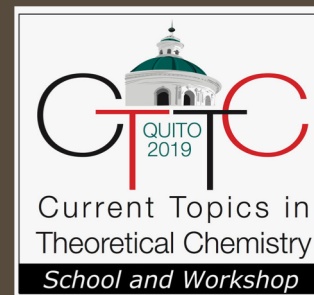




ESSENTIALS OF COMPUTATIONAL REACTIVITY

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CTCC School 2019

Quito (Ecuador)

COMPUTATIONAL CHEMISTRY

Branch of chemistry that uses digital technologies in solving chemical problems



methods of theoretical chemistry
translated into working computer
programs in order to produce results

- **Theories:** Rules postulated to govern the behaviour of physical systems.
Non universally applicable.

$$\hat{H}\Psi = E\Psi \quad \vec{F} = m\vec{a}$$

- **Modeling:** Introduction of approximations into a more general theory.

$$\Psi(\vec{r}, \vec{R}) = \Psi(\vec{r}; \vec{R})\Psi(\vec{R}) \quad ; \quad V_{\sigma}(\vec{r}) = \int_{\Gamma} \frac{\sigma^{ASC}(\vec{s})}{|\vec{r} - \vec{s}|} d^2s$$

COMPUTATIONAL CHEMISTRY

Branch of chemistry that uses digital technologies in solving chemical problems



- Energetics
- Prediction of structures
- Reactivity
- Properties:
 - a) Spectra (IR, NMR, UV, etc.)
 - b) Ionization Potentials (IP) and Electron Affinities (EA)
 - c) Electron Distribution (unpair electrons, electron localization and delocalization, aromaticity, etc.)
 - ...

COMPUTATIONAL REACTIVITY

Non-experimental studies of the **chemical reactivity** of molecular systems

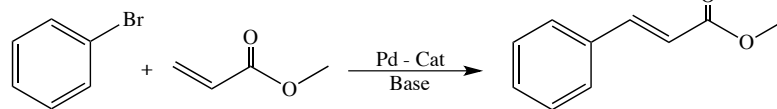


the chemical's ability to react with other substances

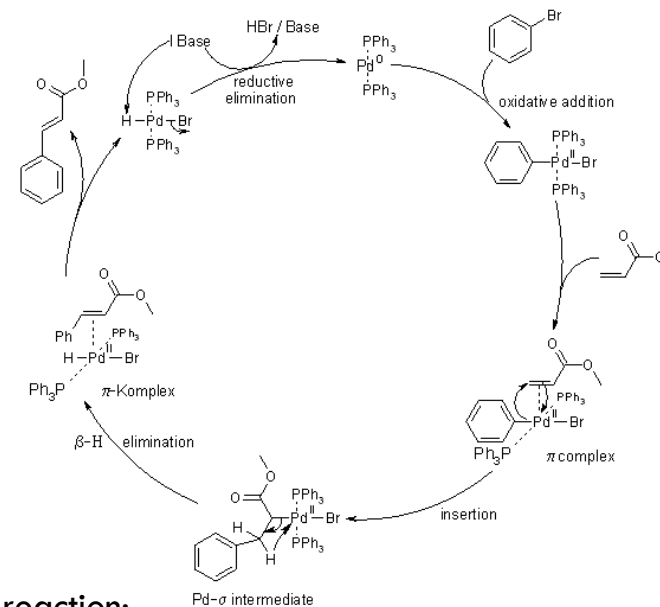
Main objectives: Identification and rationalization of:

- **reaction mechanisms**
- **kinetics**
- **thermodynamics**

of chemical processes that involve several steps.



Mechanism of the Heck reaction:



ENERGY CALCULATIONS: Theories

Molecular Mechanics

Se aplican las leyes de la Física Clásica para modelar los sistemas moleculares.

Quantum Mechanics

Se basa en la resolución aproximada de la **ecuación de Schrödinger electrónica** (ESE), porque en la mayoría de casos se trabaja sobre la **aproximación de Born-Oppenheimer**.

