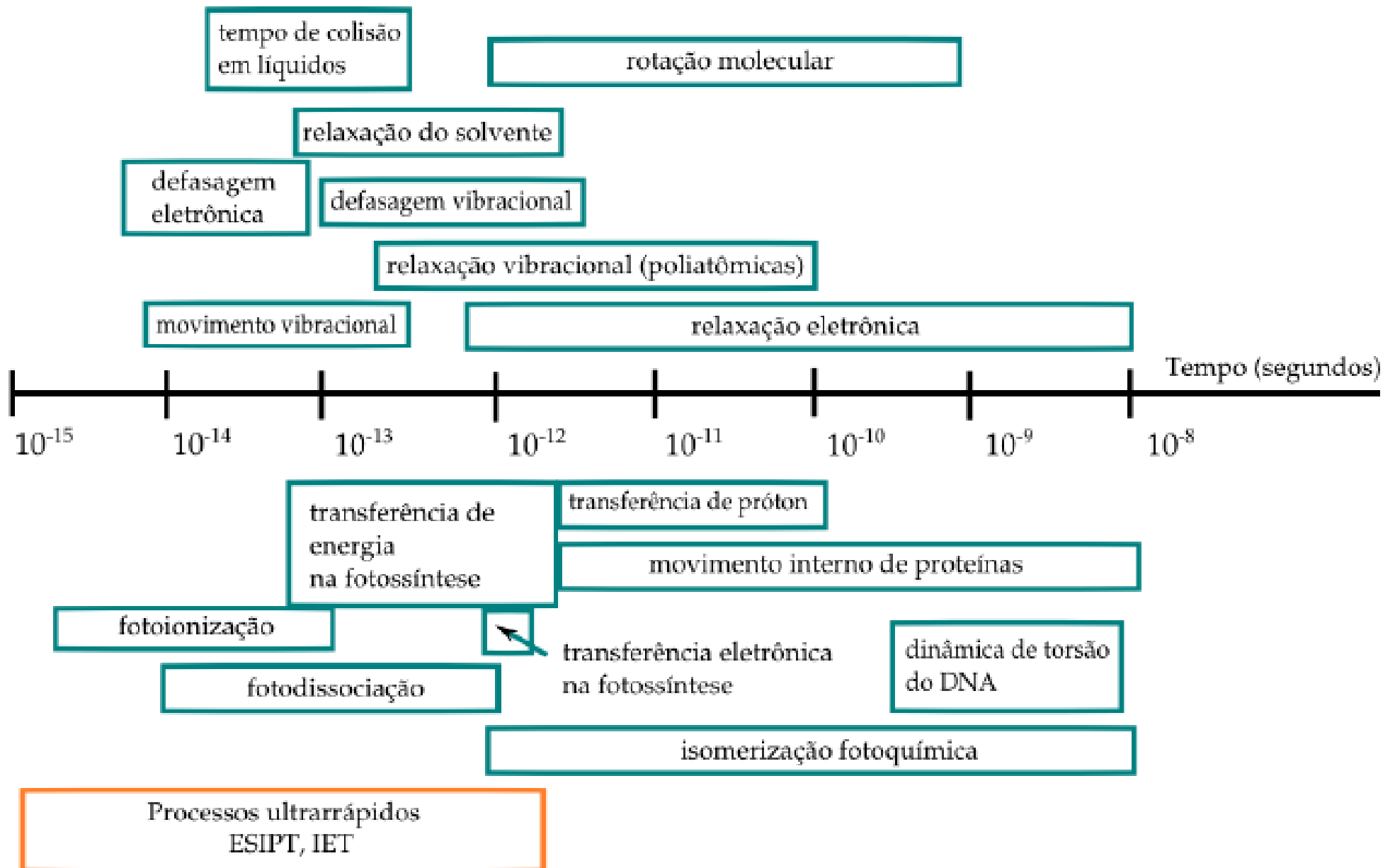


Dynamic Processes in Molecular Systems



adapted from *Chemical Dynamics in Condensed Phases*, A. Nitzan, Oxford Press.

Quantum Dynamics of Electrons and Nuclei

Time-dependent Schrödinger equation (1926):

$$i\hbar \frac{\partial}{\partial t} \Psi(r, R, t) = \left[\frac{\hbar^2}{2m} \nabla_r^2 + \frac{\hbar^2}{2M} \nabla_R^2 + V(r, R) \right] \Psi(r, R, t)$$

Relativistic quantum mechanics is obtained where quantum mechanics and special relativity simultaneously apply (1928).

