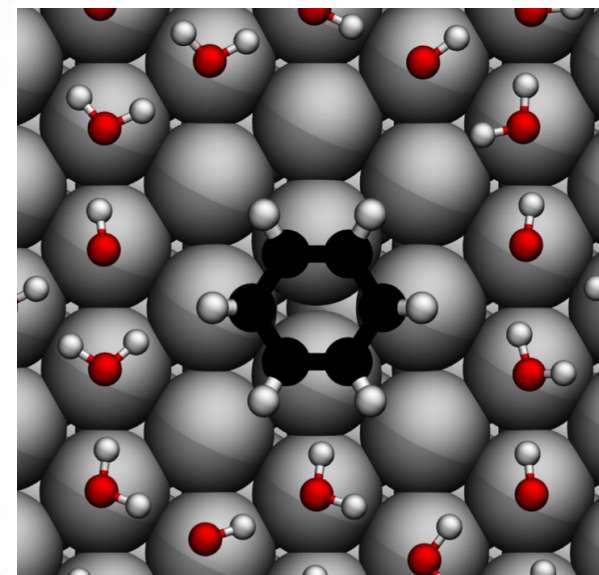
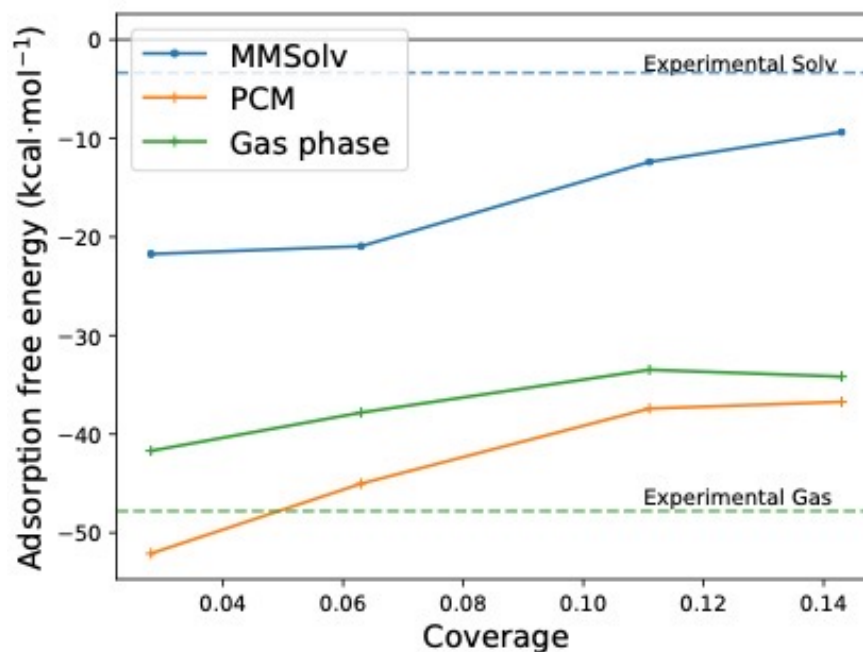


MMSolv is validated against experiments

Adsorption of benzene at the Pt/water interface

MM - AMBER
TIP3P
uff - CM5 charges
GAL17

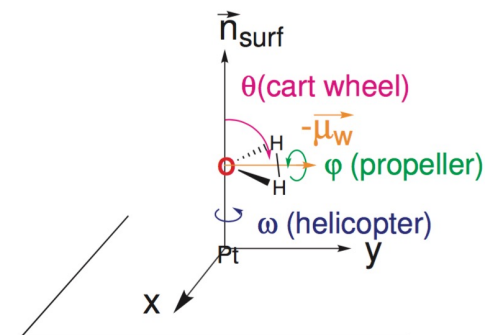
DFT - VASP
PBE+dDsC
PAW approach
Cutoff 400eV



GAL17 under the hood

Polarized Gaussian describes chemisorption

$$V_G(\vec{r}_{M,O}) = \varepsilon_a e^{-b_{\parallel} \cdot r_{\parallel}^2} e^{-b_{\perp} \cdot r_{\perp}^2}$$



Angle correction for water orientation

$$V_{\text{ang}} = \left(1 - \frac{1}{e^{-s_{\text{ang}}(r_{O,\text{surf}}/r_{\text{ang}}-1)} + 1} \right) \sum_{n=1}^4 a_n \cos(n\theta) + \sum_{i=1}^2 \frac{A_{H\text{surf}}}{r_{H_i,\text{surf}}^5}$$

Lennard-Jones potential describes physisorption

→ Fit 12 parameters to 210 PBE-dDsC water adsorption energies $\{r, \theta, \phi\}$

GAL17 under the hood

Polarized Gaussian

$1/r^{12}$ & $1/r^5$ not the best...

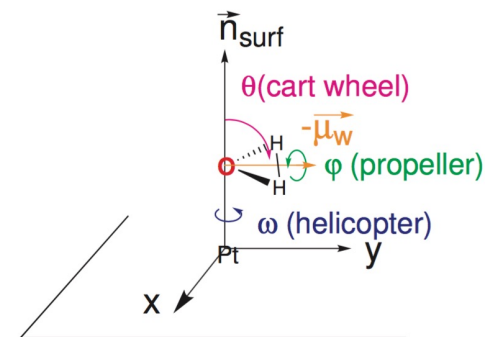
Angular correction for water or

$$V_{\text{ang}} = \left(1 - \frac{1}{2} \cos^2 \theta + 1 \right) \sum_{n=1}^{\infty} a_n \cos(n\theta) + \sum_{l=0}^{\infty} A_l \frac{1}{r^l}$$

Lennard-Jones potential de

surface specific

→ Fit 12 parameters to 210 PBE-dDsC water adsorption energies $\{r, \theta, \phi\}$



GAL21 The last generation

Polarized Gaussian describes chemisorption

$$V_G(\vec{r}_{M,O}) = \varepsilon_a e^{-b_{\parallel} \cdot r_{\parallel}^2} e^{-b_{\perp} \cdot r_{\perp}^2}$$

Angle correction for water orientation

$$V_A(r_{M,O}, \theta) = \frac{(e^{-r_{M,O}/R_O})^2}{\sum_{M_i \in \Omega(O)} e^{-r_{M_i,O}/R_O}} \sum_{n=1}^4 a_n \cos(n\theta)$$

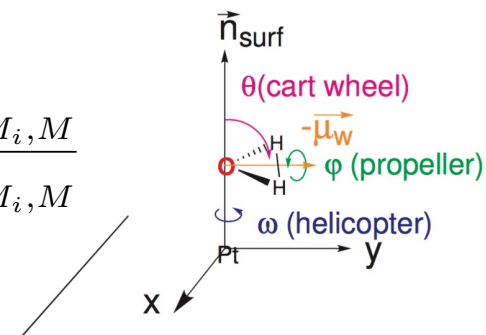
Tang-Toennies potential describes physisorption & repulsion

$$V_{TT}(r) = A e^{-B \cdot r} - \left[1 - \sum_{k=0}^6 \frac{(B \cdot r)^k}{k!} e^{-B \cdot r} \right] \frac{C_6}{r^6}$$

$$V_{M,H}(r_{M,H}) = A_H e^{-r_{M,H} \cdot B_H}$$

Local Norm

$$\vec{n}(M) = \sum_i \frac{\vec{r}_{M_i,M}}{r_{M_i,M}^5}$$



GAL21 The last generation

Polarized Gaussian

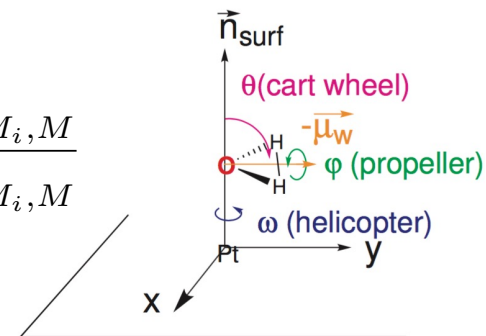
An

*1/r¹² & 1/r⁵ not the best...
 → TT potential for M, O
 → Exponential decay for M, H*

$$A(r_{M,O}, \theta) = \frac{(e^{-r_{M,O}/R_O})^2}{\sum_{M_i \in \Omega(O)} e^{-r_{M_i,O}/R_O}} \sum_{n=1}^4 a_n \cos(n\theta)$$

Local Norm

$$\rho(M) = \sum_i \frac{r_{M_i,M}}{r_{M_i,M}^5}$$



Tang-Toennies potential describes physisorption & repulsion

$$V_{TT}(r) = Ae^{-B \cdot r} - \left[1 - \sum_{k=0}^6 \frac{(B \cdot r)^k}{k!} e^{-B \cdot r} \right] \frac{C_6}{r^6}$$

$$V_{M,H}(r_{M,H}) = A_H e^{-r_{M,H} \cdot B_H}$$

GAL21 The last generation

Polarized Gaussian describes chemisorption

$$V_G(\vec{r}_{M,O}) = \varepsilon_a e^{-b_{\parallel} \cdot r_{\parallel}^2} e^{-b_{\perp} \cdot r_{\perp}^2}$$

Angle correction for water orientation

$$V_A(r)$$

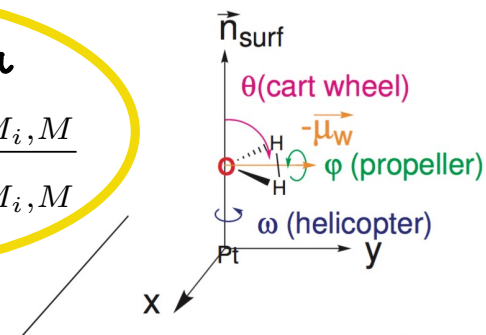
Tang-Toenn $V_{TT}(r)$ chemisorption & repulsion

$$V_{TT}(r) = \left[1 - \sum_{k=0}^{\infty} \frac{(B \cdot r)^k}{k!} e^{-B \cdot r} \right] \frac{C_6}{r^6}$$

$$V_{M,H}(r_{M,H}) = A_H e^{-r_{M,H} \cdot B_H}$$

Local Norm

$$\vec{n}(M) = \sum_i \frac{\vec{r}_{M_i,M}}{r_{M_i,M}^5}$$



Need a planar surface
→ Local Norm

GAL21 The last generation

Polarized Gaussian describes chemisorption

$$V_G(\vec{r}_{M,O}) = \varepsilon_a e^{-b_{\parallel} r_{\parallel}^2} e^{-b_{\perp} r_{\perp}^2}$$

Angle correction for water orientation

$$V_A(r_{M,O}, \theta) = \frac{(e^{-r_{M,O}/R_0})^2}{\sum_{M_i \in \Omega(O)} e^{-r_{M_i,O}/R_0}} \sum_{n=0}^4 a_n \cos(n\theta)$$

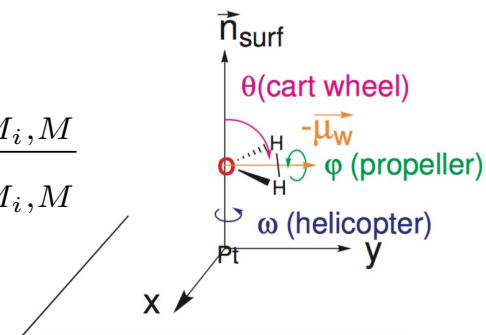
Tang-Toennies potential des

$$V_{TT}(r) = A e^{-B \cdot r} \left[1 - \sum_{k=0}^6 \frac{(B \cdot r)^k}{k!} \right]$$

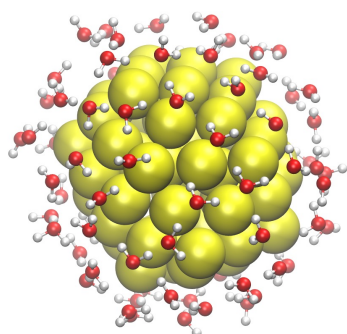
Surface specific
→ Linear or quadratic
dependance on the GCN

Local Norm

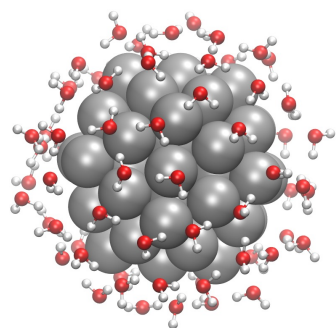
$$\vec{n}(M) = \sum_i \frac{\vec{r}_{M_i,M}}{r_{M_i,M}^5}$$



