



## **Auto**medated Reaction **Me**chanisms and **Kin**etics

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# Contents

1. Introduction	3
2. How to cite the program	4
3. Installation	4
4. Program execution and running the tests	5
5. Finding reaction mechanisms and solving the kinetics	6
a) Description of the input files	7
b) Running the dynamics in a single processor	14
c) Running the dynamics in multiple processors	15
d) Analyzing the dynamics results	16
e) Running all low-level calculations using a single script	17
f) Running the high-level calculations	18
g) Aborting amk calculations	19
h) Directory tree structure of <code>wrkdir</code>	20
i) Relevant information	20
j) Details of the kinetics simulations	26
6. Other capabilities	28
a) van der Waals complexes	28
b) Scanning dihedral angles	30
c) Fragmentation	31
d) Advanced options	32
e) Biased dynamics	37
7. Summary of all keywords and options	40
8. References	43

## 1. Introduction

AutoMeKin (amk) program package has been designed to discover reaction mechanisms and solve the kinetics in an automated fashion, using chemical dynamics simulations. The basic idea behind this program is to obtain transition state (TS) guess structures from trajectory simulations performed at very high energies or temperatures. From the obtained TS structures, minima and product fragments are determined following the intrinsic reaction coordinate (IRC). Then, with all the stationary points, the reaction network is constructed. Finally, the kinetics is solved using the Kinetic Monte Carlo (KMC) method.

The program is interfaced with MOPAC2016, Qcore and Gaussian 09 (G09), but work is in progress to incorporate more electronic structure programs.

This tutorial is thought to guide you through the various steps necessary to predict reaction mechanisms and kinetics of unimolecular decompositions. To facilitate the presentation, we consider, as an example, the decomposition of formic acid (FA). The present version of the program can also be used to study homogeneous catalysis, but additional refinements are needed to make the code more general and user-friendly. This capability will be fully incorporated and described in the next released. Users are encouraged to read references 1-2 before using AutoMeKin package.

The present version has been tested on CentOS 7, Red Hat Enterprise Linux and Ubuntu 16.04.3 LTS. If you find a bug, please report it to the main developer ([emilio.nunez@usc.es](mailto:emilio.nunez@usc.es)). Comments and suggestions are also welcome.

## 2. How to cite the program

If you use **AutoMeKin2021**, please cite the following publications:

- 1) [Martinez-Nunez, E. et al. \*J. Comput. Chem.\*, \*\*2021\*\*, \*42\*, 2036-2048.](#)
- 2) [Martinez-Nunez, E. \*J. Comput. Chem.\* \*\*2015\*\*, \*36\*, 222–234.](#)
- 3) [Martinez-Nunez, E. \*Phys. Chem. Chem. Phys.\* \*\*2015\*\*, \*17\*, 14912–14921.](#)
- 4) MOPAC2016, Version: 16.307, James J. P. Stewart, Stewart Computational Chemistry, web-site: [HTTP://OpenMOPAC.net](http://OpenMOPAC.net).

If you use the older version **tsscads2018**, please cite, instead of ref 1 above, the following one:

- 1) [Rodriguez, A. et al. \*J. Comput. Chem.\*, \*\*2018\*\*, \*39\*, 1922–1930.](#)

If Entos Qcore code is employed for the low-level calculations, you must cite:

[Manby, F. R. et al., ChemRxiv.7762646 \(2019\). DOI: 10.26434/chemrxiv.7762646.v2](#)

If the vdW sampling is employed, you must cite this publication

[Kopec, S. et al. \*Int. J. Quantum Chem.\* \*\*2019\*\*, \*119\*, e26008](#)

If the BXDE sampling is employed, you must cite the following two publications:

- 1) [Hjorth Larsen, A. et al. \*J. Phys. Condens. Matter\*, \*\*2017\*\*, \*29\*, 273002](#)
- 2) [Jara-Toro, R. A. et al. \*ChemSystemsChem\* \*\*2020\*\*, doi: 10.1002/syst.201900024.](#)

If you publish the statistics of the reaction network, NetworkX python library must be cited as well:

[Hagberg, A. A.; Shult, D. A.; Swart, P. J. In Exploring network structure, dynamics, and function using NetworkX, 7th Python in Science Conference \(SciPy2008\), Pasadena, CA USA, Varoquaux, G.; Vaught, T.; Millman, J., Eds. Pasadena, CA USA, 2008; pp 11-15.](#)

Finally, if you use the post-processing analysis bots, the following reference must be cited:

[Hutchings M. et al., \*J. Chem. Theory Comput.\* \*\*2020\*\*, \*16\*, 1606-1617](#)

## 3. Installation

To install the program follow the instructions given in the [Wiki](#)

The recommended option is to use an [auto-installer](#) script, which eases the burden of installing third-party packages. The script installs singularity and downloads the latest container image from [sylabs](#). An instance of the container is started using a sandbox image deployed under `$(TMPDIR-/tmp)` folder. The container comes with all AutoMeKin's tools installed in `$AMK`

## 4. Program execution and running the tests

To start using any of the scripts described below, you have to load the amk/2021 module (unless you use singularity):

```
module load amk/2021
```

After loading the module, you may want to run tests taken from the [examples](#) folder. Run the following script to run all tests:

```
run_test.sh
```

**Note that each test takes from a few seconds to several minutes.** The results of each test will be gathered in a different directory.

If you want to run a subset of tests use the following:

```
run_test.sh --tests=FA, FATHERmo
```

which will run FA and FATHERmo tests only. These are the tests available in this version: assoc, assoc\_qcore, rdiels\_bias, diels\_bias, FA\_biasH2, FA\_biasH2O, FA\_bxde, FA\_singletraj, FA, FATHERmo, FA\_programopt, vdW, FA\_ck, FA\_qcore, FA\_bxde\_qcore and ttors.

## 5. Finding reaction mechanisms and solving the kinetics

The first step in our strategy for finding reaction mechanisms involves running classical trajectories, using MOPAC2016 or Entos Qcore. The trajectories sample the potential energy surface at the selected semiempirical level (the default is PM7), and AutoMeKin locates transition states by using the bond breaking/formation search (BBFS) algorithm described in the amk papers.<sup>1-2</sup> Then, reactants and products connected by the transition states (TSs) are obtained by intrinsic reaction coordinate (IRC) calculations. Finally, a reaction network is constructed with all the elementary reactions predicted by the program. To increase the efficacy of AutoMeKin, this process may be carried out in an iterative fashion as described in reference <sup>1</sup>. Once the reaction network has been predicted at the semiempirical level, the user can calculate rate constants for all the elementary reactions and run Kinetic Monte Carlo (KMC) calculations to predict the time evolution of all the chemical species involved in the global reaction mechanism and to calculate product ratios.

All the above steps can be run in an automatic fashion, using a single script as described below. However, AutoMeKin allows you the possibility to run the steps separately. This is important for checking purposes and, particularly, for the screening of structures, since you may need to adjust the screening parameters to your system (see below).

In a subsequent step, the collection of TSs located at the semiempirical level are reoptimized using a higher level of electronic structure theory. Notice that, depending on the selected level of theory, the total number of reoptimized TSs may differ from that obtained with the semiempirical Hamiltonian. For each reoptimized TS, IRC calculations are performed to obtain the associated minima (reactant and products). The reaction network is then constructed for the high level of theory. As for the low-level computations, the last step involves the calculation of rate constants and product ratios. As detailed below, all the high-level steps can be run separately, employing different scripts, or in an automatic way, using a single script. At present, all the high-level electronic structure calculations are performed with the G09 program.

To follow the guidelines of this tutorial, you can try the formic acid (FA) test case that comes with the distribution. Make a working directory ([wrkdir](#)) and copy files FA.dat and FA.xyz from [path\\_to\\_program/examples](#) to your [wrkdir](#). All scripts (described below) must be run from your [wrkdir](#).

**CAVEAT:** use short names for the [wrkdir](#) and the input files. Good choices are short acronyms (using capital letters) like FA for formic acid.

a) Description of the input files

The following are files read by amk, and therefore, they must be present in [wrkdir](#).

**name.xyz** (FA.xyz in our example), where name refers to the name for our system; the recommendation is to use acronyms like FA for Formic Acid or short names. This file contains an initial input structure of our system in XYZ format:

5			
C	0.000000	0.000000	0.000000
O	0.000000	0.000000	1.220000
O	1.212436	0.000000	-0.700000
H	-0.943102	0.000000	-0.544500
H	1.038843	0.000000	-1.634005

Please provide here a stable conformer of the reactant molecule. A general recommendation is to provide here a structure previously optimized with the method selected with the keyword `LowLevel` (or eventually `LowLevel_TSopt`). **If your input structure is fragmented, then, kinetics results (if available) are meaningless. In this case you should use biased MD to smash together the fragments and obtain a TS for the bimolecular process, like in the diels\_alder example.**

**This file is mandatory except for association and vdW samplings** where two XYZ files are needed instead ([see below](#)).