Dirac equation:

“The fundamental laws necessary for the mathematical treatment of a large part of physics and the whole of chemistry are thus completely known, and the difficulty lies only in the fact that application of these laws leads to equations that are too complex to be solved.”

The electron-nucleus problem in molecular structures

Molecular Schrödinger Equation:

$$\hat{H}_{mol}(r, R)\Psi(r, R) = E\Psi(r, R)$$

$$\hat{H}_{mol}(r, R) = \hat{T}_e(r) + V_{eN}(r, R) + V_{ee}(r) + \hat{T}_N(R) + V_{NN}(R)$$

$$\hat{T}_N = \sum_n^{N_{nuc}} \frac{P_j^2}{2M_n} \quad V_{ee} = \frac{1}{2} \sum_{i \neq j} \frac{e^2}{|\vec{r}_i - \vec{r}_j|} \quad V_{eN} = - \sum_{j,n} \frac{Z_n e^2}{|\vec{r}_j - \vec{R}_n|}$$

$$\hat{T}_e = \sum_j^{N_e} \frac{p_j^2}{2m_e} \quad V_{NN} = \frac{1}{2} \sum_{n \neq m} \frac{Z_n Z_m e^2}{|\vec{R}_n - \vec{R}_m|}$$

The total hamiltonian:

$$\hat{H} = \hat{H}_{el} + \hat{H}_{ph} + \hat{H}_{el-ph} = \sum_{\kappa} E_{\kappa} b_{\kappa}^{\dagger} b_{\kappa} + \sum_{\alpha} \left(\hat{n}_{\alpha} + \frac{1}{2} \right) \hbar \omega_{\alpha} + \hat{V}_{el-ph}$$

typical solution:

$$|\Psi\rangle = \sum_{\kappa, \mathbf{n}} C_{\kappa, \mathbf{n}} \left[|\Phi_{\kappa}\rangle \prod_{\alpha=1}^N \frac{1}{\sqrt{n_{\alpha}!}} (a_{\alpha}^{\dagger})^{n_{\alpha}} |0\rangle \right]$$

where $|\Phi_{\kappa}\rangle$ is a Slater determinant and $\mathbf{n} \equiv (n_1, n_2, \dots, n_N)$

The electron-nucleus problem in molecular structures: Born-Oppenheimer (Adiabatic) Approximation

1927

№ 20

ANNALEN DER PHYSIK

VIERTE FOLGE. BAND 84

1. *Zur Quantentheorie der Molekeln;* *von M. Born und R. Oppenheimer*

Es wird gezeigt, daß die bekannten Anteile der Terme einer Molekel, die der Energie der Elektronenbewegung, der Kernschwingungen und der Rotationen entsprechen, systematisch als die Glieder einer Potenzentwicklung nach der vierten Wurzel des Verhältnisses Elektronenmasse zu (mittlerer) Kernmasse gewonnen werden können. Das Verfahren liefert u. a. eine Gleichung für die Rotationen, die eine Verallgemeinerung des Ansatzes von Kramers und Pauli (Kreisel mit eingebautem Schwungrad) darstellt. Ferner ergibt sich eine Rechtfertigung der von Franck und Condon angestellten Betrachtungen über die Intensität von Bandenlinien. Die Verhältnisse werden am Beispiel der zweiatomigen Molekeln erläutert.

Historical note:

“On the quantum mechanics of electrons in crystal lattices”, Felix Bloch (1928)

The electron-nucleus problem in molecular structures: Born-Oppenheimer (Adiabatic) Approximation

On the Quantum Theory of Molecules

M. Born^a, J.R. Oppenheimer^b

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Abstract

It will be shown that the familiar components of the terms of a molecule; the energy of electronic motion, of the nuclear vibration and of the rotation, correspond systematically to the terms of a power series in the fourth root of the ratio of electron mass to (average) nuclear mass. The treatment yields among other things an equation for the rotation, which represents a generalization of the treatment of Kramers and Pauli (top with built-in fly-wheel). Furthermore, there appears a justification of the considerations of Franck and Condon on the intensity of band lines. The relationships are illustrated for the diatomic molecule.