Solving a differential equation with respect to either:

the position \rightarrow *deterministic*

wave function \rightarrow *probabilistic*

$$V_{spring} = K_{str}(r - r_0)^2$$

$$V_{Lennard-Jones} = 4\varepsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right]$$

ENERGY CALCULATIONS: Theories

Molecular Mechanics

Se aplican las leyes de la Física Clásica para modelar los sistemas moleculares.

- La energía potencial del sistema viene dada por una función analítica llamada **campo de fuerzas**.
- No se consideran los electrones. Se considera cada átomo como una partícula.
- A cada átomo se le asigna como mínimo un radio y una carga neta parcial (comúnmente también una tipología).
- Los enlaces se tratan como si fueran *muelles*, con constantes de fuerza y distancias de equilibrio determinadas. **No se pueden romper enlaces**.
- Otras interacciones no enlazantes como fuerzas electrostáticas o de van der Waals se incluyen típicamente en el campo de fuerza a través de la Ley de Coulomb y potenciales tipo Lennard-Jones, respectivamente.

Quantum Mechanics

Se basa en la resolución aproximada de la **ecuación de Schrödinger electrónica (ESE)**, porque en la mayoría de casos se trabaja sobre la **aproximación de Born-Oppenheimer**.

- Proporcionan la función de onda electrónica y la energía potencial del sistema del estado fundamental electrónico y/o otros estados excitados.

Semiempiric methods

- Resolución aproximada de la eq. de Schrödinger electrónica mediante el uso de parámetros empíricos obtenidos previamente a partir de datos experimentales o cálculos (ab initio) muy precisos.
- Coste computacional bajo.

Ab initio methods

- Resolución aproximada de la ESE a partir de los postulados de la MQ.
- No se necesitan datos experimentales. La energía y la función de onda del sistema dependen sólo de la posición de los núcleos.
- Coste computacional relativo.



QUANTUM MECHANICS

Table of Contents

- Born-Oppenheimer Approximation
- Potential Energy Surfaces
- Statistical Mechanics
- First calculations: Energy Calculations
 - Basis Sets
 - Structure
- Transition State Theory (TST)
- Factors that affect Reaction Rates and Thermodynamics.
General Considerations

BORN-OPPENHEIMER APPROXIMATION:

$$\Psi(\vec{r}, \vec{R}) = \underbrace{\Psi(\vec{r}; \vec{R})}_{\Psi_{elec}} \underbrace{\Psi(\vec{R})}_{\Psi_{nuc}}$$

Schrödinger equation: $\hat{H}\Psi = E\Psi$

Hamiltonian terms can be also splitted: $\hat{H} = \hat{T}_N + \underbrace{\hat{T}_e + \hat{V}_{ee} + \hat{V}_{eN} + \hat{V}_{NN}}_{\hat{H}_{elec}}$

Electronic
Schrödinger
equation:

$$\hat{H}_{elec}\Psi_{elec} = E(\vec{R})\Psi_{elec}$$

Potential Energy
Surface (PES)

- \hat{T}_N = Kinetic energy of nuclei
- \hat{T}_e = Kinetic energy of electrons
- \hat{V}_{ee} = Potential energy between electrons (difficult)
- \hat{V}_{Ne} = Potential energy nuclei – electrons (attraction)
- \hat{V}_{NN} = Potential energy between nuclei (repulsión)

\neq

$$(\hat{T}_N + E(\vec{R}))\Psi(\vec{R}) = E_{tot}\Psi(\vec{R})$$

Usually it is treated classically, without taking into account nuclear wave functions.