**name.dat** (where name can be anything, from just the name of the system to something that identifies the type of calculation you are carrying out; in our case FA.dat). This file contains all parameters of the calculation and has different sections, which are explained as follows. **This file is mandatory in all cases.**

The file name.dat is organized in four sections: `General`, `Method`, `Screening` and `Kinetics`, which are explained in detail below. Each section contains lines with several “**keyword value(s)**” pairs with the following syntax:

**keyword value(s)**

**keyword** is a case-sensitive string and it must be the first field of the line.

**value(s)** can be strings, integers or floats and is/are the value(s) of the keyword: **value(s)[keyword]**.

**At least one blank space must be kept between keyword and value(s).** A few keywords include some additional lines right below the keyword line (see [Biased dynamics](#)).

Below you will find a detailed explanation of the keywords grouped together in the different sections. For each section, only the most important keywords are described. Additional keywords can be found in [Advanced options](#).

**General.** In this section the electronic structure details are provided. The following is an example of the keywords employed in this section for the FA.

```
--General--
molecule      FA
LowLevel       mopac pm7
HighLevel      g09 b3lyp/6-31G(d,p)
HL_rxn_network complete
IRCpoints      30
charge         0
mult           1
```

List of “**Keyword** value(s)” for this section:

**molecule** value

[value is one string with no blank spaces; **mandatory keyword**]

value is the name of the system and **it must match the name of the XYZ file without the extension** (FA in our example). **For association and vdW sampling there is no XYZ file at the beginning and value[molecule] is just the name of the system.**

**LowLevel** values

[two values: two strings; the second string accepts blank spaces; default values: mopac pm7]

The first value is the program and the second the semiempirical method. So far, qcore and mopac are valid programs. For qcore only xtb method is implemented, and for mopac, any of the semiempirical methods of MOPAC2016 can be employed to run the MD simulations. You can use a combination of MOPAC keywords.

If you do not employ the keyword `LowLevel_TSopt`, explained below in [advanced options](#), both the low-level TS optimizations and MD simulations are carried out using the semiempirical method specified by the second value. This is in general a good choice both in terms of efficacy and efficiency, and also because all structures will be re-optimized later using ab initio/DFT methods as specified with the keyword `HighLevel`.

However, if you know that semiempirical methods do not work well for your system, and although they are going to be employed for the MD sampling (there is no other choice at the moment), you can still pick one of the ab initio/DFT methods already at this stage for the TS optimizations using the keyword `LowLevel_TSopt` explained below in [advanced options](#). However, note that this will be much more CPU time consuming.



**HighLevel** [two values: two strings; no blank spaces in each string; **mandatory keyword except for association**]

The first value is the program (g09 or qcore are the possible choices) and the second indicates the level of theory employed in the high-level calculations. For gaussian, you can employ a dual-level approach, which includes a higher level to refine the energy, as shown in the following example:

```
HighLevel g09 ccSD(t)/6-311+G(2d,2p)//b3lyp/6-31G(d,p)
```

For gaussian, supported methods are HF, MP2 and DFT for geometry optimizations and HF, MP2, DFT and CCSD(T) for single point energy calculations.

For qcore, the method is specified in an additional file named qcore\_template. An example of such file is given in the FA\_qcore example. This option also allows an extra keyword: hessianmethod, which could accept the values 'analytic' or 'semianalytic'.

**HL\_rxn\_network** value(s)

[one or two values: first is a string, and second (if present) is an integer; default value: reduced]

The first value can be complete or reduced. The value complete indicates that all the TSs will be reoptimized and in this case no second value is needed.

Alternatively, you may use reduced as the first value (the default), followed by a second value (an integer) which indicates the maximum energy (in kcal/mol and relative to the reference starting structure) of a transition state to be calculated at the high level.

**IRCpoints** value

[value is an integer; default value: 100]

value is the maximum number of IRC points (in each direction) computed at the high-level. Note that g09 calculations need much fewer points than Entos Qcore.

**charge** value

[value is an integer; default value: 0]

value is the charge of the system.

## Memory value

[value is an integer; default value: 1]

value is the number of GB of memory employed in the gaussian high-level calculations.

## mult value

[value is an integer; default value: 1]

value is the multiplicity of the system. Note that this keyword is only employed in the HL calculations. If you want to run the LL calculations with a specific multiplicity, this should be specified in the **LowLevel** keyword using any of the possibilities that [MOPAC offers](#).

**Method.** Here the user provides details of the method employed for sampling structures. In our FA example, we have the following:

```
--Method--
sampling MD
ntraj 10
```

List of “**Keyword** value(s)” for this section:

## sampling value

[value is one string with no blank spaces; default value: MD]

value can be: **MD**, **MD-micro**, **BXDE**, **external**, **ChemKnow**, **association** and **vdW**

**MD** and **MD-micro** refer to the type of initial conditions used to run the MD simulations. **MD-micro has not been implemented yet for qcore** With **BXDE** the rare-event acceleration method named BXDE is invoked.<sup>3</sup> The BXDE module employs the “Atomistic Simulation Environment” (ASE) library of Python,<sup>4</sup> which must be referenced whenever **BXDE** is employed.

**MD** allows the user to include partial constraints in the trajectories, which may be useful for large systems (see the “advanced users” section for more details).

**external** allows trajectory data to be read from the results of an external (MD) program. The trajectory data (in XYZ format) must be stored in a directory named **coordir** using one file per trajectory which should be called `name_dynX.xyz`, where `name` is `value[molecule]`, and `X` is the number of each trajectory ( $X = 1 - ntraj$ ). The keyword `ntraj` must be set accordingly.

**ChemKnow** makes all possible combinations of bond breakages/formations which are consistent with preset valencies of the atoms and with products lying below the maximum energy of the system. Once the combinations are known, the starting and ending points are obtained after a constrained MD simulation with external forces applied to break/form the selected bonds. Then, a NEB calculation tries to obtain a path connecting both states, and the highest point of the NEB is subjected to TS optimization. This sampling does not need to include the number of trajectories and **has not been implemented yet for qcore**.

**CAVEAT:** To use **MD-micro** the initial structure needs to be fully optimized and a frequency calculation can not afford imaginary frequencies. Otherwise choose **MD**

**association** and **vdW** are employed to sample van der Waals structures, present some peculiarities and therefore are explained in detail in [van der Waals complexes](#).

MD, MD-micro, external and BXDE samplings accept the following keywords (ChemKnow also accepts the keyword **neighbors**):

#### **barrierless** value

[value is one string: yes or no; default value: no]

value can be yes, in which case barrierless processes are searched. The keyword **neighbors** explained below is related to this one.

#### **neighbors** values

[three values: first is a string and last two are floats; default values (see table below)]

The first value is an atomic symbol and the two numbers are the minimum and maximum number of neighbors of the corresponding atoms. This keyword is needed if atoms other than those in the table below are present in your system and/or if you want to change the default values. The number of neighbors is employed to locate **barrierless processes** and are also employed by **ChemKnow**. For instance, if you want to consider dissociations leading to atomic hydrogen, you must add the following line:

```
neighbors H 0 1
```

The default values are listed in this table:

Atom	Min # of neighbors	Max # of neighbors	Atom	Min # of neighbors	Max # of neighbors
H	1	1	Mg	0	2
Li	0	1	Al	1	3

Be	0	2	Si	1	4
B	1	3	P	1	5
C	1	4	S	1	6
N	1	3	Cl	0	1
O	1	2	Br	0	1
F	0	1	I	0	1
Na	0	1			

### ntraj value

[value is an integer; default value: 1]

value is the number of trajectories. We strongly recommend here to avoid using big numbers of trajectories. Instead, the user should try to run different batches of trajectories as indicated below with a small number of trajectories each one. One trajectory is recommended for BXDE.

### seed value

[value is an integer; **only valid for MD and MD-micro**; default value: 0]

value is the seed of the random number generator. It can be employed to run a test trajectory. See the FA\_singletraj.dat file in the examples. **Only use this keyword for testing.**

**Screening.** Some of the initially located structures might have very low imaginary frequencies, be repeated or correspond to transition states of van der Waals complexes formed upon fragmentation of the reactant molecule. To avoid or minimize low-(imaginary)frequency structures, redundancies and van der Waals complexes, amk includes a screening tool, which is based on the following descriptors: energy, SPRINT coordinates,<sup>5</sup> degrees of each vertex and eigenvalues of the Laplacian matrix.<sup>1</sup> While the lowest eigenvalues of the Laplacian (eigL) are employed to discriminate fragmented structures, comparing the descriptors for any pair of structures, a mean absolute percentage error (MAPE) and a biggest absolute percentage error (BAPE) are obtained.