Historical note:

“On the quantum mechanics of electrons in crystal lattices”, Felix Bloch (1928)

The electron-nucleus problem in molecular structures

This problem is extremely difficult,

$$\hat{H}_{mol}(r, R)\Psi(r, R) = E\Psi(r, R)$$

Therefore one has to make approximations; the most important one is the separation of electronic and nuclear degrees of freedom

It is based on the fact that $M_n \gg m_e \Rightarrow v_n \ll v_e$

So that the nuclear dynamics is put aside for the electronic dynamics.

We start by treating the nuclear momenta (P) and coordinates (R) as classical variables.

The electronic problem becomes

$$\begin{aligned} \left(\hat{T}_e(r) + V_{ee}(r) + V_{eN}(r, R) + V_{NN}(R) \right) \psi_a(r; R) &= \varepsilon_a \psi_a(r; R) \\ \left(\hat{T}_e(r) + V_{ee}(r) + V_{eN}(r, R) \right) \psi_a(r; R) &= (\varepsilon_a - V_{NN}) \psi_a(r; R) \end{aligned}$$

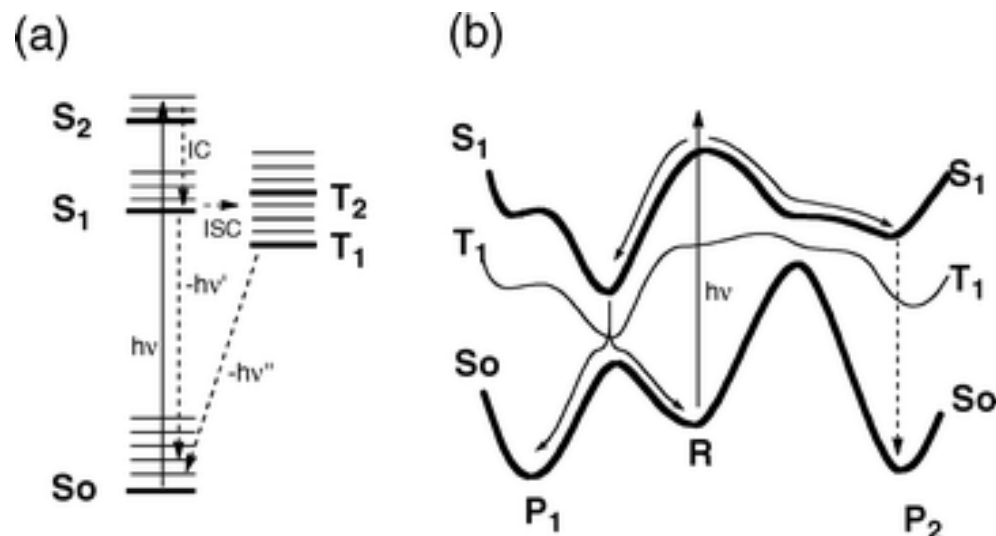
Potential Energy Surface (PES): $U_a(R) \equiv \varepsilon_a(R) - V_{NN}(R)$

Potential energy landscape for the electrons in the approximation that nuclear dynamics is decoupled from electronic dynamics.

$\psi_a(r, R) = \langle r, R | \psi_a \rangle$ is called the adiabatic electronic wavefunction

Potential Energy Surfaces (PES)

photoinduced dynamics



(a) Jablonski diagram,
 (b) reaction coordinate,
 (c) Potential Energy Surface (PES)

S_n = singlet states
 S_0 = ground state
 T_n = triplet states
 $L1$ = lowest triplet
 R = reactant state
 P_n = product states
 I = intermediary state (metastable)
 $h\nu$ = photon energy
 TS = transition state
 CI = conical intersection (diaboloic intersection)
 ISC – inter-system crossing

The electronic problem in molecular structures

To solve the electronic problem and to obtain $U_a(R)$

$$\hat{H}_{el}(R)\psi_a(r; R) = \varepsilon_a\psi_a(r; R)$$
$$\left(\hat{T}_e(r) + V_{ee}(r) + V_{eN}(r, R)\right)\psi_a(r; R) = (\varepsilon_a - V_{NN})\psi_a(r; R)$$

One can use various methods:

The so-called first principles (ab-initio)

- Hartree-Fock
- Density Functional Theory based methods
- Configuration Interaction
- Etc.