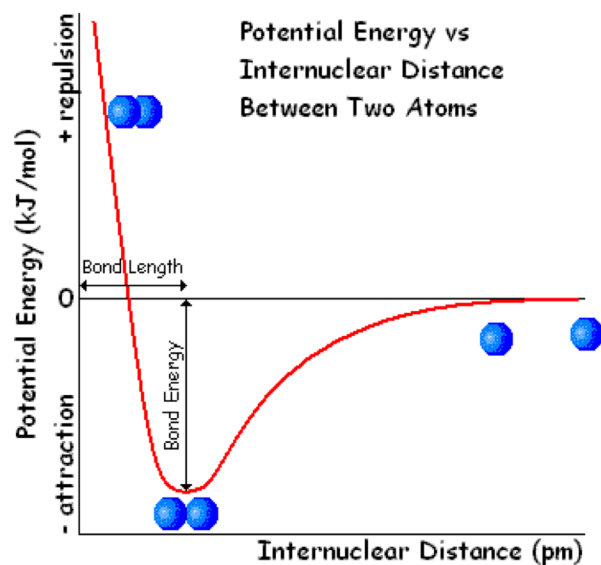
POTENTIAL ENERGY SURFACES

$$\hat{H}_{elec} \Psi_{elec} = E(\vec{R}) \Psi_{elec}$$

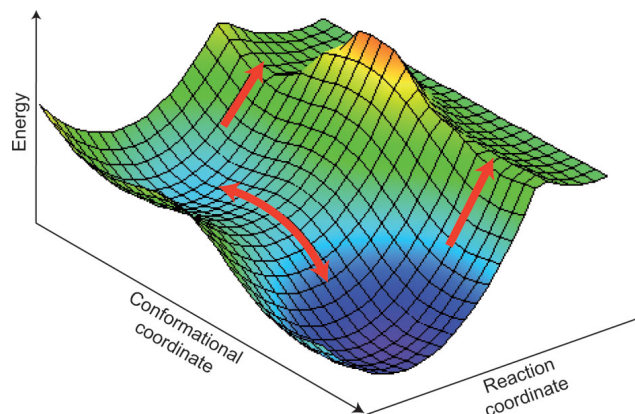
Dimensionality: $3N-6(5)$

(N =Number of atoms)

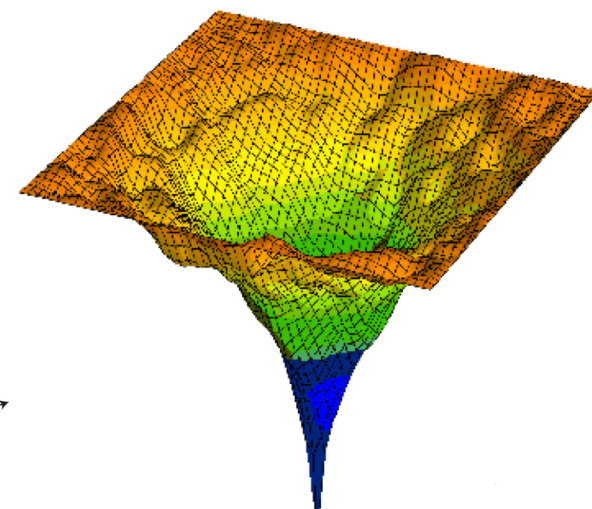
Constructing a complete PES for molecules containing more than three or four atoms is virtually impossible.



Dissociation of diatomic molecule



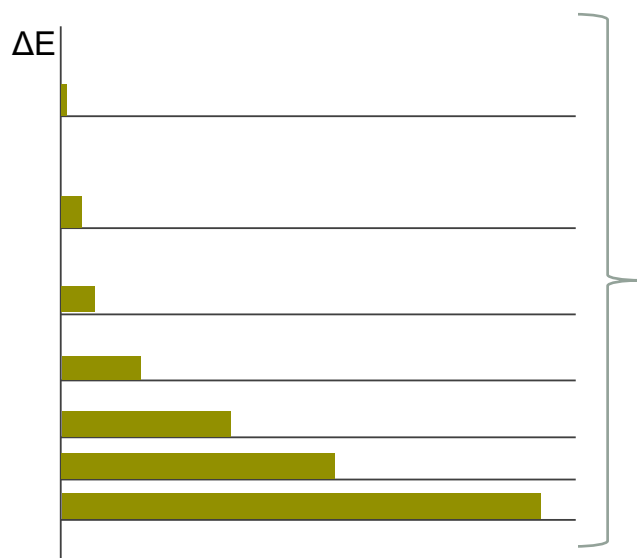
Reaction mechanism



Conformational changes in a big system

STATISTICAL MECHANICS

From E_{elec} to macroscopic properties \rightarrow Statistical mechanics



Distribution of states

At a finite temperature, there is a distribution of molecules in all possible (quantum) energy states

