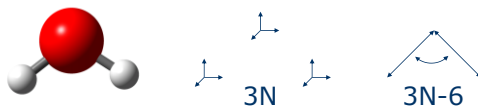


Geometrie molekul

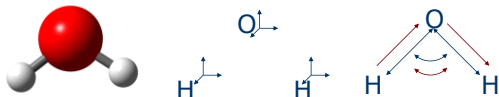
Reprezentace molekul v prostoru

- ♦ kartézský systém 3N
 - N je počet jader
- ♦ vnitřní souřadnice 3N-6



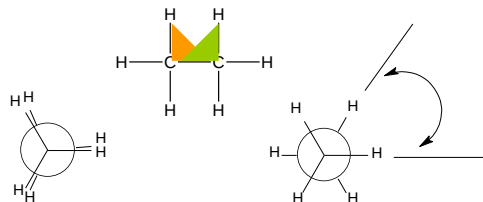
Popis molekul ve 3D

- ♦ stačí jen souřadnice?
- ♦ chybí definice atomů – protonové číslo, značka
- ♦ vnitřní souřadnice – nesmí chybět i topologická informace

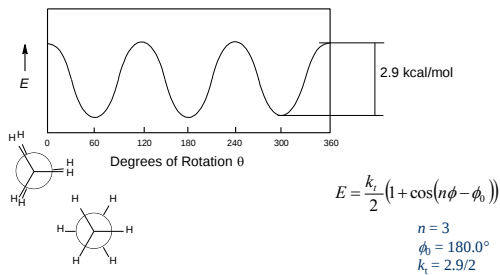


Torzní úhel

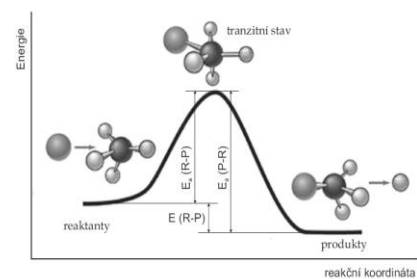
- ♦ mezirovinný úhel



Motivace I



Motivace II



Aproximace

Born-Oppenheimerova

$$\Psi_{tot}(\mathbf{r}, \mathbf{R}) = \Psi_{jad}(\mathbf{R}) \Psi_{el}(\mathbf{r}; \mathbf{R}) \quad H_{el} \Psi_{el} = E \Psi_{el}$$

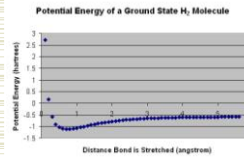
parametr elektronická Sch. r.

zanedbání relativistických efektů, spin-orbitální vazby, spin elektronů a jader

$$H_{el} = -\frac{1}{2} \sum_i \Delta_i + \frac{1}{2} \sum_{i \neq j} \frac{1}{r_{ij}} - \sum_{i,A} \frac{Z_A}{r_{iA}}$$

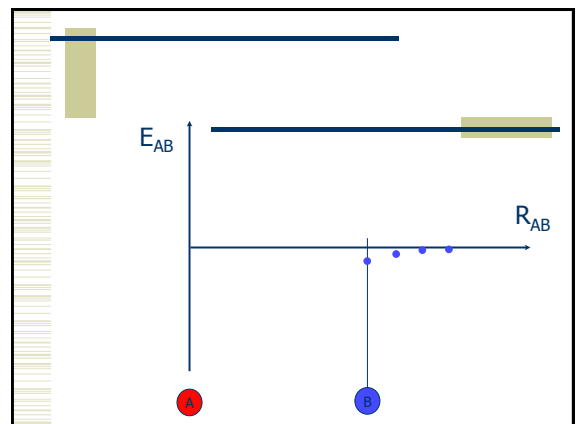
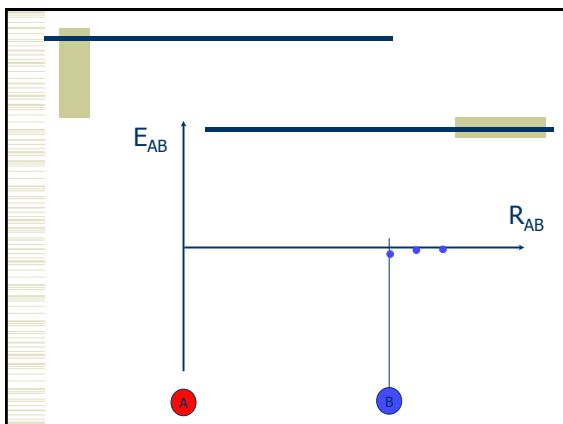
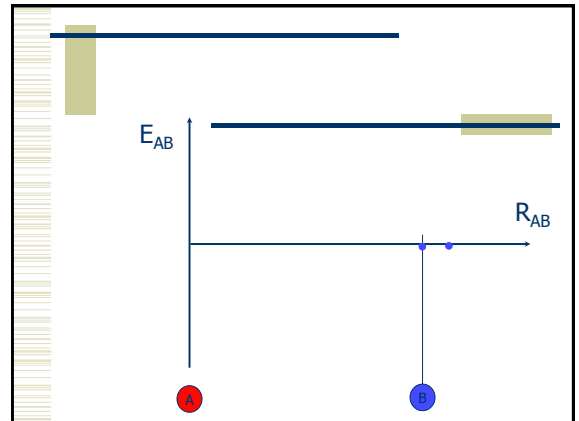
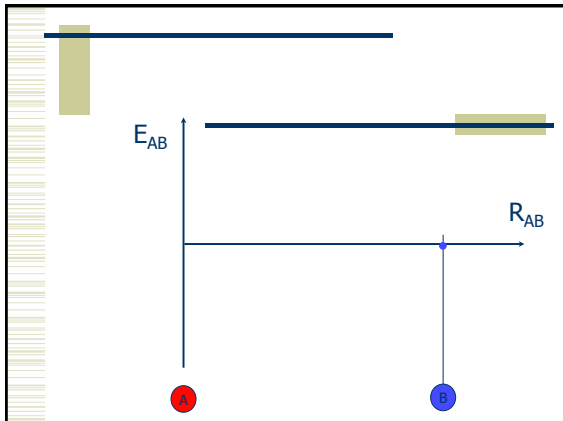
Born-Oppenheimerova aproximace

