C7790 Introduction to Molecular Modelling
TSM Modelling Molecular Structures

Lesson 25
Large Models - Ensembles Averages

PS/2020 Distant Form of Teaching: Rev1

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Context

macroworld   **microworld**

states
(thermodynamic properties, G, T,…)

phenomenological thermodynamics

equilibrium (equilibrium constant)
kinetics (rate constant)

free energy
(Gibbs/Helmholtz)

partition function

statistical thermodynamics

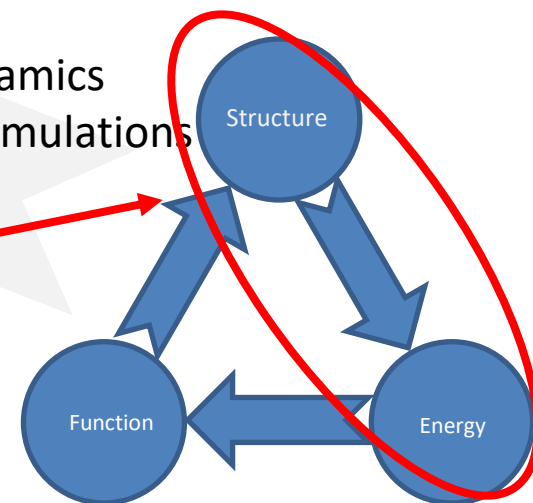**microstates**
(mechanical properties, E)

microstate ≠ 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
- …

Structure

Function   Energy

Revision: Statistical thermodynamics

Statistical approach:

Statistical physics (statistical mechanics) relates two levels of description of physical reality, namely the macroscopic and microscopic levels. In a more traditional sense, it deals with the study of the properties of macroscopic systems or systems, considering the microscopic structure of these systems (**statistical thermodynamics**). The founders were Ludwig Boltzmann and Josiah Willard Gibbs.
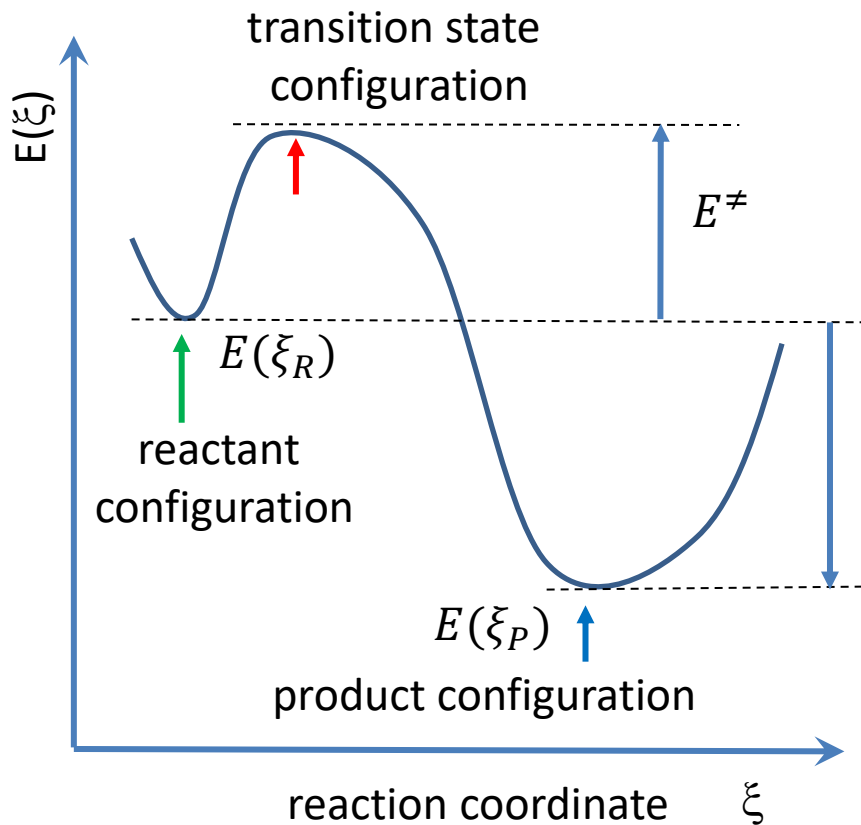
Level of description:

- particles and interactions between them
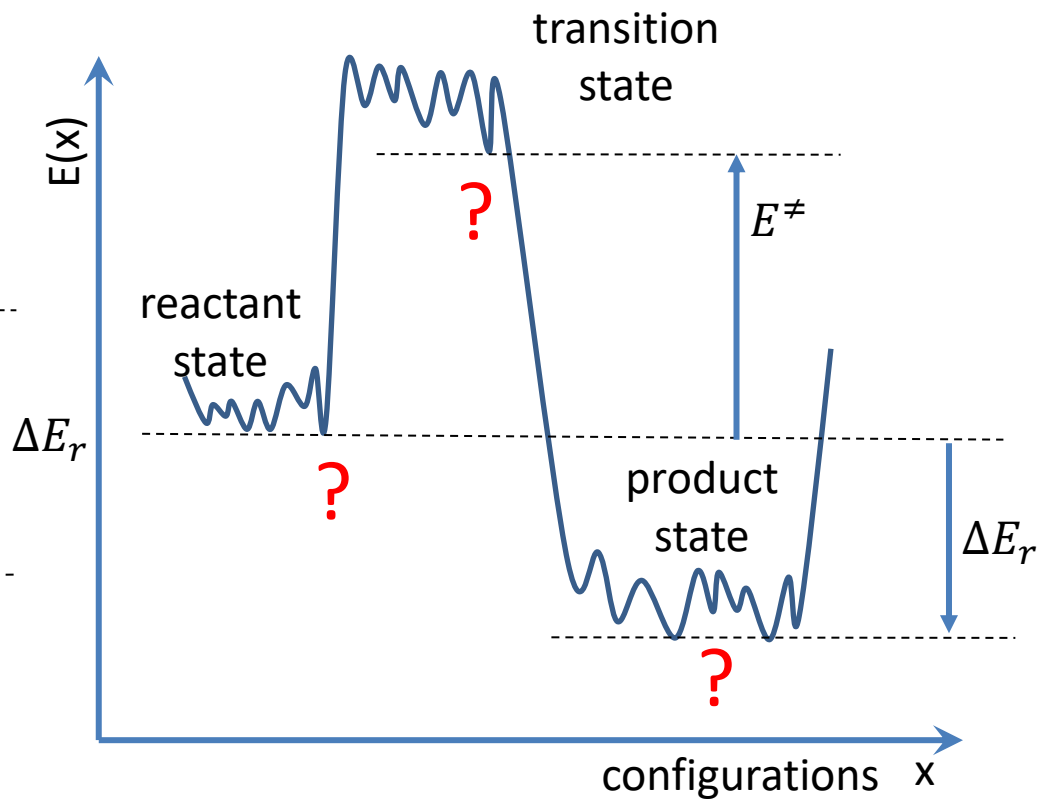- equations of motions

Main summary:

➢ It is not possible to model microstates with the size of macrosystems.
➢ Thus, simplified models (in size) are employed instead.
➢ Th size of model determines the modeling approach.

wikipedia.cz, simplified

Revision: PES

Small models

Large models

- ➤ Increasing degrees of freedom (model size) result in increased roughness of PES.
- ➤ The only reasonable description of large models is to use statistical weighting using right sampling technique.

Revision: System properties

The observable value ($\overline{M}$) of the property M can be determined by two approaches:
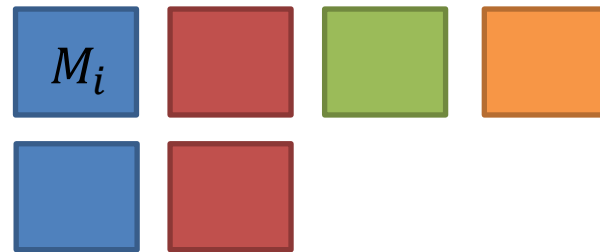
Time average:

$M(t)$

t

snapshot of the system at time *t* is called a microstate

$$\overline{M} = \frac{1}{t_{tot}} \int_{o}^{t_{tot}} M(t)dt$$

We can run **molecular dynamics simulations** to get value of property by molecular modelling.

Ensemble average:

M_i

2/6   2/6   1/6   1/6

$$\overline{M} = \sum_{i=1}^{K} p_i M_i$$

We can run **Monte Carlo simulations** to get value of property by molecular modelling.

Ergodic Hypothesis

The **ergodic hypothesis** is often assumed in the statistical analysis of computational physics. It postulates that the average of a process parameter **over time** and the average over the **statistical ensemble** are the same.

Time average:

$$\overline{M} = \frac{1}{t_{tot}} \int_{o}^{t_{tot}} M(t)\,dt$$

Ensemble average:

$$\overline{M} = \sum_{i=1}^{K} p_i M_i$$

the same outcome

However, this assumption—that it is as good to simulate a system over a long time as it is to make many independent realizations of the same system—is not correct for all physical systems.

https://en.wikipedia.org/wiki/Ergodic_hypothesis