$$P(\text{probability}) \propto e^{-\epsilon/kT} \quad \text{Boltzmann factor}$$

Key feature: partition function

$$q = \sum_{i=\text{states}}^{\infty} e^{-\epsilon_i/kT}$$

- for a single molecule -

$$Q = \sum_i^{\infty} e^{-E_i/kT}$$

- collection of *non-interacting* particles -

STATISTICAL MECHANICS

The significance of partition function Q is that thermodynamic functions can be calculated from it.

$$U = kT^2 \left(\frac{\partial \ln Q}{\partial T} \right)_V$$

$$H = U + PV = kT^2 \left(\frac{\partial \ln Q}{\partial T} \right)_V + kTV \left(\frac{\partial \ln Q}{\partial V} \right)_T$$


$$S = kT \left(\frac{\partial \ln Q}{\partial T} \right)_V - kT \ln Q$$

$$G = H - TS = \dots$$

How partition function q (Q) is computed?

STATISTICAL MECHANICS

Total energy approximated as a sum of terms involving translational, rotational, vibrational and electronic states.*

$$\begin{aligned}\epsilon_{tot} &= \epsilon_{trans} + \epsilon_{rot} + \epsilon_{vib} + \epsilon_{elec} \\ q_{tot} &= q_{trans} q_{rot} q_{vib} q_{elec}\end{aligned}$$


For an isolated polyatomic molecule, the energy levels for a single conformation can be calculated within the *rigid-rotor harmonic-oscillator* (RRHO) approximation.

Translational degrees of freedom

Model: molecule in a “box”

Energy levels: $\epsilon_n = \frac{n^2 h^2}{8\pi^2 M}$

Partition function: $q_{trans} = \left(\frac{2\pi M kT}{h^2}\right) V$

$$\Delta\epsilon \ll kT$$

STATISTICAL MECHANICS

Rotational degrees of freedom

Model: “rigid-rotor” approximation

Energy levels:
$$\varepsilon_J = J(J + 1) \frac{h^2}{8\pi^2 I}$$

I(moment of inertia) = $m_1 r_1^2 + m_2 r_2^2 + \dots$

Partition function:
$$q_{rot} = \frac{8\pi^2 I kT}{h^2 \sigma}$$

$$\Delta\varepsilon \ll kT$$

Vibrational degrees of freedom

Model: harmonic oscillator

Energy levels:
$$\varepsilon_n = \left(n + \frac{1}{2}\right) h\nu$$

$$\nu = \frac{1}{2\pi} \sqrt{\frac{k}{\mu}} \quad ; \quad \mu = \frac{m_1 m_2}{m_1 + m_2}$$

Partition function:
$$q_{vib} = \prod_{i=1}^{3N_{atom}-6} \frac{e^{-h\nu_i/2kT}}{1 - e^{-h\nu_i/2kT}}$$

$$\Delta\varepsilon \sim kT$$

Electronic degrees of freedom

$$\varepsilon_i \gg kT$$

$$q_{elec} = \sum_{i=0}^{\infty} g_i e^{-\varepsilon_i/KT} \approx g_0 e^{-\varepsilon_0/KT}$$



FIRST CALCULATIONS: ENERGY CALCULATIONS

There are many types of calculations:

- Single Point Calculations for a given geometry
- Geometry optimization
- Localization of TS

Minimal Components

- **The method:** So far we will restrict to DFT/HF.
- **The basis set:** Together with the method it determines the accuracy of our calculation.
- **The structure:** The initial starting point.
- **The charge:** The total charge of our molecule
- **The multiplicity:** $2S+1$, being S the number of unpaired electrons.

BASIS SET:

A basis set is a set of functions used to create the molecular orbitals and the wavefunction.

