

# **Discovering reaction mechanisms with automated computational methods**

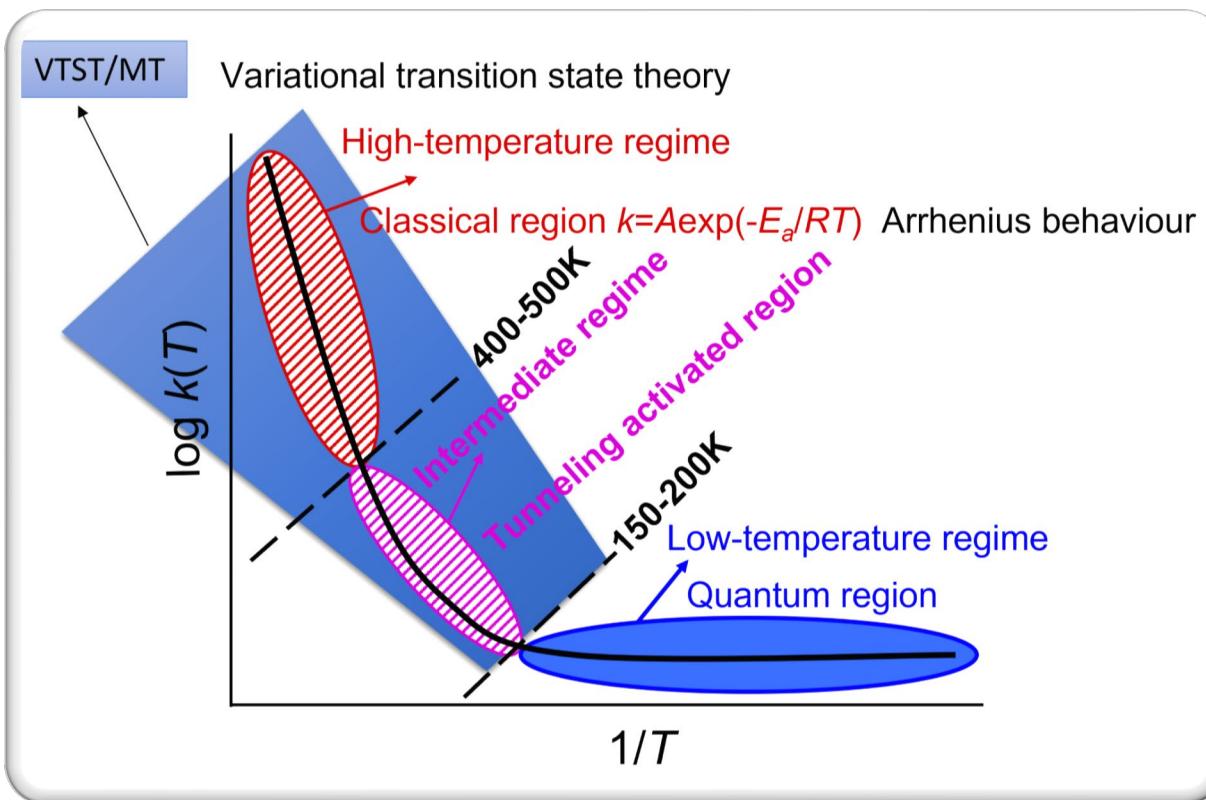
EMILIO MARTÍNEZ-NÚÑEZ

UNIVERSIDADE DE SANTIAGO DE COMPOSTELA  
SPAIN



**School on Kinetics and Dynamics of  
Chemical Reactions**  
March 18, 2024 - March 22, 2024

# Chemical kinetics

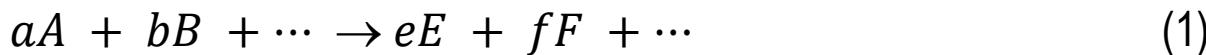


J\J



## Basic definitions:

- ✓ Homogenous reactions
- ✓ Closed system



## Rate of reaction ( $r$ )

$$r = \frac{1}{V} \left( \frac{1}{v_i} \frac{dn_i}{dt} \right) = \frac{1}{v_i} \frac{d[S_i]}{dt} \quad \text{constant } V \quad (2)$$

$$r = -\frac{1}{a} \frac{d[A]}{dt} = -\frac{1}{b} \frac{d[B]}{dt} = \dots = \frac{1}{e} \frac{d[E]}{dt} = \frac{1}{f} \frac{d[F]}{dt} = \dots \quad (3)$$

Example:  $\text{N}_2 + 3\text{H}_2 \rightarrow 2\text{NH}_3$   $r = -\frac{d[\text{N}_2]}{dt} = -\frac{1}{3} \frac{d[\text{H}_2]}{dt} = \frac{1}{2} \frac{d[\text{NH}_3]}{dt}$

Units for  $r$ : chemical kinetics:  $\text{M s}^{-1}$  ( $\text{mol L}^{-1} \text{s}^{-1}$ ),

chemical dynamics: molecule  $\text{cm}^{-3} \text{s}^{-1}$

## Rate Law

Relationship between the rate of reaction and the concentrations of species at time  $t$ .

$$r = k[A]^\alpha[B]^\beta\dots$$

$k$  is the rate coefficient

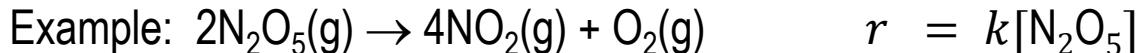
## Examples:



# Reaction Mechanism (aka reaction network)

Collection of coupled steps involving chemical transformations of molecular species. The different steps are called **elementary reactions**.

A **complex reaction** is formed by two or more elementary steps.



1.  $\text{N}_2\text{O}_5 \rightleftharpoons \text{NO}_2 + \text{NO}_3$
2.  $\text{NO}_2 + \text{NO}_3 \rightarrow \text{NO} + \text{O}_2 + \text{NO}_2$
3.  $\text{NO} + \text{N}_2\text{O}_5 \rightarrow \text{NO}_2 + \text{NO}_2 + \text{NO}_2$

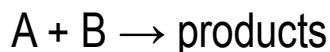
The **molecularity** is the number of molecules that react in an elementary reaction.

**Unimolecular reaction**



$$-\frac{d[\text{A}]}{dt} = k[\text{A}]$$

**Bimolecular reaction**



$$-\frac{d[\text{A}]}{dt} = -\frac{d[\text{B}]}{dt} = k[\text{A}][\text{B}]$$



$$-\frac{1}{2} \frac{d[\text{A}]}{dt} = k[\text{A}]^2$$

## Differential rate equations (aka master equation)

For a reaction mechanism, we may write the (coupled) differential rate equations. From these equations, we can predict the time evolution of the populations of all the chemical species involved in the mechanism.

Example:  $2\text{N}_2\text{O}_5(\text{g}) \rightarrow 4\text{NO}_2(\text{g}) + \text{O}_2(\text{g})$

1.  $\text{N}_2\text{O}_5 \rightleftharpoons \text{NO}_2 + \text{NO}_3$
2.  $\text{NO}_2 + \text{NO}_3 \rightarrow \text{NO} + \text{O}_2 + \text{NO}_2$
3.  $\text{NO} + \text{N}_2\text{O}_5 \rightarrow \text{NO}_2 + \text{NO}_2 + \text{NO}_2$

$$\frac{d[\text{N}_2\text{O}_5]}{dt} = -k_1[\text{N}_2\text{O}_5] + k_{-1}[\text{NO}_2][\text{NO}_3] - k_3[\text{NO}][\text{N}_2\text{O}_5]$$

...

