AutoMeKin

Automated Reaction **Me**chanisms and **Kin**etics

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1. Introduction

AutoMeKin (amk), which stands for Automated Mechanisms and Kinetics, is an automated protocol to discover chemical reaction mechanisms and simulate the kinetics at the conditions of interest. Although the method was originally designed to find transition states (TSs) from reactive molecular dynamics (MD) simulations, several new tools have been incorporated throughout the past few years. The current pipeline consists of three steps:

1) Exploration of reaction mechanisms through MD simulations or chemical knowledge-based algorithms.

2) Use of Graph Theory algorithms to build the reaction network (RXNet).

3) Kinetics simulations.

The program is interfaced with MOPAC2016, Qcore and Gaussian (G09/G16), but work is in progress to incorporate more electronic structure programs. This tutorial is thought to guide you through the various steps needed to predict reaction mechanisms and kinetics of unimolecular decompositions. To facilitate the presentation, we consider, as an example, the decomposition of formic acid (FA). 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). Comments and suggestions are also welcome.

AutoMeKin wiki page: https://rxnkin.usc.es/index.php/AutoMeKin

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: 21.129, James J. P. Stewart, Stewart Computational Chemistry, web-site: HTTP://OpenMOPAC.net.

If you use the older version **tsscds2018**, please cite, instead of ref 1 above, the following one:

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:

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 bots reactive event search algorithm, the following reference must be cited:

Hutchings M. et al., *J. Chem. Theory Comput.* **2020**, 16, 1606-1617

3. Developers team

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4. Installation

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`

More details are given in the Wiki

5. Description of the input files

The first step in our strategy for finding reaction mechanisms involves Heuristics- or MD-based methods, for which MOPAC2016 or Entos Qcore are used. The algorithm samples the potential energy surface to locate transition states by using the original BBFS algorithm,[1-2] or a new search algorithm.[9] Then, reactants and products 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 1. 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.

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. At present, the high-level electronic structure calculations can be performed with G09/G16 or with Entos Qcore.

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.

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 use 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 keywork 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      g16 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, g16 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 g16 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/g16 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 the reaction space. 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.[3] The BXDE module employs the "Atomistic Simulation Environment" (ASE) library of Python,[4] 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 (BXDE and ChemKnow also accept other keywords as seen below):

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 and about 10 for MD-based sampling.

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.**

BXDE specific keywords. This sampling (and the other BXDE-based sampling based: vdW) has a number of specific keywords as shown in this example:

```
sampling           BXDE
Friction           0.5
AdaptiveLimit      100
Window             500
Hookean            1 2 2.5 10.
```

`Friction` `value`

[`value` is a float; default `value`: `0.5`]

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

`AdaptiveLimit` `value`

[`value` is an integer; default `value`: `100`]

`value` determines how many MD steps are performed in a new box before the BXDE algorithm adaptively places a new box based upon the sampled energies.

`Window` `value`

[`value` is an integer; default `value`: `500`]

`value` determines the number of consecutive MD steps before considering a reaction to have occurred.

`Hookean` `values`

[four `values`: first (`i`) and second (`j`) are integers, third (`rt`) and fourth (k) are floats]

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^2) 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:

`ChemKnow specific keywords.` This sampling has a number of specific keywords as shown in this example:

```
sampling     ChemKnow
Graphto3D    POpt
active       1 2 3 4
startd       2.75
MaxBoF       2
MaxBoB       2
comb22       no
crossb       no
BreakRing    no
```

`Graphto3D` `value`

[`value` is a string: `POpt` or `Traj`; default `value`: `POpt`] `value` is the method employed to transform the product Graph into a 3D geometry. `POpt` performs a series of partial optimizations (with the bonds involved in the reaction coordinate frozen) where the geometry is smootly changed from reactant to product. In `Traj`, an external force is applied for the same purpose.

`active` `values`

[`values` are integers]

`values` are the labels of the atoms that participate in the reactions we are interested in. By default, all atoms in the system are active.

`startd` `value`

[`value` is a float; default `value: 2.75`]

`value` is the maximum distance between active atoms to be considered in a bond formation.