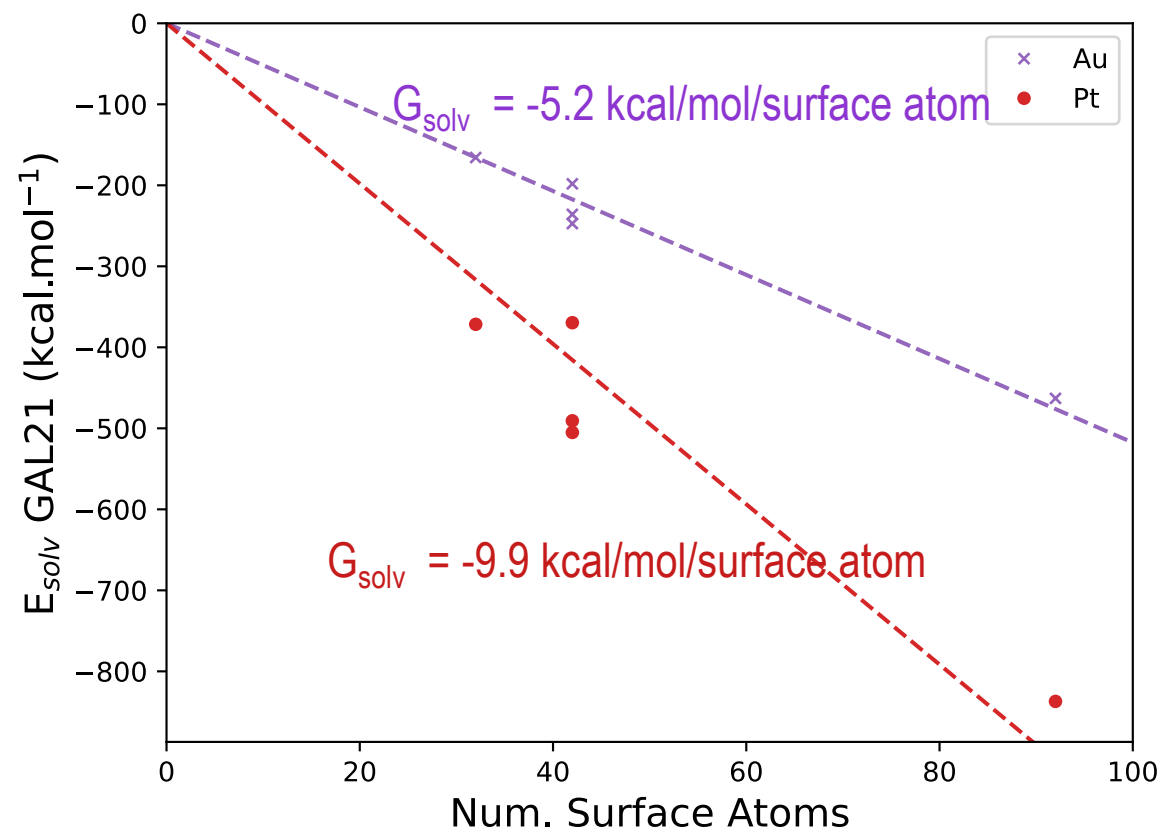
Solvation energy of NPs



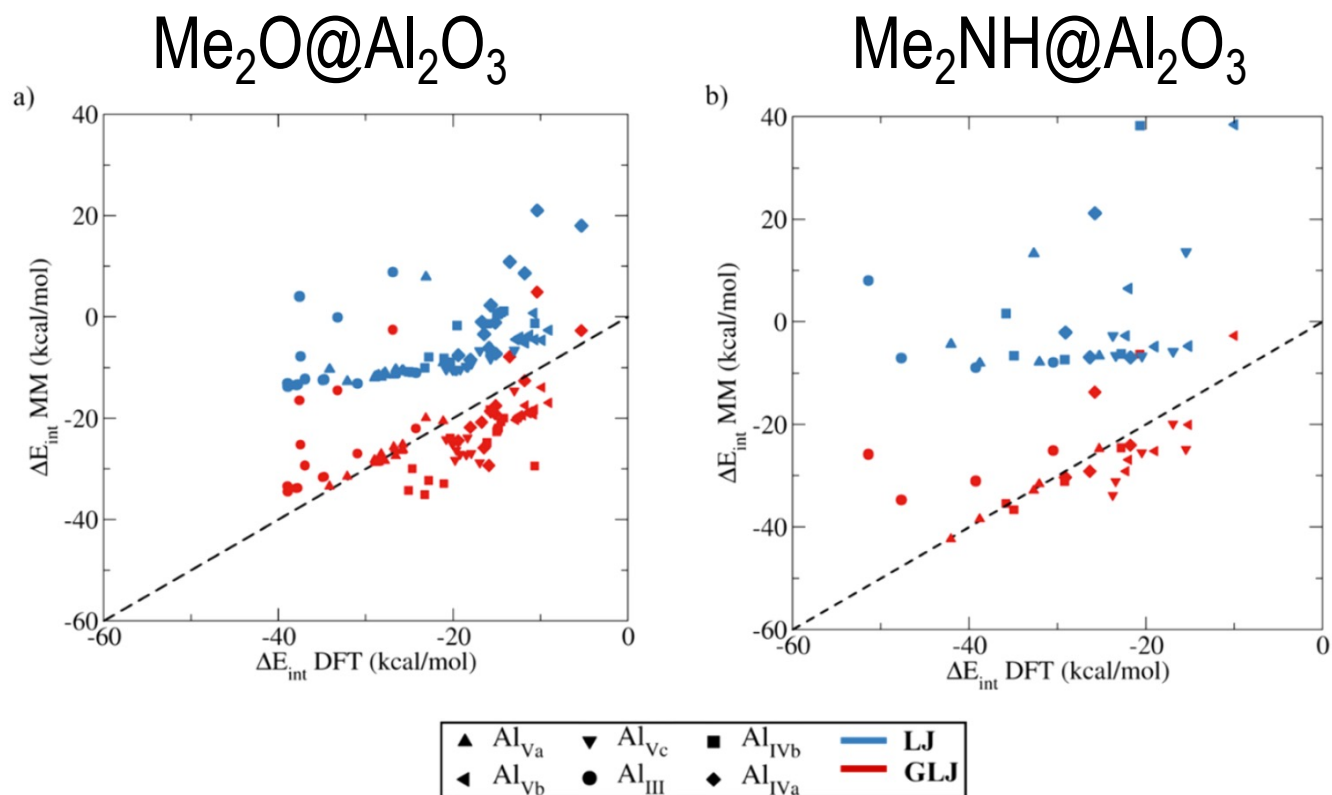
Au₅₅



Pt₅₅



Generalisation to oxides & other molecules

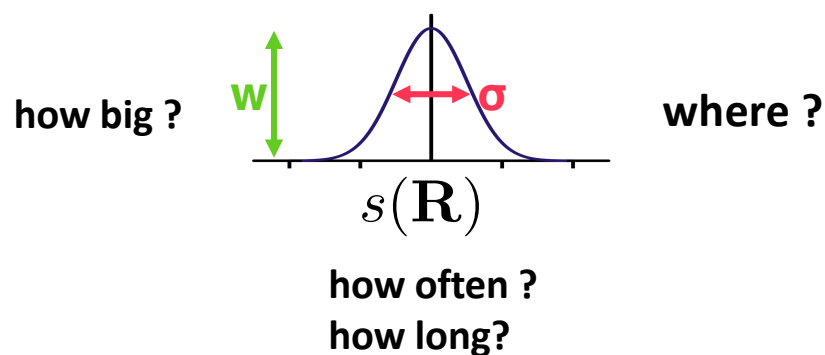


Conclusions

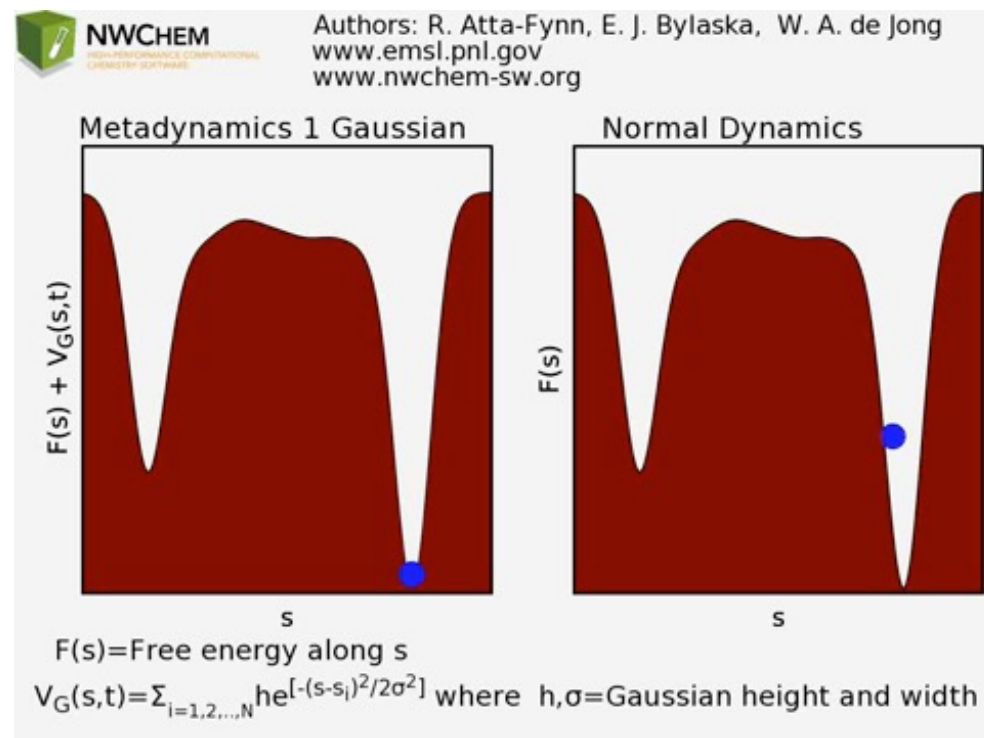
- We now have a robust metal/water force field
- We can compute solvation energies accurately at the solide/liquid interface
- We extended this approach to oxide/O-containing and N-containing molecule

Metadynamics

Trick: filling part of the PES with gaussians



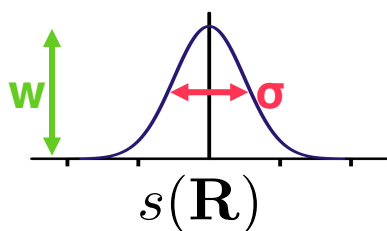
$$B_t(s) = \omega \sum_{t' < t} \exp \left(- \frac{(s_{t'} - s)^2}{2\sigma^2} \right)$$



Metadynamics

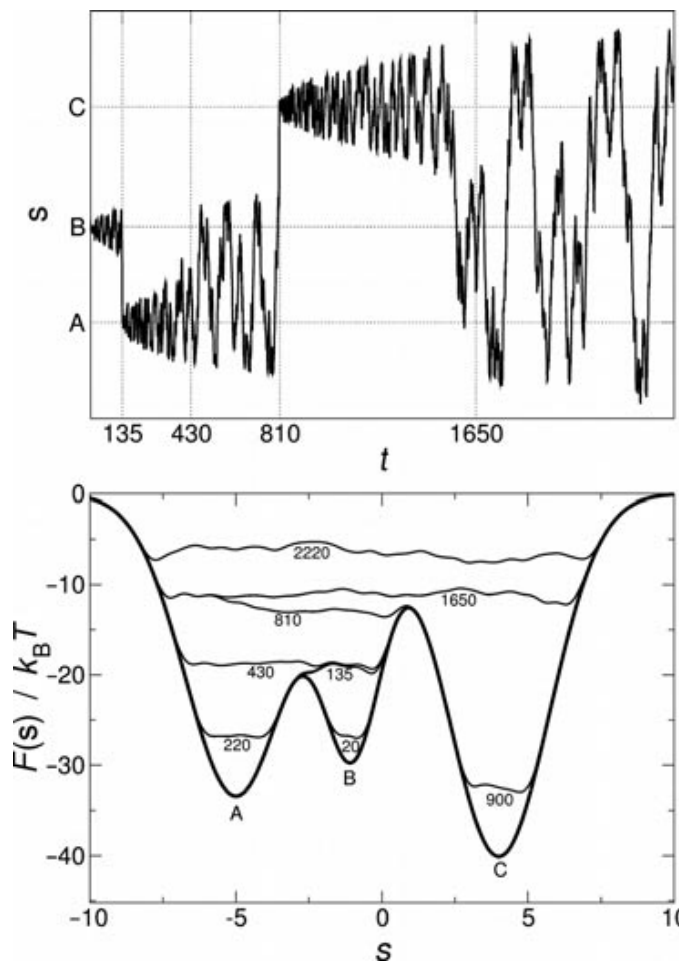
How long?

how big ?



where ?

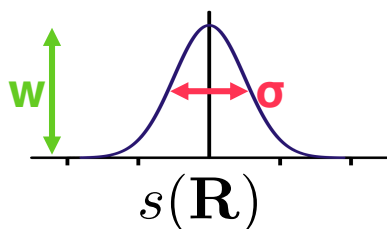
how often ?
how long?



Metadynamics

How long?

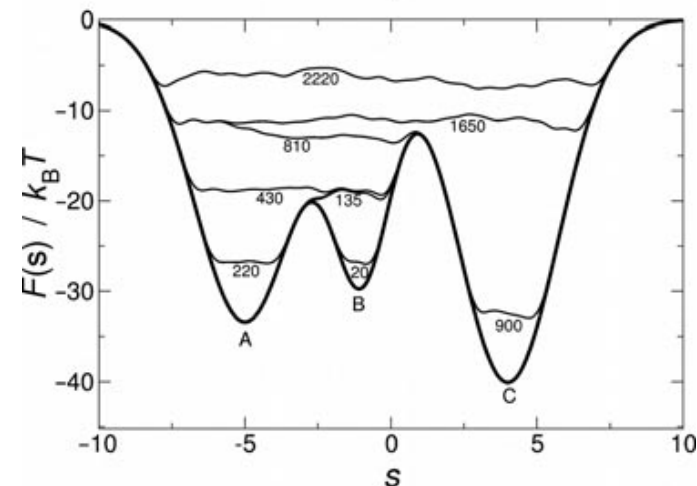
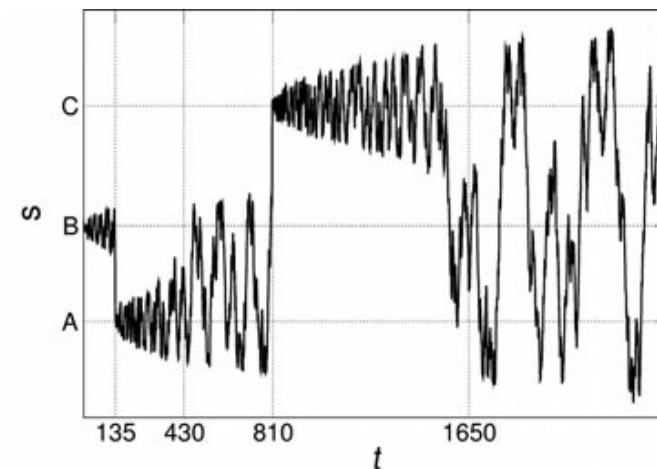
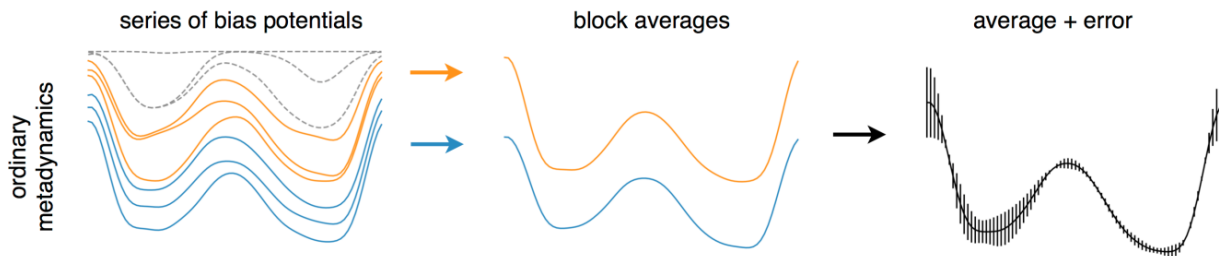
how big?



where?