$$\frac{d[\text{O}_2]}{dt} = k_2[\text{NO}_2][\text{NO}_3]$$

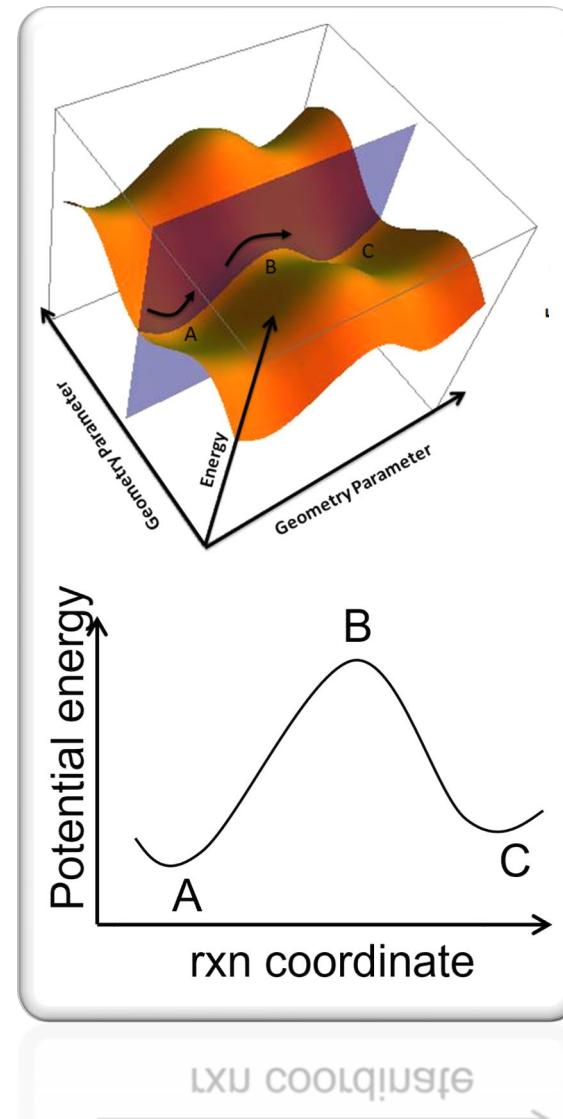
$$\frac{d\mathbf{n}(t)}{dt} = \mathbf{Mn(t)}$$

Solution of the ME: Analytical, numerical integration, KMC

# Elementary reactions

*At the molecular level:*

An elementary step involves motion across a single barrier



## Not all points matter for chemical kinetics

**Important points of the PES:** Those in which the gradient is zero (stationary points).

**Minima or equilibrium geometries:** All the eigenvalues of the Hessian are positive.

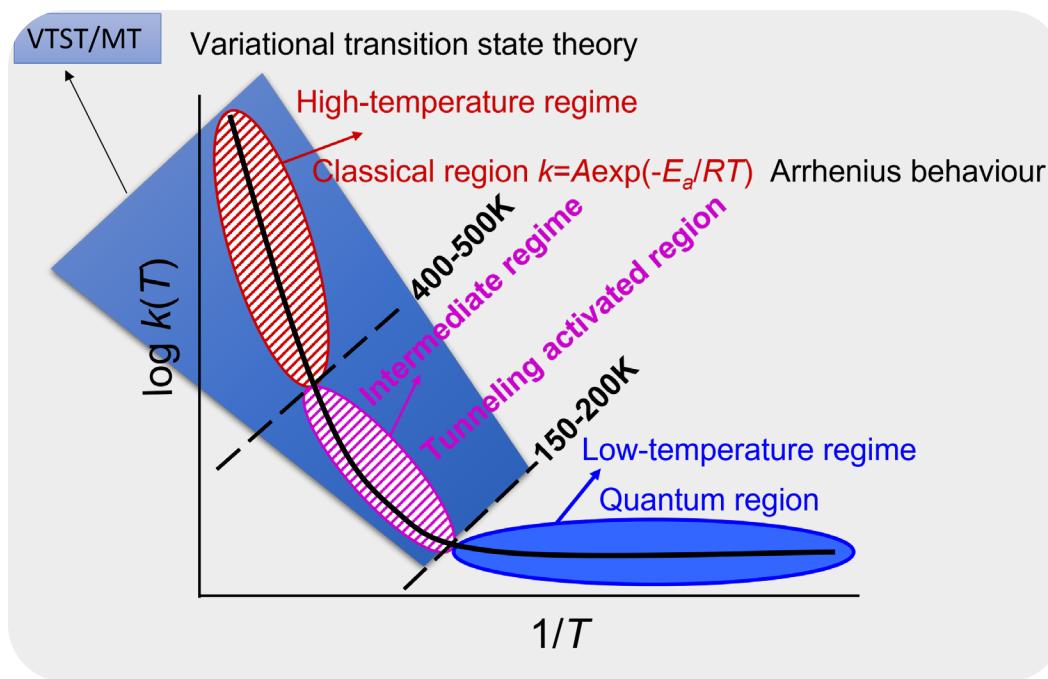
- ✓ *Global*: Lowest potential energy of the PES.
- ✓ *Local*: A point with the lowest potential in a given region.
- ✓ *Reactive intermediate*: Metastable local minimum.
- ✓ *Conformers*: Local minima interconverted by rotations about single bonds.

**Saddle points:** One or more eigenvalues of the Hessian are negative.

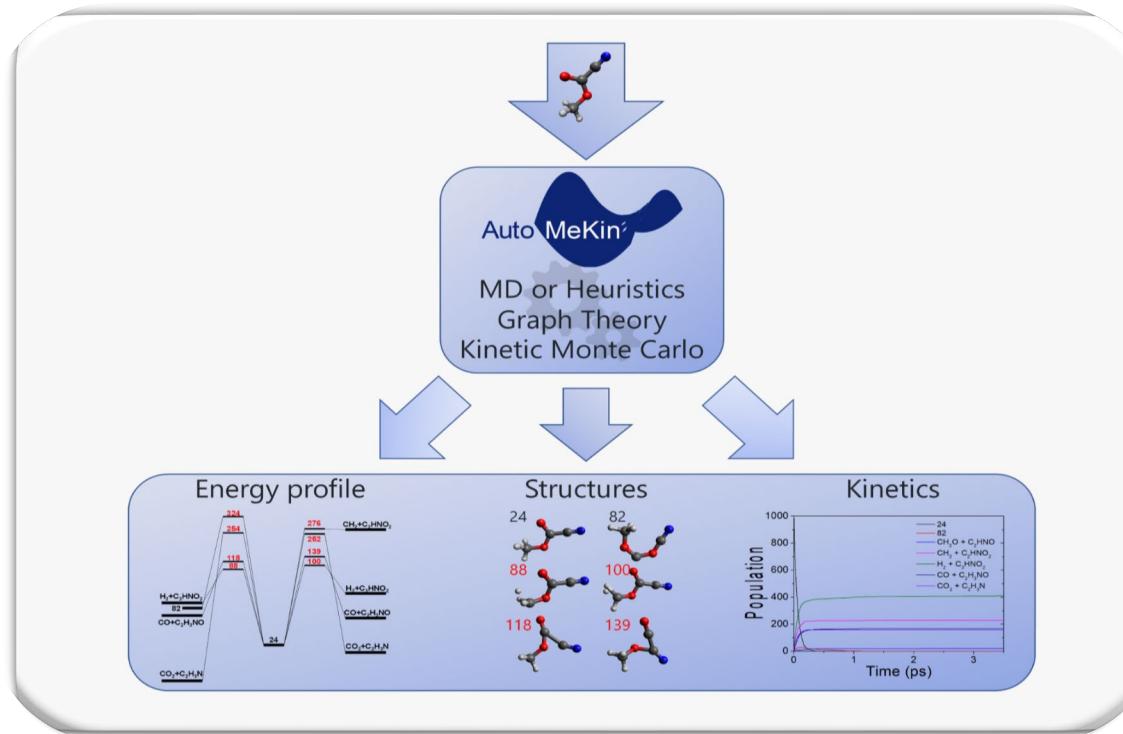
- ✓ *First order*: Only one of the eigenvalues is negative.
- ✓ *Second order*: Two eigenvalues are negative.
- ✓ *Transition state (TS)*: First order saddle point

**Note:** the Hessian is the matrix of second derivatives of the potential with respect to the coordinates (also called force constant matrix).