In this section we set a minimum value for the imaginary frequency and maximum values for MAPE, BAPE and eigL, as explained below:

```
--Screening --
imagmin 200
MAPEmax 0.008
BAPEmax 2.5
eigLmax 0.1
```

List of “**Keyword** value(s)” for this section:

### **imagmin** value

[value is an integer; default value: 0]

value is the minimum value for the imaginary frequency (in absolute value and  $\text{cm}^{-1}$ ) of the selected TS structures. Discarded structures will be stored in `tsdirLL_molecule/LOW_IMAG_TSs` to allow the user inspection of the rejected TSs.

### **MAPEmax** value

[value is a float; default value: 0]

value is the maximum value for MAPE.

### **BAPEmax** value

[value is a float; default value: 0]

value is the maximum value for BAPE.

If both, the MAPE and BAPE values calculated for two structures are below the values of MAPEmax and BAPEmax, respectively, the structures are considered equivalent, and therefore only one is kept.

As a general advice, `value[MAPEmax]` and `value[BAPEmax]` should be small. A good starting point could be the values provided in the input files of the examples. Since the HL calculations (performed with G09) have much more stringent tests for optimization than those of MOPAC, in the screening of the HL structures, `value[MAPEmax]` and `value[BAPEmax]` are set to  $\text{MIN}(\text{MAPEmax}, 0.001)$  and  $\text{MIN}(\text{BAPEmax}, 1)$ , respectively.

### **eigLmax** value

[value is a float; default value: 0]

value is the maximum value for an eigL to be considered 0. In Spectral Graph Theory, the number of zero eigLs provides the number of fragments in the system. This criterion is used to identify van der Waals complexes that are formed by unimolecular fragmentation.

**Kinetics.** This part is employed to provide details for the kinetics calculations at the (experimental) conditions you want to simulate. **This section is compulsory except for association.**

An example is given as follows.

```
--Kinetics--  
Energy 150
```

The kinetics simulations will be carried out for a canonical (fixed temperature) or microcanonical (fixed energy) ensemble, which have their associated keywords:

List of “**Keyword** value(s)” for this section:

### **Energy** value

[value is an integer; default value: 0]

value is the energy (in kcal/mol) for which microcanonical rate coefficients will be calculated.

### **Temperature** value

[value is an integer; default value: 298]

value is the temperature (in K) for which thermal rate coefficients will be calculated. At present, temperatures below 100 K are not allowed.

## b) Running the dynamics in a single processor

MD and MD-micro methods provide initial coordinates and momenta to run accelerated dynamics simulations. Select the number of trajectories with `ntraj` and remember to avoid the `seed` keyword if the number of trajectories is greater than 1. In you want to run 10 trajectories, your Method section should look like (remember that the `amk/2021` module must be loaded):

```
--Method--  
sampling MD-micro  
ntraj 10
```

The dynamics can be run either in a single processor or in parallel. To run trajectories in a single processor use the `amk.sh` script:

```
amk.sh FA.dat > amk.log &
```

The output file `amk.log` provides information about the calculations. In addition, a directory called `tsdirLL_FA` is created, which contains information that may be useful for checking purposes. We notice that the program creates a symbolic link to the `FA.dat` file, named `amk.dat`, which is used internally by several `amk` scripts. At any time, you can check the transition states that have been found using:

```
tsll_view.sh
```

The output of this script will be something like this:

ts #	File name	w_imag	Energy	w1	w2	w3	w4	traj #	Folder
2	ts2_batch4	1588i	-35.7105	206	438	461	727	1	batch4
3	ts3_batch2	458i	-78.1007	573	846	1034	1195	3	batch2
4	ts4_batch6	2010i	-17.6124	327	473	523	1078	1	batch6

where the first column is the label of each TS, the second is the filename of the optimized TS structure (located in the `tsdirLL_FA` directory), the third is the imaginary frequency (in  $\text{cm}^{-1}$ ), the fourth one is the absolute energy of the TS (in kcal/mol for MOPAC2016 and Hartrees for qcore and gaussian) and the next four numbers are the four lowest vibrational frequencies (in  $\text{cm}^{-1}$ ). Finally, the last two columns are the trajectory number and the name of the folder where the accelerated dynamics were run.

**CAVEAT:** since the dynamics employ random number seeds, the above results may differ from those obtained in your computer.

As already mentioned, the MOPAC2016 output files of the optimized TSs are stored in `tsdirLL_FA`. You can use a visualization program (e.g., Molden) to analyze your results. Try, for instance:

```
molden tsdirLL_FA/ts1_FA.out
```

You can also watch the animation of trajectories, which are stored in the `coordir` folder inside `wrkdir`:

```
molden coordir/FA_dyn1.xyz
```

We notice that the `coordir` folder is temporary. It is removed during the execution of a subsequent script.

### c) Running the dynamics in multiple processors

If you have access to several processors and want to run the dynamics in parallel, you can use the script `amk_parallel.sh`, which is executed interactively (a Zenity progress bar will appear on the screen). For instance, to submit 50 trajectories split in 5 different tasks (10 trajectories each) you should use:

```
amk_parallel.sh FA.dat 5
```

This will create temporary directories `batch1`, `batch2`, `batch3`, `batch4` and `batch5` that will be removed when the IRCs are calculated. Each of these folders includes a `coordir` directory, which contains the individual trajectories. The TSs found in each individual task will be copied in the same folder, `tsdirLL_FA`, and, as indicated above, using the `tsll_view.sh` script you can monitor the progress of the calculations. Notice that the total number of trajectories is given by `value[ntraj]` multiplied by the number of tasks. We recommend running the `amk_parallel.sh` script interactively only for checking

purposes, and particularly to carry out the screening. To run many trajectories for production, we recommend using the `llcalcs.sh` script, which is described below.

If the Slurm Workload Manager is installed on your computer, you can submit the jobs to Slurm using:

```
sbatch [options] amk_parallel.sh FA.dat ntasks
```

where `ntasks` is the number of tasks. If no options are specified, `sbatch` employs the following default values:

```
#SBATCH --output=amk_parallel-%j.log
#SBATCH --time=04:00:00
#SBATCH -c 1 --mem-per-cpu=2048
#SBATCH -n 8
```

These values can be changed when you submit the job with *options*.

**CAVEAT:** if you use Slurm Workload Manager for the `amk_parallel.sh` script, you will have to wait until all tasks are completed before going on.

#### d) Analyzing the dynamics results

1) The `amk` package includes the `irc.sh` script, which performs intrinsic reaction coordinate calculations for all the located TSs. This script also allows one to perform an initial screening of the TS structures before running the IRC calculations:

```
irc.sh screening
```

This will do the screening and stop. The process involves the use of tools from Spectral Graph Theory and utilizes `value[MAPEmax]`, `value[BAPEmax]` and `value[eigLmax]`. The redundant and fragmented structures are printed on screen as well as in the file `screening.log` which is located in `tsdirLL_FA`. MOPAC2016 output files are also gathered in `tsdirLL_FA`, and use filenames initiated by “REPEAT” and “DISCNT”, which refer to repeated and disconnected (i.e., fragmented) structures, respectively. Please check these structures and, if needed, change the above parameters. Should you change some of the above parameters (`value[MAPEmax]`, `value[BAPEmax]`, `value[eigLmax]`), you need to redo the screening with the new parameters:

```
redo_screening.sh
```

You can repeat the above process until you are happy with the screening.

Once you are confident with the threshold values, you can submit many trajectories to carry out a thorough exploration of the potential energy surface. Subsequently, you can proceed with the IRC calculations.



2) Obtaining the IRCs:

```
(sbatch [options]) irc.sh
```

3) Optimizing the minima:

```
(sbatch [options]) min.sh
```

4) Creating the reaction network:

```
rxn_network.sh
```

Once you have created the reaction network, you can grow your TS list by running more trajectories (with [amk\\_parallel.sh](#) or [amk.sh](#)). Now the trajectories will start from the newly generated minima as well as from the main structure, specified in the name .xyz file. It is important to notice that, in general, trajectories run in separate batches (i.e., performed in several tasks) may be initialized from different minima and will have different energies. In this regard, the efficiency of the code may increase if the calculations are submitted using a large number for the ntasks parameter.

Convergence in the total number of TSs can be checked doing:

```
track_view.sh
```

When you are happy with the obtained TSs or you achieve convergence, you can proceed with the next steps.