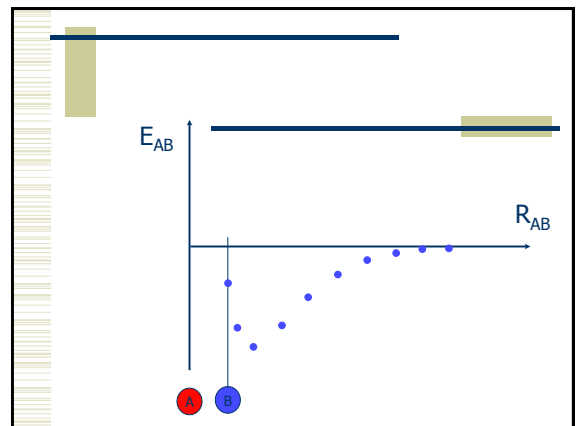
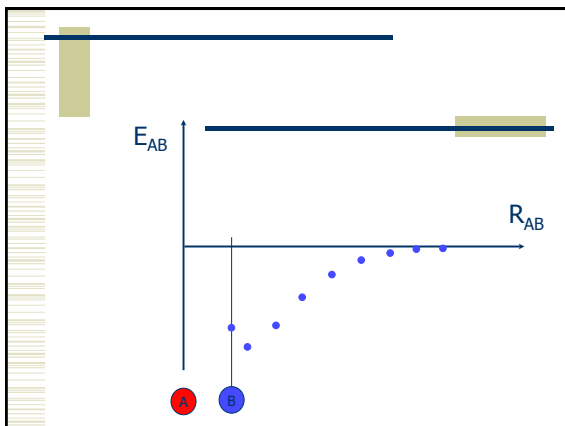
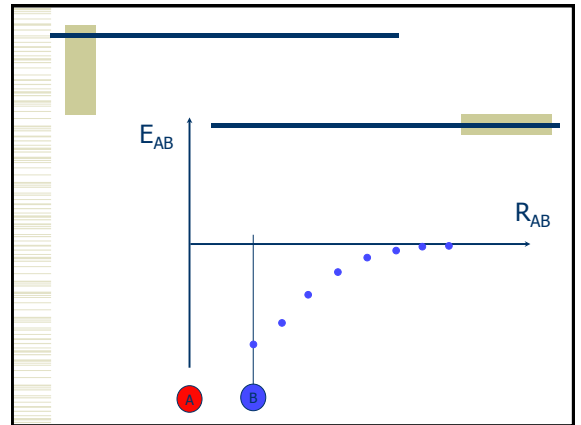
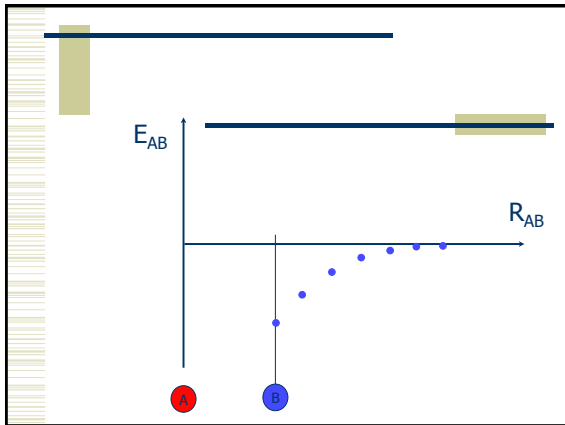
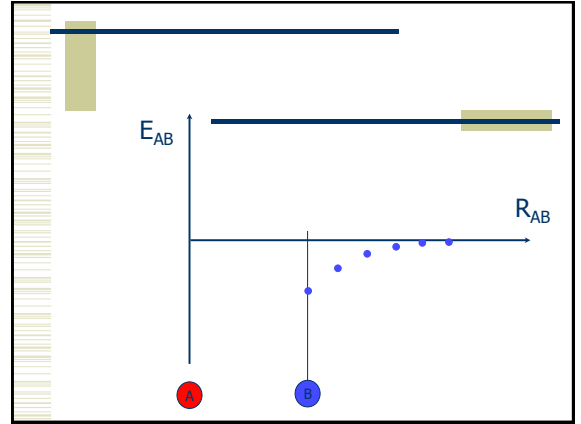
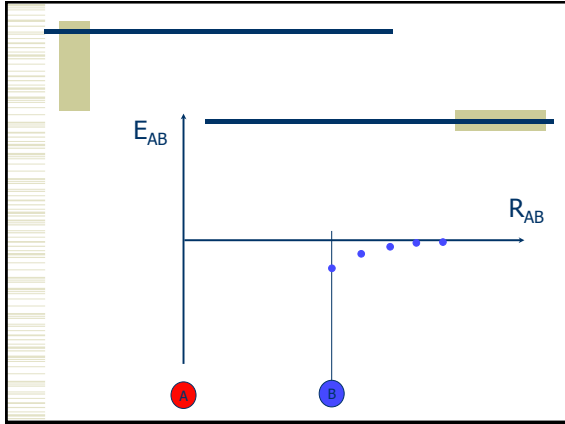
oddělení elektronického a jaderného pohybu
kvantové elektrony x klasická jádra