# Dependence on temperature: $k(T)$



# AutoMeKin (Automated Mechanisms and Kinetics)



## FULL PAPER

WWW.C-CHEM.ORG

**Journal of  
COMPUTATIONAL  
CHEMISTRY**

# An Automated Method to Find Transition States Using Chemical Dynamics Simulations

Emilio Martínez-Núñez\*

PCCP

PAPER



Cite this: *Phys. Chem. Chem. Phys.*  
2015, 17, 14912

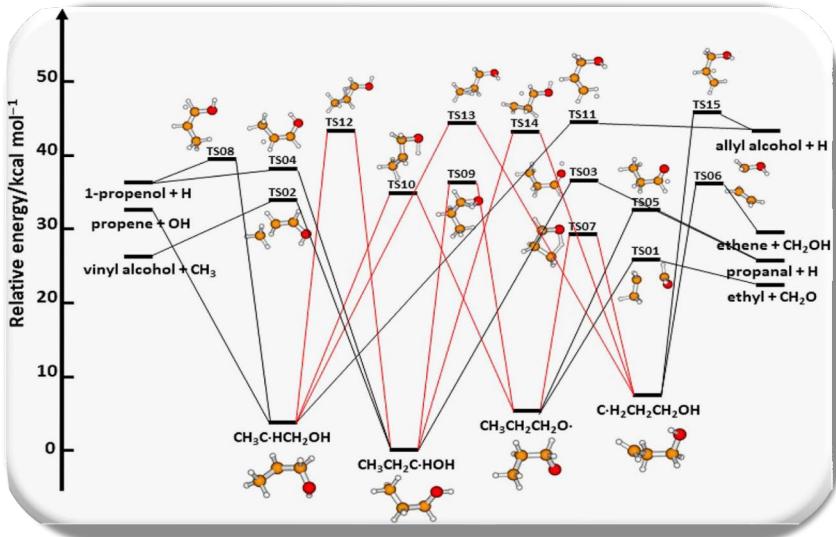
## An automated transition state search using classical trajectories initialized at multiple minima†

Emilio Martínez-Núñez

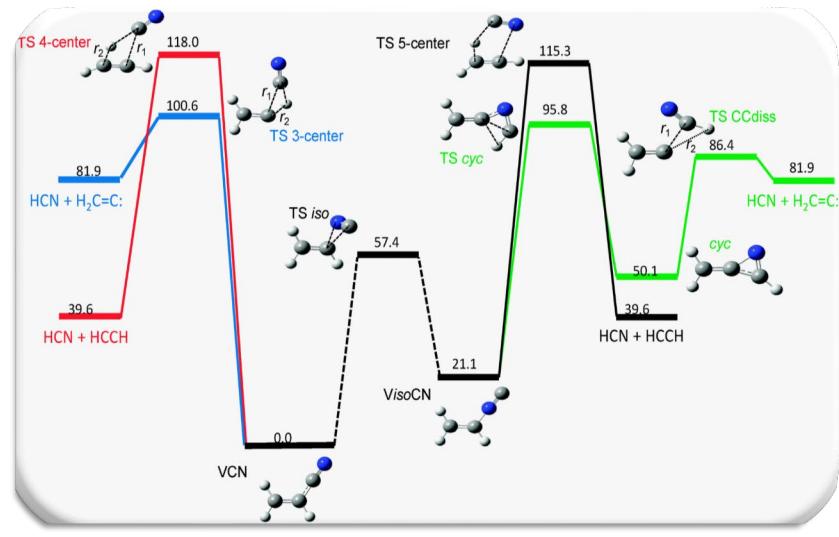


[View Article Online](#)

# AutoMeKin: Motivation

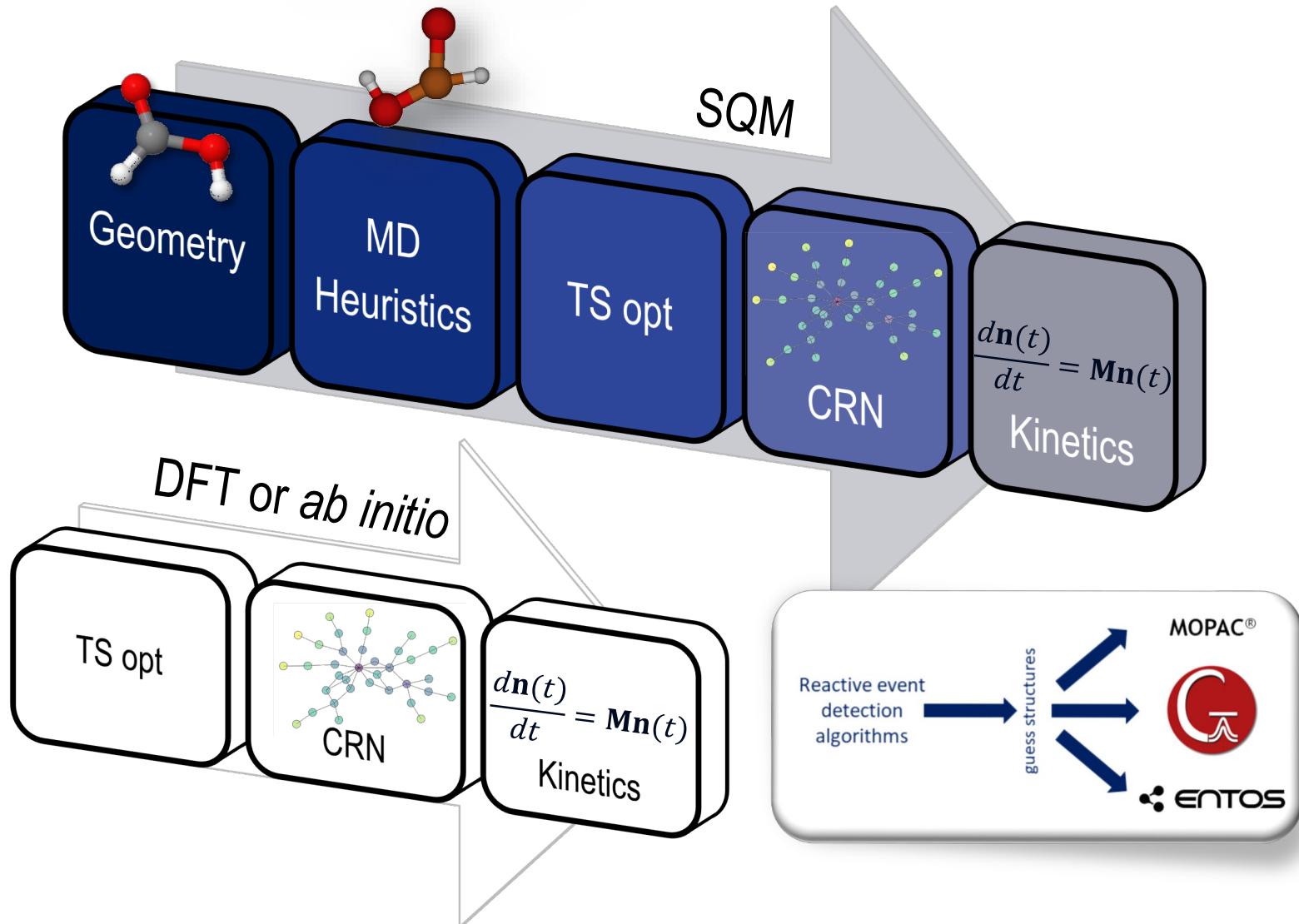


Manual search is not efficient



Possible non-intuitive pathways

# AutoMeKin: Workflow

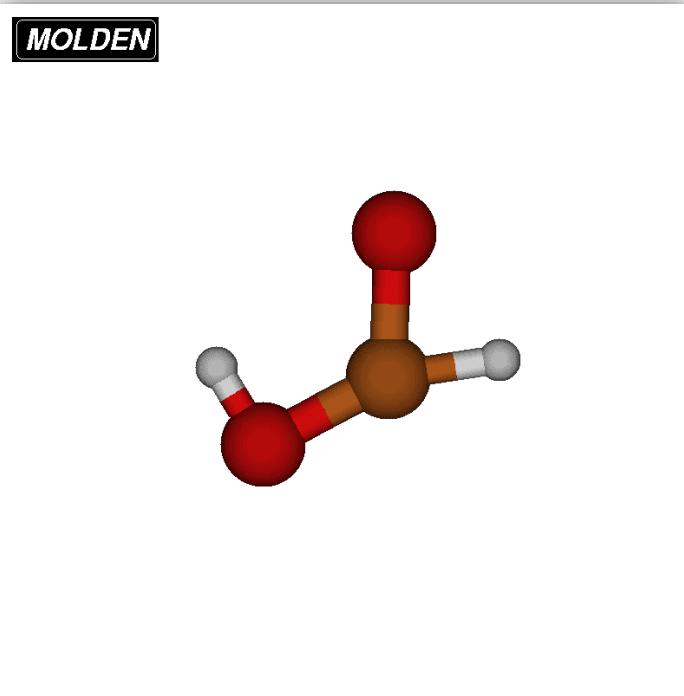


# MD simulations

Phys. Chem. Chem. Phys. 2015, 17, 14912

Standard MD: high E or T  
and short:

- ✓ QCT
- ✓ Microcanonical/canonical sampling
- ✓ Adaptive energy range
- ✓ Movie: 210 kcal/mol



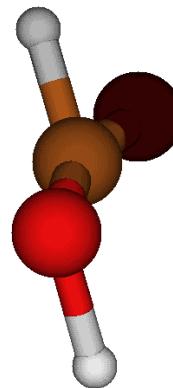
# MD simulations

ChemSystemsChem 2020, 152, e19002

Rare-event acceleration  
method (BXDE):

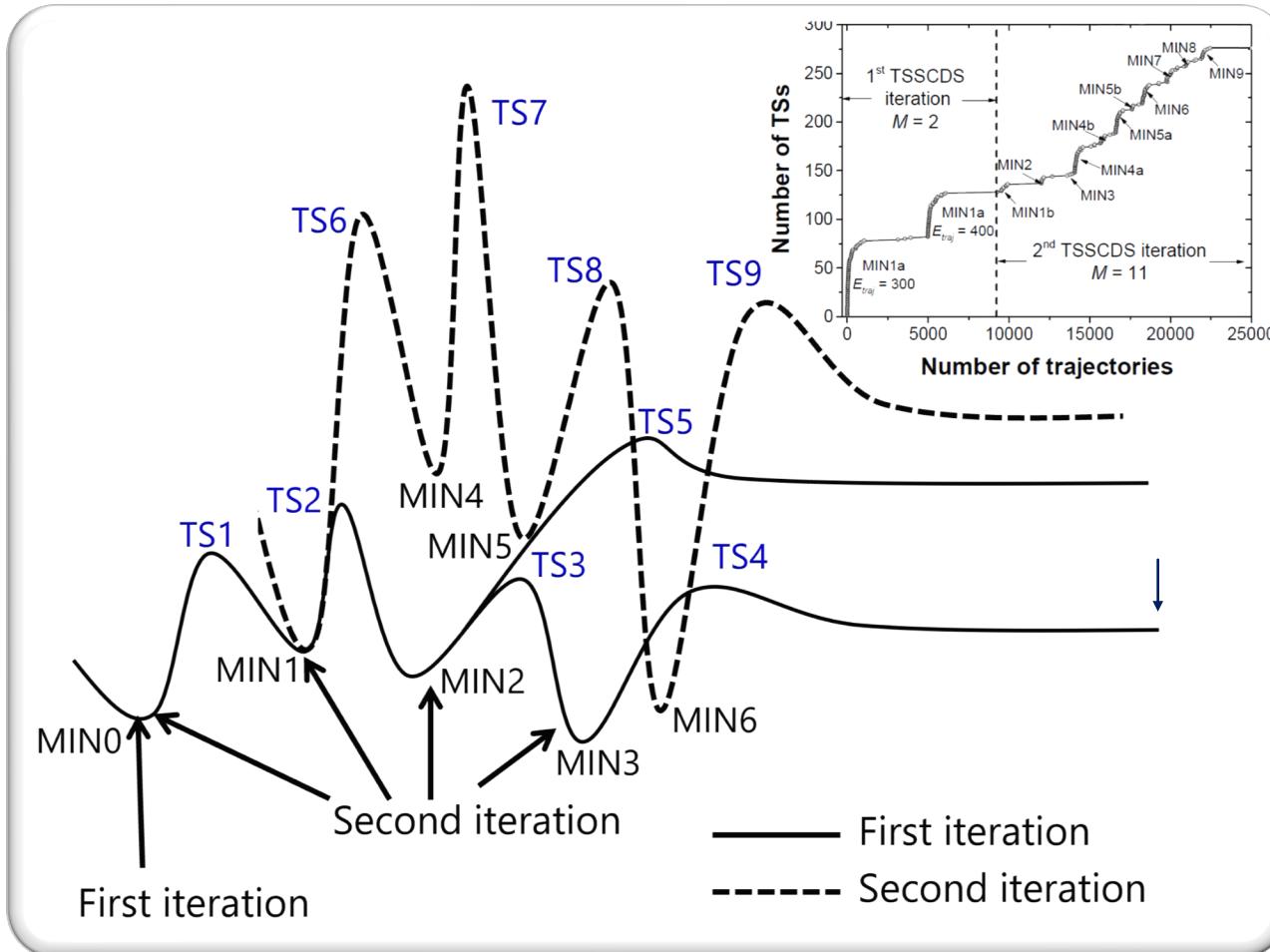
- ✓ Energy boxes
- ✓ More efficient sampling
- ✓ Loose coupling via ASE
- ✓ Movie: Langevin 1000 K