5) Solving the

6) using KMC with the parameters given in the kinetics section:

```
kmc.sh
```

7) Gathering all relevant information in folder [FINAL\\_LL\\_FA](#):

```
final.sh
```

This folder will gather all the relevant information data, which are described below.

e) Running all low-level calculations using a single script

All the above steps can be done automatically using a single script, called [llcalcs.sh](#). To run this script on a workstation with the GNU Parallel tool, type

```
nohup llcalcs.sh name.dat ntasks niter runningtasks >llcalcs.log 2>&1 &
```

where `ntasks` is the number of tasks for `amk_parallel.sh`, `niter` is the number of amk iterations, and `runningtasks` is the number of simultaneous tasks (useful if the workstation is shared by several users). The script can be run without the arguments (i.e., `name.dat`, `ntasks`, `niter` and `runningtasks`), and two pop-up windows will help you enter the arguments.

Finally, if your computer system has the Slurm job scheduler, you can submit the calculations as follows:

```
SBATCH l1calcs.sh name.dat ntasks niter
```

**CAVEAT:** the use of `l1calcs.sh` is highly recommended once you have verified that the screening process works fine for your system.

#### f) Running the high-level calculations

Once the the low-level calculations have been completed, the user can perform the high-level computations, which use the G09 program. These include the optimization of TSS, IRC calculations, optimization of minima and products, construction of the reaction network, calculation of rate coefficients and evaluation of the time evolution of the chemical species involved in the global reaction mechanism. All these steps can be performed in an automatic fashion using the `hlcalcs.sh` script, employing the following sentence (for the FA example):

```
nohup hlcalcs.sh FA.dat runningtasks >hlcalcs.log 2>&1 &
```

As for the low-level calculations, the argument `runningtasks` is the maximum number of tasks that can be run simultaneously in your computer. If your computer system has the Slurm job scheduler, the calculations can be submitted in the following way:

```
SBATCH hlcalcs.sh FA.dat
```

Although we recommend using the automatic procedure for the simulation of reaction mechanism and kinetics at the high level, it is possible to perform the calculations step by step, as described next:

1. From your `wrkdir` (FA in the example), run:

```
(SBATCH [options]) TS.sh FA.dat
```

In this case, the default values for a job submitted to Slurm are:

```
#SBATCH --time=04:00:00  
#SBATCH -n 4
```

```
#SBATCH --output=TS-%j.log
#SBATCH --ntasks-per-node=2
#SBATCH -c 12
```

2. The scripts needed to build the reaction network and solve the kinetics are the same as those described above for the *low level* calculations. Namely:

```
(sbatch [options]) IRC.sh
(sbatch [options]) MIN.sh
RXN_NETWORK.sh
KMC.sh
```

Remember that the use of Slurm involves checking that every script has finished before proceeding with the next one.

3. The product fragments are optimized using

```
(sbatch [options]) PRODs.sh
```

**CAVEAT:** Step 3 is mandatory before proceeding to step 4. Run step 3 only when you are sure the first two steps have been successfully completed and you do not need to add more transition states.

4. To make a summary of the calculations in folder [FINAL\\_HL\\_FA](#):

```
FINAL.sh
```

Notice that the high-level calculations also generate the directory [tsdirHL\\_FA](#), which is the counterpart of the [tsdirLL\\_FA](#) folder. Finally, remember that you can use the [kinetics.sh script](#) to calculate rate coefficients and product branching ratios for an energy or temperature different from that specified in the kinetics section of the name.dat file (FA.dat in our example).

g) Aborting amk calculations

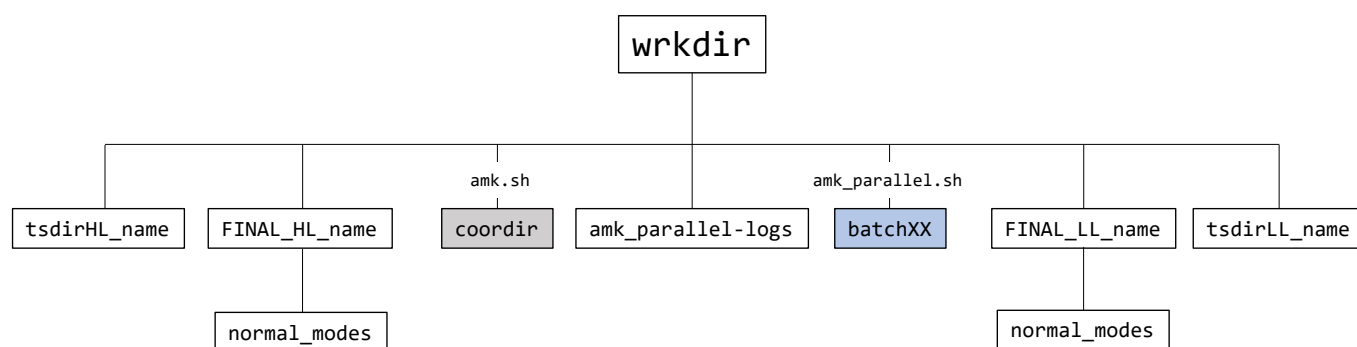
If, for any reason, you want to kill all the calculations, execute the following script from the [wrkdir](#):

```
abort.sh
```

This script kills the processes whose PID are specified in these hidden files: `.parallel.pid` and `.script.pid`. We notice that, if G09 jobs are killed, the read-write files (Gau-####) generated in the Gaussian scratch directory are not removed. The user should do it manually.

## h) Directory tree structure of `wrkdir`

The figure below shows the main folders that are generated in `wrkdir`. Folders `batchXX` (where `XX = 1-tasks`) are generated with `amk_parallel.sh`. This script is also invoked by `llcalcs.sh`, and when that happens these folders are temporary (they are removed at the end of the tasks). Directory `coordir` is only generated in those directories where `amk.sh` is executed. The `amk_parallel-logs` directory contains a series of files that give information on CPU time consumption for the different calculation steps when they were executed with GNU Parallel. Directories `tsdirLL_name` and `tsdir_HL_name` are generated at runtime and employed to generate the final files and directories. For that reason, they should not be removed. Finally, the most important files are gathered in a final directory (`FINALDIR`) which is named after the system's name: `FINAL_level_name` (with `level` being LL for low-level or HL for high level; see figure below).

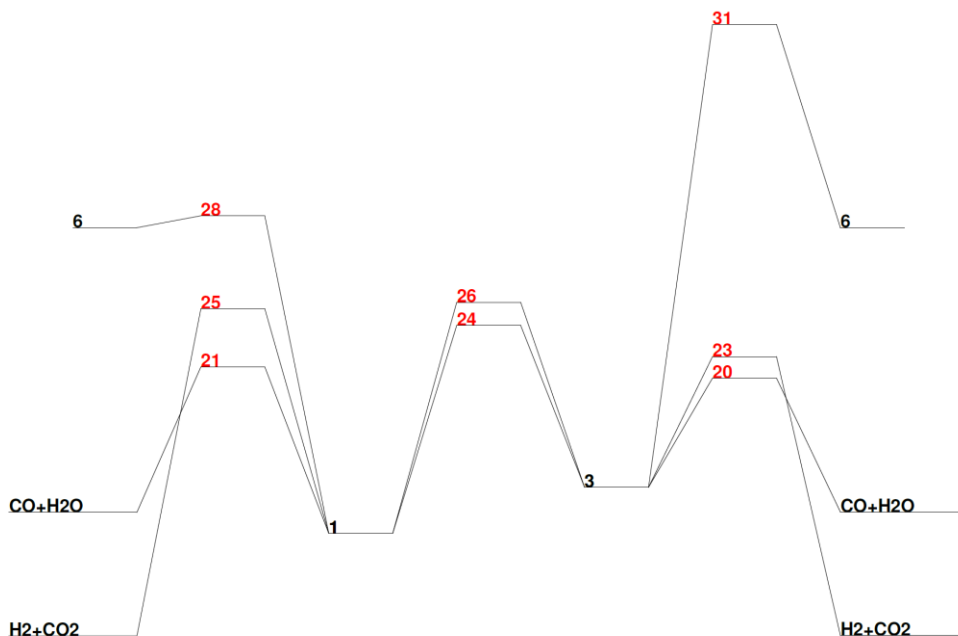


## i) Relevant information

Scripts `final.sh` and `FINAL.sh` are employed to collect all relevant information in `FINALDIR` (`FINAL_LL_FA` and `FINAL_HL_FA` in our example, respectively). These folders contain files as well as a subdirectory called `normal_modes`, which includes, for each structure, a file (in MOLDEN format) with which you can visualize the corresponding normal modes. The files included in these folders are the following.

**convergence.txt** lists the number of located transition states as a function of the number of trajectories and iteration (Only in `FINAL_LL_FA`).