Formalism used: SCF-LCAO-MO. The many-electron wavefunction (Ψ) is expressed as a product of single-electron wavefunctions called molecular orbitals (ψ) formed from a linear combination of atomic orbitals (φ) and whose coefficients, which are determined self-consistently.

$$\Psi = \prod_i^n \psi_i(\vec{r})$$

$$\psi_i = \sum_j C_{ij} \varphi_j$$

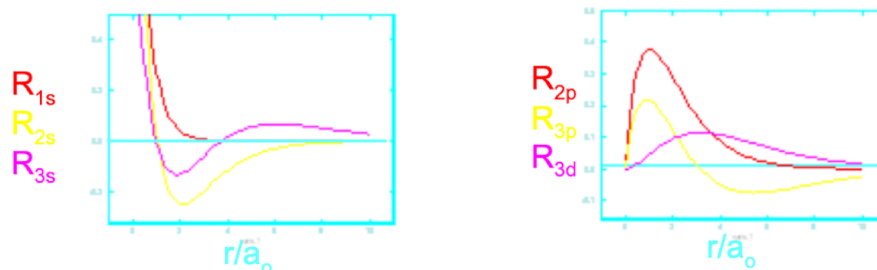
The most commonly used atomic orbitals (φ_j) are called Slater type orbitals (STOs), composed of sums of Gaussian type orbitals (GTOs).

BASIS SET:

Slater type orbitals (STOs):

$$\varphi_j = S_{nlm}(r, \theta, \phi) = R_{nl}(r) \cdot Y_{lm}(\theta, \phi) = Nr^{n-1}e^{-\zeta r} \cdot Y_{lm}(\theta, \phi)$$

STOs represent the radial distribution of electron density very well.



However, from a computational point of view, the STOs have the severe shortcoming that most of the required integrals needed in the course of the SCF procedure must be calculated numerically which drastically decreases the speed of a computation.

Gaussian type orbitals (GTOs):

$$G_{nlm}(r, \theta, \phi) = R_{nl}(r) \cdot Y_{lm}(\theta, \phi) = Nx^a y^b z^c e^{-\alpha r^2} \cdot Y_{lm}(\theta, \phi)$$

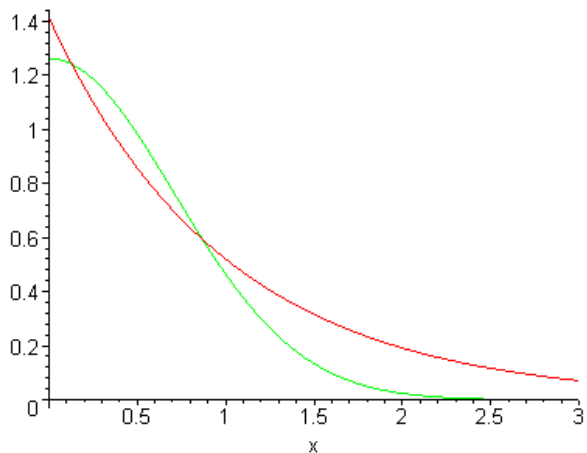
The problem is that GTOs do not represent the radial dependence of the electron density well at all.

BASIS SET:

$$\varphi_j = S_{nlm}(r, \theta, \phi) = R_{nl}(r) \cdot Y_{lm}(\theta, \phi) = Nr^{n-1}e^{-\zeta r} \cdot Y_{lm}(\theta, \phi)$$

$$G_{nlm}(r, \theta, \phi) = R_{nl}(r) \cdot Y_{lm}(\theta, \phi) = Nx^a y^b z^c e^{-\alpha r^2} \cdot Y_{lm}(\theta, \phi)$$

The main difference between STO and GTO is that in GTO the r variable in the exponential function is squared.



GTO (en verde) vs STO (en rojo)

Las funciones tipo STO tienen una interpretación física directa y, por tanto, son de manera natural buenas bases para orbitales moleculares. describen mejor la densidad electrónica cerca de los núcleos, pero son computacionalmente ineficientes.