MOLDEN



# Sampling from multiple minima

Phys. Chem. Chem. Phys. 2015, 17, 14912

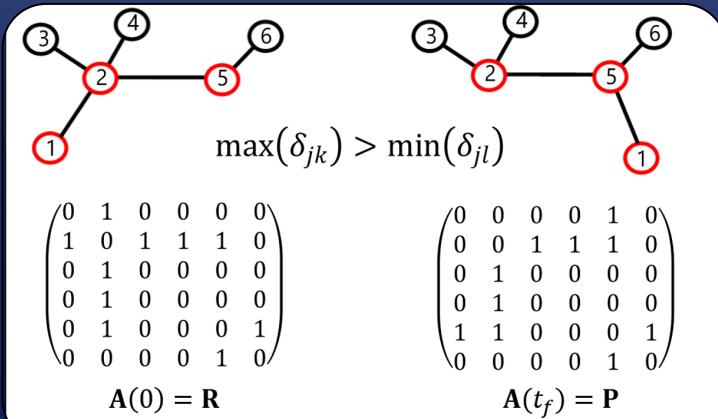


# What's different from other methods?

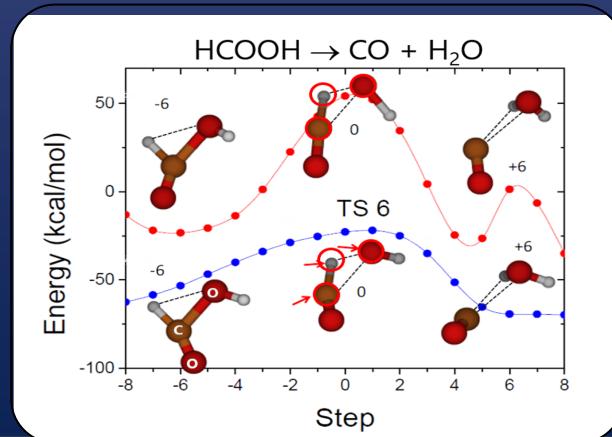
J Comput. Chem. 2015, 36, 222

## Detecting Transition States

### Graph-based detection step



### Relaxation step



$$\text{Laplacian } L = D - A$$

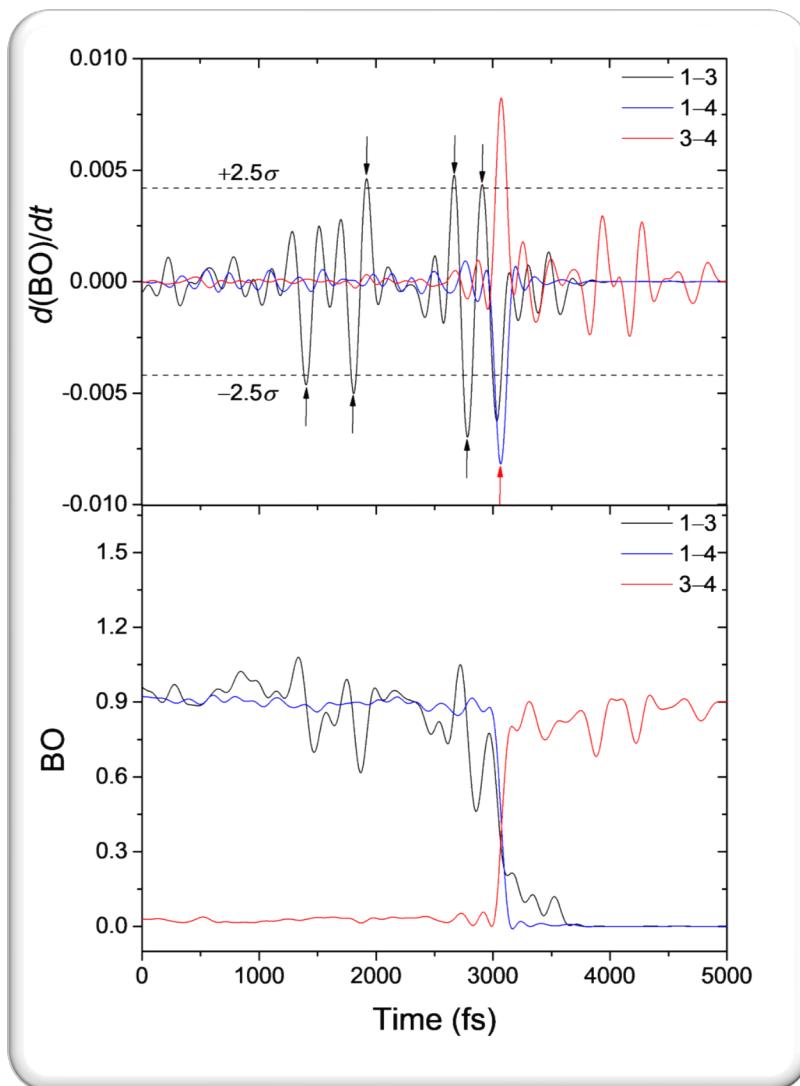
$$\begin{pmatrix} 2 & -1 & -1 & 0 \\ -1 & 2 & 0 & -1 \\ -1 & 0 & 2 & -1 \\ 0 & -1 & -1 & 2 \end{pmatrix}$$

$$\lambda = 0, 2, 2, 4$$

Multiple minima  
Spectral Graph Theory  
✓ Compare structures  
✓ Degree of fragmentation

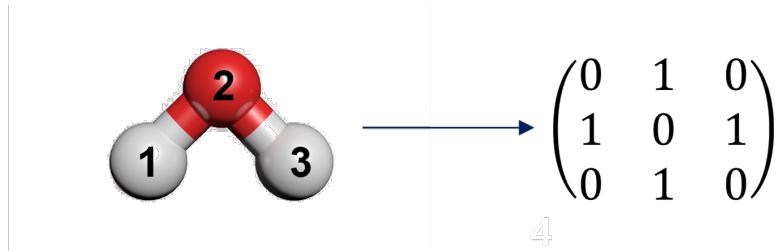
# Event detection: Bond orders

JCTC, 2020, 16, 1606

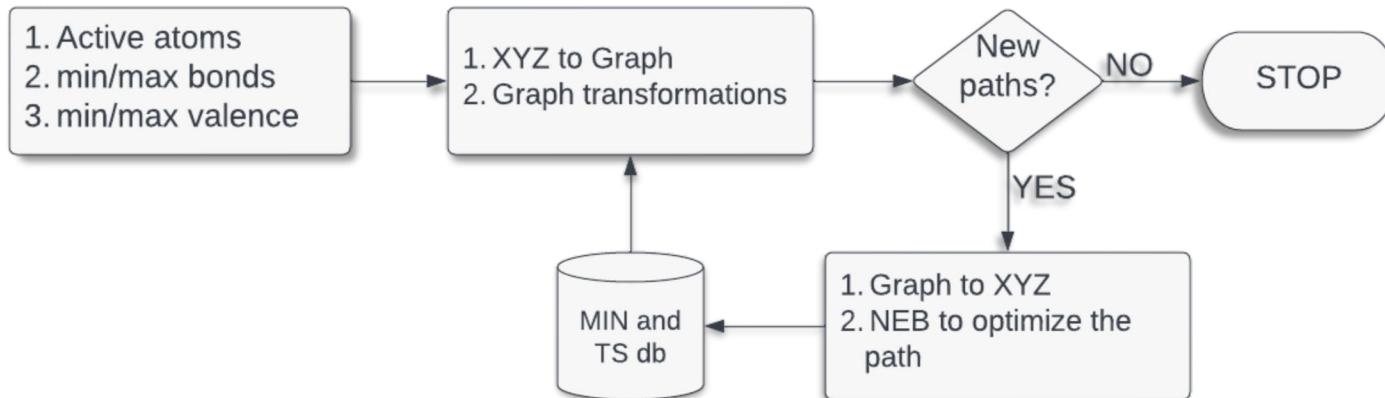


# ChemKnow module

J Comput. Chem. 2021, 42, 2036



## Graph space



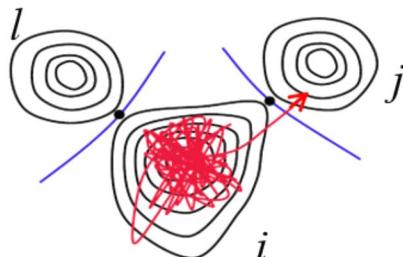
## Workflow

# Semi-automated kinetics

## Automated

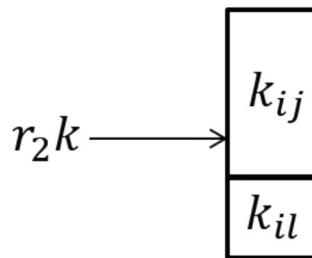
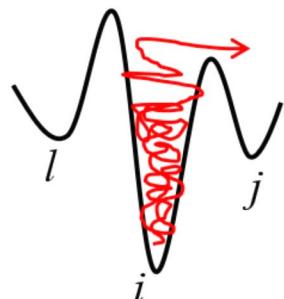
$$k(T) = \sigma \frac{k_B T}{h} e^{-\frac{\Delta G^\ddagger}{RT}}$$

$$\frac{d\mathbf{n}(t)}{dt} = \mathbf{M}\mathbf{n}(t)$$



$$t = -\frac{1}{k} \ln(r_1)$$

$$k = k_{ij} + k_{il}$$



# Semi-automated kinetics

Not automated

**Pilgrim**

<https://github.com/dafarro/Pilgrim>

$$\gamma = \Gamma \kappa$$

$$\Gamma = \frac{Q(T, s^*)}{Q^\dagger(T)} e^{-\beta \Delta E(s^*)}$$

$$\kappa = \frac{\beta \int_0^\infty dE \exp(-\beta E) P(E)}{\exp(-\beta V^{\text{AG}})}$$

## amk\_tools

ACS Phys. Chem. Au **2022**, 2, 225



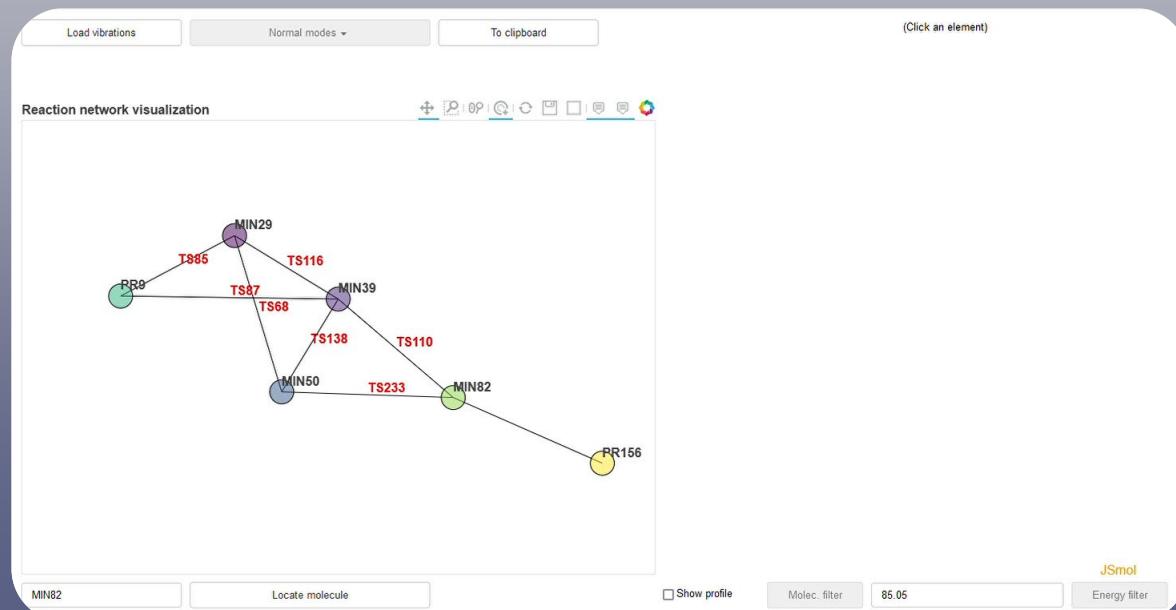
Carles Bo



Diego Garay

- ✓ Interactive HTML
- ✓ Visualize the CRN and energy diagrams

[https://github.com/dgarayr/amk\\_tools](https://github.com/dgarayr/amk_tools)



