

# C7790 Introduction to Molecular Modelling

## TSM Modelling Molecular Structures

### Lesson 20

#### Potential Energy Surface - IV (Transition States)

**PS/2020 Distant Form of Teaching: Rev1**

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# Context

## macroworld

### states

(thermodynamic properties, G, T,...)

### phenomenological thermodynamics

equilibrium (equilibrium constant)

kinetics (rate constant)

free energy

(Gibbs/Helmholtz)



partition function



### statistical thermodynamics

### microstates

(mechanical properties, E)

microstate  $\neq$  microworld

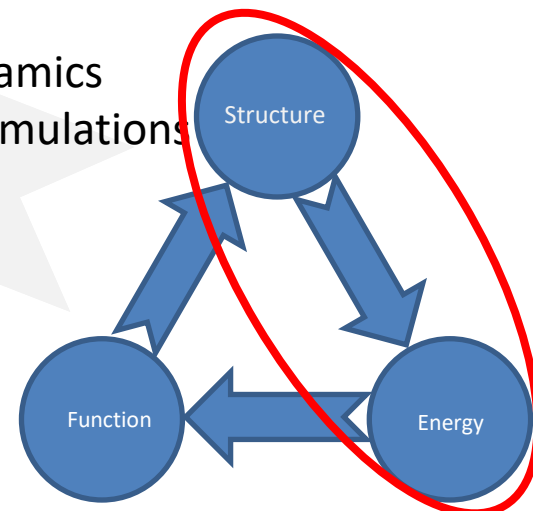
## microworld

### Description levels (model chemistry):

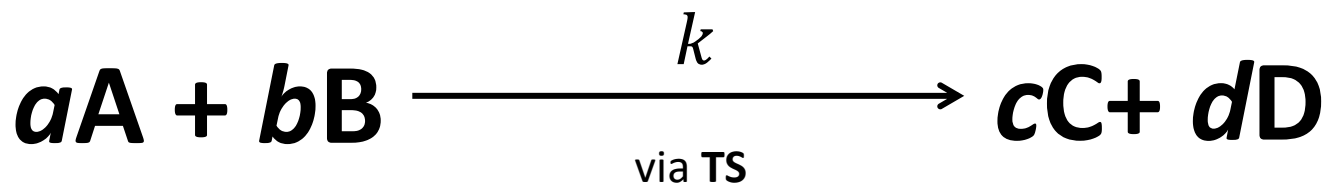
- quantum mechanics
  - semiempirical methods
  - ab initio methods
  - post-HF methods
  - DFT methods
- molecular mechanics
- coarse-grained mechanics

### Simulations:

- molecular dynamics
- Monte Carlo simulations
- docking
- ...



# Revision: Activation energy and modelling



Eyring equation

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

rate constant

activation free energy

$$\Delta G^\ddagger = \Delta G_{f,TS} - (a\Delta G_{f,A} + b\Delta G_{f,B})$$

A

We only need to know the **properties of individual components** involved in the reaction at standard conditions (or at different conditions, which are well defined).

B

easier for modelling

TS

transition state

# Revision: Partition function and modelling

Canonical partition function:

$$Q = \sum_{j=1}^K e^{-\beta E_j}$$

Helmholtz energy  $F$ :

