

tsscds1.1

transition state search using chemical dynamics simulations

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1. Introduction

tsscds-1.1 computer program 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 structures, minima and product fragments can be optimized following the intrinsic reaction coordinate (IRC), and the reaction network can thus be constructed. Finally, the kinetics is solved using Kinetic Monte Carlo (KMC) method.

The program is interfaced with MOPAC2016 and GAUSSIAN09, but work is in progress to incorporate more electronic structure programs.

2. How to cite the program

Work based on this code should include the following references:

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

This tutorial is thought to guide you through the steps to obtain the reaction mechanisms and kinetics of formic acid (FA) decomposition.

3. Installation

Untar and unzip the file tsscds-SOURCE-1.1.tar.gz:

```
tar xvfz tsscds-SOURCE-1.1.tar.gz
```

Go to tsscds-SOURCE-1.1 folder and type:

```
./configure
```

This will install tsscds in \$HOME/tsscds-1.1 by default. If you want to install it in a different directory type:

```
./configure --prefix=path_to_program
```

The program will check, among other things, that you have installed parallel and sqlite3. Additionally, "Environment modules" needs to be installed in your computer. Then, you can add to your .bash_profile the following line to use the tsscds module:

```
module use path_to_program/modules
```

You will also need g09 to run the high-level calculations and it should be run as: g09<input>output. After checking the above issues, type the following to complete the installation:

```
make  
make install
```

4. How to start using the program

To start using any of the scripts described below, you have to load tsscads/1.1 module:

```
module load tsscads/1.1
```

If you use the program in FinisTerraes infrastructure (CESGA, Spain), type the following instead:

```
module load tsscads/1.1ft2
```

5. Finding reaction mechanisms and solving the kinetics

All electronic structure calculations described in this section employ semi-empirical Hamiltonians and use MOPAC. To guide you in this tutorial you can try the formic acid (FA) test case that comes with the distribution. Make a working directory and copy files FA.dat and FA.xyz from [path_to_program/examples](#) in your working directory. All the scripts described below (except `select.sh`) should be run from your working directory.

a) Description of the input files

To find reaction mechanisms and solve the kinetics you just need two input files:

- i) **molecule.xyz**. Cartesian coordinates of the system. Example: FA.xyz.
- ii) **molecule.dat**. This contains all parameters of the calculation. Example: FA.dat.

The file has different sections explained in the following.

General section. In this section the user provides details of the system and electronic structure calculations.

```
--General section--
molecule FA
LLcalc pm7
HLcalc 1 DFT
level1 b3lyp/6-31G(d,p)
charge 0
mult 1
```

Description of the keywords

molecule: is the name of the system. A file **molecule.xyz** must exist in the folder.

LLcalc: is any of the semiempirical methods implemented in MOPAC2016. You can use a combination of MOPAC keywords. For instance, PM7 singlet excited state calculations can be run using:

```
LLcalc pm7 singlet cis c.i.=6 root=2 meci
```

HLcalc: refers to high level calculations. The number **1** in the above figure indicates that only one method will be employed, **DFT** in this case (but it could also be **HF** or **MP2**). For single point energy corrections employ **2**, and the methods can be: **HF**, **DFT**, **MP2** or **CCSDT**.

level1: indicates the level of theory of HL calculation number 1.

level2: indicates the level of theory of the energy correction.

For instance, to run b3lyp/6-31G(d,p) calculations with single point energy correction at the CCSD(T)/6-311+G(2d,2p) level of theory we should use the following:

```
HLcalc 2 DFT CCSDT
level1 b3lyp/6-31G(d,p)
level2 ccSD(t)/6-311+G(2d,2p)
```

iop: is employed to specify a iop in gaussian. Example:

```
iop iop(X/Y=Z)
```

where X, Y and Z denote the overlay, option and value, respectively.

charge: is the charge of the system.

mult: is the multiplicity of the system.

CDS (Chemical Dynamics Simulations) section. Here the user provides details of the accelerated dynamics simulations.

```
--CDS section--
sampling microcanonical
etraj 200
modes all
seed 109
ntraj 1
fs 500
```

Description of the keywords

sampling: is employed to indicate the type of sampling: microcanonical, canonical, association and external.

Microcanonical. Microcanonical sampling includes a number of specific keywords:

etraj: is the energy (in kcal/mol) of the accelerated dynamics simulations. This can be a single value (200) or a range, in which case the energy is randomly selected in the given energy range (200-300 for instance).

modes: is the number of normal modes to be initially excited. It can be **all** or you can just excite a small subset. For instance, if you want to excite only the 3 lowest frequency modes, you should employ:

```
modes 3 1,2,3
```

where the number **3** indicates the number of excited modes and **1,2,3** are the indices of the modes, which should be in a single field and separated by commas.