The semi-empirical

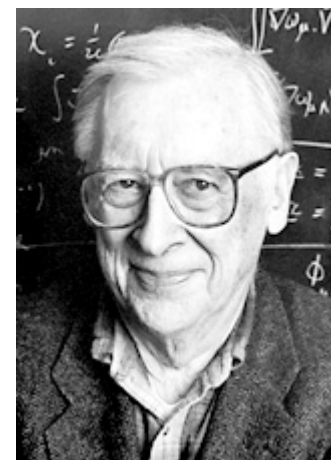
- Tight-binding
- ZINDO family
- etc.

We will come back to this problem later.

The Nobel Prize in Chemistry 1998



Walther Kohn
for his
development
of DFT



John A. Pople
for his
development of
computational
methods in
Quantum Chem

The electron-nucleus problem in molecular structures

The adiabatic electronic wavefunctions form a complete basis in the electronic Hilbert space. Hence the combined system (electrons + nuclei) can be described by the total wavefunction

$$\Psi(r; R) = \sum_a \chi_a(R) \psi_a(r, R)$$

To obtain the coefficients χ_a we insert the total wf in the molecular hamiltonian

$$\begin{aligned} \hat{H}_{mol} \Psi(r, R) &= E \Psi(r, R) \\ \sum_a \left(\hat{T}_N + \hat{H}_{el} \right) \chi_a(R) \psi_a(r, R) &= E \sum_a \chi_a(R) \psi_a(r, R) \\ \sum_a \left(\hat{T}_N + [\varepsilon_a(R) - V_{NN}] \right) \chi_a(R) \psi_a(r, R) &= E \sum_a \chi_a(R) \psi_a(r, R) \end{aligned}$$

Multiplying by $\psi_b(r, R)$, integrating over r , and using the orthogonality of ψ_a

$$- \sum_n \frac{\hbar^2}{2M_n} \left\{ \nabla_n^2 \chi_b(R) + \sum_a [2 \langle \psi_b | \nabla_n \psi_a \rangle \cdot \nabla_n + \langle \psi_b | \nabla_n^2 \psi_a \rangle] \chi_a(R) \right\} + U_b(R) \chi_b(R) = E \chi_b(R)$$

$$\hat{T}_N \chi_b(R) + \sum_a \hat{\Omega}_{a,b} \chi_a(R) + U_b(R) \chi_b(R) = E \chi_b(R)$$

The electron-nucleus problem in molecular structures

The nonadiabatic term:

$$\begin{aligned}\hat{\Omega}_{ab}(R_n) &= -\frac{\hbar^2}{M_n} \langle \psi_b | \nabla_n \psi_a \rangle \nabla_n - \frac{\hbar^2}{2M_n} \langle \psi_b | \nabla_n^2 \psi_a \rangle \\ &= -\frac{\hbar^2}{M_n} \mathbf{d}_{ab}^n \cdot \nabla_n - \frac{\hbar^2}{2M_n} \mathbf{D}_{ab}^n\end{aligned}$$

\mathbf{d}_{ab}^n is the nonadiabatic coupling matrix.

\mathbf{D}_{ab}^n is a small correction term.

The nonadiabatic term $\hat{\Omega}_{ab}(R_n)$ couples (mixes) the electronic adiabatic states.

Assuming the Born-Oppenheimer (BO) regime: $\Psi(r; R) = \chi_a(R) \psi_a(r, R)$

$$-\sum_n \frac{\hbar^2}{2M_n} \{ \nabla_n^2 + 2 \langle \psi_a | \nabla_n \psi_a \rangle \nabla_n + \langle \psi_a | \nabla_n^2 \psi_a \rangle \} \chi_a(R) + U_a(R) \chi_a(R) = E \chi_a(R)$$

$$-\sum_n \frac{\hbar^2}{2M_n} \nabla_n^2 \chi_a(R) - \frac{\hbar^2}{M_n} \mathbf{d}_{aa}^n \cdot \nabla_n \chi_a(R) - \frac{\hbar^2}{2M_n} \mathbf{D}_{aa}^n \chi_a(R) + U_a(R) \chi_a(R) = E \chi_a(R)$$

$$\mathbf{d}_{aa}^n = 0 \quad , \quad \mathbf{D}_{aa}^n = \text{small}$$

$$-\sum_n \frac{\hbar^2}{2M_n} \nabla_n^2 \chi_a(R) + U_a(R) \chi_a(R) = E \chi_a(R)$$

The nuclear problem in molecular structures

For the general situation the matrix elements associated with the nonadiabatic operator \hat{A} are a small perturbation and can be neglected.