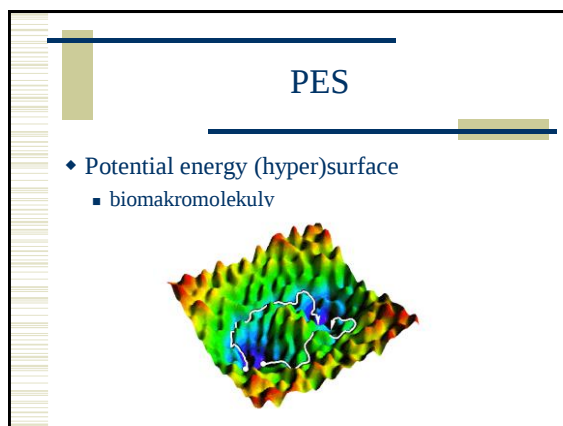
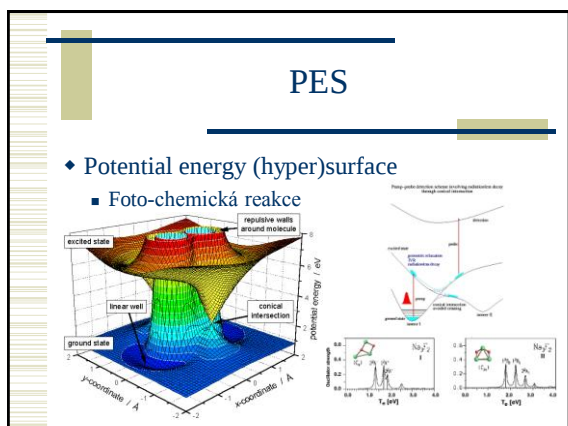
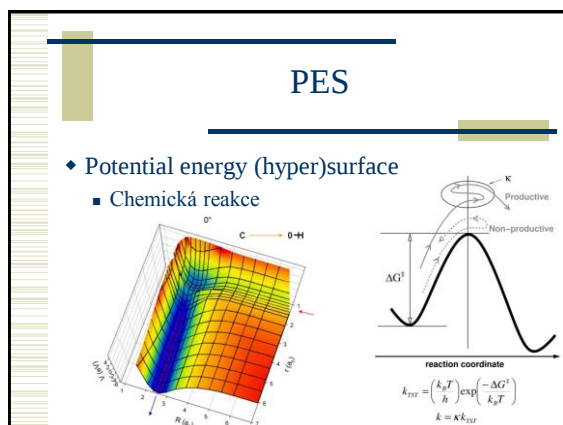
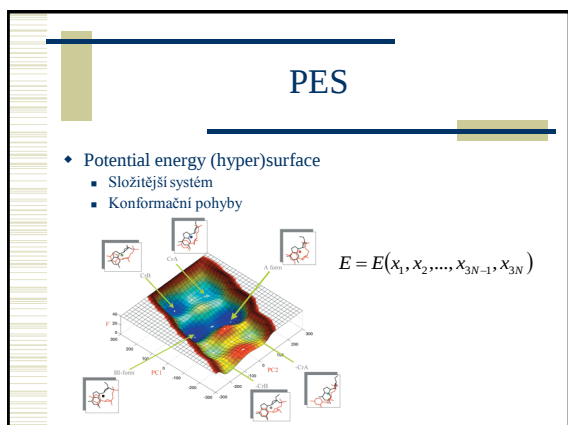
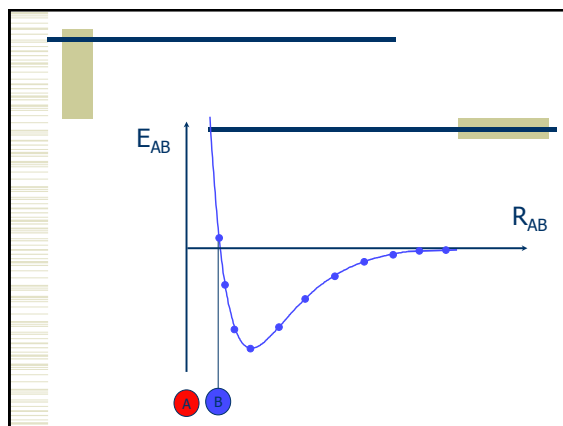
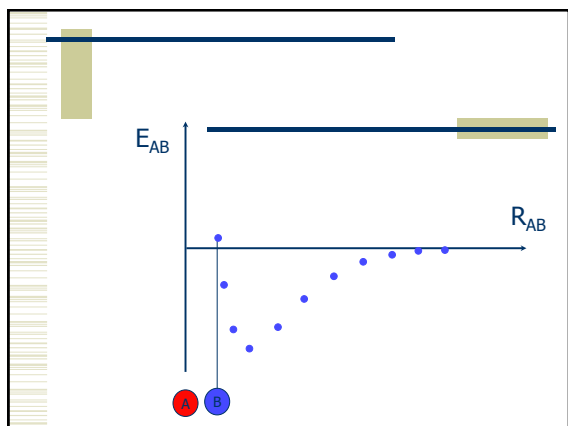