$$F = -k_B T \ln Q$$

approximation

Consider only the most important microstate

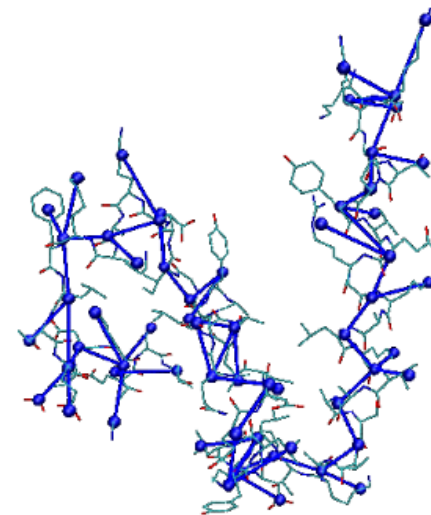
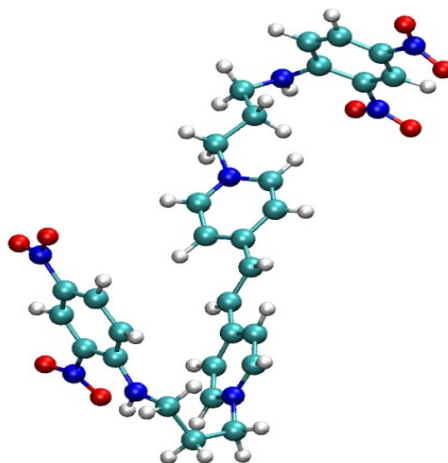
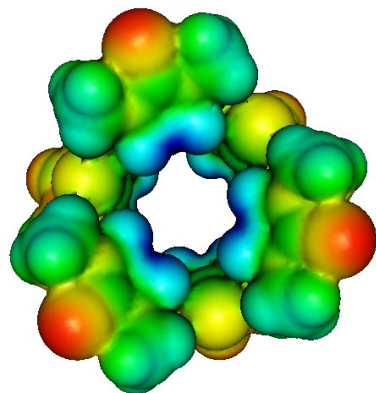
$$E_1, \underline{E_2}, E_3, \dots$$

The most important microstate is the microstate with the lowest energy.

$$F = E_1$$

It is very often used for qualitative consideration or when computationally demanding methods are employed (typically quantum chemical calculations).

# Revision: Potential energy calculations



QM (Quantum mechanics)

MM (Molecular mechanics)

CGM (*Coarse-grained mechanics*)