The Schrödinger equation for the nuclei on the $\psi_a(r, R)$ electronic state becomes

$$\hat{T}_N \chi_{a,\nu} + U_a \chi_{a,\nu} = E_{a,\nu} \chi_{a,\nu}$$

$$U_a(R) = \varepsilon_a(R) - V_{NN}$$

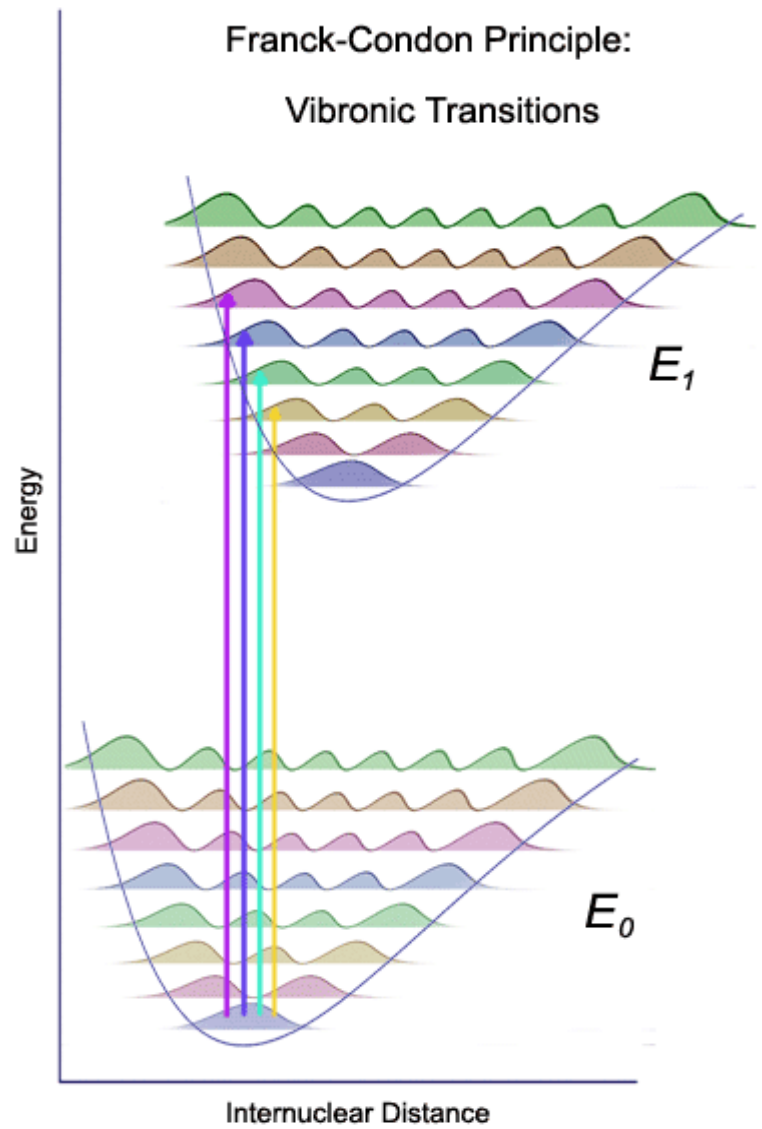
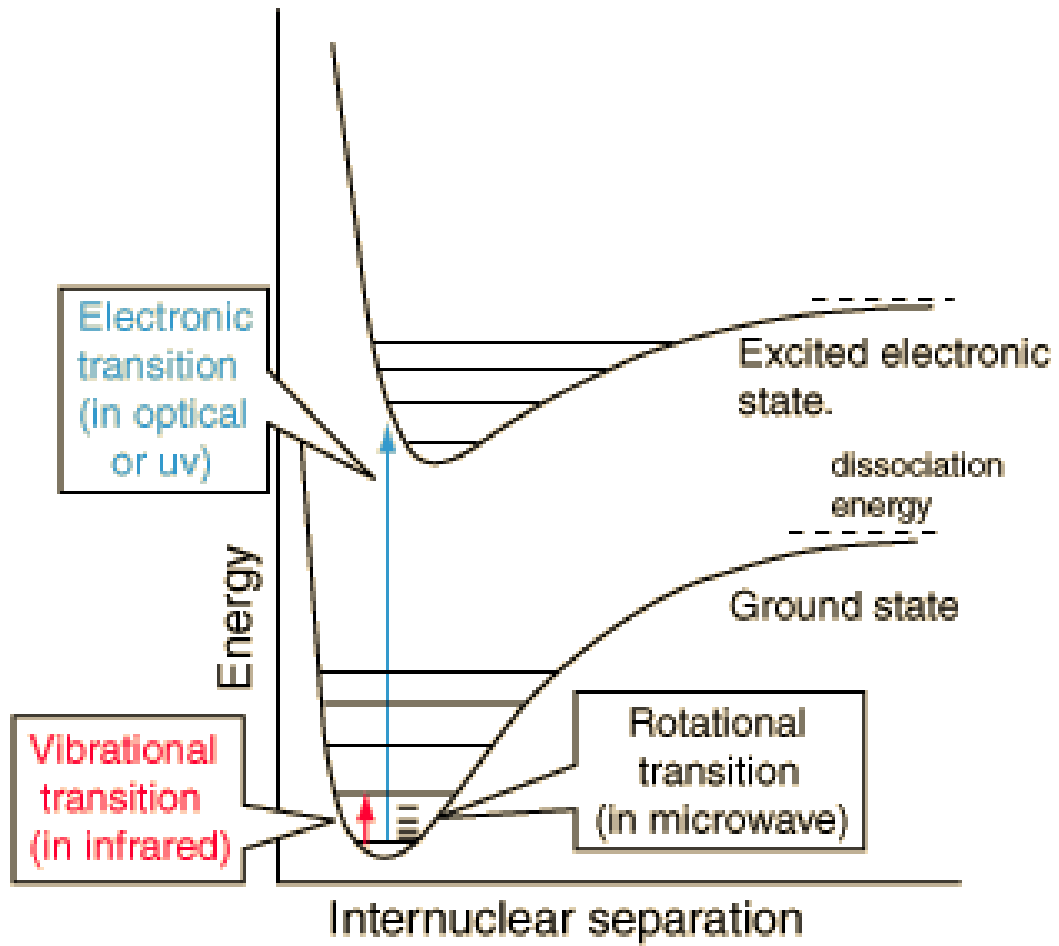
Quantum mechanical solution:

In the vicinity of the equilibrium positions for the nuclei the PES can be approximated by Harmonic potentials

$$U_a(R) \approx U_a(R_0) + \frac{1}{2} U_a''(R_0) \delta_n \delta_m$$
$$\sum_n \left\{ -\frac{\hbar^2}{2M_n} \nabla_n^2 + \frac{1}{2} \sum_m U_a''(R_0) \delta_n \delta_m \right\} \chi_{a,\nu}(R) = E_{a,\nu} \chi_{a,\nu}$$

Thus the nuclear dynamics is described by a set of independent phonons with energies

$$E_{a,\nu} = U_a(R_0) + \sum_\nu \left(n_\xi + \frac{1}{2} \right) \hbar \omega_\nu$$



HyperPhysics; Dept. of Physics, Georgia State Univ.

$$\left(\hat{T}_e(r) + V_{ee}(r) + V_{eN}(r, R) \right) \psi_a(r; R) = (\varepsilon_a - V_{NN}) \psi_a(r; R)$$

$$\sum_n \left\{ -\frac{\hbar^2}{2M_n} \nabla_n^2 + \frac{1}{2} \sum_m U_a''(R_0) \delta_n \delta_m \right\} \chi_{a,\nu}(R) = E_{a,\nu} \chi_{a,\nu}$$