Canonical. Canonical sampling includes a number of specific keywords:

temp: is the temperature of the accelerated dynamics in K. As above, it can be a single number or a range.

atoms: indicates how many atoms will move in the dynamics. It can be followed by **all** or the number and the indices of the atoms (just like above for the microcanonical sampling). The atoms that are not listed in the line starting with the keyword **atoms** will remain frozen in the dynamics simulations.

thmass: can be employed to specify the required minimum mass (in a.u.) of an atom to be initially excited. An example of an input file for a canonical example can be found in this distribution (tsscads_canonical.dat).

Common keywords of the above two samplings:

seed: can be employed to run a test trajectory. This is the seed for the random number generator. If you plan to run more than one trajectory do not use this keyword, and every trajectory will have a different random number seed.

ntraj: is the number of trajectories.

fs: is the simulation time in fs.

Association. This sampling is explained in section f.

External. With this option you can couple your dynamics results, obtained with any other code and with any initial conditions, with our BBFS algorithm. You just need to copy the dynamics xyz files (with a time step of 1 fs) in folder **coordir**. The xyz files have to be named **molecule_dynX.xyz**, where X goes from 1 to ntraj, and molecule is the name of your system. Example for 10 external trajectories.

```
--CDS section--
sampling external
ntraj 10
```

CAVEAT: Finally, if you combine external trajectories with those computed internally using MOPAC, you need to employ the same labelling in both cases.

BBFS (Bond Breaking/Formation Search) section. BBFS algorithm selects TS guess structures monitoring changes in the adjacency matrix,¹ but the user can impose some restrictions based on the energy and imaginary frequency of the structures found.

```
--BBFS section--
emaxts 200
emints -100
freqmin 200
```

Description of the keywords

emaxts: is the maximum energy (in kcal/mol) of the TSs that will be selected.

emints: is the maximum energy (in kcal/mol) of the TSs that will be selected.

The above energies are relative to the optimized structure provided in FA.xyz. In the figure below **emaxts** is set to **etraj** and **emints** is **-100** kcal/mol because the initial structure might not be the global minimum.

freqmin: is the minimum imaginary frequency (in absolute value and cm^{-1}) of the TSs that will be selected.

Screening of the structures section. To screen the structures for possible redundancies and/or fragmentations, some features of each structure are calculated: energy, SPRINT coordinates,² degrees of each vertex and eigenvalues of Laplacian matrix.³ Comparing these values for two structures, the mean absolute percentage error (MAPE) and the biggest absolute percentage error (BAPE) can be obtained. While **avgerr** and **bigerr** set maximum values for MAPE and BAPE, respectively, **thdiss** refers to the eigenvalues of the Laplacian (EL). The number of zero ELs provides the number of fragments in the system.

```
--Screening of the structures section--
avgerr 0.008
bigerr 2.5
thdiss 0.1
```

Description of the keywords

avgerr: is the maximum value of the MAPE for two structures to be considered equal.

bigerr: is the maximum value of the BAPE for two structures to be considered equal.

thdiss: is the threshold for a EL to be 0. In the above figure, if a $\text{EL} < 0.1$, then $\text{EL} = 0$.

Kinetics section. This part is employed to provide details of the kinetics calculations at the experimental conditions.

```
--Kinetics section--
Rate microcanonical
EKMC 150
MaxEn 150
imin min0
nmol 1000
Maxtime 2e24
Stepsize 1e23
ImpPaths 0.1
```


Description of the keywords

Rate: can either be *canonical* or *microcanonical*, which means that the rate constants will be calculated according to Transition State Theory (TST) or Rice-Ramsperger-Kassel-Marcus (RRKM) theory, respectively.

EKMC: is the energy of the system in kcal/mol for a microcanonical calculation.

TKMC: is the temperature of the system in K for a canonical calculation.

MaxEn: is the maximum energy of the TSs included in the reaction network. In a *microcanonical* calculation, that energy should be equated to **EKMC**. If this value is not set the default is 40 kcal/mol.

imin: is the label for the starting structure in the Kinetic Monte Carlo (KMC) simulations. If **min0** is selected instead of a number, the reference (initial) structure is the starting state in the KMC simulations.

nmol: is the number of molecules employed in the KMC simulations (placed initially at *imin* state).