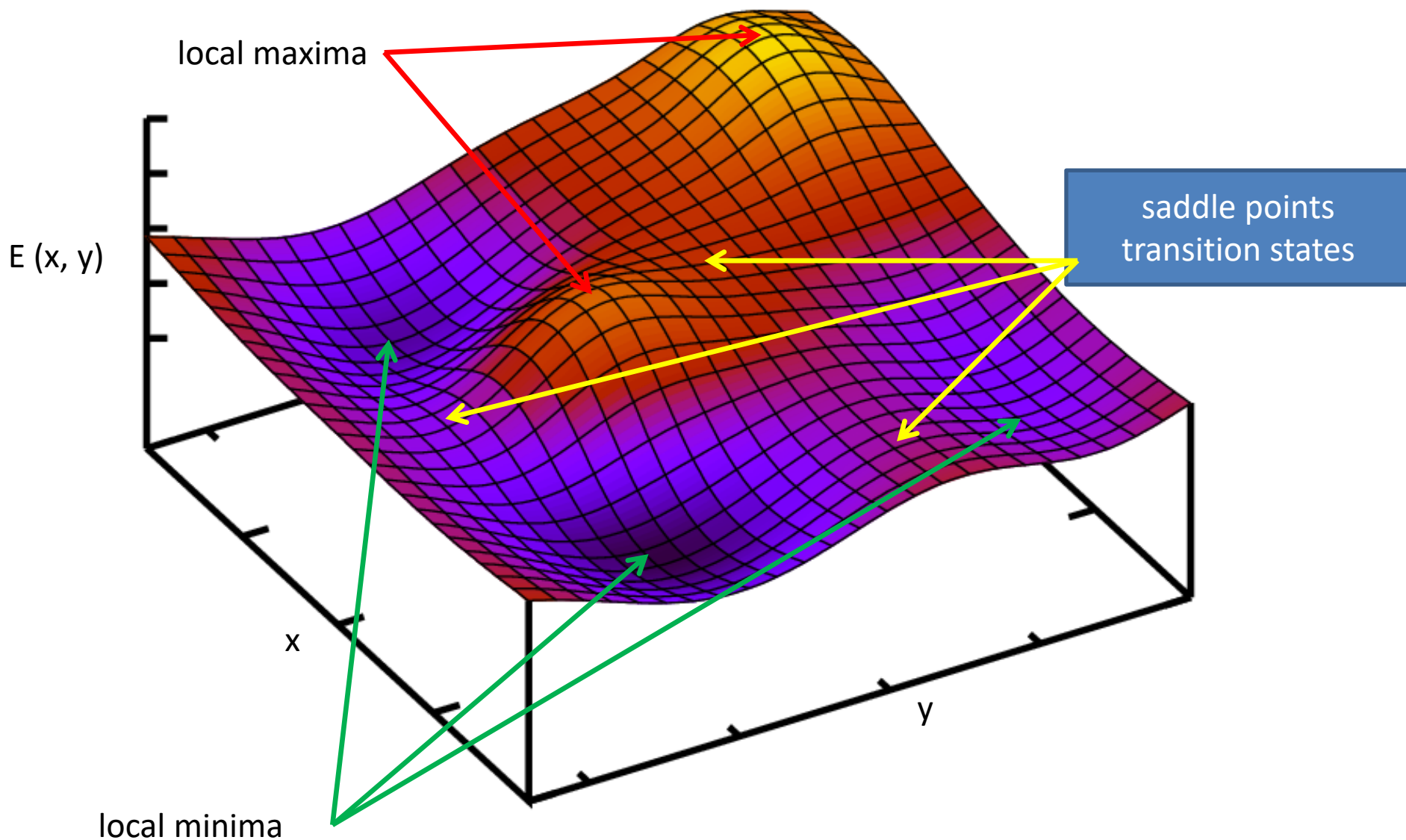
R - position of atom nuclei

R - position of atoms

R - position of beads

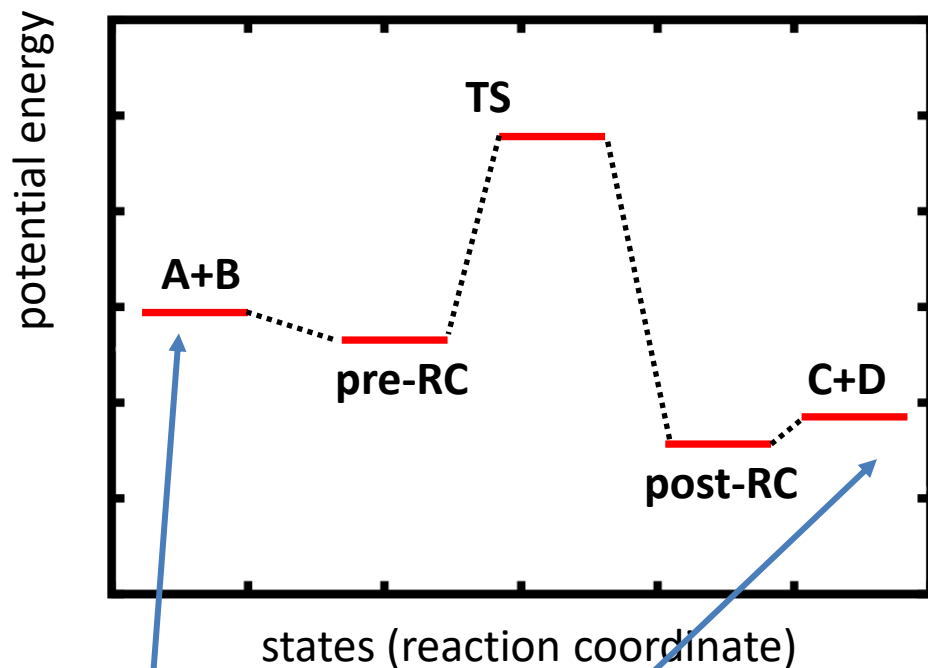
**Potential energy surface can be calculated by various method (model chemistry)!**