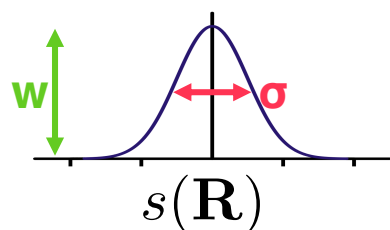
how often?
how long?

$$\bar{B}_t(s) = \frac{1}{t - t_{fill}} \sum_{t'=t_{fill}}^t B_{t'}(s)$$



Metadynamics

Well-tempered metadynamics



how often ?
how long ?

One can regulate the extent of FES exploration by tuning ΔT

how big ?

$$B_{t+1}(s) = B_t(s) + \exp\left(-\frac{B_t(s)}{\Delta T}\right) \exp\left(-\frac{(s_t - s)^2}{2\sigma^2}\right)$$

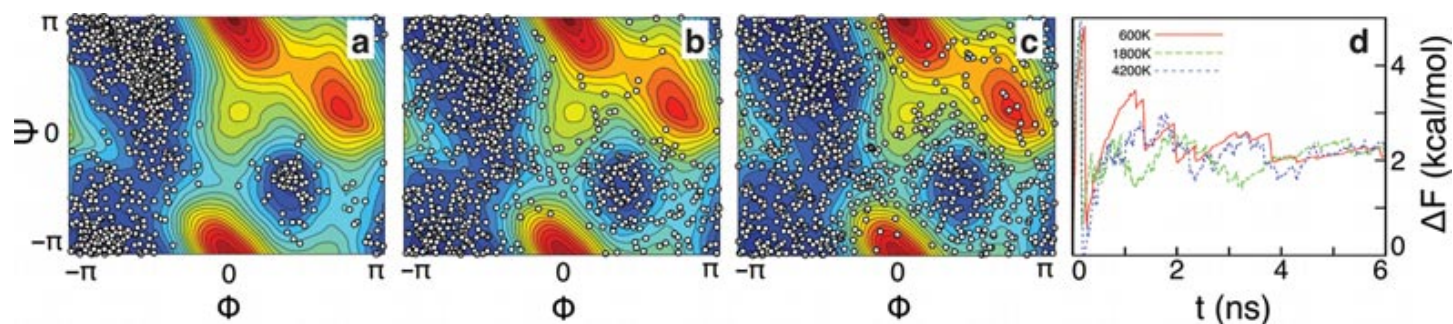
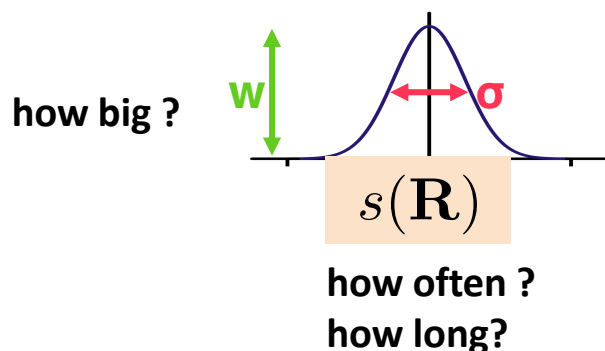


FIGURE 2 | (a–c). Projection onto the Ramachandran plot of the configurations sampled during a well-tempered metadynamics simulation of alanine dipeptide in vacuum (white dots) for different choices of ΔT [600 K (a), 1800 K (b), and 4200 K (c)]. The underlying color map shows the reference free-energy landscape. (d) Estimate of the free-energy difference between the two metastable minima C_{7ax} (1.22, -1.22) and C_{7eq} (-1.45 , 1.29) as a function of the simulation time. Angles are measured in radians.

Metadynamics

Where?



$$B_t(s) = \omega \sum_{t' < t} \exp \left(- \frac{(s_{t'} - s)^2}{2\sigma^2} \right)$$

$$\mathbf{F}_B = - \frac{dB}{dR} = -\omega \sum_{t' < t} \exp \left(- \frac{(s_{t'} - s)^2}{2\sigma^2} \right) \times \frac{ds}{dR}$$

Be careful, if this term is zero,
no force is derived from the bias which piles up!

“Identifying a set of CVs appropriate for describing complex processes is far from trivial.”

Collective variables are **derivable functions** of the microscopic coordinates \mathbf{R} . They should:

- distinguish IS/TS/FS and intermediates
- include all the slow modes of the system.
- be limited in number.

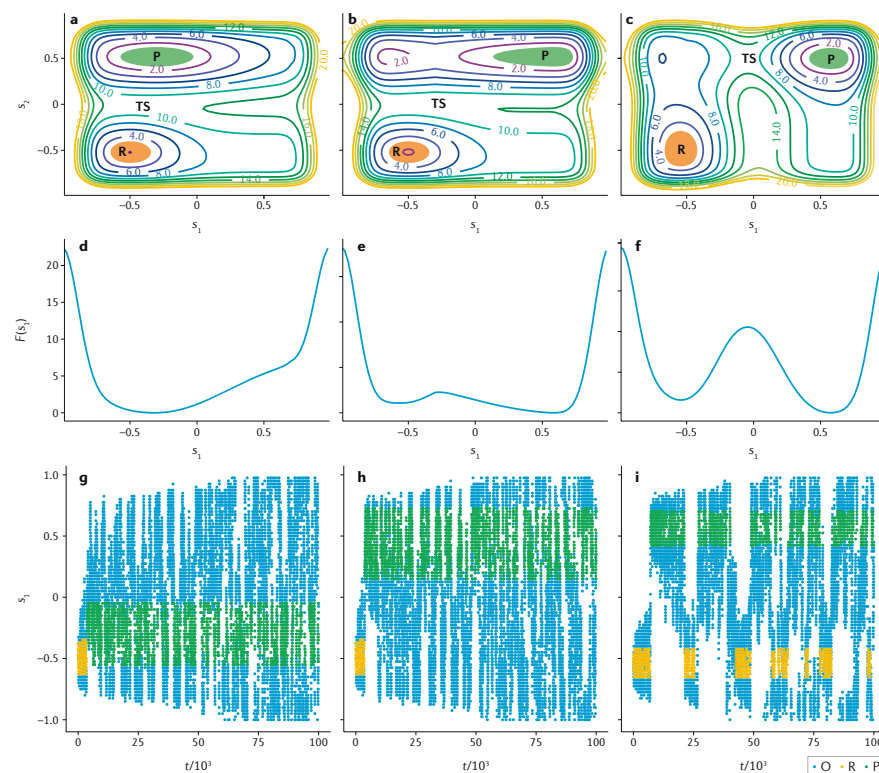
Metadynamics

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Collective variables are derivable functions of the microscopic coordinates \mathbf{R} . They should:

- distinguish IS/TS/FS and intermediates
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- be limited in number.

Fig. 2 | **Three potential energy landscapes, the corresponding free energies and metadynamics trajectories.** **a–c** | The three landscapes are representative of cases where the chosen collective variable (CV) cannot distinguish reactant (R) from product (P) (panel **a**), cannot distinguish the transition state (TS) from R (panel **b**) and can distinguish R, P and TS (panel **c**). The potential energy landscapes $V(s_1, s_2)$ are shown as functions of two coordinates (s_1 and s_2) using contour lines. Regions within $k_B T$ (where k_B is the Boltzmann constant) of the two metastable minima are coloured in orange (R state) and green (P state). s_1 represents the chosen biased CV. **d–f** | The corresponding free energies $F(s_1)$. **g–i** | Metadynamics trajectories for s_1 . Points are coloured by their location in the (s_1, s_2) space, with green and orange corresponding to the colours in panels **a–c**. Points that do not belong to the green and orange regions are shown in blue (O). t , time.



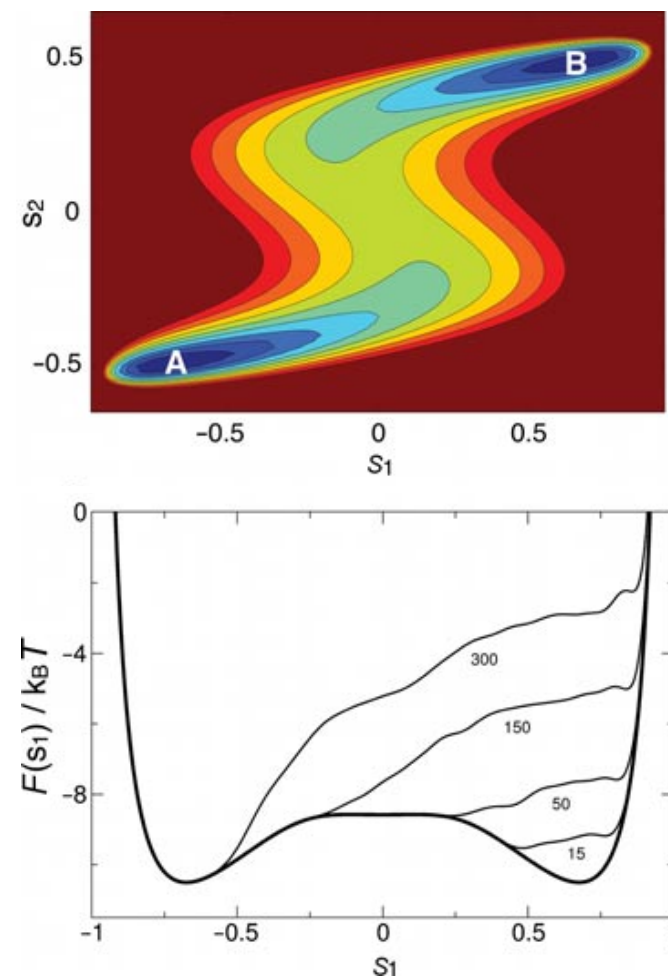
Metadynamics

“Identifying a set of CVs appropriate for describing complex processes is far from trivial.”

Collective variables are derivable functions of the microscopic coordinates \mathbf{R} . They should:

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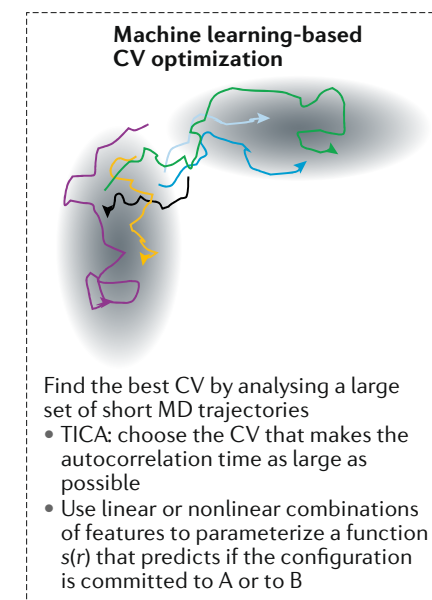
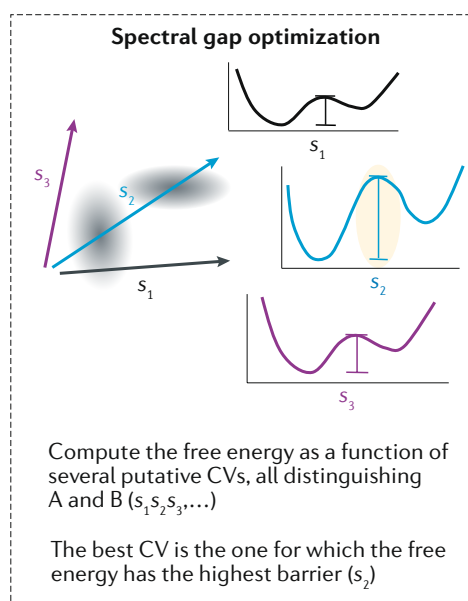
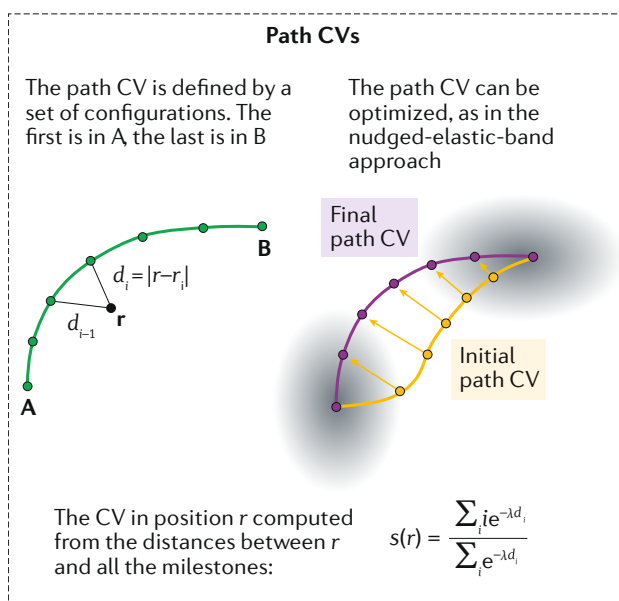
FIGURE 3 | Example of the effect of neglecting a slow degree of freedom in the collective variables (CVs) set. (Top) Model two-dimensional potential with relevant barriers both in s_1 and s_2 . (Bottom) Representation of a metadynamics simulation using only s_1 as CV. The sum of the underlying one-dimensional free-energy $F(s_1)$ (thick line) and of the metadynamics bias is shown at different times (thin lines). Neglecting s_2 in the CVs set causes strong hysteresis in the reconstructed free energy.