Los GTO son computacionalmente mas manejables pero es necesario introducir combinaciones lineales de ellas (**primitivas**) para describir los electrones internos (core).

LA SOLUCIÓN: Acondicionar una suma fija de GTOs para replicar la STO.

BASIS SET:

Minimal Basis Set: 1 Slater function per electron, independently the electron is in a core or valence orbital.

STO-3G
STO-4G
STO-6G

$$S(r, \theta, \phi) \approx \sum a_i G_i(r, \theta, \phi)$$

$$S(r, \theta, \phi) \approx a_1 G_1(r, \theta, \phi) + a_2 G_2(r, \theta, \phi) + a_3 G_3(r, \theta, \phi)$$

Expression of a STO-3G function

The minimal basis sets are not flexible enough for accurate representation of orbitals.

SOLUTION: Extended basis sets. Use multiple functions to represent each orbital.

$$\varphi_{2s}(r) = \varphi_{2s}^{STO}(r, \zeta_1) + d\varphi_{2s}^{STO}(r, \zeta_2) \quad \mathbf{d \text{ is a constant}}$$

There are several different types of extended basis sets:

BASIS SET:

Extended basis sets:

- Split-valence

- Polarized sets

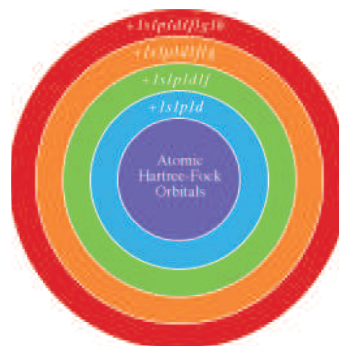
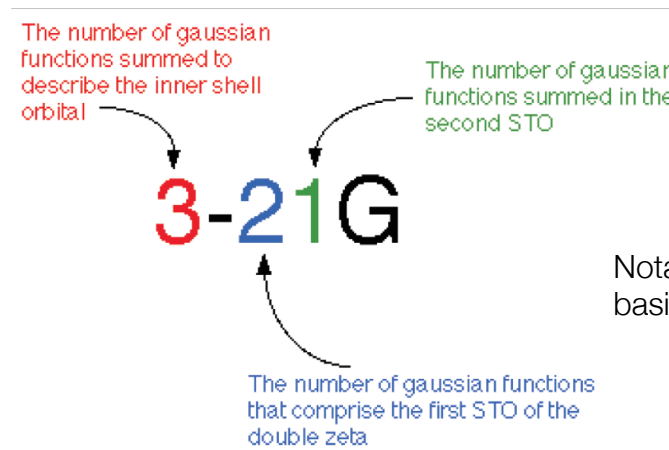
Polarization functions have one addition node

- Diffuse sets

Functions with very small exponents. They decay slowly with distance from nucleus.

- Correlated consistent sets

Dunning's basis set.





STRUCTURE:

There are different ways to determine the initial structure:

- **Obtain** the structure from:

- Experiment (X-ray)
- Research paper (Supporting Information).
- Previous (more approximate) calculation.
- Database

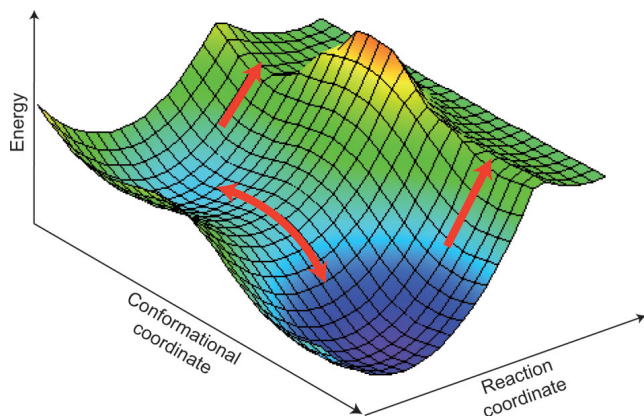
Comp. Chem. Comparison and Database Benchmark (small molecules):

<http://cccbdb.nist.gov/>

- **Construct** the structure:

- With the help of a chemistry graphic interface (gaussview, chemcraft, etc.)
- Cartesian Coordinates.
- Z-matrix coordinates.