# Revision: Transition State on PES

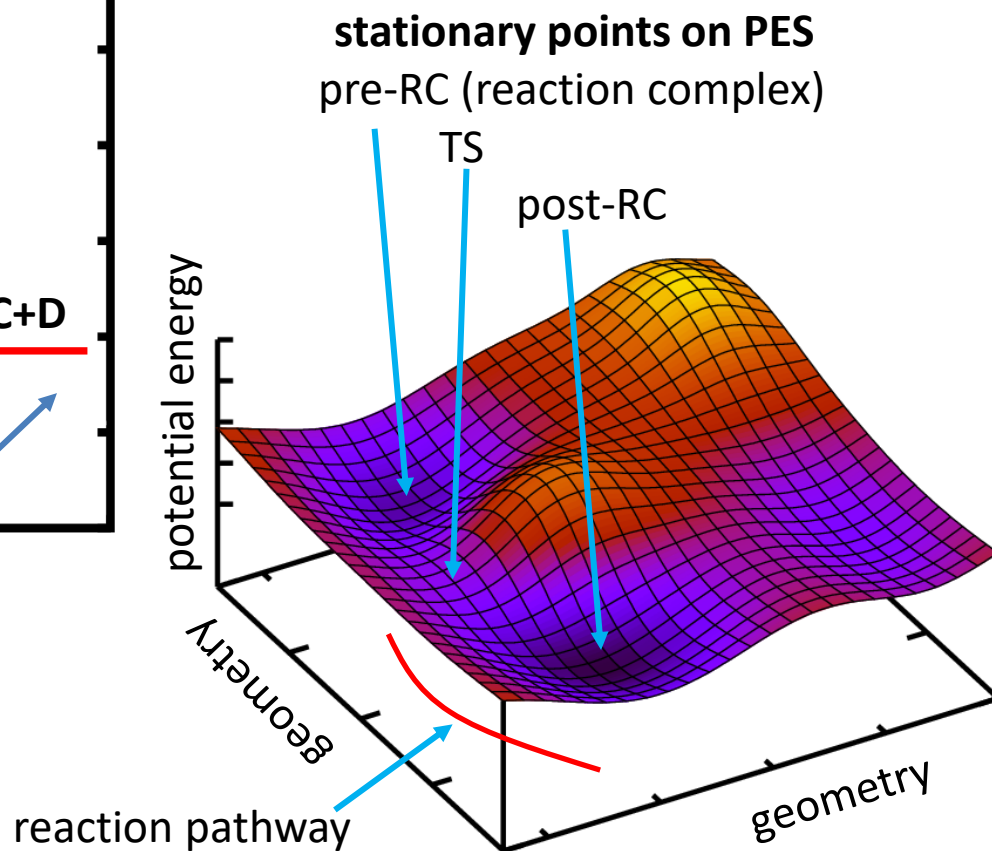


# Elementary reaction and PES

**Elementary reaction** is the transformation of reactants and products represented by **pre-reaction** and **post-reaction complexes** separated by just one **transition state**.



individual non-interacting components at standard state



# Finding Transition States on PES

If the initial geometry is already close to searched transition state:

- local optimization methods

If the reactants, products or both are known:

- semi-global optimization methods
  - Single Coordinate Driving Method
  - Synchronous Transit Methods
  - Nudged Elastic Band Methods



# Reaction Coordinate

- The **reaction coordinate** describes the geometrical changes, which are necessary for transforming reactants into products via the transition state and vice versa.
- Its correct form is not a priori known.
- Approximate reaction pathways can be obtained by:
  - nudged elastic band method
  - string method
- If the transition state is known, then the **intrinsic reaction coordinate (IRC)** can be calculated.
  - IRC describes geometrical changes resulting from going "downhill" from TS in both directions in such a way that the energy gradient in all perpendicular directions is zero.

Since the potential energy is a state function, the exact knowledge of reaction pathway is not needed. Only proper characterization of states (reactants, products, transition states) is necessary.