Metadynamics

“Identifying a set of CVs appropriate for describing complex processes is far from trivial.”

Trying to find the CVs automatically....



Metadynamics

“Identifying a set of CVs appropriate for describing complex processes is far from trivial.”

Collective variables are derivable functions of the microscopic coordinates \mathbf{R} . They should:

- distinguish IS/TS/FS and intermediates
- include all the slow modes of the system.
- be limited in number

« A high-dimensional space is costly to explore and analyzing a high-dimensional surface is far from trivial ».

Alternatives:

Bias-exchange metadynamics
Combinaison with Parallell-tempering

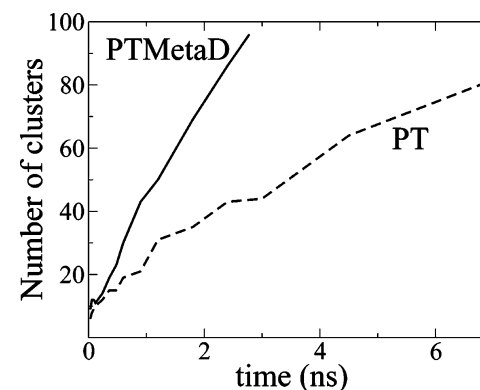


Figure 2. Number of explored clusters as a function of the simulation time, for PT (dashed) and PTMetaD (solid). PTMetaD exploration is more than 3 times faster.

Finally, a recipe...

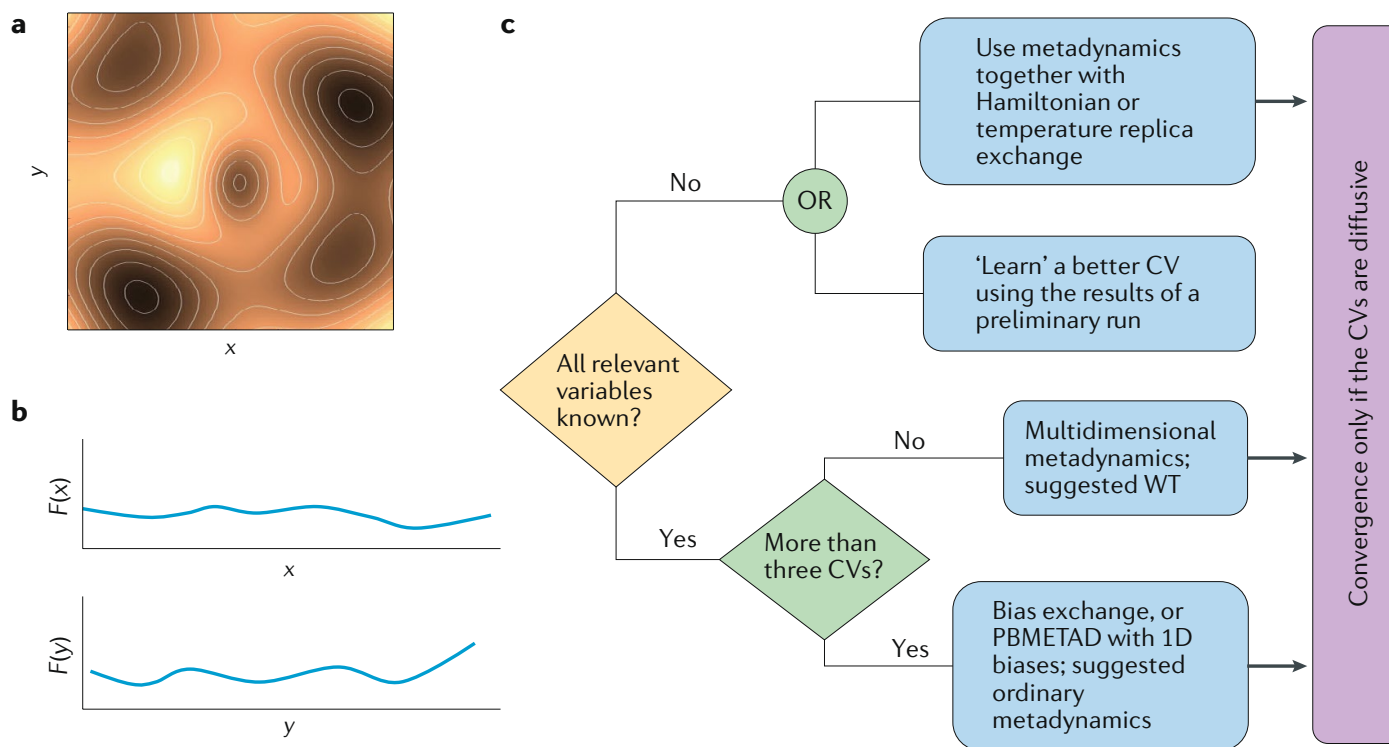


Fig. 5 | **Choosing the correct metadynamics variant. a,b** | An example of a potential energy landscape characterized by the presence of deep minima (panel a), but whose free energy F as a function of two variables (x and y) is approximately flat (panel b). This situation is rather common in practical applications. **c** | A decision tree for choosing the most appropriate version of metadynamics. CV, collective variable; PBMETAD, parallel-bias metadynamics; WT, well-tempered.

And inspiration from what has been implemented

CV Documentation

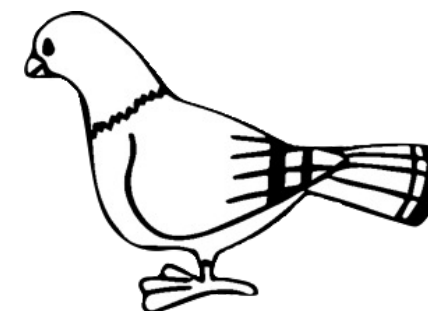
The following list contains descriptions of a number of the colvars that are currently implemented.

ADAPTIVE_PATH	Compute path collective variables that adapt to the
ALPHABETA	Measures a distance including pbc between the i
ALPHARMSD	Probe the alpha helical content of a protein struct
ANGLE	Calculate an angle.
ANTIBETARMSD	Probe the antiparallel beta sheet content of your j
CELL	Calculate the components of the simulation cell
CONSTANT	Return one or more constant quantities with or wi
CONTACTMAP	Calculate the distances between a number of pai
COORDINATION	Calculate coordination numbers.
DHENERGY	Calculate Debye-Huckel interaction energy amon
DIHCOR	Measures the degree of similarity between dihedr
DIMER	This CV computes the dimer interaction energy fo
DIPOLE	Calculate the dipole moment for a group of atoms
DISTANCE	Calculate the distance between a pair of atoms.
DISTANCE_FROM_CONTOUR	Calculate the perpendicular distance from a Willa
EEFSOLV	Calculates EEF1 solvation free energy for a grou
ENERGY	Calculate the total potential energy of the simulat
ERMSD	Calculate eRMSD with respect to a reference str
EXTRACV	Allow PLUMED to use collective variables compu
FAKE	This is a fake colvar container used by citools or
GHBFIX	Calculate the GHBFIX interaction energy among bonding interactions, JCTC, 2019. Essentially it is specifying interaction scaling parameters and ene
GPROPERTYMAP	Property maps but with a more flexible framewo
GYRATION	Calculate the radius of gyration, or other properti
PARABETARMSD	Probe the parallel beta sheet content of your prot
PATH	Path collective variables with a more flexible fr
PATHMSD	This Colvar calculates path collective variables.
PCAVARS	Projection on principal component eigenvectors

PARABETARMSD	Probe the parallel beta sheet content c
PATH	Path collective variables with a more fl
PATHMSD	This Colvar calculates path collective \
PCAVARS	Projection on principal component eigr
POSITION	Calculate the components of the positi
PROJECTION_ON_AXIS	Calculate a position based on the proj
PROPERTYMAP	Calculate generic property maps.
PUCKERING	Calculate sugar pseudorotation coordi
TEMPLATE	This file provides a template for if you v
TORSION	Calculate a torsional angle.
VOLUME	Calculate the volume of the simulation

In addition to the keywords above, by enabling optional modules you can access:

CS2BACKBONE	(from PLUMED-ISDB module) Calculat
EMMI	(from PLUMED-ISDB module) Calculat
FRET	(from PLUMED-ISDB module) Calculat
FUNNEL_PS	(from Funnel-Metadynamics (FM) mo
FUSIONPOREEXPANSIONP	(from Membrane Fusion module) A C\
FUSIONPORENUCLEATIONP	(from Membrane Fusion module) A C\
JCOUPLING	(from PLUMED-ISDB module) Calculat
MEMFUSIONP	(from Membrane Fusion module) Calc
NOE	(from PLUMED-ISDB module) Calculat
PCS	(from PLUMED-ISDB module) Calculat
PIV	(from PIV collective variable module)
PRE	(from PLUMED-ISDB module) Calculat
RDC	(from PLUMED-ISDB module) Calculat
S2CM	(from S2 contact model collective vai
SANS	(from PLUMED-ISDB module) Calculat
SASA_HASEL	(from SASA collective variable modul
SASA_LCPO	(from SASA collective variable modul
SAXS	(from PLUMED-ISDB module) Calculat



PLUMED

<https://www.plumed.org/>

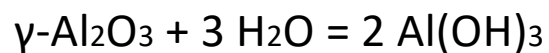
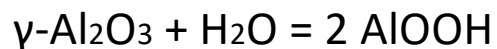


A practical exemple

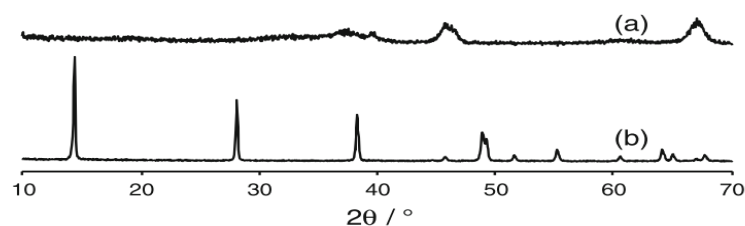
ALUMINA/WATER INTERFACE

$\gamma\text{-Al}_2\text{O}_3$ in water

γ -Alumina is very reactive towards water



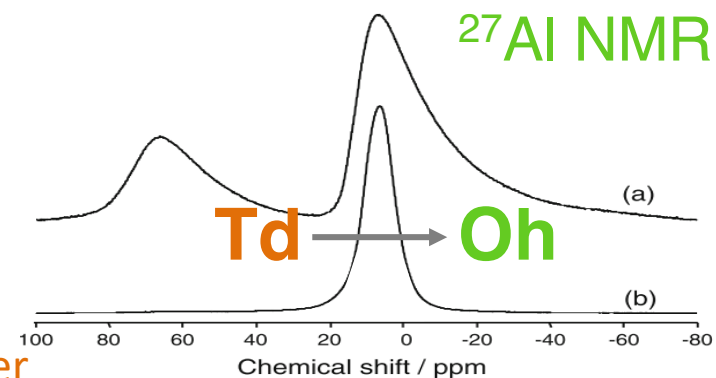
XRD



Pt/ $\gamma\text{-Al}_2\text{O}_3$
as synthesised

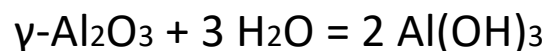
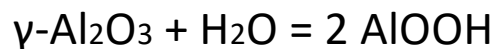
Pt/ $\gamma\text{-Al}_2\text{O}_3$
10h @ 225° C in water