$$E = f(\mathbf{R})$$

aparát klasické fyziky
molekulová mechanika
(empirický potenciál, FF)







Terciální struktura

- aby protein mohl vykonávat svou funkci musí se složit (to fold) do určité, často unikátní, 3D struktury
- skládání (folding) proteinů
 - zcela zásadní role nekovalentních interakcí
 - kolaps hydrofobního jádra proteinu
 - skládání nerealizuje žádný buněčný systém (Anfinsen) – pozor, výjimky ...

skládání
↔
denaturace

Levinthal's paradox (1969)

natolikový polypeptid

potlačení posttranslační relaxace

nepotlačení posttranslační relaxace

hydrofobní vnitřní polypeptidů obaluje nepotlačení aminokyselin

vodíkové můstky se tvoří mezi potlačení aminokyselinami na zepředu proteinu

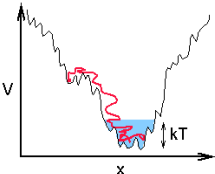
konkrétní konformace složeného polypeptidu ve vodě

Skládání proteinů

The diagram illustrates the process of protein folding. On the left, a flowchart shows the progression from a polypeptide chain to a folded protein. Key stages include: Polypeptide chain, Unfolded state, Disordered aggregates, Intermediate states, and Native state. The native state can further form oligomers or fibrils. On the right, a funnel-shaped energy landscape represents the folding process. The vertical axis is labeled 'FREE ENERGY' and the horizontal axis is 'PROTEIN STRUCTURE'. The funnel narrows from 'DISORDERED AGGREGATES' at the top to 'NATIVE STRUCTURE' at the bottom. The funnel is divided into regions: 'FOLDING' (top), 'FOLDING INTERMEDIATES' (middle), and 'FOLDING INTERMEDIATES' (bottom). The funnel is also labeled 'FOLDING INTERMEDIATES' and 'FOLDING INTERMEDIATES'.

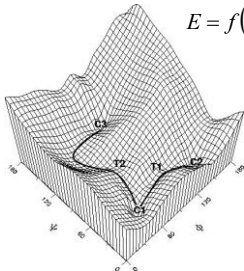
PES

- ◆ Potential energy (hyper)surface
 - Sampling – rare event



The graph shows a potential energy surface V as a function of position x . The potential energy curve has a deep well. A red line represents a trajectory that starts at a high energy state, moves down into the well, and then moves back up. A blue shaded region at the bottom of the well represents the ground state. A vertical double-headed arrow indicates the energy difference between the ground state and the transition state, labeled kT .