**Energy\_profile.pdf** is an energy diagram with the *relevant paths*, which are those that participate in the dynamics at the conditions of interest. If you change the `value[ImpPaths]` in the kinetics section of the input data (see below), you can incorporate/remove some pathways (the maximum number of TSs in the profile is 100). In our example, the energy diagram is the following:



**frag\_warnings.** contains information on failed ab initio calculations of the fragments. If all calculations are successful, the file is absent. If some of the fragment calculations failed, the file will be located in **FINAL\_HL\_FA** folder.

**MINinfo** contains information of the minima:

MIN #	DE(kcal/mol)
1	-8.341
2	0.000
3	5.288
4	6.732
5	15.441
6	82.122
7	110.400
8	188.254

Conformational isomers are listed in the same line:

1 2  
3 4 5

**TSinfo** contains information of the TSs:

TS #	DE(kcal/mol)
1	-1.624
2	1.868
3	9.644
4	25.135
5	32.821
6	37.608
7	40.956
8	44.037
9	53.173
10	58.156
11	60.015
12	85.659
13	142.228
14	188.765
15	191.650

Conformational isomers are listed in the same line:

In the above files, DE is the energy relative to that of the main structure specified in the FA.dat file (optimized with the semiempirical Hamiltonian). The integers are used to identify, independently, minima and transition states. Notice that, in this example, MIN 2 corresponds to the structure specified in FA.xyz.

**table.db** with table being min, prod and ts, which refer to the minima (intermediates), product fragments and transition states, respectively. These are SQLite3 tables containing the geometries, energies and frequencies of minima, products and TSs, respectively. The different properties can be obtained using the `select.sh` script:

```
select.sh FINALDIR property table label
```

where property can be: natom, name, energy, zpe, g, geom, freq, formula (only for prod) or all, and label is one of the numbers shown in RXNet (see below), which are employed to label each structure. At the semiempirical level, the energy values correspond to heats of formation. For high-level calculations, the tables collect the electronic energies. As an example, to obtain the geometry of the first low-level transition state of FA, you should use:

```
select.sh FINAL_LL_FA geom ts 1
```

**CAVEAT: MOPAC** optimizations of minimum-energy structures (**min**) might not be fully optimized and, consequently, imaginary **frequencies** might arise for minima. Additionally, the frequencies obtained for fragments (**prod**) are meaningless as these structures are not optimized.

**RXNet** contains information of the complete reaction network, that is all the elementary reactions found by the amk program (the file shown below and the following ones were cut and show only up to TS 31).

TS #	DE(kcal/mol)	Reaction path information
====	=====	=====
1	-1.6	PR2: CO + H2O <---> PR2: CO + H2O
2	1.9	MIN 1 <---> MIN 2
3	9.6	MIN 3 <---> MIN 4
4	25.1	MIN 1 <---> MIN 1
5	32.8	PR2: CO + H2O <---> PR1: H2 + CO2
6	37.6	MIN 4 <---> PR2: CO + H2O
7	41.0	MIN 1 <---> PR2: CO + H2O
8	44.0	PR1: H2 + CO2 <---> PR1: H2 + CO2
9	53.2	MIN 1 <---> MIN 4
10	58.2	MIN 2 <---> PR1: H2 + CO2
11	60.0	MIN 2 <---> MIN 5
12	85.7	MIN 2 <---> MIN 6
13	142.2	MIN 3 <---> MIN 6
14	188.8	MIN 2 <---> MIN 8
15	191.7	MIN 7 <---> MIN 8

As can be seen, for each transition state, this file specifies the associated minima and/or product fragments and their corresponding identification numbers. Notice that TS, MIN and PR have independent identification numbers. If you use the option `complete` for the keyword `HL_rxn_network` (in the `General` section of the input data), all the TSs will be reoptimized in the high-level calculations. You may reduce significantly the number of TSs to be reoptimized in the HL calculations, and therefore the reaction network, if you use the option `reduced`. If it is employed without an argument, TSs associated to PR  $\leftrightarrow$  PR steps (i.e., bimolecular reactions) and to interconversion between optical isomers will not be reoptimized in the HL calculations. You may include a number as an argument of this option:

```
HL_rxn_network reduced 55
```

In this case, besides the above TSs, all TSs having relative energies larger than 55 kcal/mol will not be considered for HL optimizations, that is, they will not be included in the HL reaction network. We notice that the last argument must be an integer.

**RXNet.barrless.** Barrierless reactions are included in this file (only when MOPAC and g09 are employed). The user must be aware that the channels are those consistent with the values of the keyword `neighbors` explained above. These channels are not considered in the kinetics, but they are plotted in the complete graph indicated below.

TS #	DE(kcal/mol)	Reaction path information			
====	=====	=====	=====	=====	=====
1	152.8	MIN	1	---->	PR6: HO + CHO
2	170.4	MIN	3	---->	PR7: HO + CHO
3	150.6	MIN	6	---->	PR8: HO + CHO

Note that here TS refers to a dynamical TS and no saddle point exists in these paths.

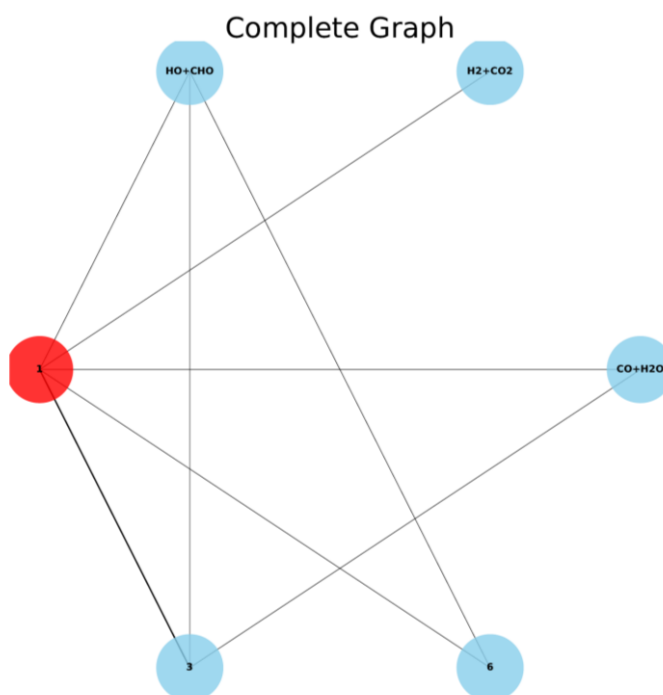
**RXNet.cg.** By default (see below) the KMC calculations are “coarse-grained”, that is, conformational isomers form a single state, which is taken as the lowest energy isomer. Such reaction network, which also removes bimolecular channels, is the following:

TS #	DE(kcal/mol)	Reaction path information			
====	=====	=====	=====	=====	=====
6	37.6	MIN	3	---->	PR2: CO + H2O      CONN
7	41.0	MIN	1	---->	PR2: CO + H2O      CONN
9	53.2	MIN	1	<---->	MIN 3              CONN
10	58.2	MIN	1	---->	PR1: H2 + CO2      CONN
11	60.0	MIN	1	<---->	MIN 3              CONN
12	85.7	MIN	1	<---->	MIN 6              CONN
13	142.2	MIN	3	<---->	MIN 6              CONN
14	188.8	MIN	1	<---->	MIN 8              DISCONN
15	191.7	MIN	7	<---->	MIN 8              DISCONN

The last column with the flag “CONN” or “DISCONN” indicates whether the given process is connected with the others (CONN) or whether it is isolated (DISCONN). This flag is useful when you choose a starting intermediate for the KMC simulations, because that intermediate should be connected with the others. If you want to include all conformational isomers explicitly in the KMC simulations, you need to construct the reaction network by using the `allstates` option, as described in the next section.

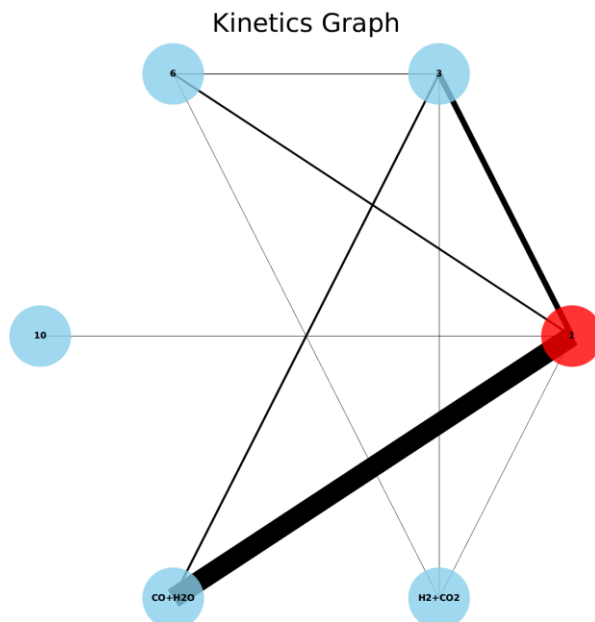
**RXNet.rel** is similar to **RXNet.cg**, but only collects the relevant paths, that is, those included in the **Energy\_profile.pdf** file. A maximum of 100 TSs are printed in this file. If this number is reached, both **Energy\_profile.pdf** and **RXNet.rel** would be incomplete, and the pathways drawn in **Energy\_profile.pdf** could be less than those that appear in **RXNet.rel**.