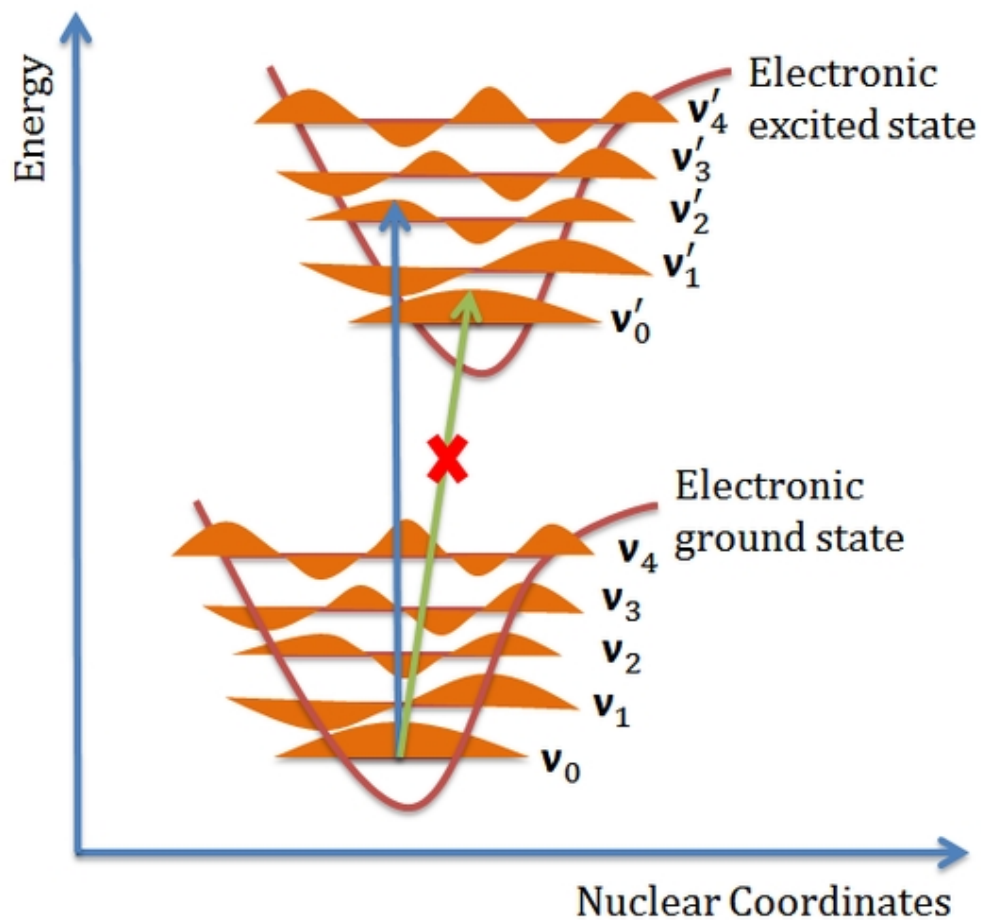


Fig. 2 Franck-Condon energy diagram

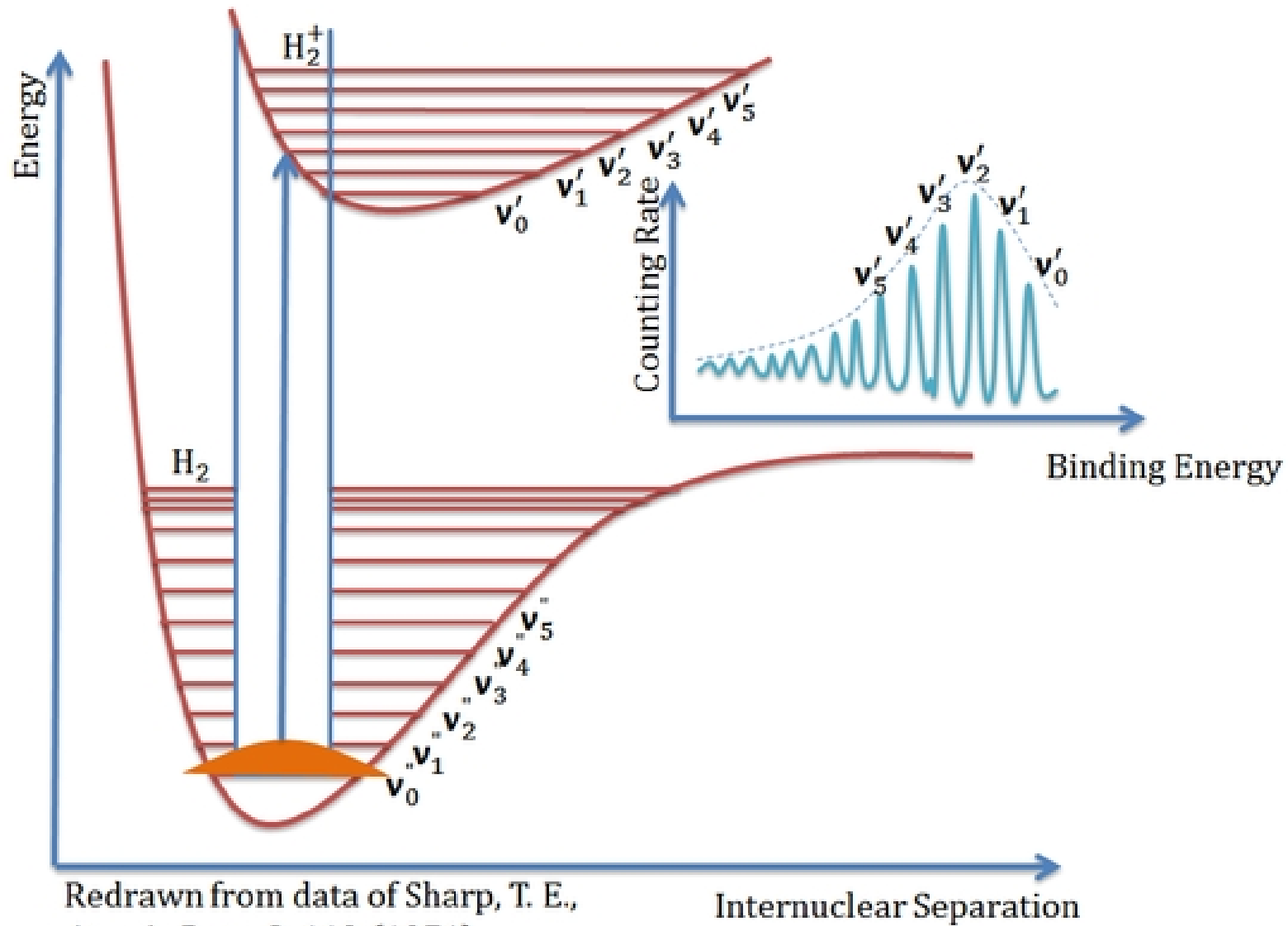
ChemWiki- UC Davis

Franck-Condon Principle and the adiabatic approximation:

It assumes that the electronic transition is much faster than the nuclear motion, so that we can consider the nuclear fixed (or the electronic transition occurring instantaneously).