PES



A 3D wireframe plot of a Potential Energy Surface (PES). The surface is represented by a grid of points connected by lines, showing a complex energy landscape with several peaks and valleys. A reaction coordinate path is highlighted with a thick black line, starting from a reactant state (labeled 'R') in a valley, passing through a transition state (labeled 'TS') at a saddle point, and ending at a product state (labeled 'P') in another valley. The axes are labeled with numerical values: the vertical axis ranges from 0 to 100, and the horizontal axes range from 0 to 100.

$$E = f(\mathbf{R}_i)$$

Ramachandranův diagram

Ramachandranův diagram ukazuje možné konformace ϕ a ψ dihedrálů polypeptidů (pozor G)

The Ramachandran Plot.

The diagram illustrates the Ramachandran plot, which shows the allowed conformational space for the backbone dihedral angles ϕ and ψ of a polypeptide chain. The plot is divided into four quadrants, each representing a different type of secondary structure:

- Beta-sheet** (Top Left, red area): ϕ is negative, ψ is positive.
- Left handed alpha-helix** (Top Right, yellow area): ϕ is negative, ψ is negative.
- Right handed alpha-helix** (Bottom Left, red area): ϕ is positive, ψ is negative.
- Other** (Bottom Right, yellow area): ϕ is positive, ψ is positive.

The plot also shows the allowed conformational space for the side chain dihedral angle χ_1 , which is indicated by the blue arc labeled ≈ 180 in the diagram.

Hyperplocha potenciální energie

Obrázek 6.1: Panel A ukazuje plochu potenciální energie E závislou na dvou proměnných x_1 a x_2 , vedlejší panel zobrazuje tutéž plochu ve formě mapy. Bod R představuje reaktanty a bod P produkty.

Figure 6.1 consists of two panels, A and B, illustrating a potential energy surface (PES). Panel A is a 3D wireframe plot showing the potential energy E as a function of two coordinates, x_1 and x_2 . The vertical axis is labeled 'Energy' and ranges from 0.0 to 1.0. The horizontal axes are x_1 and x_2 , both ranging from -4 to 4. The surface shows a prominent saddle point labeled 'vrstevnice $E = \text{konst.}$ ' and a local minimum labeled 'minimum E '. Points R and P are marked on the surface. Panel B is a 2D contour map of the same potential energy surface. The axes are x_1 and x_2 , both ranging from -4 to 4. The map shows concentric contour lines representing different energy levels. Points R and P are marked on the map, and a curved arrow indicates the reaction path from R to P. The label 'vrstevnice $E = \text{konst.}$ ' is also present in panel B.

Zajímavé body

stacionární body

$$\frac{\partial E}{\partial x_i} = 0,$$

$$\mathbf{H} = \begin{pmatrix} \frac{\partial^2 E}{\partial x_1^2} & \frac{\partial^2 E}{\partial x_1 \partial x_2} & \cdots & \frac{\partial^2 E}{\partial x_1 \partial x_n} \\ \frac{\partial^2 E}{\partial x_2 \partial x_1} & \frac{\partial^2 E}{\partial x_2^2} & \cdots & \frac{\partial^2 E}{\partial x_2 \partial x_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial^2 E}{\partial x_n \partial x_1} & \frac{\partial^2 E}{\partial x_n \partial x_2} & \cdots & \frac{\partial^2 E}{\partial x_n^2} \end{pmatrix}$$

**Hessova matice
(křivost)**

$$\begin{pmatrix} \lambda_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \lambda_n \end{pmatrix}$$

vlastní čísla Hessovy matice

$$\frac{\partial E}{\partial x_i} = 0,$$

stacionární body

$$\mathbf{H} = \begin{pmatrix} \frac{\partial^2 E}{\partial x_1^2} & \frac{\partial^2 E}{\partial x_1 x_2} & \cdots & \frac{\partial^2 E}{\partial x_1 x_n} \\ \frac{\partial^2 E}{\partial x_2 x_1} & \frac{\partial^2 E}{\partial x_2^2} & \cdots & \frac{\partial^2 E}{\partial x_2 x_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial^2 E}{\partial x_n x_1} & \frac{\partial^2 E}{\partial x_n x_2} & \cdots & \frac{\partial^2 E}{\partial x_n^2} \end{pmatrix}$$

Hessova matice (křivost)

$$\begin{pmatrix} \lambda_1 & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & \lambda_n \end{pmatrix}$$

vlastní čísla Hessiany matice

Hyperplocha potenciální energie

Obrázek 6.1: Panel A ukazuje plochu potenciální energie E závislou na dvou proměnných x_1 a x_2 , vedlejší panel zobrazuje tutéž plochu ve formě mapy. Bod R představuje reaktanty a bod P produkty.