Maxtime: is the maximum simulation time (units of s (ps) for a canonical(microcanonical) calculation).

Stepsize: is the stepsize for intermediate printout (same units as Maxtime).

ImpPaths: is the minimum percentage of processes occurring through a particular pathway that has to be achieved in order to be considered relevant and finally plotted in an energy diagram (vide infra). If you want to plot them all use 0.

b) Running the accelerated dynamics

Canonical and microcanonical sampling methods provide initial coordinates and momenta to run accelerated dynamics simulations. Select the number of trajectories with **ntraj** and remember to delete **seed**. In you want to run 10 trajectories your CDS section should look like:

```
--CDS section--
sampling microcanonical
etraj 200
modes all
ntraj 10
fs 500
```

And the dynamics can be run using:

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

You may want to have a look at the output file `tsscads.log`, which gives you information of the calculations. Besides, a working directory called `tsdirLL_FA` is created with some temporary information that might be checked throughout the calculations. For instance, a file named `tlist` is created inside the folder, which can be best viewed using:

```
tssl1_view.sh
```

The output will be something like this:

ts #	MOPAC file name	w_imag	Energy	w1	w2	w3	w4	traj #	Folder
1	ts1_FA	1587.3i	-35.71	204.3	438.3	461.3	726.8	1	FA
2	ts2_FA	2009.6i	-17.61	327.2	472.7	522.7	1078.6	2	FA
3	ts3_FA	2930.8i	-20.17	450.6	586.9	908.6	997.2	7	FA

where the first column is the label of each TS, the second is the MOPAC output file name, the third is the imaginary frequency (in cm^{-1}), the fourth one is the energy in kcal/mol, 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 accelerated dynamics were run.

CAVEAT: since the dynamics employ random number seeds, the results shown in the above figure may differ from those obtained in your computer, and the next few explanations refer to the tsvlist file shown above.

MOPAC files are stored also in [tsdirLL_FA](#) Try, for instance:

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

You can also watch the animation of the trajectory, which is stored in [coordir](#) folder inside [FA](#):

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

c) Running several trajectories

If you have access to several processors and want to run the dynamics in parallel you can use the script [tsscads_parallel.sh](#). For instance, to submit 50 trajectories split in 5 different tasks (10 trajectories each) you should use:

```
tsscads_parallel.sh FA.dat 5
```

This will create the directories [batch1](#), [batch2](#), [batch3](#), [batch4](#) and [batch5](#). All TSs will be copied in [tsdirLL_FA](#). If you have slurm workload manager you can submit the jobs to slurm using:

```
sbatch [options] tsscads_parallel.sh FA.dat 5
```

which employs the following default values when no options are specified:

```
#SBATCH --time=01:00:00
#SBATCH -n 40
#SBATCH --output=tsscads_parallel-%j.log
#SBATCH -p shared
#SBATCH --qos=shared
```

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

CAVEAT: the use slurm workload manager might be faster but you have to wait until all tasks are completed before going on.

d) Screening the structures, IRC, minima, reaction network, and kinetics

1) Since `irc.sh` script includes an initial screening of the TS structures, you can check the screening this way:

```
irc.sh screening
```

The above sentence will do the screening and stop. The process involves the use of tools from Spectral Graph Theory using the three threshold values indicated above: ***avgerr***, ***bigerr*** and ***thdiss***. The redundant and fragmented structures are printed on screen as well as in the file **`screening.log`**. When you start obtaining these structures, please check them and change the above parameters if needed.

Should you change some of the above parameters (***avgerr***, ***bigerr***, ***thdiss***) 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”. Now, 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 `tscds_parallel.sh`), which will start the dynamics from the newly generated minima. Convergence in the total number of TSs can be obtained doing:

```
track_view.sh
```

When you are happy with the obtained TSs or you achieved convergence, you can proceed.

5) Solving the kinetics using KMC:

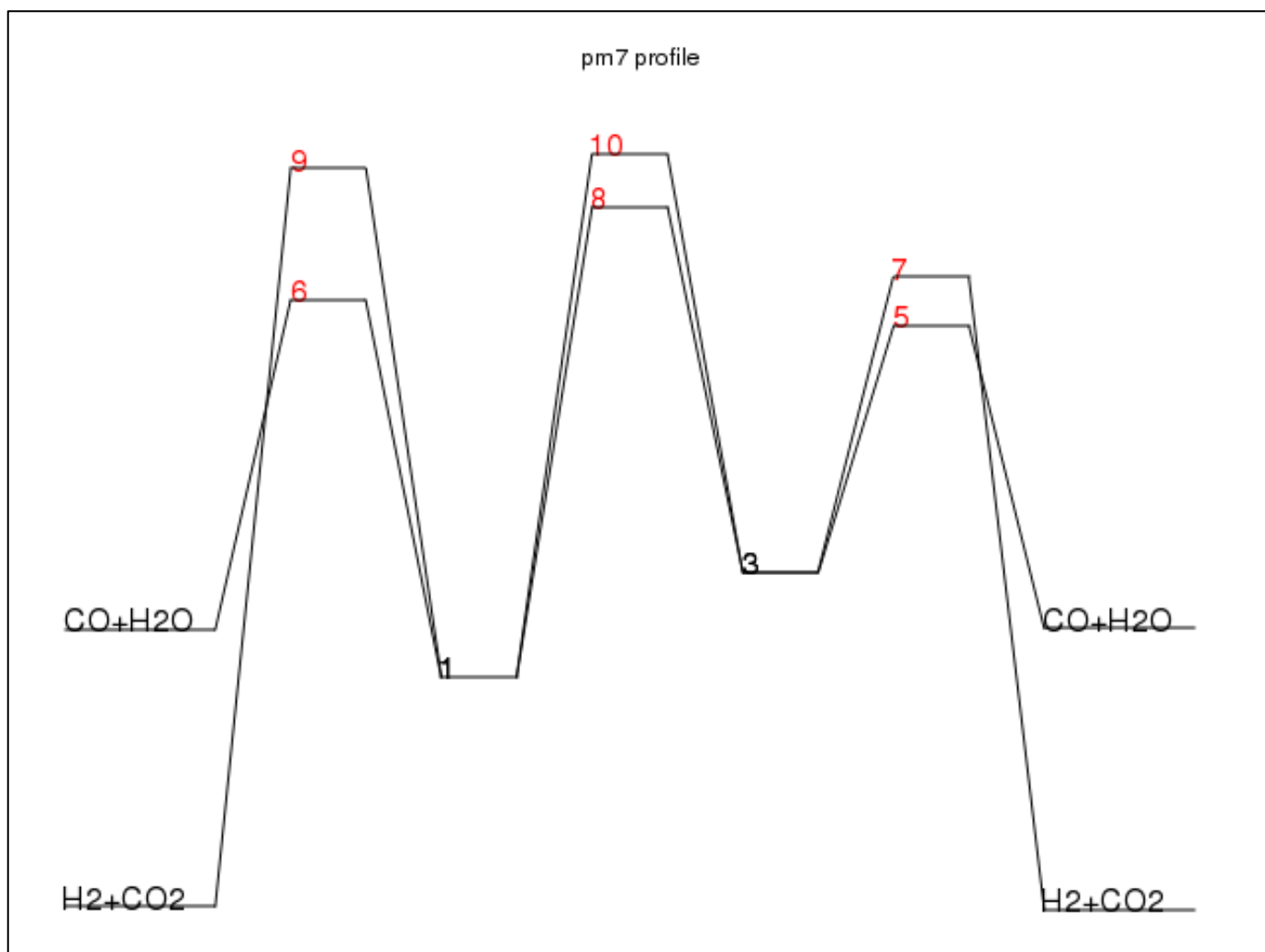
```
kmc.sh
```

6) Gathering all relevant information in folder [FINAL_LL_FA](#):

```
final.sh
```

This folder contains several files:

Energy_profile.gnu: is an energy diagram with the **relevant paths** and it can be viewed with gnuplot. If you change the value of `ImpPaths` in the kinetics section, you will incorporate/remove some pathways.



MINinfo: contains information of the minima:

```
MIN #    DE(kcal/mol)
  1      -8.340
  2       0.000
  3       5.283
  4       6.710
  5      15.338
```

Conformational isomers are listed in the same line:

```
1 2
3 4 5
```

TSinfo: contains information of the TSs:

```
TS #    DE(kcal/mol)
  1       1.873
  2       9.625
  3      25.137
  4      32.852
  5      37.596
  6      40.962
  7      43.960
  8      53.165
  9      58.155
 10      60.011
 11      90.312
```