**However, at least some crude representation of reaction pathway is necessary to find transition state.**

Locating Transition Structures

# Local Methods

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# Local Methods

- **Transition state (TS)** is a **saddle point** on PES.

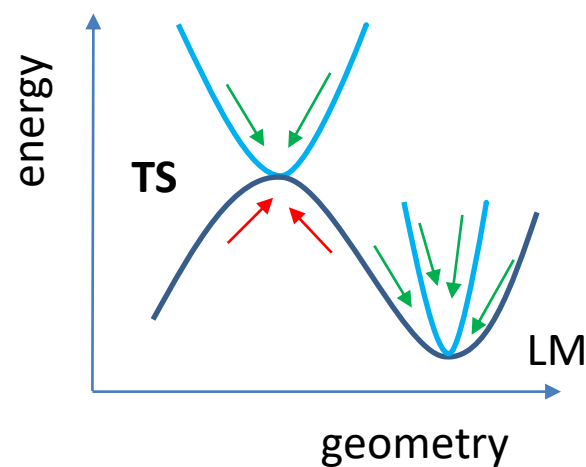
- The saddle point is a **stationary point**:
$$\frac{\partial E(\mathbf{R})}{\partial \mathbf{R}} = 0$$

- PES curvature at the saddle point provides **one negative Hessian H eigenvalue**:

$$\mathbf{H}\mathbf{c}_k = \lambda_k \mathbf{c}_k$$

all positive  $\lambda_k$  - local minimum (LM)  
one negative, other positive  $\lambda_k$  - **first order saddle point transition state - TS**

- Searching for a transition state structure is more complex procedure than searching for a local minima because:



LM geometry optimizers:

- move geometry "downhill" only

**TS geometry optimizers:**

- move geometry "uphill" along negative eigenvector
- at the same time, move geometry "downhill" along the other degrees of freedom

# Local Methods, cont.

## Transition state geometry optimizers:

- pseudo-second order methods (quasi-Newton methods) need to be employed
- **starting geometry (structure) must be very close to the saddle point**
- **initial Hessian must be of high quality**
  - empirical Hessians employed in local geometry optimization are not usable
  - **Hessian calculated at the same level theory** as used during geometry optimization is good choice. However, this is computationally very demanding.
- for difficult cases, Hessian need to be recalculated at the same level of theory at each geometry optimization step (quasi-Newton -> full Newton method). This is extremely computationally demanding and suitable only for small molecular systems.

## Starting structure for SP (TS) search can be found by **pseudo-global optimization methods**:

- single coordinate driving method
- linear and quadratic synchronous transit methods
- nudged elastic methods
- string methods
- others ....

# Local Methods - Practical Realizations

## Transition structure search in Gaussian

request optimization of the transition state

```
%Chk=ts.chk  
# PM3 Opt(CalcFC,TS,NoEigenTest,MaxCycle=25)  
  
transition state optimization  
  
XX  
X .....
```

**CalcFC** force constants (Hessian) are calculated on the input geometry

**CalcAll** force constants (Hessian) are calculated on each geometry during optimization (full Newton-Raphson method)

do not waste computational time on bad structures

skip very tight requirements on starting structures  
if the starting structure is not of good quality, the optimization can fail

# Validation of TS

- It is necessary to validate the nature of stationary state representing the transition state employing vibrational analysis.
- Only ONE normal mode must be imaginary, the other normal modes must be represented by frequencies, which are real numbers.
- Atom movement along imaginary vibrational mode must follow the intended reaction change (formation/breaking bonds).

Locating Transition Structures

# Semi-global Methods

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**Single Coordinate Driving (SCD) Method**

**Synchronous Transit (ST) Methods**

**Nudged Elastic Band (NEB) Methods**

# Single Coordinate Driving Method

**Single coordinate driving (SCD) method** is a simple approach for finding initial structures for the transition state geometry optimization.

SCD is a special case of potential energy surface scan methods (limited to a single geometry parameter).