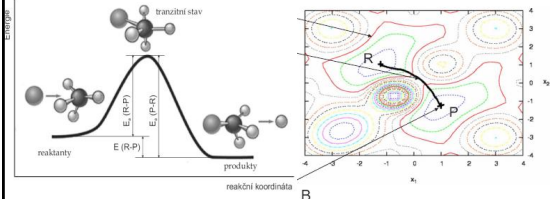
Panel A: 3D plot of the potential energy surface E as a function of coordinates x_1 and x_2 . The surface is shown as a red wireframe mesh. The vertical axis is labeled 'Energy' and ranges from 0.0 to 1.0. The horizontal axes are labeled x_1 and x_2 , both ranging from -4 to 4. A saddle point is labeled 'sedlo' and a minimum is labeled 'minimum E'. Points R and P are marked on the surface.

Panel B: 2D contour map of the potential energy surface E as a function of coordinates x_1 and x_2 . The axes are labeled x_1 and x_2 , both ranging from -4 to 4. The energy levels are indicated by color-coded contours. Points R and P are marked on the contour map, corresponding to the same locations as in Panel A. Arrows indicate the reaction path from R to P.

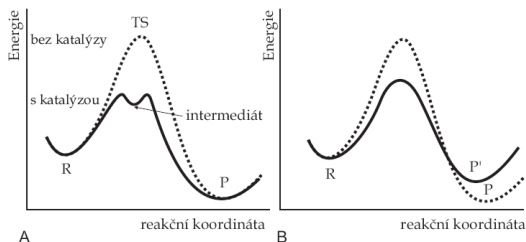
Figure 1 consists of two panels, A and B, illustrating the energy landscape of the two-dimensional Ising model. Panel A is a 3D surface plot showing the energy E as a function of coordinates x_1 and x_2 . The energy surface is characterized by a central peak labeled 'sedlo' (saddle point) and a central valley labeled 'minimum E'. A path is shown on the surface, starting from a point 'R' and ending at a point 'P'. Panel B is a 2D contour plot of the same energy landscape, showing the energy levels as contour lines. The same features are visible: a central peak labeled 'sedlo' and a central valley labeled 'minimum E'. A path is shown on the contour plot, starting from a point 'R' and ending at a point 'P'. The axes for both panels are labeled x_1 and x_2 , ranging from -4 to 4.

Hyperplocha potenciální energie

The figure consists of two parts. The left part is a reaction coordinate diagram showing the energy profile of a reaction. The y-axis is labeled 'Energy' and the x-axis is labeled 'reakční koordináta'. The curve starts at a reactant state (labeled 'reaktanty'), rises to a peak labeled 'transiční stav', and then falls to a product state (labeled 'produkty'). Energy levels are indicated by horizontal lines: $E(R,P)$ for reactants, $E(P,R)$ for products, and $E(R,R)$ for the transition state. The activation energy is labeled $E(R,P)$. Ball-and-stick models illustrate the molecular structures at each stage. The right part is a 2D potential energy surface (PES) plot with axes r_1 and r_2 . It shows a complex landscape of energy contours. A black arrow indicates the reaction path from a reactant state (R) to a product state (P) through a saddle point. A local minimum is marked with a blue dot and labeled 'B'.

[illegible]

Obrázek 6.3: Panel A ukazuje srovnání reakční koordináty nekatalyzované reakce (přerušované) s reakční koordinátou za přítomnosti katalyzátoru, jehož přítomnost vede ke snížení aktivizační bariéry a tedy ke zvýšení rychlosti reakce. Panel B ukazuje srovnání dvou reakčních cest z reaktantu R do údojí produktů P' a P. Termodynamiky jsou výhodnější produkty P, ale bude-li bariéra pro přechod z R do P oproti bariéře R-P' výrazně vyšší, bude pozorován vznik produktů P'. V takovém případě jde o kineticky řízenou reakci.

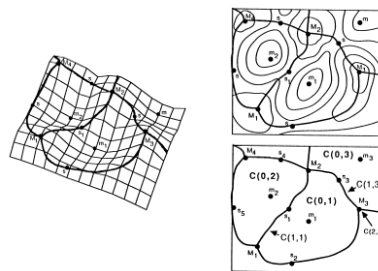


PES



The figure illustrates the Potential Energy Surface (PES) for a molecular system. It consists of three parts:

- 3D Surface Plot:** A 3D representation of the PES showing a grid of points and a path connecting minima. The surface is colored with a gradient from blue (low energy) to red (high energy).
- 2D Contour Plots:** Two 2D contour plots showing the PES. The top plot shows the overall shape with labels M_1 through M_{10} and C_1 through C_{10} . The bottom plot shows a zoomed-in view of the central region with labels $C(0,2)$, $C(0,1)$, $C(1,1)$, $C(1,3)$, $C(2,3)$, $C(0,3)$, M_1 through M_{10} , and C_1 through C_{10} .