**graph\_all.pdf** is a graph displaying **RXNet.cg** reaction network. The nodes correspond to reactant, intermediates and products, and the widths of the edges are proportional to the number of paths connecting the corresponding nodes. The starting node is shown in red.



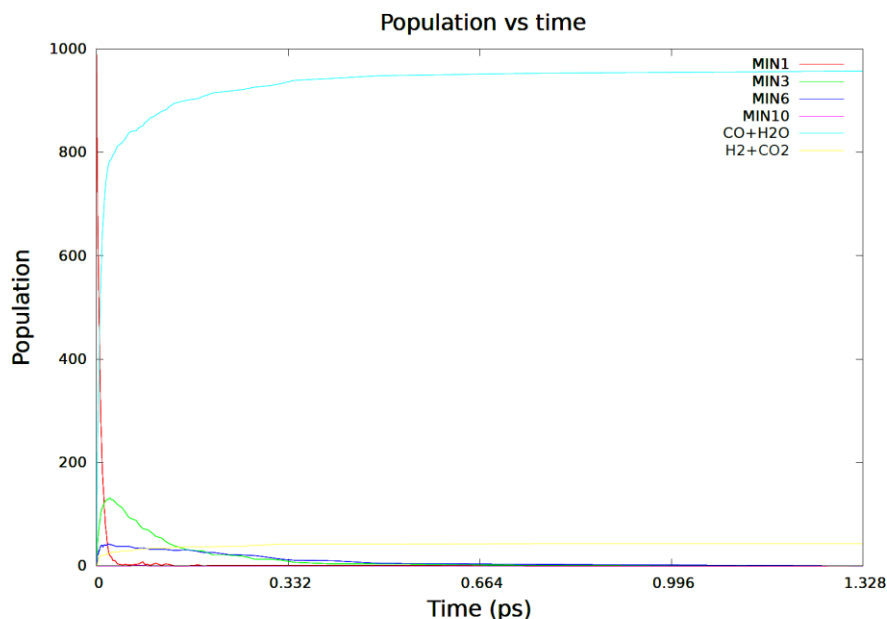
**graph\_kin.pdf** is a graph displaying only those nodes actively participating in the kinetics at the chosen temperature  $T$  or energy  $E$ . Here, the widths of the edges are proportional to the total (forward + backward) flux in the kinetics simulations. The starting node is shown in red.





**rxn\_x.txt** ( $x = \text{all, kin, stats}$ ) are files with information relevant for the reaction network analysis made with NetworkX python library.<sup>6</sup> Each line of **rxn\_all.txt** lists the nodes (first two columns) and the weight (last column), which is the number of paths connecting the two nodes. For **rxn\_kin.txt** the weight is the total flux in the kinetics simulations. These two files are employed to construct **graph\_all.pdf** and **graph\_kin.pdf**, respectively. In **rxn\_stats.txt**, some properties of the reaction network are listed, like the average shortest path length, the average clustering coefficient, the transitivity, etc. The user is encouraged to read the NetworkX documentation and ref<sup>7</sup>.

**kineticsFvalue** contains the kinetics results, namely, the final branching ratios and the population of every species as a function of time. In the name of the file, **F** is either “**T**” or “**E**” for temperature or energy, and “**value**” is the corresponding value. For instance, the kinetics results for a canonical calculation at 298 K would be printed in a file called **kineticsT298**. A file called **populationFvalue.pdf** is also available. It is a plot with the population of each species as a function of time. A maximum of 20 species (the most populated ones) are plotted. The following figure shows an example of such a plot obtained for the decomposition of FA using the PM7 stationary points.



## j) Details of the kinetics simulations

Except for vdW sampling, in the KMC simulations the different conformational isomers form a single state, which speeds up the calculations. If you prefer to treat each conformational isomer as a single state or rerun the kinetics at a different temperature or energy, you can use `kinetics.sh` script as detailed below. For vdW sampling, the `allstates` option is enforced when running `llcalcs.sh`.

The kinetics calculations can be rerun for a temperature/energy different from that specified in the input file after the keywords `Temperature` or `Energy`. This can be easily done using the `kinetics.sh` script with the following arguments:

```
kinetics.sh value calc (allstates)
```

where `value` is the new value of the temperature (in K) or energy (in kcal/mol) depending on your initial choice in the Kinetics section of the input file, and `calc` is either `l1` (for low-level) or `h1` (for high-level). Finally, with no other options, the conformational isomers will form a single state (as above), and using `allstates` as the last argument, the calculations will regard every conformational isomer as a different state. Each calculation will create a new folder `FINAL_XL_FA_Fvalue` (with X = H,L and F=T,E)

As explained above, the use of very tight criteria in the screening process might lead to redundant TS structures in the FINAL directories. In those cases, the user can remove those structures as shown in the following example:

```
remove_ts.sh 2 4 7
```

where 2, 4 and 7 are the labels of the TSs to be removed (for the LL calculations). The corresponding script for the HL calculations is `REMOVE_TS.sh`. These two scripts will create a new `FINAL_XL_FA` (with X = H, L) directory where the selected TS structures have been removed.

## 6. Other capabilities

### a) van der Waals complexes

AutoMeKin includes an option to predict van der Waals (vdW) complexes. In principle two related sampling options are available: `association` and `vdW`. While `association` runs a number of structure optimizations for randomly rotated fragments, `vdW` is a more powerful option representing a natural extension of our `bbfs` method to study vdW complexes.<sup>8</sup> The input files for these two options slightly differ from those explained previously, as detailed below.

**association.** Here, a number of full optimizations are performed starting from random orientations of A and B. An example of such input file can be found in [path\\_to\\_program/examples/assoc.dat](#). Two additional input files are also needed for this example, `Bz.xyz` and `N2.xyz`, which are also available in the same folder. The `assoc.dat` file contains the following data:

```
--General--
molecule Bz-N2
fragmentA Bz
fragmentB N2

--Method--
sampling association
rotate    com com 4.0 1.5
Nassoc    50

--Screening--
MAPEmax 0.0001
BAPEmax 0.5
eigLmax 0.05
```

This type of sampling only needs three sections: `General`, `Method` and `Screening`. Some further **keyword** value(s) pairs are needed for this sampling:

**fragmentA** value

[value is one string with no blank spaces; **mandatory keyword**]

value is the name of fragment A (Bz in our case). A file with the Cartesian coordinates `Bz.xyz` must be present in [wrkdir](#).

**fragmentB** value

[value is one string with no blank spaces; **mandatory keyword**]

value is the name of fragment B (N2 in our case). A file with the Cartesian coordinates N2.xyz must be present as well.

### **rotate values**

[four values: first two can be strings or integers and last two are floats; default values: com com 4.0 1.5]

The first two values are the pivot positions of the random rotations: the center of mass (com) of fragment A and the center of mass of fragment B in our example (these pivots could be labels of atoms and therefore integers). The last two values are the distance (in Å) between both pivots and the minimum intermolecular distance between any two atoms of both fragments, respectively.

### **Nassoc value**

[value is an integer; default value: 100]

value is the total number of intermolecular structures considered in the sampling. With this sampling, you cannot perform kinetics. However, you still need to provide the parameters for the screening. To run the calculations, just type:

```
amk.sh assoc.dat
```

This job will submit Nassoc independent optimizations to find the structures. After the jobs finished, the script will automatically remove duplicates and select the best association “complex”.

**Note that you cannot use `amk_parallel.sh` with this option, as this script is only employed to run MD simulations.**

You can check the optimized structures in folder `assoc_Bz_N2`. The program will also select the “best” structure according to the minimum number of structural changes between the complex and the individual fragments and its energy. The structure selected will be called `Bz-N2.xyz`. For fragments containing metals, the selection is also based on the valence of the metal center. The file `assoclist_sorted` (in the `assoc_Bz_N2` folder) collects a summary of the structures and their energies, as well as the MOPAC2016 output files of each of them, which are called `assocN.out`, where N is a number from 1 to Nassoc.