`MaxBoF/MaxBoB` `value`

[`value` is an integer; default `value: 2`]

`value` is the maximum number of bonds formed (n_F)/broken (n_B) to make all possible (n_F, n_B) combinations for Graph transformations.

`comb22` `value`

[`value` is a string: `yes` or no; default `value`: no]

By default, the (2,2) combination is not considered.

`crossb` `value`

[`value` is a string: `yes` or no; default `value`: no]

A check can be done to see if the closest distance between the paths followed by the atoms in their rearrangements is lower that a threshold value (a potential problem in planar molecules or planar regions of a molecule). By default, this check is not done.

`BreakRing` `value`

[`value` is a string: `yes` or no; default `value`: no]

By default, a bond that belongs to a ring is not broken in (0,1) tranformations. However, there might be ring opening reactions of our interest.

`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,[5] degrees of each vertex and eigenvalues of the Laplacian matrix.[1] 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 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/G16) 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 MIN(MAPEmax, 0.001) and MIN(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, only temperatures in the range 100-9999 K are allowed.

6. Running the program

To modify your environment information so that you can use the program, load the `amk/2021` module every time a new session is opened (only if you do not use the container option):

```
module load amk/2021
```

a) Tests

You may want to run tests taken from the `examples` folder. The following command line script runs 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. To run FA and FAthermo tests, use the following:

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

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`.

b) Low-level calculations

All low-level calculations can be run using the command line script `llcalcs.sh`:

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

where `ntasks` is the number of parallel tasks, `niter` is the number of iterations, and `runningtasks` is the number of simultaneous tasks. 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.

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

```
sbatch llcalcs.sh name.dat ntasks niter
```

This is an example to run 10 iterations of our low-level workflow for FA. Every iteration includes 50 tasks (MD, BXDE, etc), 20 of them running simultaneously.

```
nohup llcalcs.sh FA.dat 50 10 20 >llcalcs.log 2>&1 &
```

c) High-level calculations

Having completed the low-level calculations, the user can perform the high-level computations, which use Gaussian (g09 or g16) or Entos Qcore. These calculations can be run employing the following script:

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

If your computer system has the Slurm job scheduler, the calculations can be submitted in the following way:

```
sbatch hlcalcs.sh FA.dat
```

d) Step-by-step low-level calculations

This section explains how to run one iteration of our workflow. This might be useful for getting acquainted with the program and didactic purposes, but the recommended option for production runs is to use the iterative `llcalcs.sh` and `hlcalcs.sh` scripts explained above.

To run AutoMeKin in a single processor use amk.sh script with the name of the input file as argument:

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

The ouput 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   wrkdir
     3       ts3_batch2    458i    -78.1007    573    846   1034   1195      3   wrkdir
     4       ts4_batch6   2010i    -17.6124    327    473    523   1078      1   wrkdir
```

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 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 cm^{-1}). Finally, the last two columns are the trajectory number and the name of the folder where the structure was obtained.

CAVEAT: since the dynamics employ random number seeds, the above results may differ for this type of calculations although using a sufficiently large number of trajectories (see below), the important TSs should appear in all runs.

As already mentioned, the 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.molden
```

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.

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 Manage for the `amk_parallel.sh` script, you will have to wait until all tasks are completed before going on.

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 ouput 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.

Obtaining the IRCs:

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

Optimizing the minima:

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

Building 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.

Rnning the kinetics at the conditions of interest:

```
kmc.sh
```

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) Step-by-step high-level calculations

Although the recommended option for running the high-level calculations is to use `hlcalcs.sh`, it is possible to perform the calculations step by step, as described next:

From your `wrkdir` (`FA` in the example), run the following scripts:

Optimizing the TSs

```
(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
```

Building the high-level reaction network, optimizing the minima and running the kinetics:

```
(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.

Optimizing the product fragments:

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

CAVEAT: The previous step is mandatory before proceeding gather all information in the final folder.

Gathering all relevant information in folder `FINAL_HL_FA`:

```
FINAL.sh
```

Notice that the high-level calculations also generate the directory `tsdirHL_FA`, whose structure is similar to `tsdirLL_FA`. Finally, remember that you can use the `kinetics.sh` to calculate rate coefficients and product branching rations for an energy or temperature different from that specified in the kinetics section.

f) Aborting the calculations

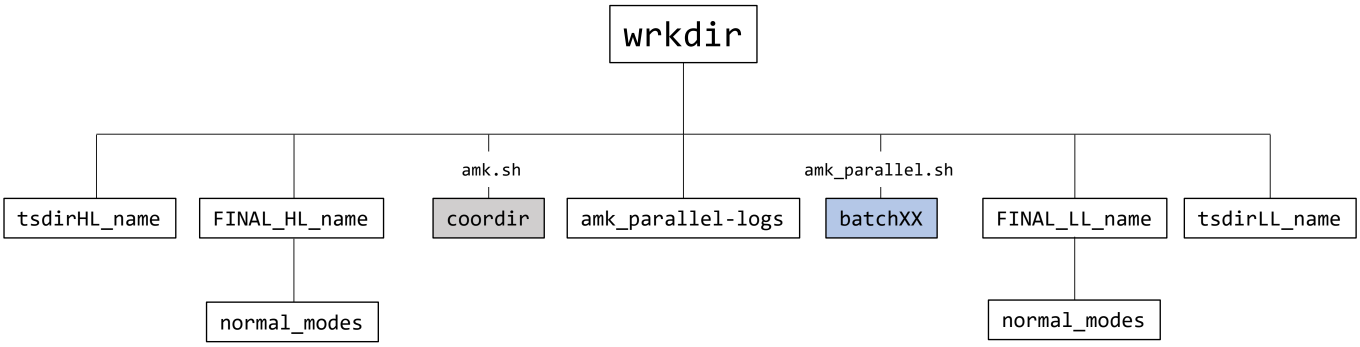
If, for any reason, you want to kill the iterative calculations, execute the following script from the `wrkdir`:

```
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/G16 jobs are killed, the read-write files (Gau-#####) generated in the Gaussian scratch directory are not removed. The user should do it manually.

g) 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 are 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).