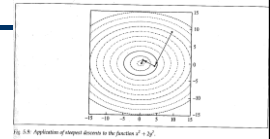


optimalizace geometrie

- ♦ hledání nejbližšího minima
- ♦ hledání globálního minima
 - PES je komplexní, problém lokálního uzavření
 - metody prohledávání PES

nejbližší minimum

- ♦ optimalizace
 - simplexová metoda
 - s využitím gradientů
 - s využitím znalosti křivosti
- ♦ kde začít?
 - chemická intuice
 - problém lokálního uzavření



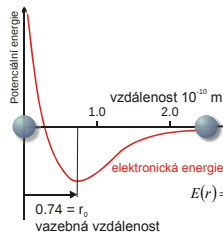
komplexnější prohledávání

- ♦ Monte Carlo
- ♦ genetické algoritmy
- ♦ vzorkování fázového prostoru
 - přidali jsme i kin. energii (umožňuje překonávat bariéry)

máme minimum!

- ♦ Další analýza
 - křivost v okolí, E ve všech směrech roste

Harmonický oscilátor



využijeme Taylorův rozvoj energie v minimu

$$f(x) = \sum_{n=0}^{\infty} \frac{f^{(n)}(a)}{n!} (x-a)^n.$$

$$E(r) = E(r_0) + \frac{1}{1!} \frac{\partial E(r_0)}{\partial r} (r-r_0) + \frac{1}{2!} \frac{\partial^2 E(r_0)}{\partial r^2} (r-r_0)^2 + \dots$$

$$E(r) = \frac{k}{2} (r-r_0)^2$$

Harmonický oscilátor

$$\hat{H} = \frac{\hat{p}^2}{2m} + \frac{1}{2} m \omega^2 \hat{x}^2$$

analogie

$$(a^2 - b^2) = (a+b)(a-b)$$

$$(a^2 + b^2) = (a+ib)(a-ib), \quad i^2 = -1$$

$$a = \frac{1}{\sqrt{2m\hbar\omega}} (\hat{p} - iom\hat{x}) \quad \text{anihilační operátor}$$

$$a^+ = \frac{1}{\sqrt{2m\hbar\omega}} (\hat{p} + iom\hat{x}) \quad \text{kreační operátor}$$

Harmonický oscilátor

$$\hat{H} = \frac{\hat{p}^2}{2m} + \frac{1}{2}m\omega^2\hat{x}^2 = \hbar\omega\left(\hat{a}^+\hat{a} + \frac{1}{2}\right)$$

stačí najít řešení: $\hat{a}^+\hat{a}|\psi_\lambda\rangle = \lambda|\psi_\lambda\rangle$

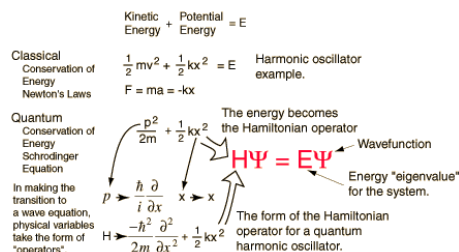
$$\langle\psi_\lambda|\hat{a}^+\hat{a}|\psi_\lambda\rangle = \langle\psi_\lambda|\hat{a}\hat{a}^+|\psi_\lambda\rangle = \lambda \geq 0$$

$$a\hat{a}^+|\psi_\lambda\rangle = (\hat{a}^+\hat{a} + 1)|\psi_\lambda\rangle = \lambda b|\psi_\lambda\rangle \quad [\hat{a}^+, \hat{a}] = \hat{a}^+\hat{a} - \hat{a}\hat{a}^+ = 1$$

$$\hat{a}^+|\psi_\lambda\rangle = (\lambda + 1)|\psi_{\lambda+1}\rangle$$

stav $|\psi_\lambda\rangle$ vlastní číslo λ anihilační operátor
 $|\psi_\lambda\rangle$ $\lambda - 1$

Harmonický oscilátor lehčeji

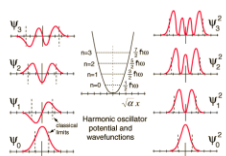


Harmonický oscilátor

$$\lambda = 0, 1, \dots$$

$$E_n = \hbar\omega\left(n + \frac{1}{2}\right), \quad n = 0, 1, \dots$$

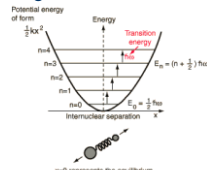
kvantování



$$\lambda = 0$$

$$E_n = \frac{1}{2}\hbar\omega = \frac{1}{2}\hbar\nu$$

energie zákl. vibračního stavu



Harmonický oscilátor - důsledky

♦ řešení

$$E_n = (n + 1/2)\hbar\nu = (n + 1/2)\hbar\left(\frac{k}{m_{\text{eff}}}\right)^{1/2}$$