TRANSITION STATE THEORY



1.

Born-Oppenheimer approximation leads to a mental picture of nuclei moving in a PES.

2.

The nuclear dynamics is treated by classical mechanics.

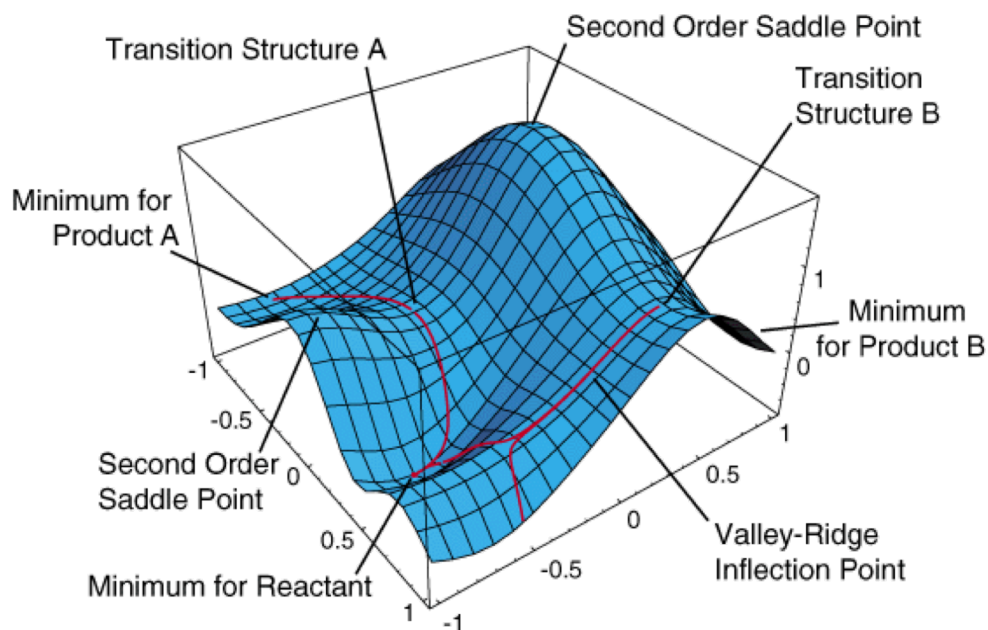
Easiest path → Lowest energy path

Highest energy point → Transition structure

Its energy (relative to the reactant complex) determines the **reaction rate** within *Transition State Theory*.

TRANSITION STATE THEORY

Topological characterization of the PES



There are a few relevant critical points (zero gradient) of the PES:

- **Minima** characterize stable geometries.
- Saddle points of first order (one negative Hessian eigenvalue) correspond to **transition states (TS)**.

TRANSITION STATE THEORY

1929 → With Michael Polany, Henry Eyring performs first quantum mechanical calculations of reaction rates.

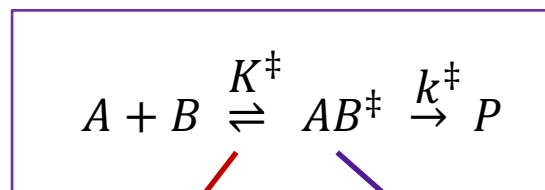
“developed a quantum mechanical way to think about reaction rates.”

Which was that way?



Rate law: $\frac{dP}{dt} = k[A][B]$

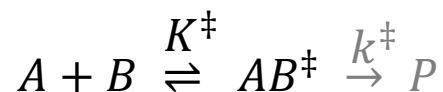
TST:



3.