# Last version: 2021.1137

J. Comput. Chem. 2021, 42, 2036



Pablo  
Tahoces



Roberto  
Rodríguez

- ✓ GitHub & syllabs
- ✓ Web site
- ✓ Notebook



Aurelio  
Rodríguez

<https://rxnkin.usc.es/index.php/AutoMeKin>

The screenshot shows a table with two rows of job information:

ID	Description	Status	Graph	Report	Data	Delete
1952	FA	✓	🕒	🕒	🕒	🕒
1959	your job description here	✓	🕒	🕒	🕒	🕒

Below the table, there is a "New Job" button and an "Acknowledgements" section featuring logos for USC, Xunta de Galicia, and CESGA.

The screenshot shows a browser window displaying the GitHub repository for AutoMeKin. Below the browser is a terminal window showing the following command-line session:

```

git clone https://github.com/automekin/automekin.git
cd automekin
pip install .
python setup.py install
./automekin

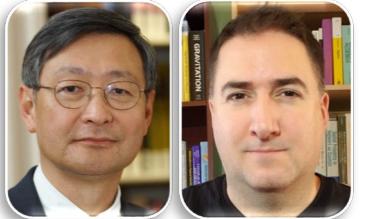
```

The terminal also displays a portion of a script file containing Python code for generating input files for reaction mechanism calculations.

# AutoMeKin: Applications

System	Reference
Pyrolysis of isoprene	Combust. Flame <b>2022</b> , 242, 112206
Fragmentation of indole	ACS Phys. Chem. Au <b>2022</b> , 2, 225
Diglycine and dialanine	JCTC <b>2021</b> , 17, 5556
Photoisomerization of a charged styryl dye	J. Am. Soc. Mass. Spectrom. <b>2021</b> , 32, 284
Formation of formaldehyde in cold astrophysical regions	A&A <b>2021</b> , 656, A148
Fragmentation of octaazapentalene	Monatsh Chem. <b>2021</b> , 152, 421
Syngas oxy-combustion in supercritical CO <sub>2</sub>	J. CO <sub>2</sub> Util <b>2021</b> , 49, 101554
Electron-transfer-induced cleavage in Tryptophan	JPCA <b>2021</b> , 125, 2324
Cycloaddition of cyclic nitrone	Tetrahedron <b>2020</b> , 76, 130764
Ozonolysis of $\alpha$ -pinene	ChemSystemsChem <b>2020</b> , 152, e19002.
vdW interactions	IJQC <b>2019</b> , 119, e26008
Fragmentation of L-Cysteine	JPCA <b>2019</b> , 123, 3685
Thermal decomposition of 1-propanol	JPCA <b>2018</b> , 122, 4790
Tetrahydrofuran oxidation	Combust Flame <b>2018</b> , 191, 252
Photolysis of methyl cyanoformate	ApJ <b>2017</b> , 849, 15
Hydroformylation of ethylene	Chem. Sci. <b>2017</b> , 8, 3843
Fragmentation of protonated uracil	PCCP <b>2016</b> , 18, 22712
Photolysis of acryloyl chloride	PCCP <b>2016</b> , 18, 5019
Photolysis of propenal	PCCP <b>2015</b> , 17, 14912
HCN elimination from vinyl cyanide	PCCP, <b>2015</b> , 17, 6948

- ✓ Atmospheric chemistry.
- ✓ Astrochemistry.
- ✓ Non-covalent interactions.
- ✓ Homogeneous catalysis.