• povolené přechody jen mezi sousedními hladinami $\Delta n = \pm 1$

$$\Delta E = E_{n+1} - E_n = \hbar\nu = \hbar\left(\frac{k}{m_{\text{eff}}}\right)^{1/2}$$

odtud lze spočítat k

vibrační analýza

- ♦ optimalizace geometrie
- ♦ výpočet Hessovy matice $\mathbf{H}$
- ♦ silové konstanty $\sim$ vibrační frekvence!

$$\mathbf{H} = \begin{pmatrix} \frac{\partial^2 E}{\partial x_1^2} & \frac{\partial^2 E}{\partial x_1 \partial x_2} & \dots & \frac{\partial^2 E}{\partial x_1 \partial x_n} \\ \frac{\partial^2 E}{\partial x_2 \partial x_1} & \frac{\partial^2 E}{\partial x_2^2} & \dots & \frac{\partial^2 E}{\partial x_2 \partial x_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial^2 E}{\partial x_n \partial x_1} & \frac{\partial^2 E}{\partial x_n \partial x_2} & \dots & \frac{\partial^2 E}{\partial x_n^2} \end{pmatrix} \quad H_{ij}^m = \frac{H_{ij}}{\sqrt{M_i M_j}}$$

mass-weighted hessian
 - diagonalizace dává k/m

vibrační analýza – další souvislosti

- ♦ Aparát statistické termodynamiky dovoluje výpočet termodynamických funkcí z partiční funkce Q (např. $G = -k_B T \ln Q_{\text{NPT}}$)
- ♦ Partiční funkci molekuly získáme ze znalosti – hmotnosti, rotační konstanty (geometrie) a vibračních frekvencí

výpočty ΔG

$$\Delta G = \Delta H - T\Delta S \quad \leftarrow \text{přes partiční funkci, statistická termodynamika}$$

$$\Delta H = \Delta U + P\Delta V$$

$$\Delta U = \Delta E^{el} + \Delta E^{ZPE}$$

výpočet vibračních frekvencí

QCh – např. CBS

vibrační analýza

♦ Dovoluje vypočítat

- IR, Ramanova spektra molekul
 - pozor: empirické škálování frekvencí, anharmonicity
- Termodynamické vlastnosti systému
- Kinetiku chemických procesů (dva/tři body na PES – R/P a TS)

Scaling Frequencies and Zero-Point Energies

Frequencies computed with methods other than Hartree-Fock are also scaled to similarly eliminate known systematic errors in calculated frequencies. The following table lists the recommended scale factors for frequencies and for zero-point energies and for use in computing thermal energy corrections (the latter two items are discussed later in this chapter), for several important calculation types:[†]

Method	Scale Factor	
	Frequency	ZPE/Thermal
HF/3-21G	0.9085	0.9409
HF/6-31G(d)	0.8929	0.9135
MP2(Full)/6-31G(d)	0.9427	0.9646
MP2(FC)/6-31G(d)	0.9434	0.9676
SVWN/6-31G(d)	0.9833	1.0079
BLYP/6-31G(d)	0.9940	1.0119
B3LYP/6-31G(d)	0.9613	0.9804

chemické reakce

- ♦ lokalizace nejen R a P, ale i TS, který je spojuje
- ♦ vibrační analýza TS (vlastní vektor s im. frekvencí „spojuje“ R a P)

PES

♦ Potential energy (hyper)surface

- Chemická reakce

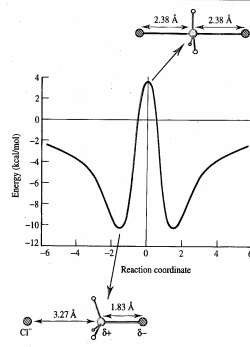
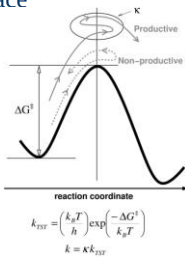
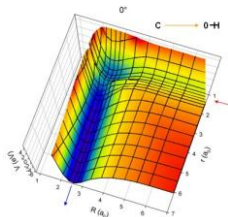


Fig. 5.21. The energy profile for the gas-phase $\text{Cl}^- + \text{MeCl}$ reaction. (Adapted in part from Chandrosskhar J., S. F. Smith and W. L. Jorgensen 1985. Theoretical Examination of the $\text{S}_{\text{N}}2$ Reaction Involving Chloride Ion and Methyl Chloride in the Gas Phase and Aqueous Solution. Journal of the American Chemical Society 107:154–163.)