Conformational isomers are listed in the same line:

```
8 10
```

table.db: with *table* being *min*, *prod* or *ts*. These are sqlite3 tables containing the geometries, energies and frequencies of minima, products and TSs, respectively. The different properties can be obtained using the following, which should be run from the [FINAL_LL_FA](#) folder:

```
select.sh 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) employed to label each structure. For instance, to obtain the geometry of the first transition state you should use:

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

RXNet: contains information of the reaction network.

TS #	DE(kcal/mol)	-----Path info-----			
1	1.873	MIN	1 <-->	MIN	2
2	9.625	MIN	3 <-->	MIN	4
3	25.137	MIN	1 <-->	MIN	1
4	32.852	PROD	1 <-->	PROD	2
5	37.596	MIN	4 <-->	PROD	2
6	40.962	MIN	1 <-->	PROD	2
7	43.960	MIN	3 <-->	PROD	1
8	53.165	MIN	1 <-->	MIN	4
9	58.155	MIN	2 <-->	PROD	1
10	60.011	MIN	2 <-->	MIN	5
11	90.312	PROD	2 <-->	PROD	7

PROD 1 H2 + CO2
PROD 2 CO + H2O
PROD 7 H2 + CO2

RXNet.cg: cg stands for “coarse-grained”. By default (see below) the KMC calculations are “coarse-grained”, i.e., conformational isomers form a single state (corresponding to the lowest energy isomer). Such reaction network, which also removes bimolecular channels is shown in the figure below.

TS #	DE(kcal/mol)	-----Path info-----			
5	37.596	MIN	3 <-->	PROD	2
6	40.962	MIN	1 <-->	PROD	2
7	43.960	MIN	3 <-->	PROD	1
8	53.165	MIN	1 <-->	MIN	3
9	58.155	MIN	1 <-->	PROD	1
10	60.011	MIN	1 <-->	MIN	3

PROD 1 H2 + CO2
PROD 2 CO + H2O
PROD 7 H2 + CO2

Finally, the normal modes of TSs and minima are collected in [normal_modes](#) folder in molder format.

As indicated above, by default, in the KMC simulations, the different conformational isomers form a single state, which speeds up the calculations. If you prefer that each conformational isomer will be a single state in the KMC calculations, you should run the RXN again, and solve the kinetics with the new conditions:

```
rxn_network.sh allstates
kmc.sh
final.sh
```

e) Summary of the steps needed to find reaction mechanisms and solve the kinetics

1. Load tsscds module:

```
module load tsscds/1.1
```

2. Run the accelerated dynamics in parallel:

```
(sbatch [options]) tsscds_parallel.sh molecule.dat ntasks
```

3. Run the irc calculations:

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

4. Optimize the minima:

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

5. Create a reaction network:

```
rxn_network.sh
```

6. Here, you might want to iteratively run tsscds going back to step 2.

7. Solve the kinetics:

```
kmc.sh
```

8. Create [FINAL_LL_molecule](#) folder:

```
final.sh
```

All the above steps can be done using a single script:

```
llcalcs.sh molecule.dat ntasks niter
```

Where niter is the number of iterations. If zenity is available in your linux distribution, the script can be run without arguments, and a GUI will help you enter the arguments.

The use of [llcalcs.sh](#) is recommended once you have verified that the screening process works fine for your system.

f) Finding intermolecular complexes between two molecules

The input file for this type of calculation is slightly different. An example of such input file can be found in [path_to_program/examples/assoc.dat](#) (see figure below). Two more additional files are also needed for this example `cat.xyz` and `co.xyz`, which are also available in the same folder.

```
--General section--
LLcalc pm7
charge 0

--CDS section--
sampling association
A= cat
B= co
rotate 2 com 2.0 1.0

--Screening of the structures section--
avgerr 0.0001
bigerr 5
thdiss 0.1
```

This type of sampling only needs three sections: General, CDS and Screening.

This sampling is employed to optimize complexes between two fragments A and B. It just needs three keywords in the CDS section.

Description of the keywords

A: is the name of fragment A. A file with the Cartesian coordinates `fragA.xyz` must be present also.

B: is the name of fragment B. A file with the Cartesian coordinates `fragB.xyz` must be present also.

rotate: refers to the method employed to optimize the complexes. The calculation is carried out by taking 100 relative structures of both fragments, obtained via random rotations. Thus, the next two fields **2 com** indicate the pivot positions of the rotations: atom 2 of fragment A and the center of mass (com) of fragment B. The last two numbers **2.0** and **1.0** are distances in Å that indicate the distance between both pivots and the minimum intermolecular distance between any two atoms of both fragments, respectively. With this sampling, you do not need BBFS and kinetics sections. However, you still need to provide the parameters for the screening (*vide supra*).

To run the calculations:

```
tsscads.sh assoc.dat
```

This job will submit 100 jobs to find the structures. After the jobs finished, the script will automatically remove duplicates and select the best association “complex”.

You can check the optimized structures in folder [assoc_cat_co](#). 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 `cat_co.xyz`. For fragments containing metals (like in this example), the selection is also based on the valence of the metal center.

The file [assoc_cat_co/assoclist_sorted](#) collects a summary of the structures and their energies, and the MOPAC2016 output files of each of them are called `assocN.out`, where N is a number from 1 to 100.

6. Biased dynamics

A number of methods are available in this distribution to bias the dynamics towards specific reaction pathways. So far, these are the available options:

1) In this algorithm,⁴ 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 adding the following keyword in the CDS section:

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

That would “freeze” two bond distances connecting atoms 1-13 and 2-8, respectively. The labels of the atoms must follow the line starting with **nbondsfrozen**.

2) The second algorithm bias the dynamics towards a particular reaction mechanism. Suppose you want to get the H₂ elimination transition states from formic acid. There is an example of this option in [path_to_program/examples/FA_biasH2.dat](#). You would also need FA.xyz file.

In this case, the reaction coordinate is composed of bond distances: 3-5, 1-4, and 4-5. While the first two bonds have to break, the last one has to form in this process. The following keywords should be added to the CDS section:

```
nbondsbreak 2
3 5
1 4
nbondsform 1
4 5
Kapparep 100
Kappa 100
rmin 0.5
iexp 1
irange 10
```

Keywords **nbondsbreak** and **nbondsform** follow the same syntax as **nbondsfrozen** above. The other keywords are explained below.

A similar test can be performed on the same molecule to get the H₂O elimination TS, whose input file is also available in [path_to_program/examples/FA_biasH2O.dat](#).

Additionally, a Diels-Alder reaction has also been tested (ethylene+1,3-butadiene→cyclohexene) and. the input files can be copied from [path_to_program/examples/diels_bias.dat](#) and [path_to_program/examples/diels.xyz](#).

In practice, a bias potential is added to the potential energy obtained using the semi-empirical Hamiltonian. The bias potential has the following simple form:

$$V = \sum_{i=1}^{nbondsbreak} V_{rep}(r_i) + \sum_{j=1}^{nbondsform} V_{attrac}(r_j)$$

$$V_{rep}(r_i) = \frac{\kappa_{rep}}{r_i}$$

$$V_{attrac}(r_j) = \frac{r_{min}^{iexp}}{2} \times \frac{\kappa}{r_j^{2 \times iexp}} - \frac{\kappa}{r_j^{iexp}}$$

Where κ_{rep} , κ , r_{min} and $iexp$ are parameters (corresponding to the keywords **Kapparep**, **Kappa**, **rmin** and **iexp**), and their units are such that the potential energy is in kcal/mol and the distances in Å. Additionally, the keyword (parameter) **irange** corresponds to the time window (in fs) employed by BBFS.¹ This parameter takes a default value of 20 fs when nonbiased simulations are performed.

The following table shows the parameters employed for the above examples:

	Diels-Alder rxn	H ₂ elimination from FA	H ₂ O elimination from FA
κ_{rep}	200	100	100
κ	200	100	100
r_{min}	0.5	0.5	0.5
$iexp$	1	1	1
irange	10	10	10

The units are such that the potential energy is in kcal/mol and the distances in Å.

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

tsscads.sh inputfile

Should you try this second option, you have to optimize the parameters for your own system, perhaps starting from those collected in the above table.

7. Reaction mechanisms and kinetics using high-level calculations

The High-Level (HL) calculations are carried out by g09.

1. From your working directory (FA in the example), run:

```
(sbatch [options]) TS.sh molecule.dat
```

The default values in this case for a job submitted to slurm are:

```
#default sbatch FT2 resources
#SBATCH --time=04:00:00
#SBATCH -n 8
#SBATCH --output=tsscads_parallel-%j.log
#SBATCH -p shared
#SBATCH --qos=shared
#SBATCH --ntasks-per-node=2
#SBATCH -c 10
```

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

```
(sbatch [options]) IRC.sh
(sbatch [options]) MIN.sh
RXN_NETWORK.sh (allstates)
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 2 steps have been successfully completed and you do not need to add more transition states.

4. Finally, to make a summary of the calculations in folder [FINAL_HL_FA](#):

```
FINAL.sh
```

References

1. Martínez-Núñez, E., An automated method to find transition states using chemical dynamics simulations. *J. Comput. Chem.* **2015**, *36*, 222-234.
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