**vdw.** For this option, the first part is common to association, and the program runs Nassoc independent optimizations to get an initial structure of the complex. From that point onwards, the program performs

BXDE simulations to find TSs and intermediates for the system. Here is the inputfile `vdW.dat` that you can find in the [examples](#) folder:

```
--General--
molecule Bz-N2
fragmentA Bz
fragmentB N2

--Method--
sampling vdW
rotate com com 4.0 1.5
Nassoc 10
ntraj 1
fs 500

--Screening--
MAPEmax 0.0001
BAPEmax 0.5
eigLmax 0.01

--Kinetics--
Energy 150
```

As with other MD-based sampling methods, [amk\\_parallel.sh](#) can be employed here as well.

## b) Scanning dihedral angles

Dihedral angles can be scanned using script [tors.sh](#). You will need the inputfile and the XYZ file in your [wrkdir](#) and just type:

```
tors.sh inputfile file
```

The first argument is the name of the inputfile and the second one can be: **all** (default) or **file**. Using **all**, all the rotatable angles are scanned, while if you use **file**, the four indices that specify the dihedrals you want to scan must be present in file “dihedrals”.

The dihedrals will be scanned and the highest point(s) along the scan(s) will be subjected to TS optimizations.

In general, dihedral scans are automatically performed in all parallel calculations (except with `vdW` and `assoc` samplings). For big and/or highly flexible molecules these automated scans can be very CPU intensive, and they can be avoided adding the keyword `torsion` with the value `no` to your Method section like in the next example:

```
--Method--
sampling MD
ntraj 10
torsion no
```

The default value is `yes`.

### c) Fragmentation

The fragmentation patterns and breakdown curves can be modelled using the script [amk\\_frag.sh](#). This script will iteratively fragment not only the parent molecule but also the fragments that come out of the primary fragmentation. The user can add more fragments and spin states to take into account. Usage:

```
amk_frag.sh
```

The inputfile must have an additional section called "Fragmentation", as in this example:

```
--Fragmentation--  
minsize 4  
systems 1  
CH3O+ 3
```

The new keywords are explained below.

#### **minsize** value

[value is an integer; default value: 4]

value is the minimum number of atoms for a fragment to be considered in secondary fragmentations.

#### **systems** ns

sys(1)      mult(1)

sys(2)      mult(2)

...

sys(ns)     mult(ns)

ns is the number of additional fragments (or systems) to be considered in secondary fragmentations (default value: 0), besides those obtained in the fragmentation of the parent molecule. These could be fragments with other spin state, or fragments that are obtained through a barrierless process. This line must be followed by ns lines with two columns each one: the formula of each system (sys) and its multiplicity (mult). Note that for the formula the chemical symbols of the atoms must be sorted following AutoMeKin's convention: alphabetic order.

In the example above, only fragments with number of atoms greater than or equal to 4 are further fragmented and an additional system has been added: CH<sub>3</sub>O<sup>+</sup> in its triplet state.

This workflow creates a new folder: M3Cinp containing files that can be read by program [M3C](#) to simulate the breakdown curves of the studied molecule.

## d) Advanced options

The following are keywords that can be useful for experienced users.

### General

#### **iop** value

[value is one string with no blank spaces; no default value]

value is a gaussian IOp string or any other additional keyword you want to add. Example:

```
HighLevel g09 mpwb95/6-31+G(d,p)
iop      iop(3/76=0560004400)
```

#### **LowLevel\_TSopt** values

[two values: two strings; no blank spaces in each string; default values: mopac value[LowLevel]]

First value is the program and second value is the electronic structure level employed to optimize the TSs at the low-level stage. **This keyword is employed if you want to use g09 (which is the only ab initio program interfaced with amk) for the low-level TS optimizations, as shown in the example below but take into account that it is very CPU-time consuming.** Besides the TSs, the starting minimum in name.xyz is also optimized at this level of theory.

```
LowLevel_TSopt g09 hf/3-21g
```

#### **recalc** value

[one value: one integer; by default this keyword is not employed; **only with mopac**]

If the last point of the IRC is an intermediate, MOPAC will try to optimize it. For difficult cases, the user can employ this keyword like in this example:

```
recalc 10
```

which tells MOPAC to recalculate the Hessian every 10 steps in the EF optimization. For small values, the calculation is costly but is also very effective in terms of convergence.



## Method

### **atoms** value(s)

[one or two values: first is a string with no blank spaces or an integer and second (if present) is a string with no blank spaces; **only with MD**; default value: all]

The first value can be all (in which case no other values are needed) or the number of atoms initially excited followed by a second value (string), which is the list of atoms separated by commas (without blank spaces). It is analogous to modes (explained below). This is an example where atoms 1, 2 and 3 are initially excited.

```
atoms 3 1,2,3
```

### **etraj** value

[value is an integer or string with no blank spaces; **only with MD-micro**; no default]

If an integer, value is the energy (in kcal/mol) of the MD-micro simulations. If value is a range as in the example below, the energy is randomly selected in the given energy range.

```
etraj 200-300
```

If etraj is not specified, the program automatically employs the following range of energies:  $[16.25 \times (s - 1) - 46.25 \times (s - 1)]$  kcal/mol, where  $s$  is the number of vibrational degrees of freedom of the system. The values 16.25 and 46.25 have been determined from the formic acid results and making use of RRK theory. The program automatically adjusts the range to obtain at least 60% reactivity at the boundaries.

### **factorflipv** value

[value is a float; **only with MD and MD-micro**; no default]

Using the default options, trajectories are halted when the simulation time reaches the value [ fs ] keyword (see below) or when there an interatomic distance,  $r_{ij}$ , reaches 5 times its initial value  $r_{ij}^0$ , which is regarded as a fragmentation. Using **factorflipv** fragmentation can be prevented because the atomic velocities change their sign:

$$\vec{v}_k = \begin{cases} -\vec{v}_k & \text{if } k = i \text{ or } j \\ -0.9 \times \vec{v}_k & \text{if } k \neq i \text{ or } j \end{cases}$$

whenever the following relationship is fulfilled:

$$r_{ij} \geq \text{FP} \times r_{ij}^0$$

where FP is value[`factorflipv`]. We recommend this value to be in the range 3.0-5.0.

### **fs** value

[value is an integer; default value: 500 for MD and MD-micro and 5000 for BXDE]

value is the simulation time (in fs) in MD, MD-micro and BXDE samplings. Notice that this is the maximum simulation time, because when any interatomic distance reaches 5 times its initial value, the simulation stops. To run 2 ps trajectories the following should be employed:

```
fs 2000
```

### **fric** value

[value is a float; **only with BXDE**; default value: 0.5]

value is the friction coefficient (in a.u.) employed in the Langevin dynamics of a BXDE simulation.

### **Hookean** values

[four values: first (*i*) and second (*j*) are integers, third (*rt*) and fourth (*k*) are floats; **only with BXDE**]

Hookean keyword can be employed with any BXDE-based dynamics sampling. It employs ASE's Hookean class to conserve molecular identity (<https://wiki.fysik.dtu.dk/ase/ase/constraints.html#the-hookean-class>). A Hookean restorative force with spring constant given by the fourth value (in eV/Å<sup>2</sup>) is applied between two atoms of indices given by the first and second values if the distance between them exceeds a threshold (third value). For instance, the following example tethers atoms at indices 1 and 2 together:

```
Hookean 1 2 2.5 10.
```

### **modes** value(s)

[one or two values: first is a string with no blank spaces or an integer and second (if present) is a string with no blank spaces; **only with MD-micro**; default value: all]

The first value can be all (in which case no other values are needed) or the number of modes initially excited followed by a second value (string), which is the list of modes separated by commas (without blank spaces). It is analogous to atoms (explained above).

### **multiple\_minima** value

[value is one string: yes or no; default value: yes]

value can be yes, in which case the exploratory simulations start from multiple minima, or no, where the all the MD simulations start from the input initial structure.