^{27}Al NMR

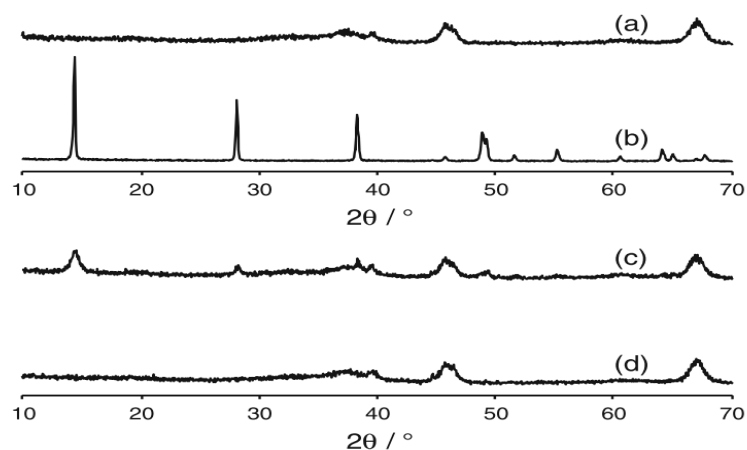


γ -Al₂O₃ in water and in presence of biomass

γ -Alumina is very reactive towards water



XRD



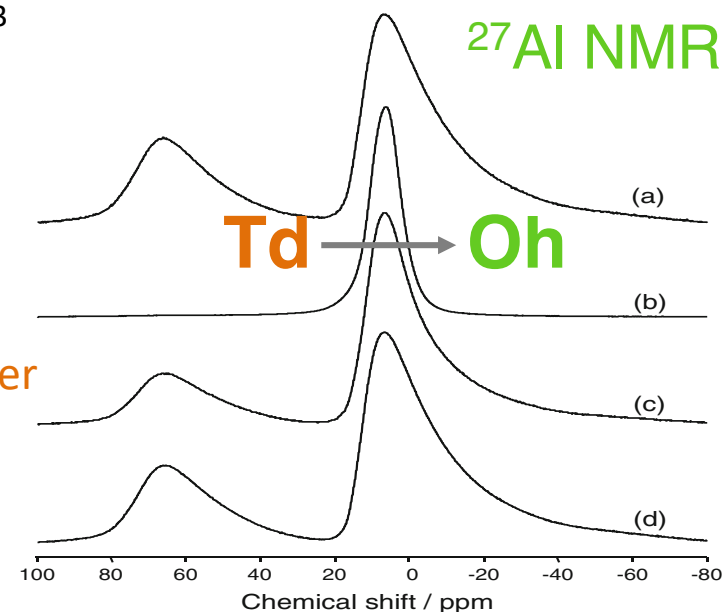
Pt/ γ -Al₂O₃
as synthesised

Pt/ γ -Al₂O₃
10h @ 225°C in water

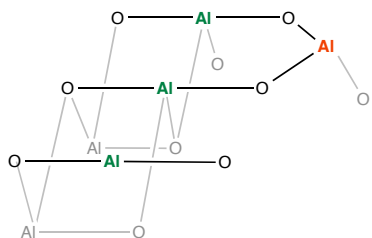
+5wt% glycerol

+5wt% sorbitol

²⁷Al NMR

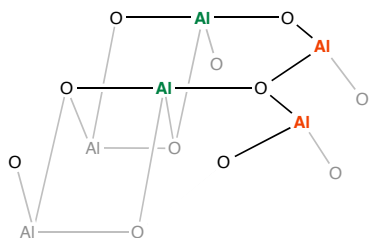


Building a model of the γ -Al₂O₃ / water interface



(110) surface

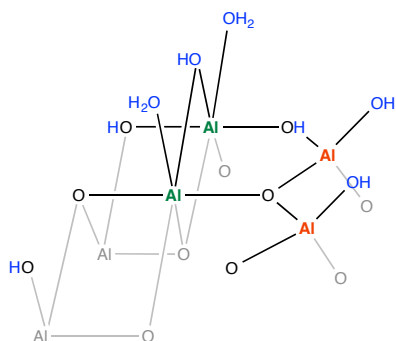
Building a model of the γ - Al_2O_3 / water interface



(110) surface

Migration of Al: **two Td sites**

Building a model of the γ - Al_2O_3 / water interface

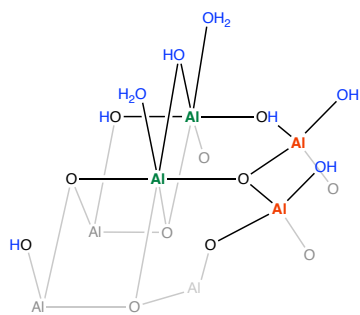


(110) surface

Migration of Al: **two Td sites**

Chemisorption of 5 H_2O

Building a model of the γ -Al₂O₃ / water interface



(110) surface

CP2K 2.5.1

PBE+D3

GPW approach

DZVP-MOLOPT GTH

pseudos

Molecular Dynamics

T = 330 K, CSV

md-step = 0.5 fs

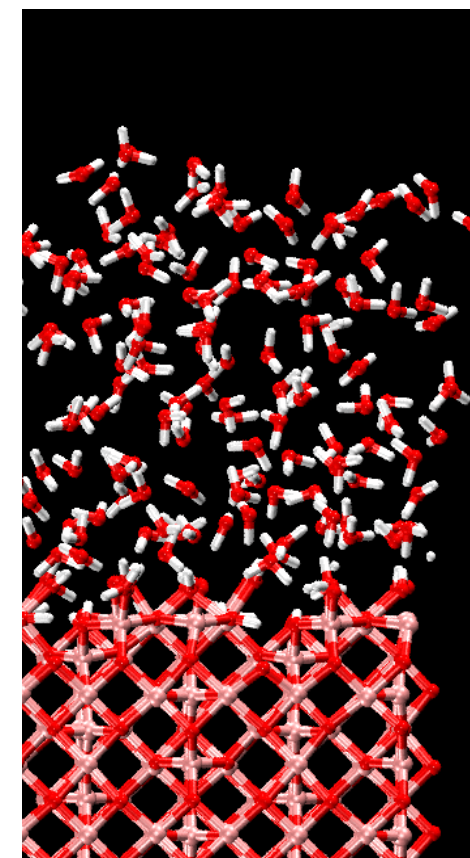
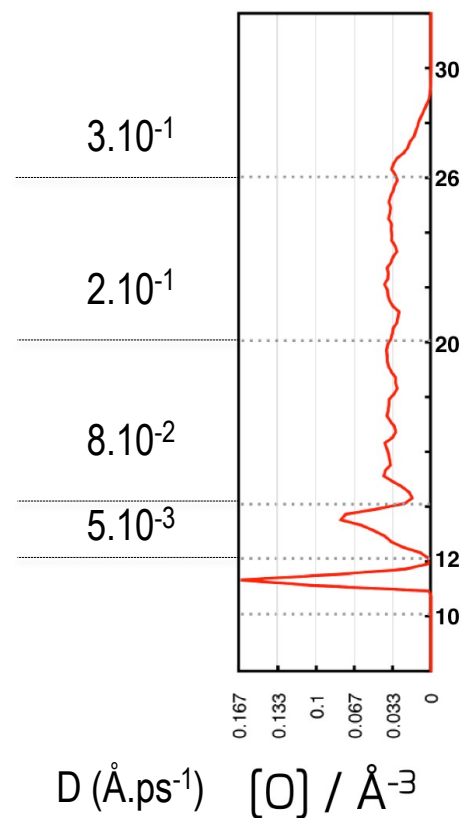
thermalisation = 35 ps

production = 27.5 ps

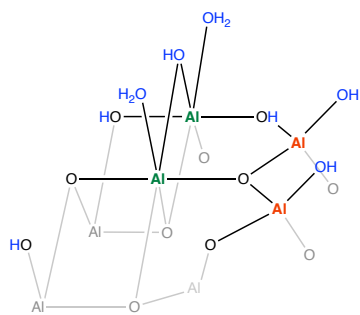
Most hydrophilic facet (110)

Two Td sites

Chemisorption of 5 H₂O, the
~15 Å of water, free to move



Building a model of the γ -Al₂O₃ / water interface



(110) surface

CP2K 2.5.1

PBE+D3

GPW approach

DZVP-MOLOPT GTH

pseudos

Molecular Dynamics

T = 330 K, CSVR

md-step = 0.5 fs

thermalisation = 35 ps

production = 27.5 ps

Most hydrophilic facet (110)

Two Td sites

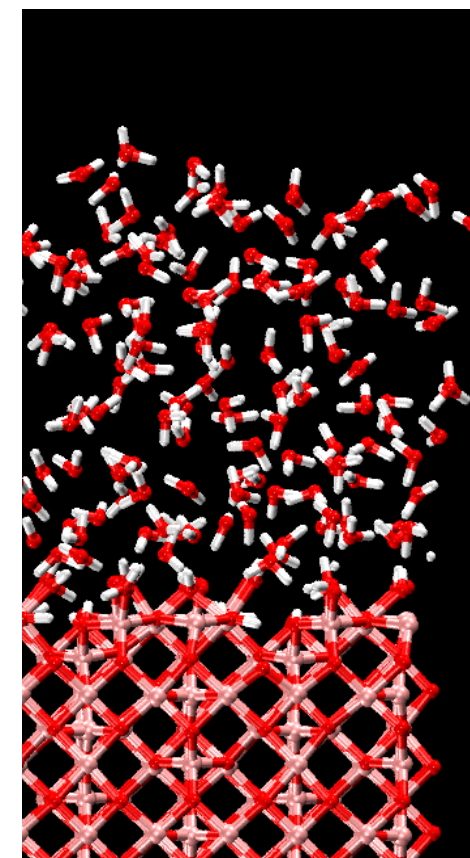
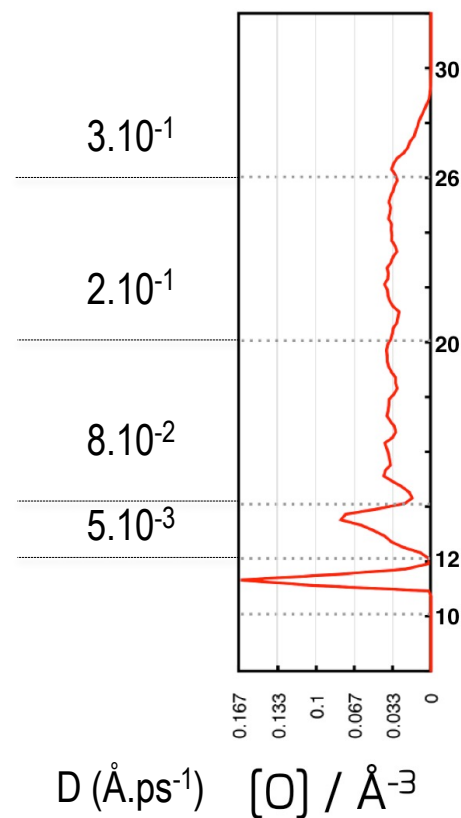
Chemisorption of 5 H₂O

~15 Å of water, free to move

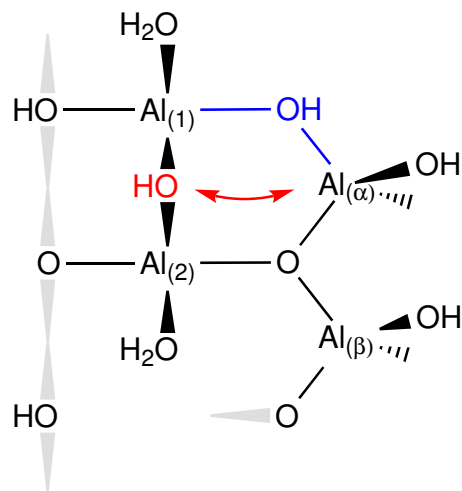


We observed H-transfers

The water has a very slow dynamic at the interface



Failed attempts...



metadynamics #1

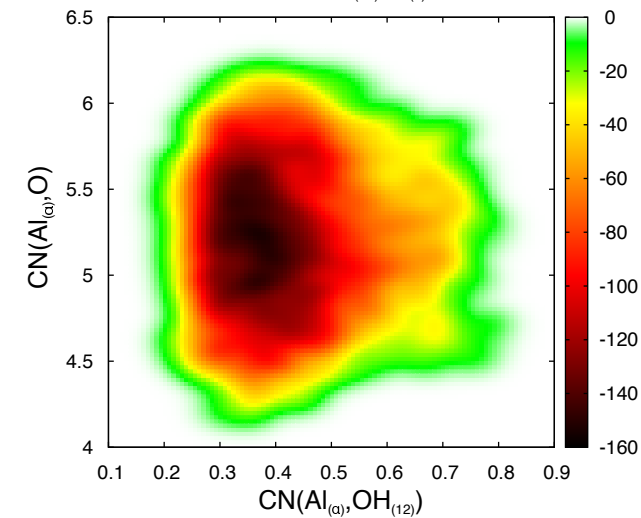
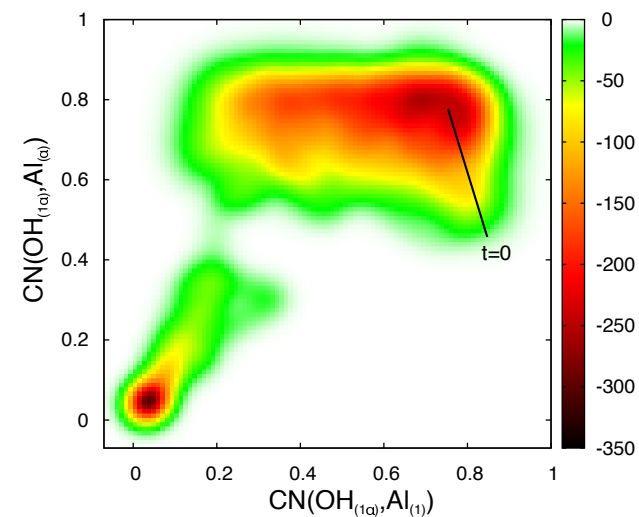
$$\text{CN}(\text{Al}_{(\alpha)}, \text{OH}_{(1\alpha)})$$

$$\text{CN}(\text{Al}_{(1)}, \text{OH}_{(1\alpha)})$$

metadynamics #2

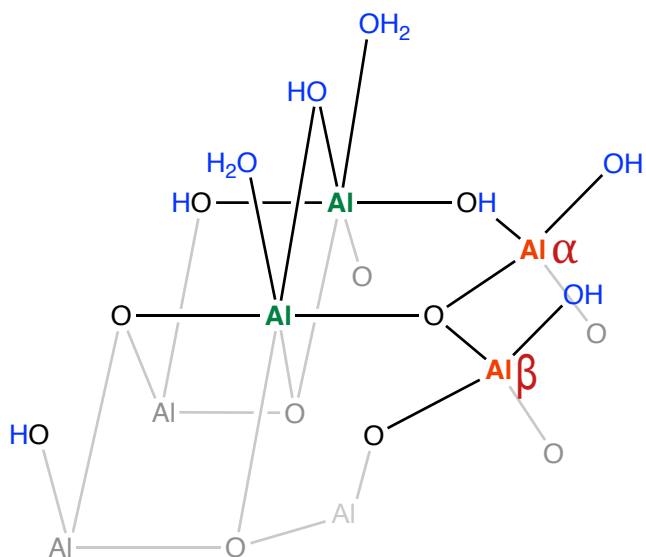
$$\text{CN}(\text{Al}_{(\alpha)}, \text{OH}_{(12)})$$

$$\text{CN}(\text{Al}_{(\alpha)}, \text{O})$$

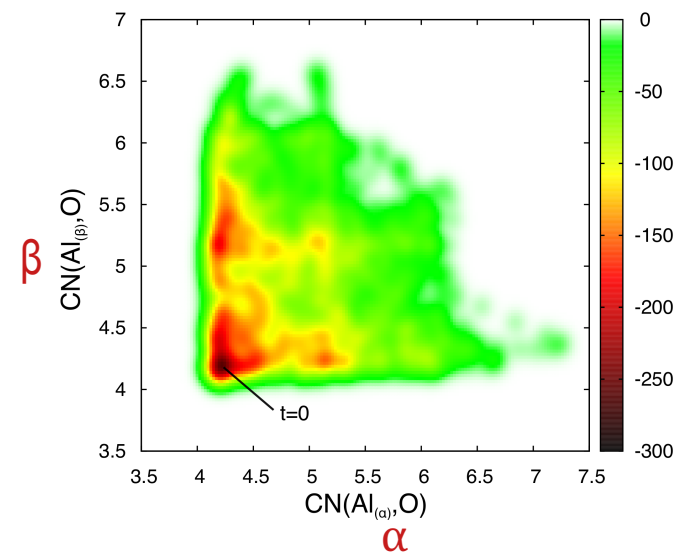


Failed attempts...