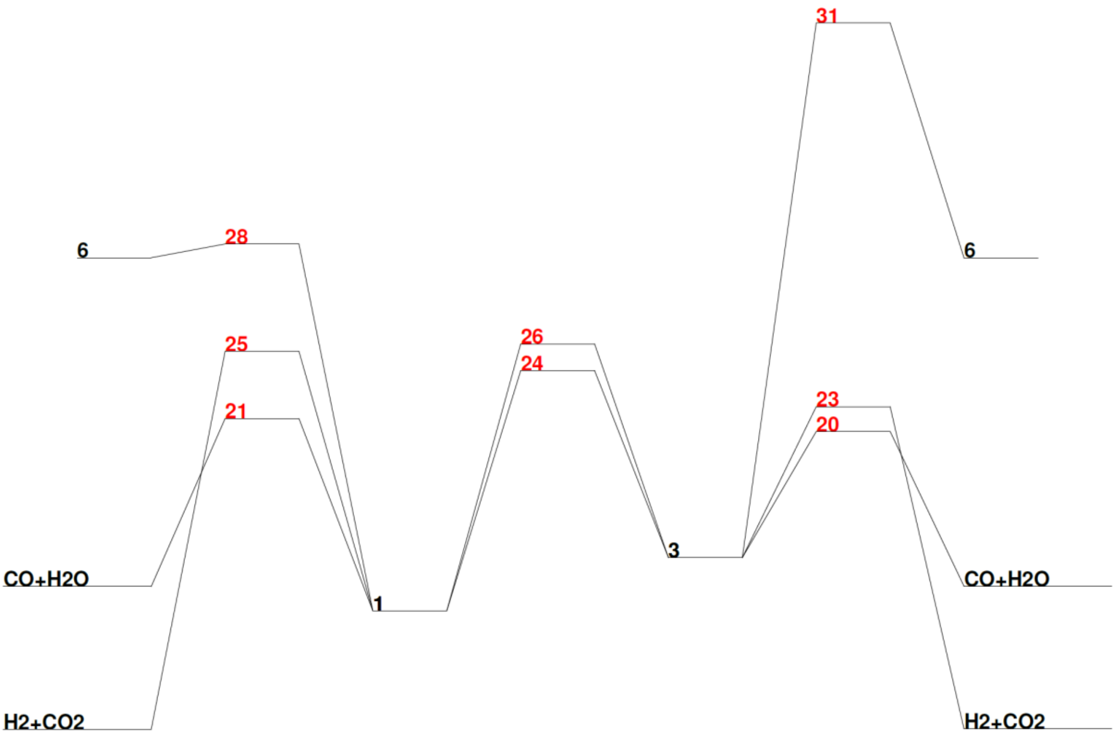
7. Results

a) 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. The file is 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:
9 11
```

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 select.sh:

```
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. Please note that for the hybrid calculations involved through the use of keyword LowLevel_TSopt, energies, zpe and frequencies in the tables are those obtained with MOPAC, while the geometry in ts.db is the one obtained at the g09/g16 level of theory.

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 15).

```
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 `<-->` 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/g16 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:

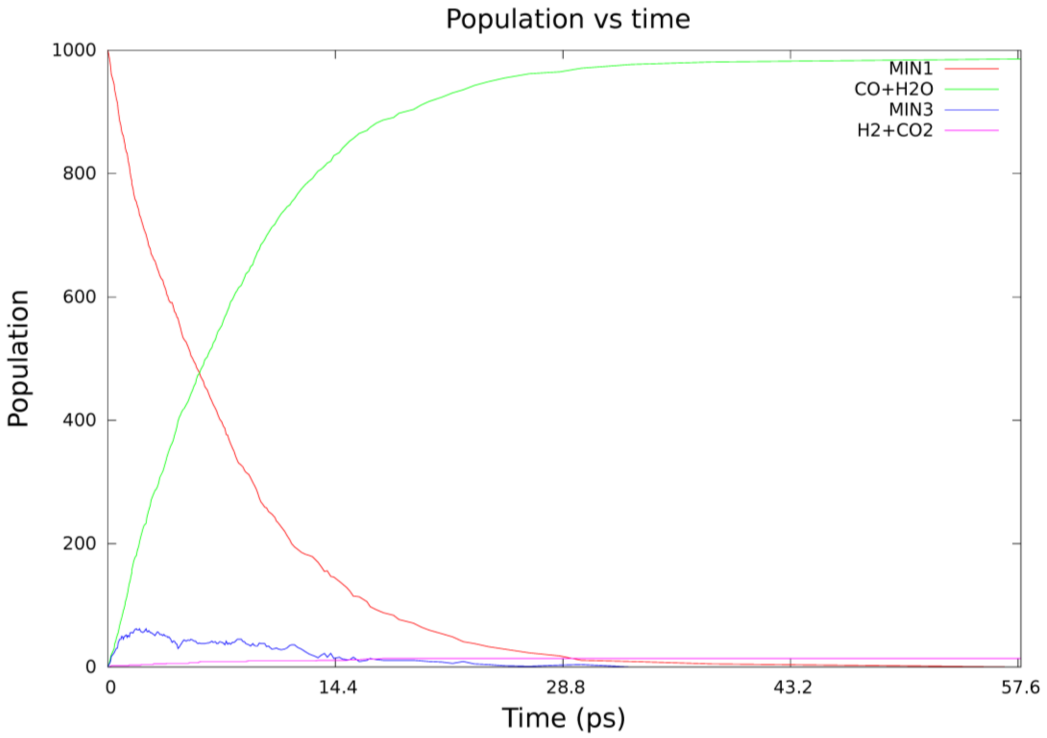
```
TS #   DE(kcal/mol)     Reaction path information
 ====   ============     ========================
    6       37.6       MIN    3 ----> PR2:  CO + H2O        CONN
    7       41.0       MIN    1 ----> PR2:  CO + H2O        CONN
    9       53.2       MIN    1 <--->       MIN    3        CONN
   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. 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.

`rxn_x.txt` (`x = all, kin, stats`) are files with information relevant for the reaction network analysis made with NetworkX python library.[6] 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 7.