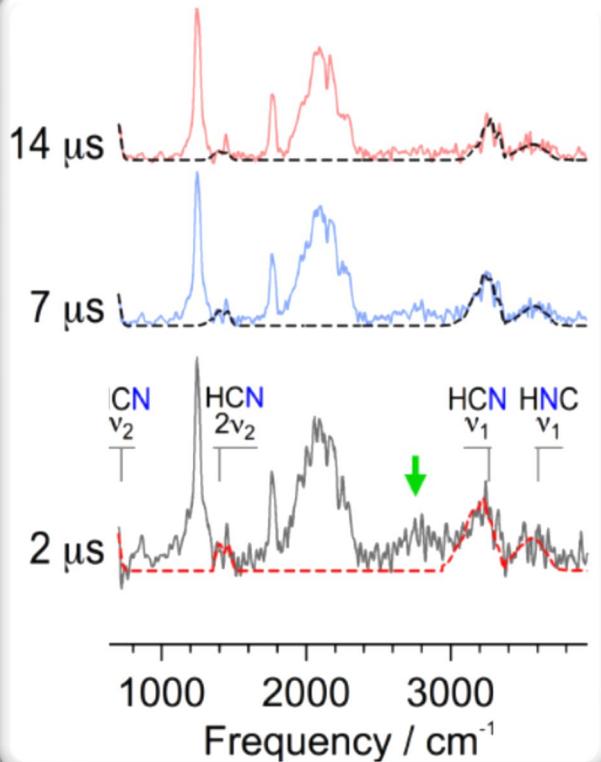


# Photolysis of methyl cyanoformate

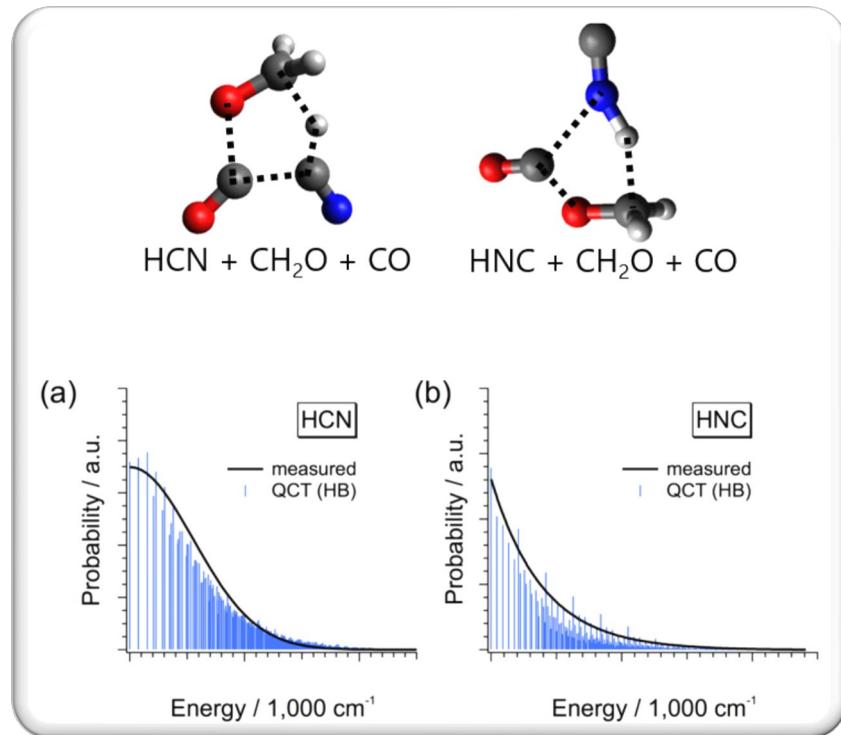
ApJ. 2017, 849, 15

24

**Time-resolved IR spectra**  
Evidence of HCN(HNC) formation



**AutoMeKin & QCT**  
TSs & Vibrational distros



Dani  
Peláez

25

# vdW interactions

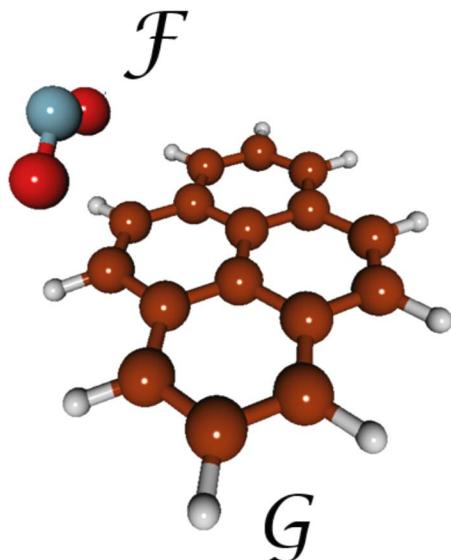
Int. J. Quantum Chem. 2019, 119, e26008

## New A matrix

F: Molecule F

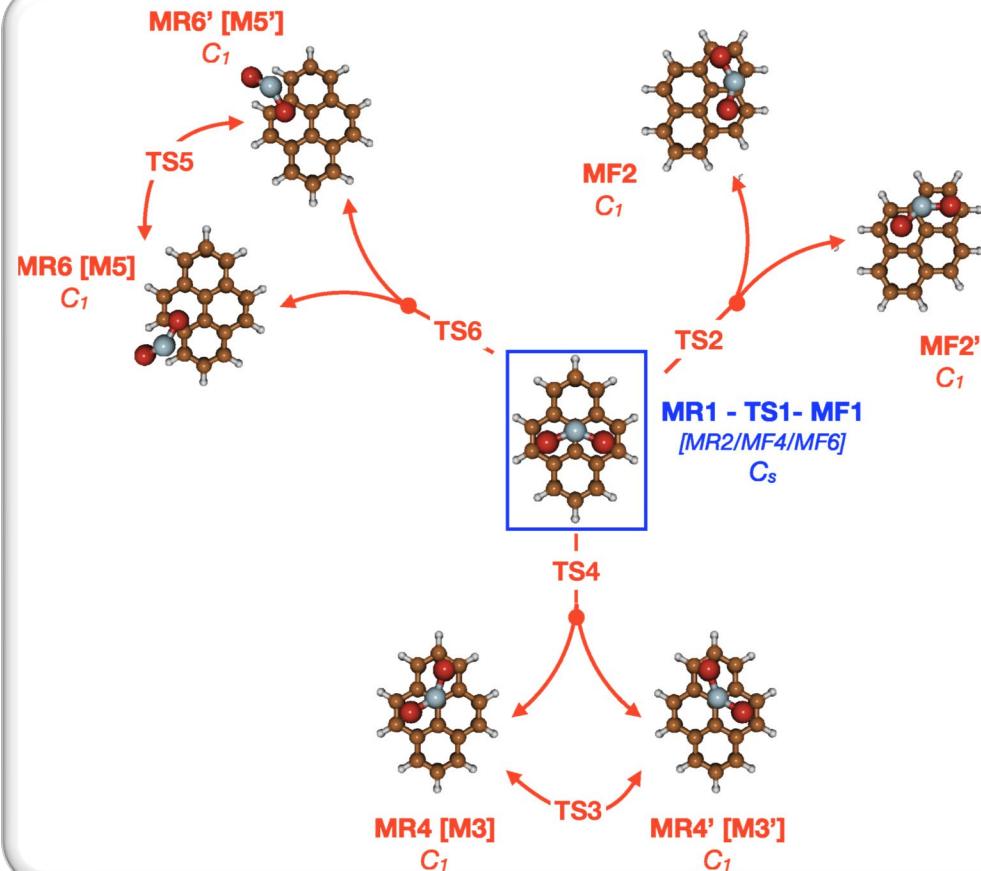
G: Molecule G

$$A = \begin{pmatrix} F & FG \\ FG & G \end{pmatrix}$$



## NO<sub>2</sub>-pyrene

Most stable minimum-energy structures



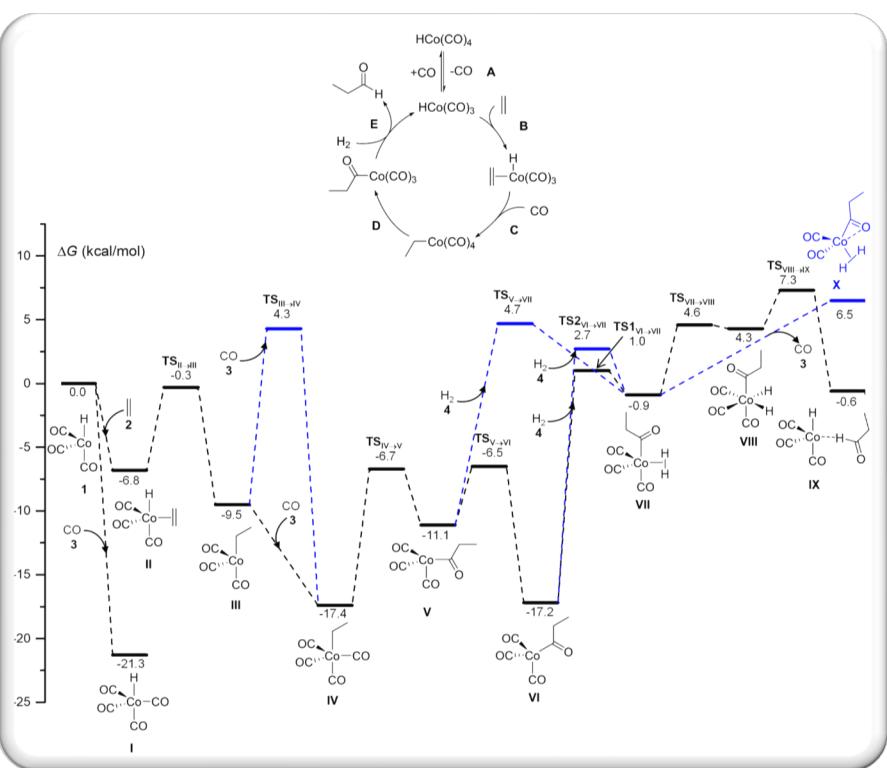
Jesús  
Varela

26

# Hydroformylation of ethylene

Chem. Sci. 2017, 8, 3843

## Reaction mechanism

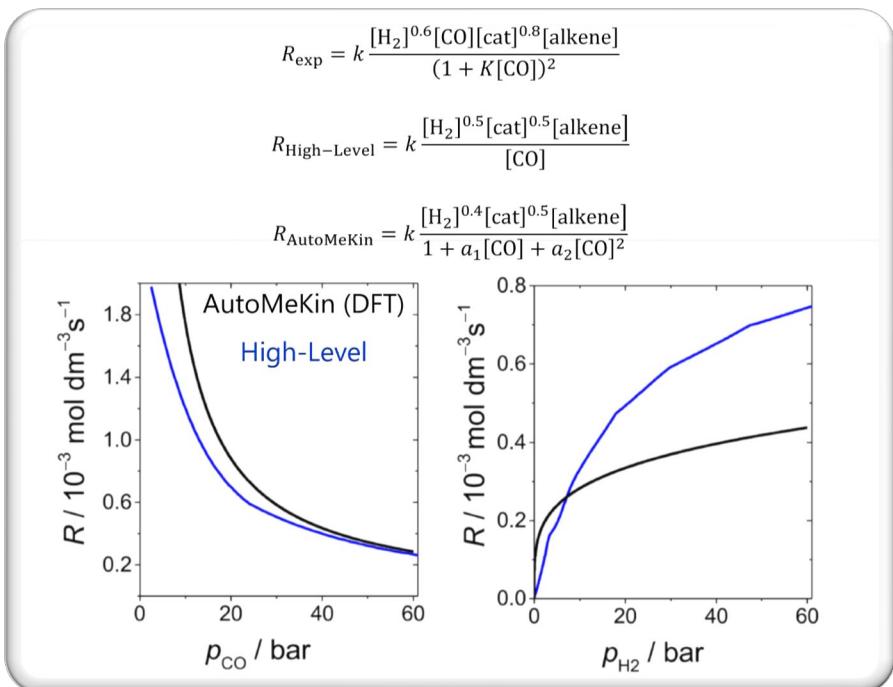


## Rate law

$$R_{\text{exp}} = k \frac{[\text{H}_2]^{0.6} [\text{CO}]^{0.8} [\text{alkene}]}{(1 + K[\text{CO}])^2}$$

$$R_{\text{High-Level}} = k \frac{[\text{H}_2]^{0.5} [\text{cat}]^{0.5} [\text{alkene}]}{[\text{CO}]}$$

$$R_{\text{AutoMeKin}} = k \frac{[\text{H}_2]^{0.4} [\text{cat}]^{0.5} [\text{alkene}]}{1 + a_1[\text{CO}] + a_2[\text{CO}]^2}$$