More general?

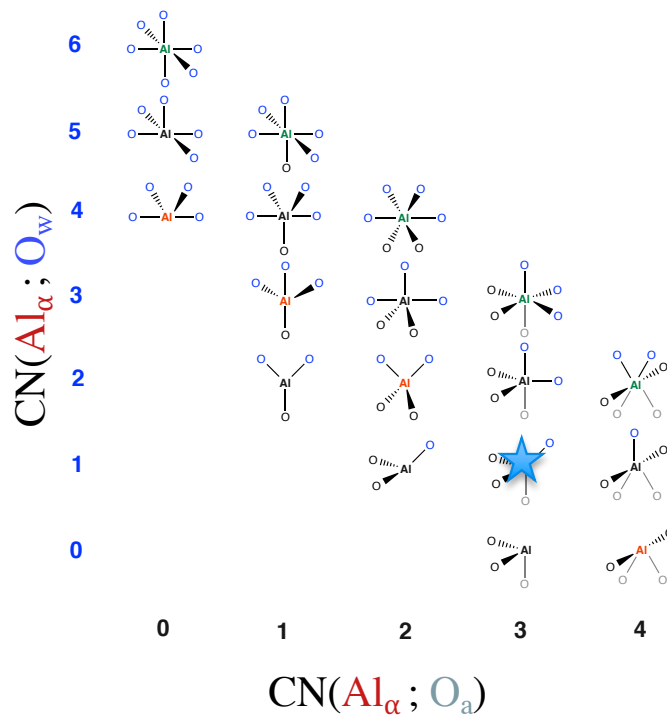
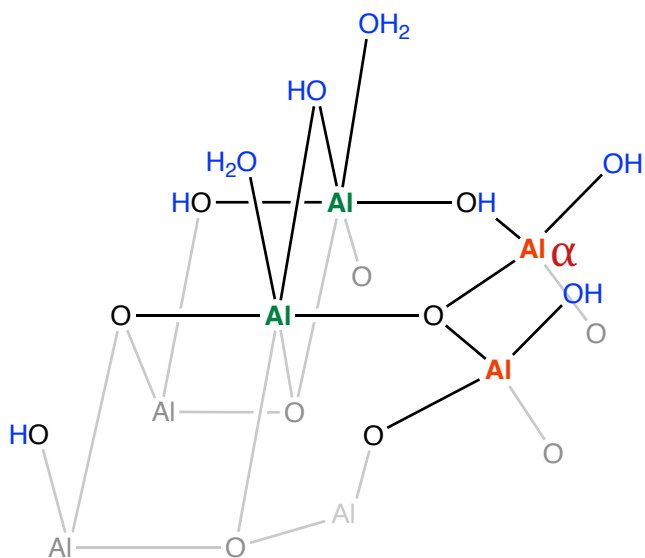


metadynamics #3
 $CN(Al_\alpha; O)$
 $CN(Al_\beta; O)$



Failed attempts...

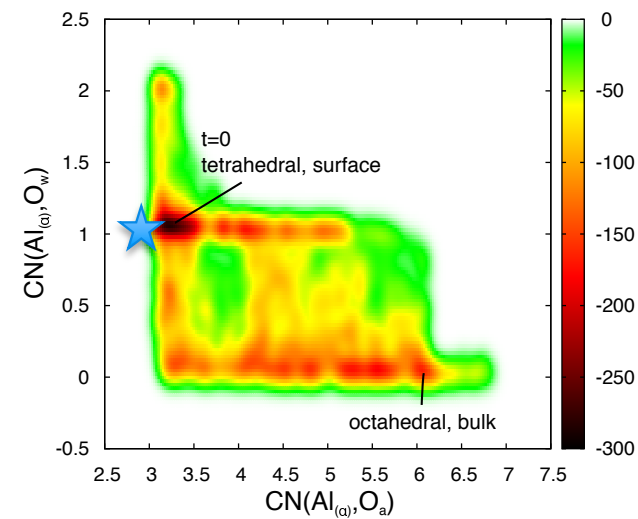
Focused on Al_α but separating O_a and O_w



metadynamics #4

$CN(Al_\alpha; O_a)$

$CN(Al_\alpha; O_w)$



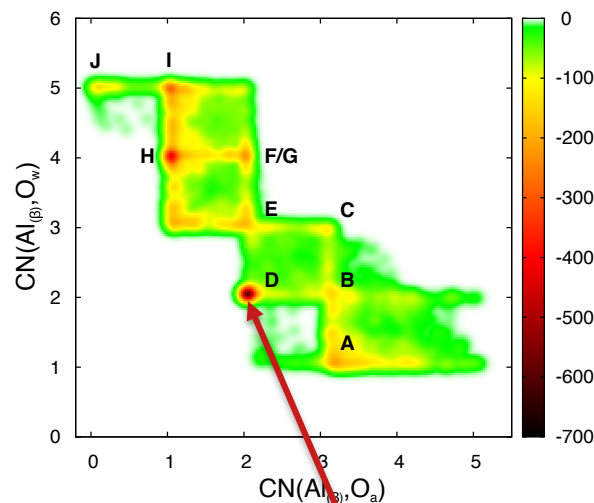
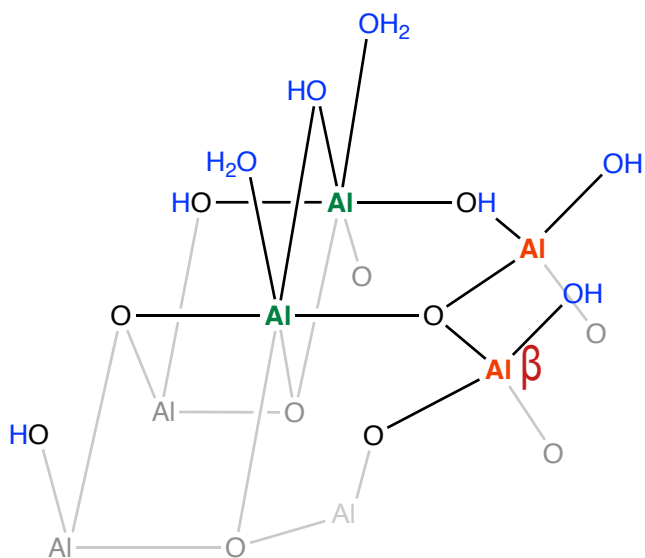
Failed attempts...

Focused on Al_β but separating O_a and O_w

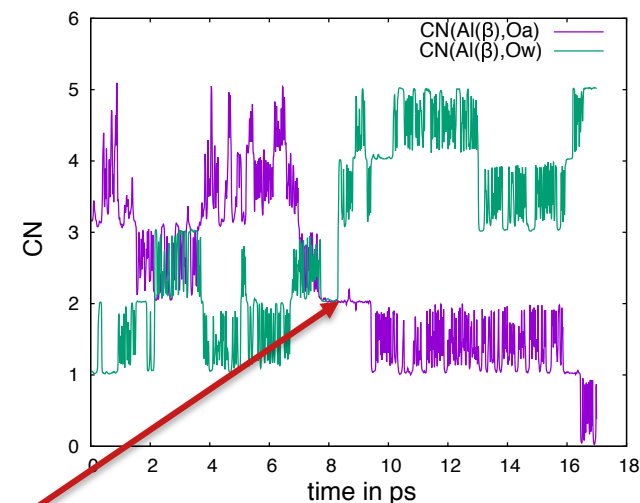
metadynamics #5

$\text{CN}(\text{Al}_\beta; \text{O}_a)$

$\text{CN}(\text{Al}_\beta; \text{O}_w)$



(a) Reconstructed free energy profile

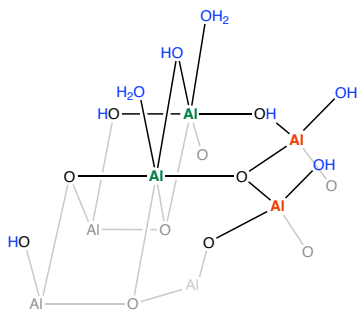


(b) time evolution of the CVs

$$\mathbf{F}_B = -\frac{dB}{dR} = -\omega \sum_{t' < t} \exp\left(-\frac{(s_{t'} - s)^2}{2\sigma^2}\right) \times \frac{ds}{dR}$$

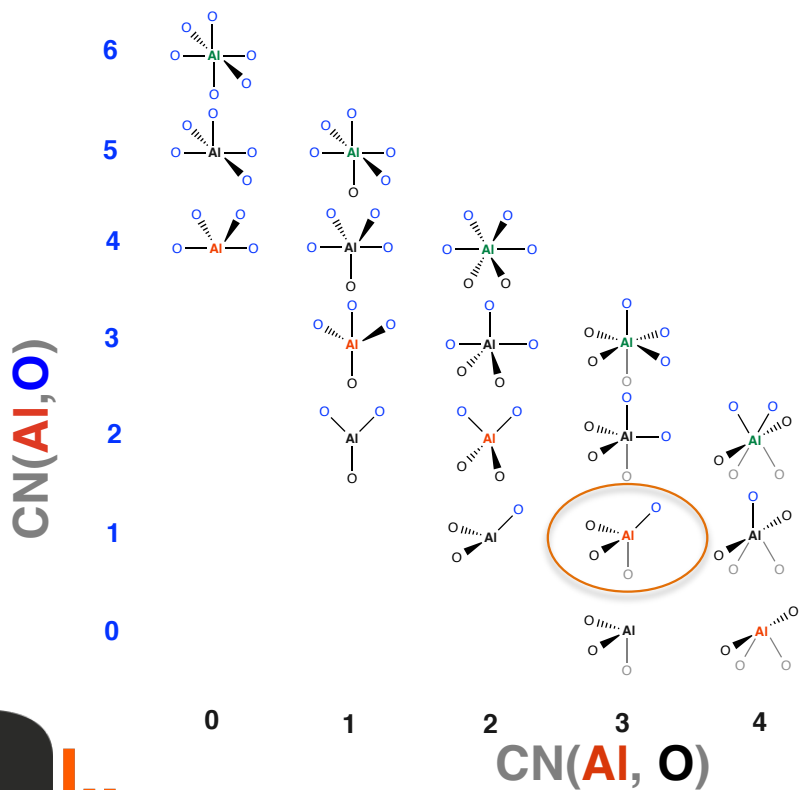
$$s(r_{ij}) = \frac{1 - \left(\frac{r_{ij} - d_0}{r_0}\right)^n}{1 - \left(\frac{r_{ij} - d_0}{r_0}\right)^p}$$

We need to play on the parameters of the CN to avoid a zero force.