`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.



b) Visualization tools

The Python library amk-tools developed by Diego Garay (Institute of Chemical Research of Catalonia Prof. Carles Bo Research group) is a useful package to parse, process and transform the reaction networks created by AutoMeKin (https://github.com/dgarayr/amk_tools). All the data contained in `FINALDIR` can be easily accessed using these tools.

The commandline script `amk_gen_view.py` allows to generate visualizations directly taking arguments from STDIN:

```
amk_gen.py FINALDIR RXNFILE
```

where RXNFILE is the name of the RXNet files explained above (RXNet, RXNet.cg or RXNet.rel). Additional arguments that may be passed are:

--barrierless. Include the barrierless routes stored in *RXNet.barrless*.

--vibrations NVIBR. Add only *NVIBR* normal modes to the visualization. Default is -1, meaning that ALL modes are included.

--paths [SOURCE] [TARGET] Locate paths in the network connecting SOURCE to TARGET, to include energy profile visualizations in the dashboards. When both SOURCE and TARGET are specified, a simple search is performed including only the routes that connect both nodes. If --*paths* is passed without further specification, all possible cyclic paths along the network are searched (much slower). If only

SOURCE is specified, all cyclic paths are also searched, and then filtered to only keep these with connections to SOURCE.

--cutoff_path CUTOFF. Maximum depth for two-ended path search (number of intermediate nodes between SOURCE and TARGET), default is 4.

--outfile FILENAME. Name of the output HTML file containing the dashboard.

--title TITLE. Title shown in the dashboard.

The following example shows how to create interactive plots from RXNet.cg file including all paths found at low level for Formic Acid (FA):

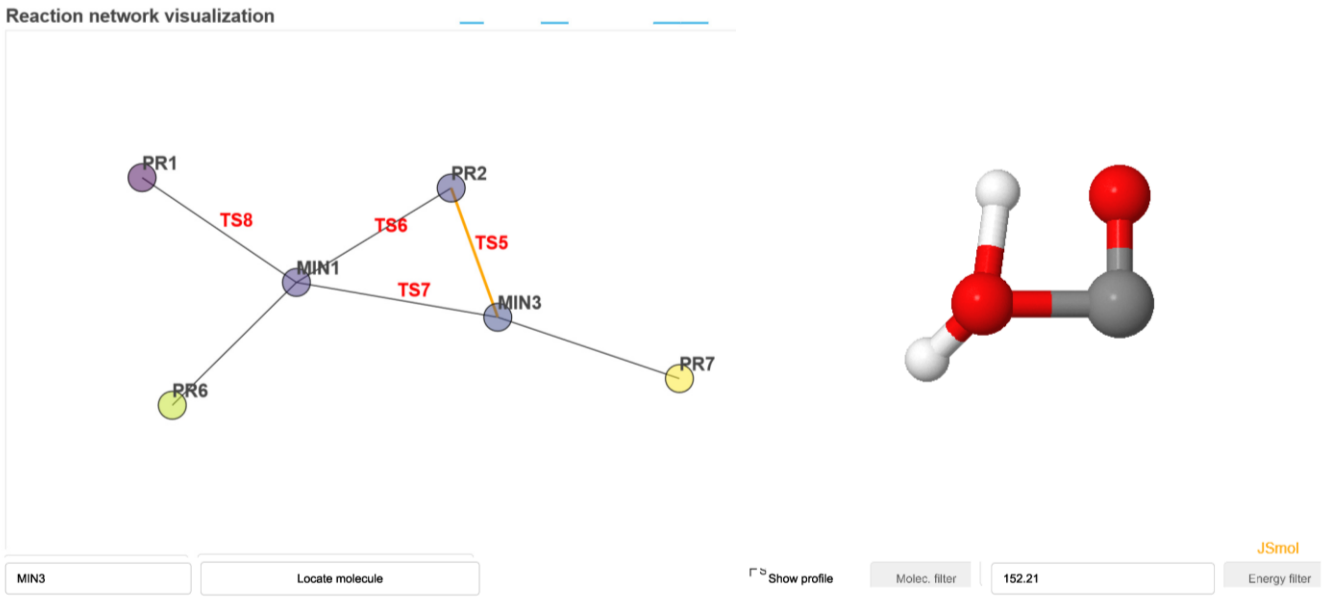
```
amk_gen.py FINAL_LL_FA RXNet.cg --b --paths
```