## Dimerization of C<sub>60</sub>

Carbon 2023, 213, 118209

C<sub>60</sub>+C<sub>60</sub> molecular bonding revisited and expanded

Jorge Laranjeira,<sup>1,\*</sup> Karol Strutyński,<sup>2</sup> Leonel Marques,<sup>1</sup> Emilio Martínez-Núñez,<sup>3</sup> and Manuel Melle-Franco<sup>2,†</sup>

<sup>1</sup>Departamento de Física and CICECO, Universidade de Aveiro, 3810-193 Aveiro, Portugal

<sup>2</sup>Departamento de Química and CICECO, Universidade de Aveiro, 3810-193 Aveiro, Portugal

<sup>3</sup>Departamento de Química Física, Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain

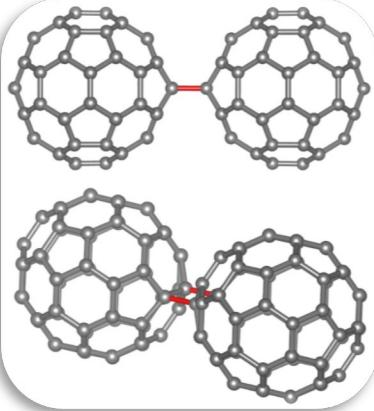


- ✓ DFT with dispersion: TPSS-Def2-TZVPP-D3BJ/B3LYP-6-31G(d,p)-D3BJ
  - ✓ 41 dimers (previously 12).

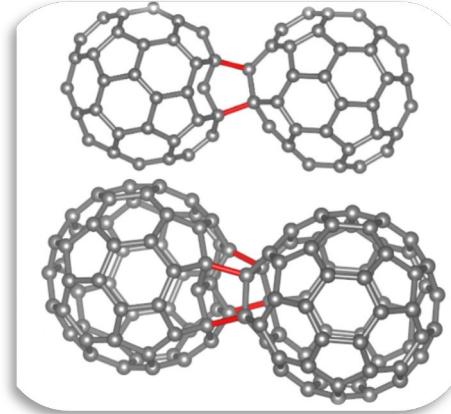
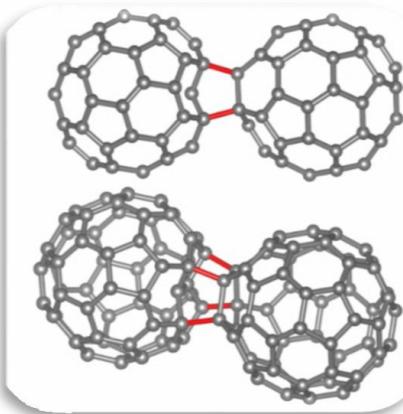
✓ At 298 K C<sub>60</sub> is a van der Waals solid

✓ Subjected to HPHTs molecules bond to each other covalently.

< 8 GPa



> 8 GPa



# Integration within the Cathedral package

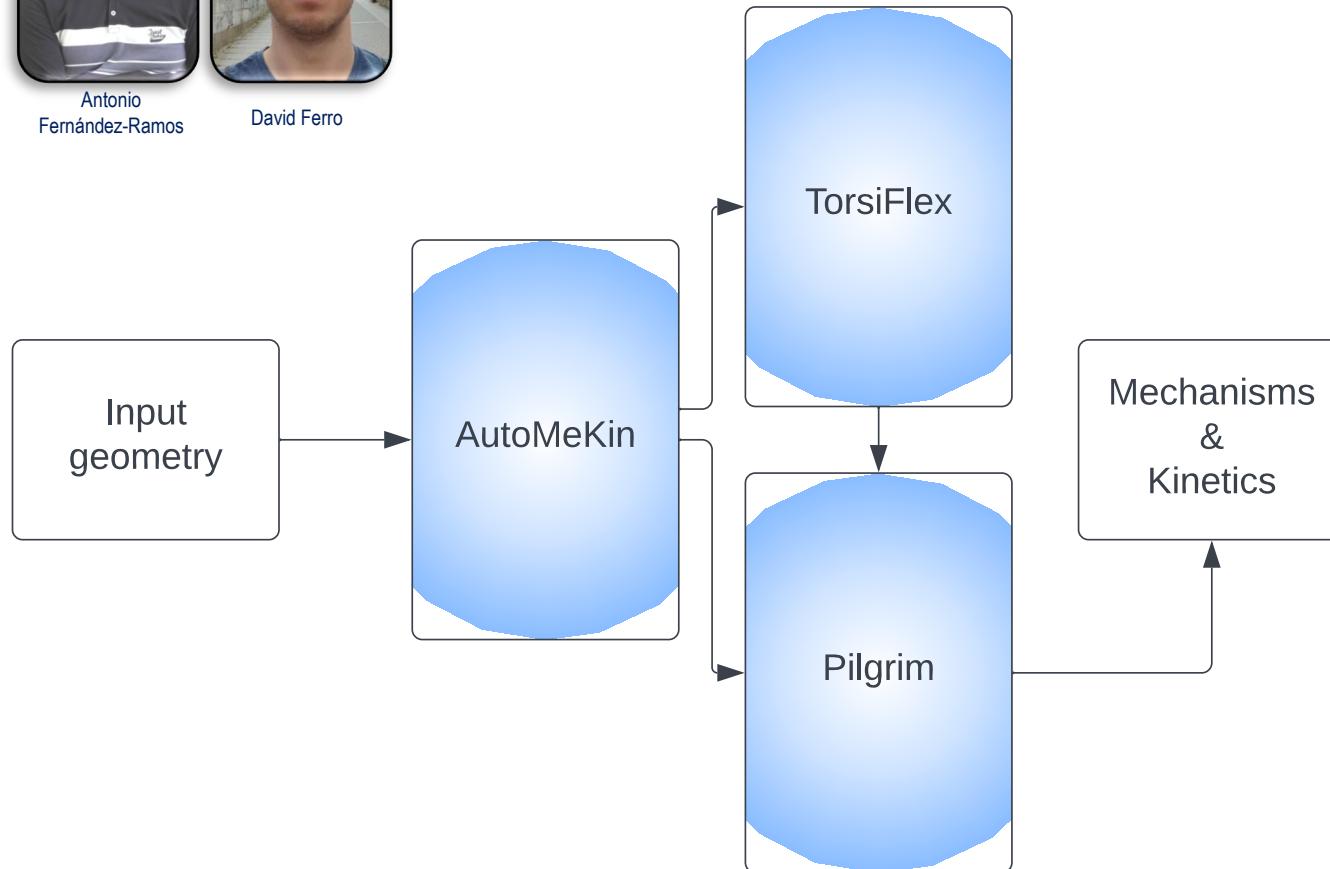


Antonio  
Fernández-Ramos



David Ferro

<https://github.com/cathedralpkg>



## Acknowledgements



George Barnes



Carles Bo



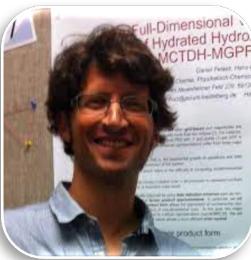
Diego Garay



Dave Glowacki



Sabine Kopec



Dani Peláez



Aurelio Rodríguez



Roberto Rodríguez



Robin Shannon



Pablo Tahoces



Saulo Vázquez