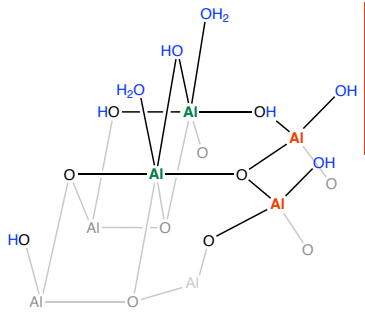


Reactivity of the $\gamma\text{-Al}_2\text{O}_3$ / water interface

Td \longrightarrow Oh



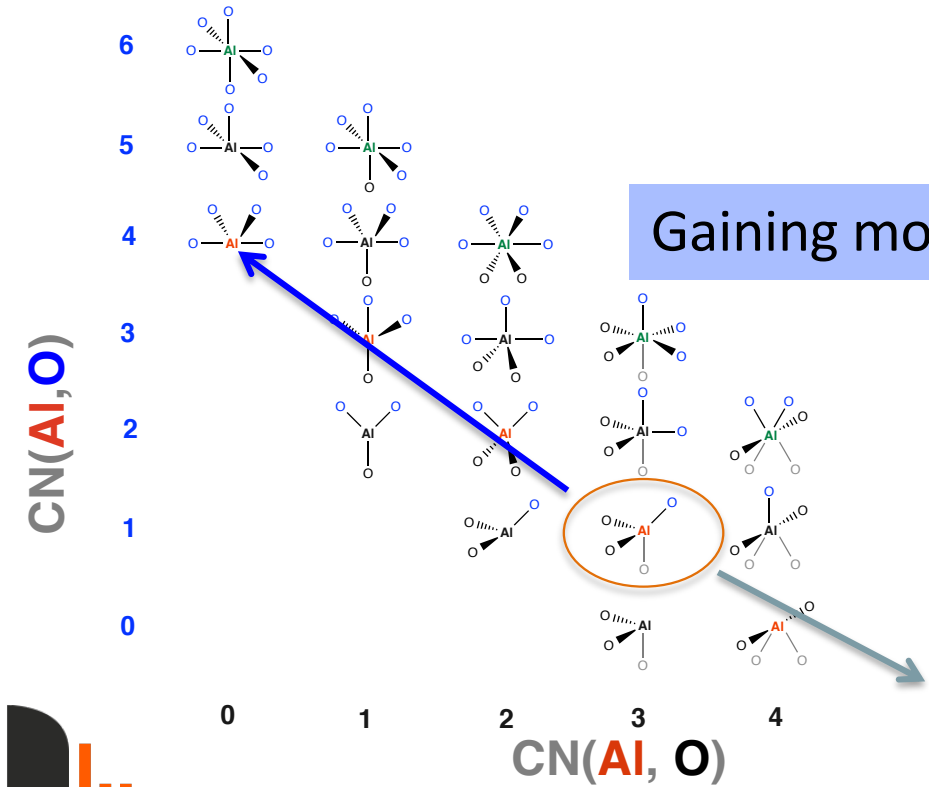
Reactivity of the γ -Al₂O₃ / water interface



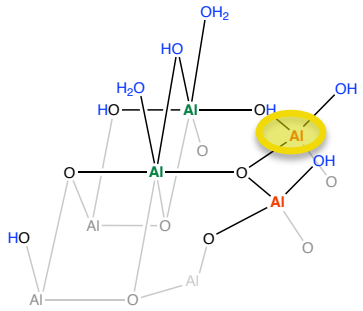
Td → **Oh**

Gaining more water in the coordination sphere

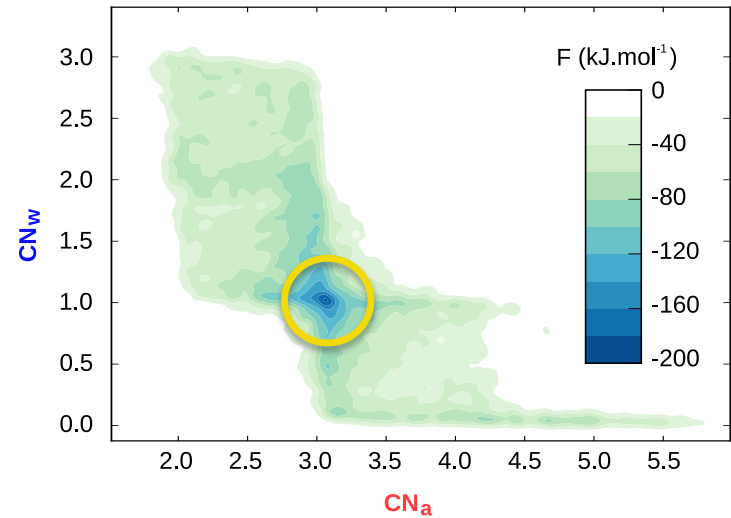
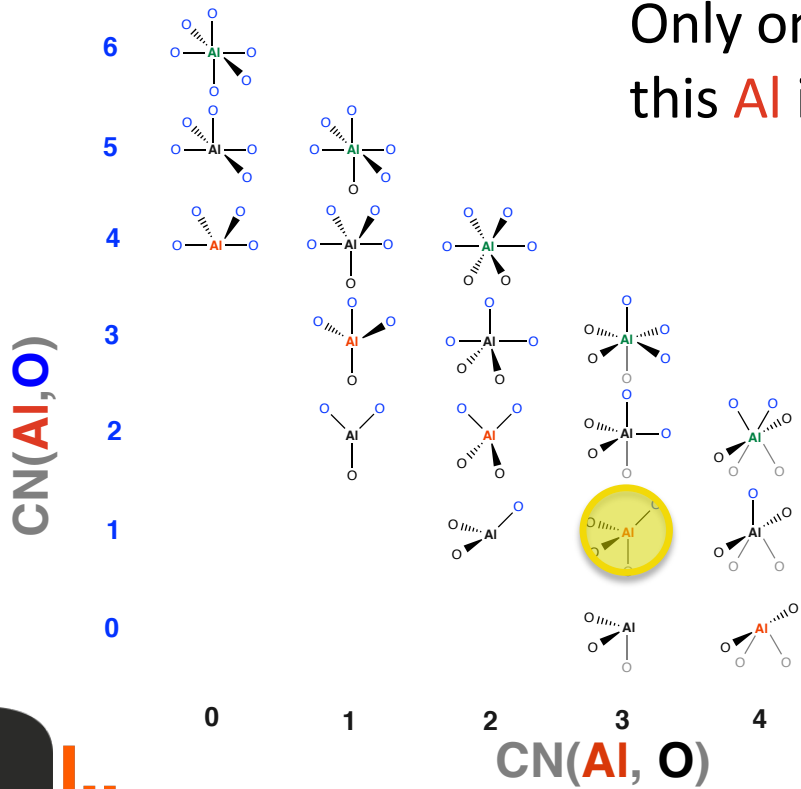
Diving into the alumina network



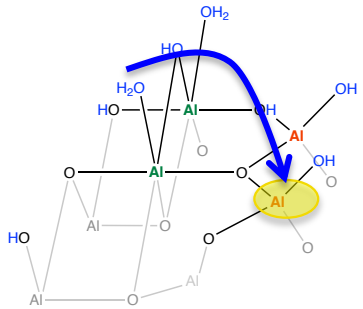
First tetrahedral Al



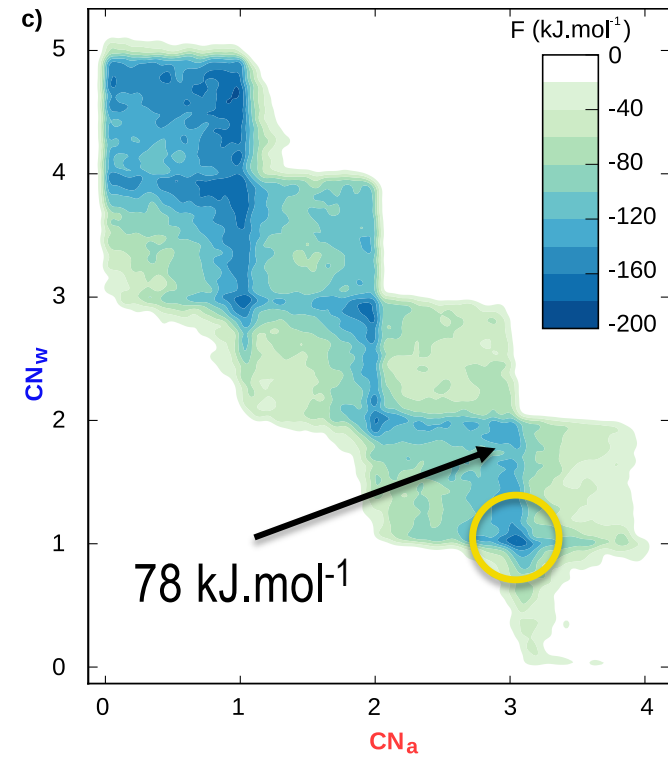
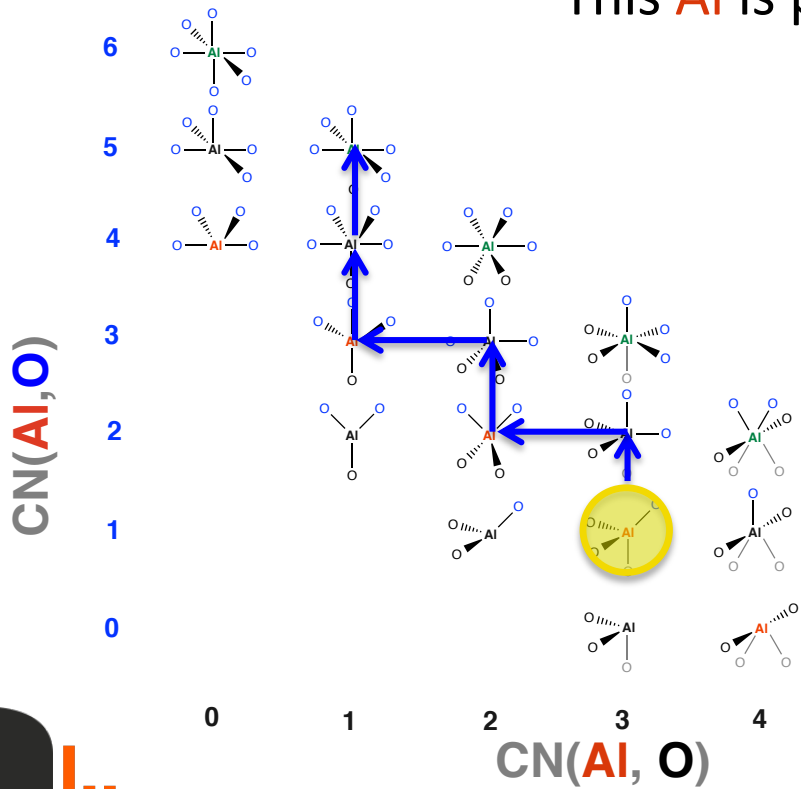
Only one clear minimum:
this **Al** is hard to hydrate and is not very mobile



Second tetrahedral Al



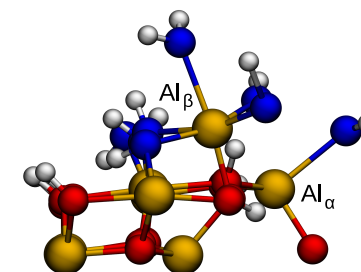
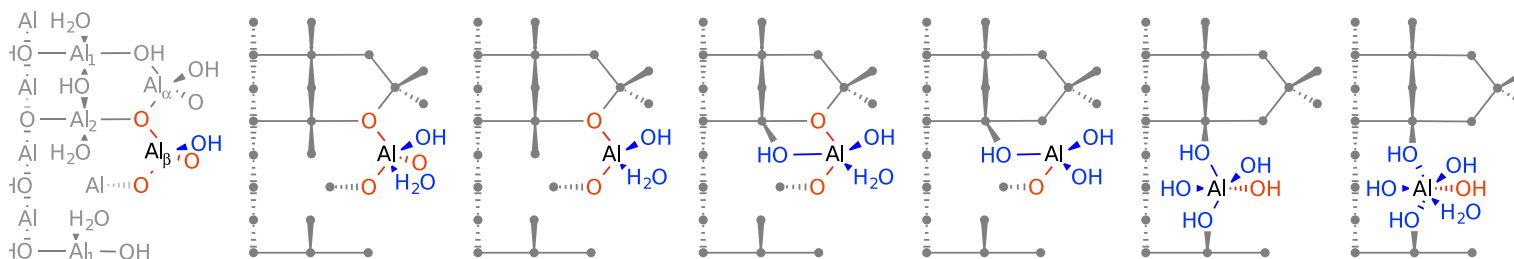
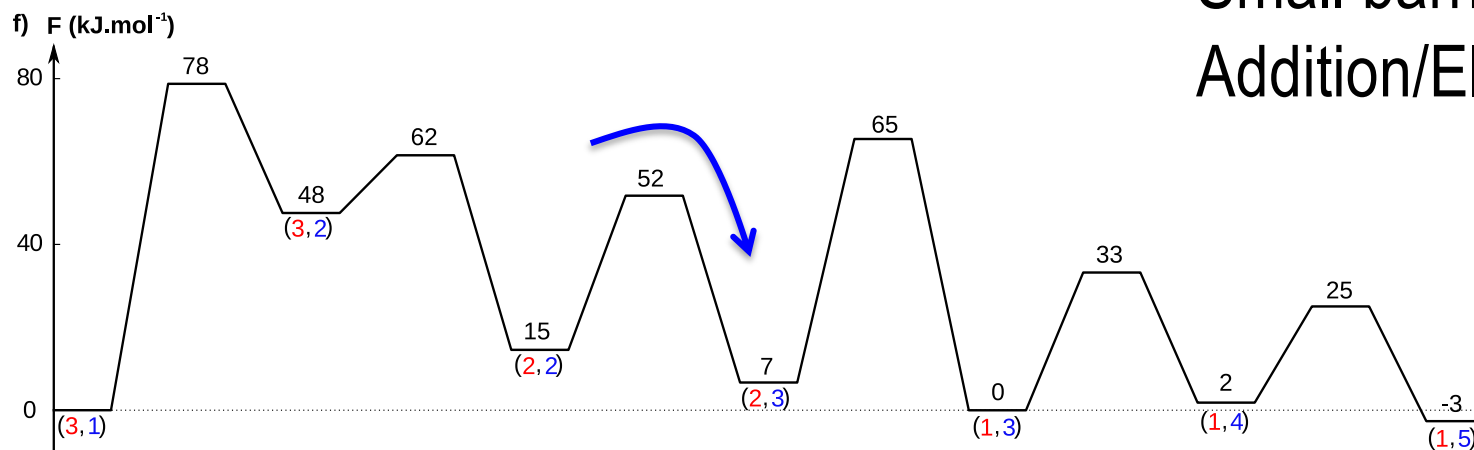
This **Al** is pretty mobile!!