## **post\_proc** value(s)

[from one to three values: first value is a string (bbfs, bots or no), the second and third are integers or floats; default values: bbfs 20 1 for all samplings except association where the only default value is no]

The first value is the post-processing algorithm employed to detect reaction events and it can be bbfs (the default), bots<sup>9</sup> or no (if no algorithm is applied; this makes only sense for the purpose of testing the MD module). For bbfs two more values can follow: the time window (in fs) employed by bbfs and the number of guess structures selected per candidate. Possible choices for this last number can be 1 or 3. Example:

```
post_proc bbfs 20 1
```

If bots (for bond order time series) is employed (**only with BXDE, vdW and external**), the algorithm developed by Hutchings et al. is employed,<sup>9</sup> which is based on peak finding on the first time derivative of the bond orders. In this case the two additional values are the cutoff frequency (in  $\text{cm}^{-1}$ ) for the low-pass filter used to smooth bond order time series, and the number of standard deviations considered to identify peaks associated with reactive events. The default values for this algorithm are:

```
post_proc bots 200 2.5
```

## **temp** value

[value is an integer or string with no blank spaces; **only with MD and BXDE**; no default]

If an integer, value is the temperature (in K) of the MD or BXDE simulations. If a range (**only valid for MD**), the temperature is randomly selected in the given range. In the absence of the temp keyword, the program automatically defines the following range of temperatures:  $[5452.04 \times (s - 1)/natom - 15517.34 \times (s - 1)/natom]$  K, which has been optimized for formic acid. However, as for etraj, the boundaries are adjusted “on the fly” to obtain a minimum reactivity of 60%. **For BXDE, temp has only one value (with 1000 being the default).**

## **thmass** value

[value is an integer; **only with MD**; default value: 0]

value is the required minimum mass (in a.u.) of an atom to be initially excited.

## Use\_LET value

[value is one string: yes or no; **only with mopac**; default value: no for all samplings except ChemKnow]  
If value is yes, then mopac TS optimizations that fail throwing the error: "NUMERICAL PROBLEMS BRACKETING LAMDA" are rerun using LET keyword (this allows more of the potential energy surface to be sampled: [http://openmopac.net/manual/error\\_messages.html](http://openmopac.net/manual/error_messages.html)). To help the user judge whether to use this keyword, the results of the optimizations using LET are collected in the file *stats\_let* located in *tsdirLL\_molecule*. This file contains several lines (one per iteration) with two numbers: the first is the number of optimized TSs, and the second is the number of total attempts using LET.

## Screening

### tight\_ts value

[value is one string: yes or no; default value: yes]

value can be yes, in which case only first order saddles are considered, or no if we want to keep also higher order saddles.

## Kinetics

### imin value

[value is an integer or one string: min0; default value: min0]

value is the starting minimum for the KMC simulations. value can be an integer, which identifies the desired structure or min0, which refers to the input structure. All the minima are listed in MINinfo file and the user must examine RXNet.cg file to check that the minimum is indeed connected with the other ones (last column of each pathway indicates this fact).

### nmol value

[value is an integer; default value: 1000]

value is the number of molecules for the KMC simulations.

### Stepsize value

[value is an integer; default value: 10]

value is the number of reactions that have to take place before printing the population in the KMC runs.

### MaxEn value

[value is an integer; default value: 100 for thermal kinetics or 3/2 the value of Energy for microcanonical kinetics]

value is the maximum allowed energy (in kcal/mol and relative to the input structure) for a TS to be included in the reaction network.

### ImpPaths value

[value is a float; default value: 0]

value is the minimum percentage of processes occurring through a particular pathway (in the KMC simulation) that has to be achieved in order to be considered relevant and finally included in Energy\_profile.pdf and in RXNet.rel. The default value of 0 means that pathways which are overcome at least once by the KMC simulations are included in these files. To reduce to number of channels drawn in Energy\_profile.pdf and printed in RXNet.rel you can increase the default value. Notice that these pathways may refer to the “coarse-grained” mechanism (default option) or to the complete mechanism that includes conformational isomers (obtained by using the allstates option as described above). For practical reasons, a **maximum of 100 TSs** will be drawn in Energy\_profile.pdf and printed in RXNet.rel. If this maximum value is reached (which can be checked in RXNet.rel), it means that part of the channels are missing in these files.

### e) Biased dynamics

AutoMeKin includes several methods to bias the dynamics towards specific reaction pathways. So far, these are the available options (**only for MD and MD-micro**):

1) The first option uses the AXD algorithm described in Ref <sup>10</sup>, with which selected bond lengths are not allowed to stretch more than 30% with respect to their initial values. This can be useful to prevent the breakage of certain bonds. This option can be used invoked using the following **keyword nfr** pair:

**nbondsfrozen nfr**

fr\_i(1) fr\_j(1)

fr\_i(2) fr\_j(2)

...

```
fr_i(nfr) fr_j(nfr)
```

[nfr, fr\_i(1,...,nfr) and fr\_j(1,...,nfr) are integers; default nfr: 0]

where nfr is the number of constrained bonds. The line containing this **keyword** nfr pair must be followed by nfr lines, each one with two values (fr\_i(1,...,nfr) and fr\_j(1,...,nfr), which are integers) indicating the indexes (labels) of the atoms that form each constrained bond, as in the following example

```
nbondsfrozen 2
1 13
2 8
```

This would “freeze” two bond distances connecting atoms 1 and 13 and 2 and 8, respectively.

2) The second algorithm bias the dynamics towards a particular reaction channel. An example of this option is provided in file [path\\_to\\_program/examples/FA\\_biasH2.dat](#) (you also need FA.xyz), which illustrates a way to search for H<sub>2</sub> elimination transition states from formic acid. For this we use two sets of keywords to apply constant external forces to break or form bonds. For bond breakage we use the following:

**nbondsbreak** nbr

```
br_i(1) br_j(1) force(1)
```

```
br_i(2) br_j(2) force(2)
```

...

```
br_i(nbr) br_j(nbr) force(nbr)
```

[nbr, br\_i(1,...,nbr) and br\_j(1,...,nbr) are integers and force(1,...,nbr) are floats; default nbr: 0]

where nbr is the number of bonds we want to break. The line containing this **keyword** nbr pair must be followed by nbr lines, each one with three values (br\_i(1,...,nbr), br\_j(1,...,nbr) and force(1,...,nbr), of which the first two are integers and the last a float). These three numbers indicate the indexes (labels) of the atoms that form each bond we want to break, and the magnitude of the applied external force (in kcal/mol/Å), respectively.

For bond formation we use the analogous keyword **nbondsform** as in this example (taken from FA\_biasH2.dat):

```
nbondsform 1
4 5 30
nbondsbreak 2
```

```
3 5 80
1 4 80
```

A similar test can be performed on the same molecule to get the TS for H<sub>2</sub>O elimination. The corresponding input file, FA\_biasH2O.dat, is also available in directory [path\\_to\\_program/examples](#). Additionally, a retro Diels-Alder reaction has also been tested (cyclohexene → ethylene+1,3-butadiene), using the input files rdiels\_bias.dat and rdiels.xyz provided in the amk distribution.

The above examples can be tested using the [amk.sh](#) script:

```
amk.sh inputfile
```

## 7. Summary of all keywords and options

sampling <sup>1</sup>	LowLevel <sup>2</sup>	General	Method	Screening	Kinetics
MD	mopac	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo, recalc	ntraj, seed, atoms, factorflipv, fs, multiple_minima, post_proc: bbfs, temp, thmass, nbondsfrozen, nbondsbreak, nbondsform, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
	qcore	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo	ntraj, seed, fs, multiple_minima, post_proc: bbfs, temp	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
MD-micro	mopac	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo, recalc	ntraj, seed, etraj, factorflipv, fs, modes, multiple_minima, post_proc: bbfs, nbondsfrozen, nbondsbreak, nbondsform, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
BXDE	mopac	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo, recalc	ntraj, fs, fric, Hookean, multiple_minima, post_proc: bbfs, bots, temp, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
	qcore	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo	ntraj, fs, fric, Hookean, multiple_minima, post_proc: bbfs, temp	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
external	mopac	molecule, LowLevel, HighLevel,	ntraj, post_proc: bbfs, bots, Use_LET	imagmin, MAPEmax,	Energy, Temperature, imin, nmol,



		HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo, recal		BAPEmax, eigLmax	Stepsize, MaxEn, ImpPaths
	qcore	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo	ntraj, post_proc: bbfs	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
ChemKnow	mopac	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo, recal	active, nbonds, startd, neighbors, comb22, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
associati on	mopac	molecule, fragmentA, fragmentB, LowLevel	rotate, Nassoc	MAPEmax, BAPEmax, eigLmax	
	qcore	molecule, fragmentA, fragmentB, LowLevel	rotate, Nassoc	MAPEmax, BAPEmax, eigLmax	
vdW	mopac	molecule, fragmentA, fragmentB, LowLevel, HighLevel, IRCpoints, charge, Memory, iop, LowLevelTSopt, pseudo, recal	rotate, Nassoc, ntraj, fs, fric, Hookean, multiple_minima, post_proc: bbfs, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
	qcore	molecule, fragmentA, fragmentB, LowLevel, HighLevel, IRCpoint, charge, Memory, iop, LowLevelTSopt, pseudo	rotate, Nassoc, ntraj, fs, fric, Hookean, multiple_minima, post_proc: bbfs	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths

<sup>1</sup>Value of sampling keyword (in section: Method). <sup>2</sup>First value of LowLevel keyword, i.e., program, (in section General).



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