Driven geometry parameter should represent the geometry change occurring during the reaction. Suitable coordinates can be:

- distance of formed bond
  - distance of broken bond
  - dihedral angle representing rotation around bond during a conformational change
  - others ...
- The SCD method can suffer from **driving hysteresis**. Two different driving pathways can be observed when driving from the reactant or product state.



# Synchronous Transit Methods

## Linear synchronous transit (LST) method

- Geometry parameters (Cartesian or internal coordinates) vary linearly between initial (reactants) and final (products) states:
- The order of atoms in  $\mathbf{R}_{reactants}$  and  $\mathbf{R}_{products}$  must be the same!

$$\mathbf{R}_i = \frac{N - i}{N} \mathbf{R}_{reactants} + \frac{i}{N} \mathbf{R}_{products} \quad i = 0, 1, 2, \dots, N$$

- The guess of transition state geometry is taken as a geometry with the maximum energy.
- The structure with maximum energy is usually far away from the correct transition state.
- Thus, the geometry obtained by LST must be optimized using a local method.

## Improved versions:

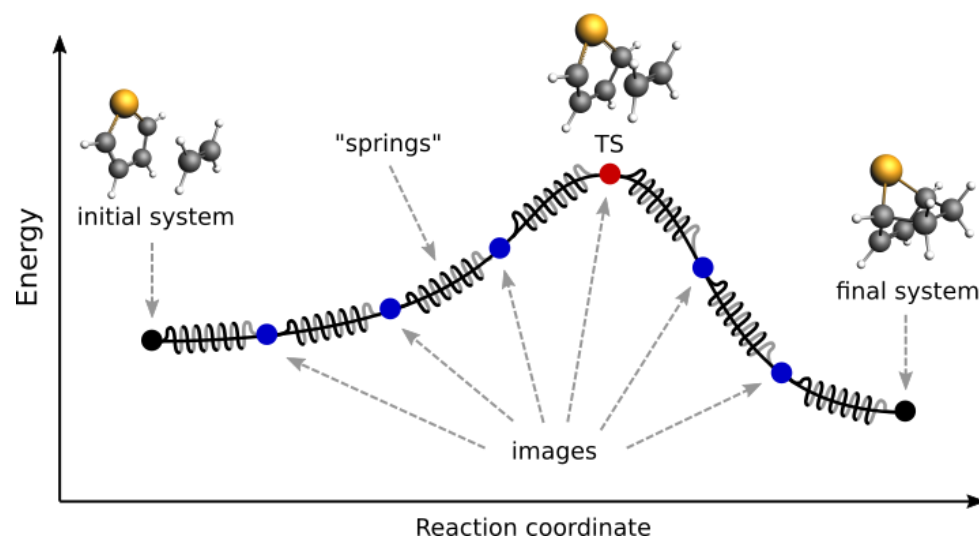
- QST2 - quadratic synchronous transit between reactants and products
- QST3 - quadratic synchronous transit between reactants and products via crude approximation of transition state

# Nudged Elastic Band Method

**Nudged elastic band (NEB) method** is an approach for finding reaction paths and transition structures.

- Reaction path is represented by beads. Each bead represent a specific system geometry.
- NEB ensures equidistant spacing between beads by springs.
- Potential energy is minimized in all perpendicular degrees of freedom.
- Due to path discrimination, only guess of transition state geometry is obtained, which need to be refined by local optimization.

The **string method (SM)** is similar as NEB. SM uses splines to achieve equidistant bead separation.



<https://www.scm.com/doc/AMS/Tasks/NEB.html>

# Summary

- Finding transition states is necessary step for quantification of reaction kinetics.
- Broad range of methods is available to locate either correct TS or at least its estimate.
- In comparison with characterization of reactants and products, finding transition structures is much difficult task.
- Nature of found transition states needs to be verified by vibrational analysis.
- Transition state must be a stationary state with only one imaginary molecular vibrations.