Mechanism of an interfacial reaction



Small barrier!
Addition/Elimination

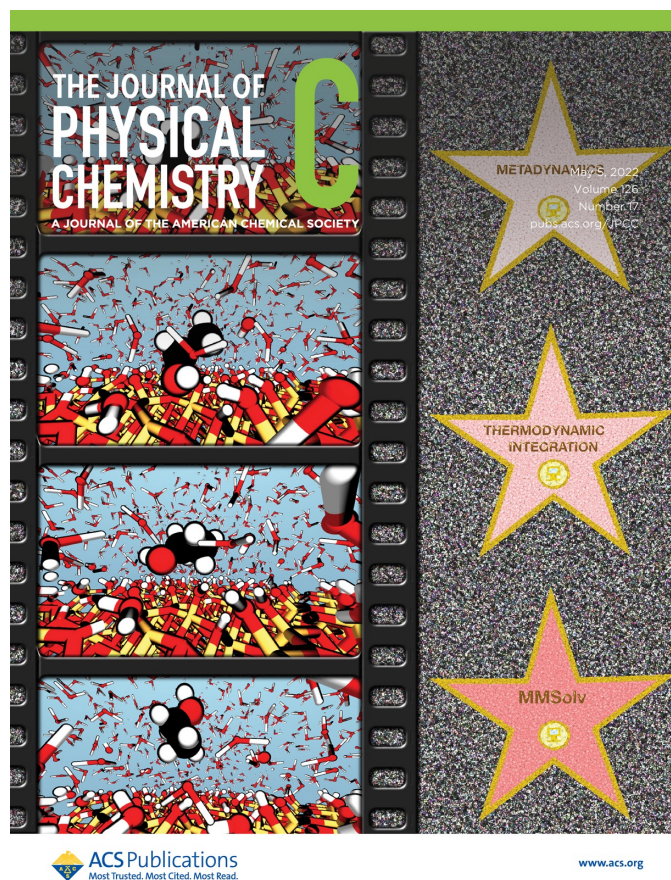


Adsorption of a model alcohol at the interface

Adsorption



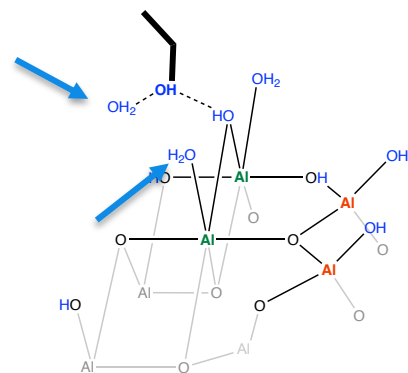
Desorption



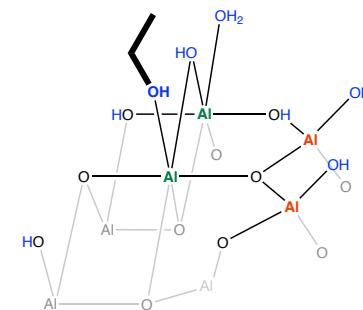
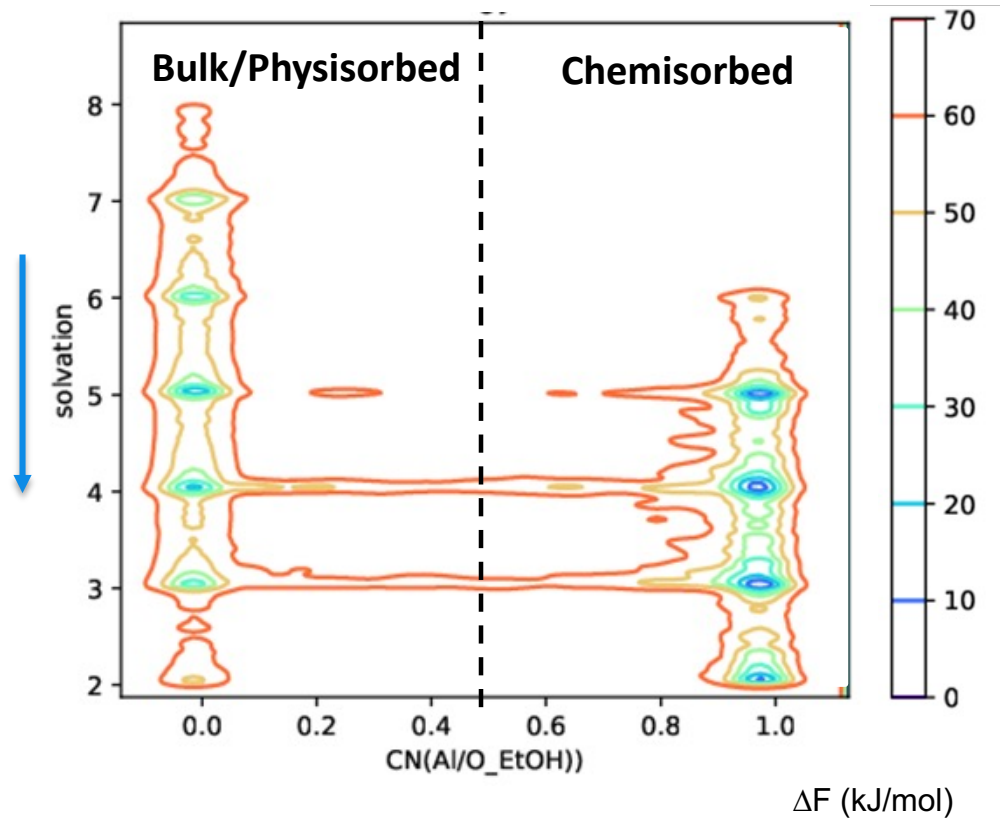
Comparison of methods

- Metadynamics
 - Thermodynamics Integration
 - PCM
 - MMSolv
- Metadynamics is the most informative
- MMSolv is the most efficient (solvation contribution at the MM level)

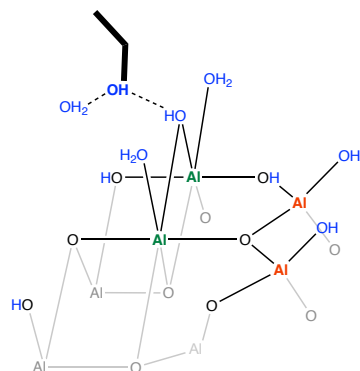
Adsorption of a model alcohol at the interface



desolvation

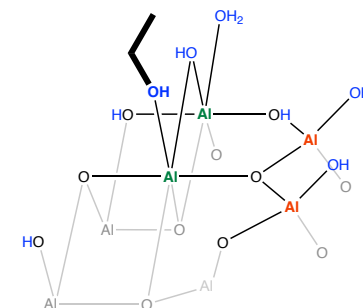
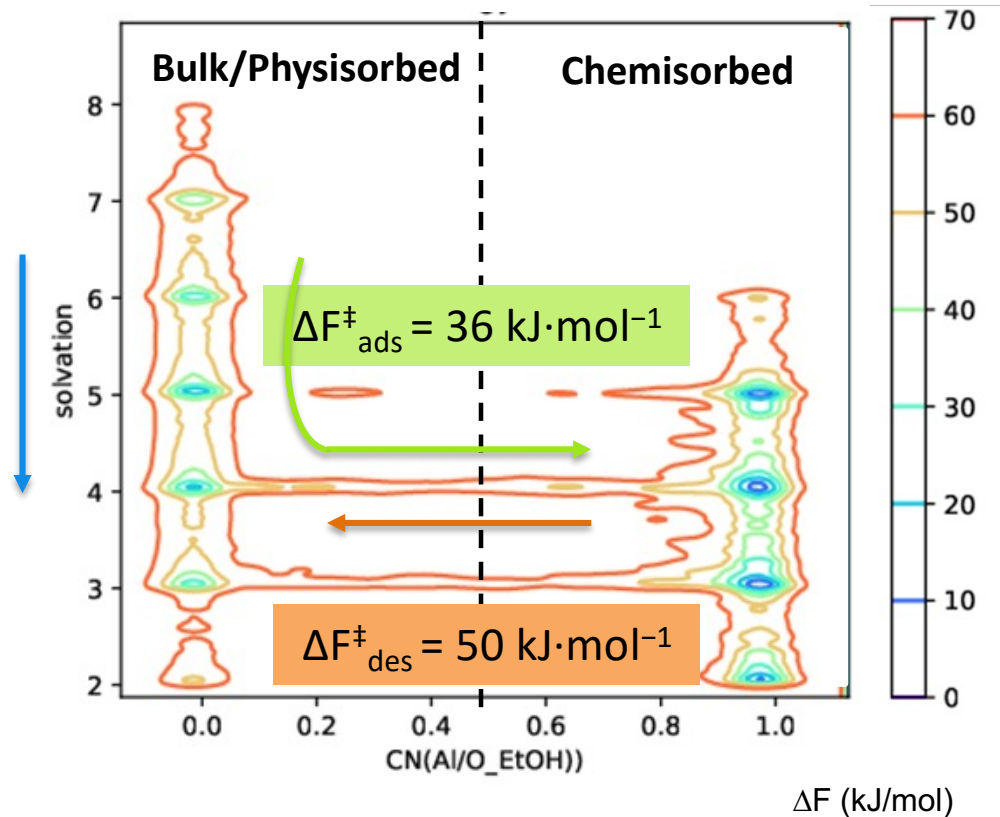


Adsorption of a model alcohol at the interface



desolvation

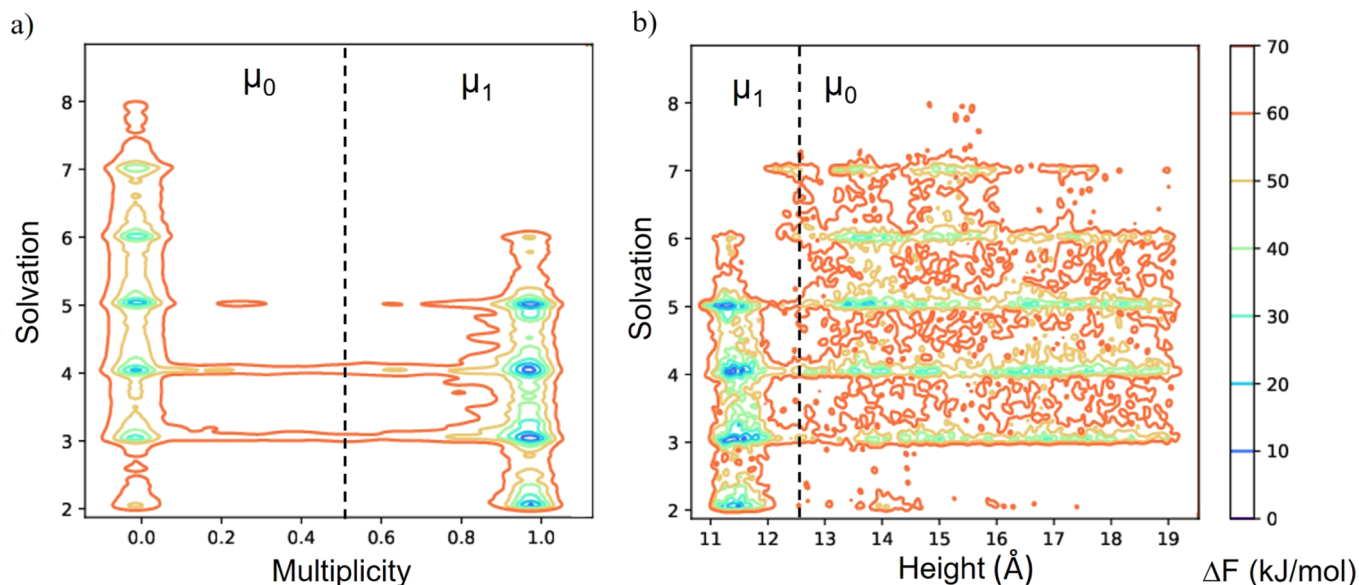
$$\Delta F_{\text{desolv}}^{\ddagger} \sim 20 \text{ kJ}\cdot\text{mol}^{-1}$$



ab initio metadynamics
 $\Delta F_{\text{ads}} = -14 \text{ kJ}\cdot\text{mol}^{-1}$

MMSolv
 $\Delta F_{\text{ads}} = -10 \text{ kJ}\cdot\text{mol}^{-1}$

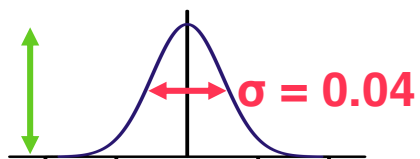
In more details...



After few trials...

- 3CV rather complex
- Well-tempered metadynamics (bias factor of 100)
- Four walkers
- 20463 gaussians (204.6 ps)

$W = 3.3 \text{ kJ/mol}$



Every 10fs.

$$\begin{aligned}
 CV_{\text{solv}} = & \text{CN}(\text{O}_{\text{ethanol}}; \text{H}_{\text{water}} \cup \text{H}_{\text{ethanol}}) \\
 & + \text{CN}(\text{H}_{\text{ethanol}}; \text{O}_{\text{water}} \cup \text{O}_{\text{ethanol}}) \\
 & + \text{CN}(\text{Al}_{(n)}; \text{O}_{\text{water}})
 \end{aligned}$$

$$\text{CN}(A; B) = \sum_{i \in A} \sum_{j \in B} s_{ij}$$

with

$$s_{ij} = \begin{cases} 1 - \left(\frac{r_{ij} - d_0}{r_0}\right)^n & \text{if } r > d_0 \\ 1 - \left(\frac{r_{ij} - d_0}{r_0}\right)^m & \text{if } r < d_0 \\ 1 & \text{if } r < d_0 \end{cases}$$

Exploring the PES/FES of complex systems

A challenge in $3n$ or $3N-6$ dimensions...

Don't neglect geometry optimization and toy systems

Be imaginative!

Chemist's intuition is still very valuable 😊