While this one creates the corresponding plots for the paths that connect MIN1 with the H_2 + CO_2 products:

```
amk_gen.py FINAL_LL_FA RXNet.cg --paths MIN1 H2+CO2
```

More details can be found here: https://github.com/dgarayr/amk_tools/blob/master/UserGuide.md

Example of an interactive dashboard (for FA), with the reaction network on the left and a selected edge (TS) on the right. Clicking on "Show profile" enables visualization of the energy profile as well.



c) Kinetics simulations at different temperatures

The kinetics calculations can be rerun for a temperature/energy different from that specified in the input file after the keywords `Temperature` or `Energy`. You may also want to use the `allstates` option (see below). This can be easily done using the `kinetics.sh` command line script:

```
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, and calc is either ll (for low-level) or hl (for high-level). Finally, with no other options, the conformational isomers will form a single state (default for all sampling except vdW). However, using allstates as the last argument, the calculations will regard every conformational isomer as a different state (default for vdW). Each calculation will create a new folder named FINAL_XL_molecule_Fvalue (with X = H,L and F=T,E)

d) Removing unwanted TS structures

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.

8. Other capabilities

a) van der Waals complexes

AutoMeKin includes an option to find 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.[8] 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 provides a workflow to iteratively discover fragmentation pathways not only the parent molecule but also for the fragments resulting from the primary fragmentation. Usage:

```
nohup amk_frag.sh > amk_frag.log 2>&1 &
```

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 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_3O^+ 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 system.

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 g16 mpwb95/6-31+G(d,p)
iop       iop(3/76=0560004400)
```

CAVEAT: care must be taken when `LowLevel_TSopt` (see below) is employed with `iop`, as this keyword will also be activated in `LowLevel_TSopt` calculations. If the `iop` is only desired for high-level gaussian calculations, then, the keyword should be removed while running the low-level computations.

`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/g16` 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:

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

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
```

`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`[9] 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,[9] 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 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). 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 [10], with which selected bond lengths are not allowed to stretch more than 50% with respect to their initial values. This can be useful to prevent the breakage of certain bonds. This option can be invoked using the following "**keyword** value" 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 the "**nbondsfrozen** 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. This keyword has not been tested thoroughly and the more robust Hookean keyword (see above) is suggested.

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_2 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_2O 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
```

9. Summary of all keywords and options

sampling[1]	LowLevel[2]	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,	ntraj, fs, Friction, Hookean, multiple_minima, post_proc: bbfs,	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize,

		charge, Memory, mult, iop, LowLevelTSopt, pseudo, recalc	bots, temp, Use_LET		MaxEn, ImpPaths
	qcore	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo	ntraj, fs, Friction, Hookean, multiple_minima, post_proc: bbfs, temp	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
external	mopac	molecule, LowLevel, HighLevel, HL_rxn_network, IRCpoints, charge, Memory, mult, iop, LowLevelTSopt, pseudo, recalc	ntraj, post_proc: bbfs, bots, 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, 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, recalc	active, nbonds, startd, neighbors, comb22, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
association	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, recalc	rotate, Nassoc, ntraj, fs, Friction, Hookean, multiple_minima, post_proc: bbfs, Use_LET	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize, MaxEn, ImpPaths
	qcore	molecule, fragmentA, fragmentB, LowLevel,	rotate, Nassoc, ntraj, fs, Friction, Hookean,	imagmin, MAPEmax, BAPEmax, eigLmax	Energy, Temperature, imin, nmol, Stepsize,

		HighLevel, IRCpoint, charge, Memory, iop, LowLevelTSopt, pseudo	multiple_minima, post_proc: bbfs		MaxEn, ImpPaths

[1]Value of sampling keyword (in section: Method). [2]First value of LowLevel keyword, i.e., program, (in section General).

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