Equilibrium!! Activated complex
or Transition State
(intermediate)

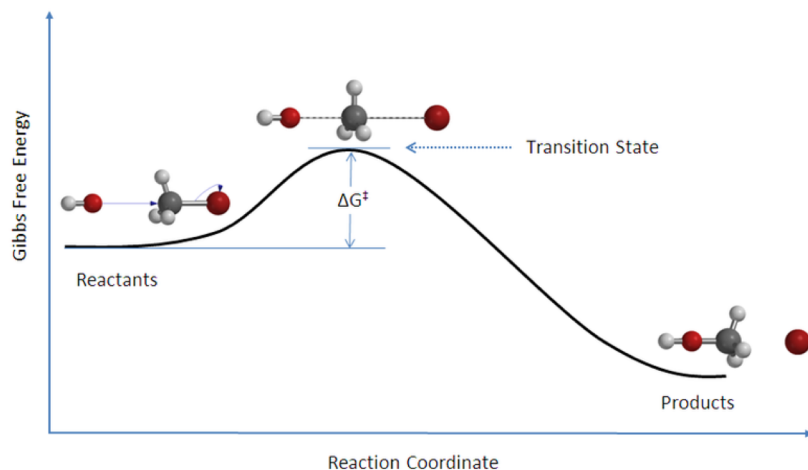
TRANSITION STATE THEORY



If reactants are in equilibrium with the activated complex:

$$K^\ddagger = \frac{[AB^\ddagger]/c^\circ}{[A]/c^\circ [B]/c^\circ} = \frac{[AB^\ddagger]c^\circ}{[A][B]} \quad c^\circ = \text{standard concentration}$$

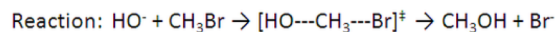
Equilibrium constant from partition functions:



$$K^\ddagger = \frac{N_A q_{AB^\ddagger}^o}{q_A^o q_B^o} e^{-\frac{\Delta E_a^o}{RT}} \quad q_X^o = \text{standard molar partition function of X}$$

ΔE_a^o resembles ΔE_{reac}^o in Arrhenius equation

TST takes a thermodynamic constant and applies that to the TS.



TRANSITION STATE THEORY

$$K^\ddagger = \frac{N_A q_{AB^\ddagger}^o}{q_A^o q_B^o} e^{-\frac{\Delta E_a^o}{RT}}$$

$$k = \frac{k_B T}{h} K^\ddagger$$

Demonstration

4.

No recrossing of TS.

Expression that related the overall rate constant k in terms of the equilibrium constant K^\ddagger .

by the thermodynamic relation:

$$\begin{aligned}\Delta^\ddagger G &= -RT \ln k \\ \Delta G &= \Delta H - T\Delta S\end{aligned}$$

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

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

Transition State Theory

$$k = A e^{-\frac{E_a}{RT}}$$

Arrhenius equation

FACTORS THAT AFFECT REACTION RATES AND THERMODYNAMICS.

-General considerations-

■ Solvent

The environment can change the thermodynamics and kinetics of the reaction mechanism. Even the solvent can change the reaction mechanism or explicitly enter into the mechanism.

Explicit vs Implicit description.

[Link.](#)

■ Dispersion Energy

Electronic interactions at long range. Typically not properly addressed in density functionals. A correction has to be added (the most typical: Grimme correction).

[Link.](#)

■ Experimental concentrations

$$\Delta G' = \Delta G^\circ + \Delta G^{\circ/*} (pH, [React], [Prod]) \quad \Delta G^{\circ/*} = \sum RT \ln \left(\frac{[Prod]_{exp}}{\left(\frac{1}{24.5}\right)} \right) - \sum RT \ln \left(\frac{[Reag]_{exp}}{\left(\frac{1}{24.5}\right)} \right)$$

■ Identification of the proper TS in catalytic cycles

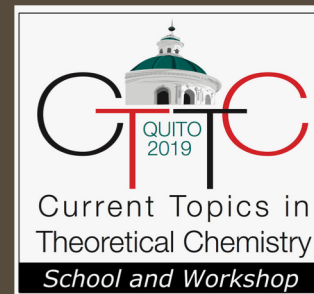
Concatenation of two energy profiles of the catalytic cycle.

[Link.](#)



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