It successfully explains the difference reason for why peaks in a optical spectrum have different intensities or are even absent

$$M = \langle \hat{\mu}_{ab} \rangle \langle \chi_{b,\nu'} | \chi_{a,\nu} \rangle$$



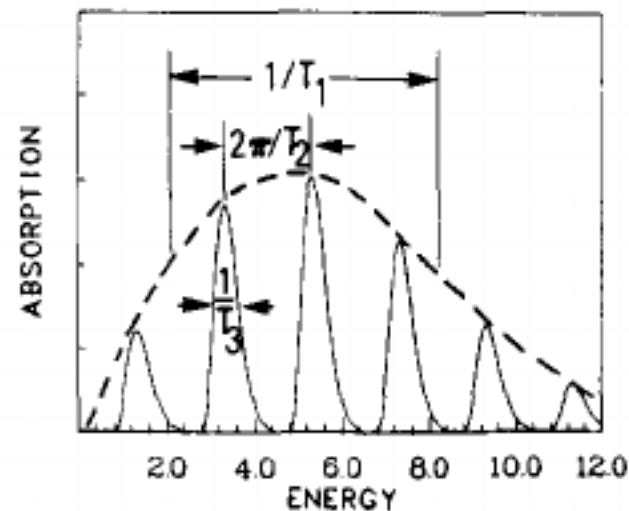
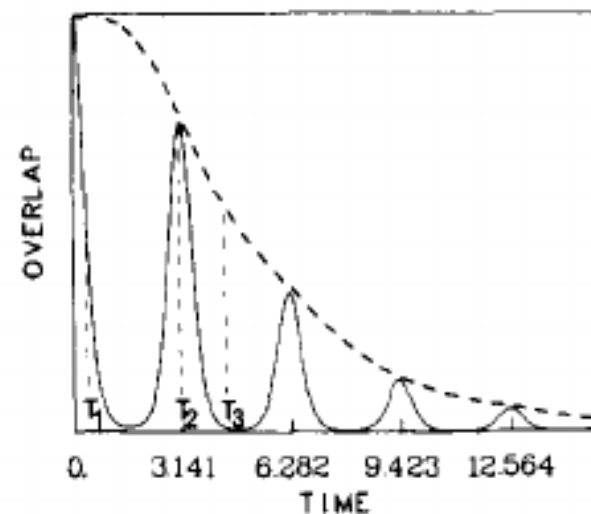
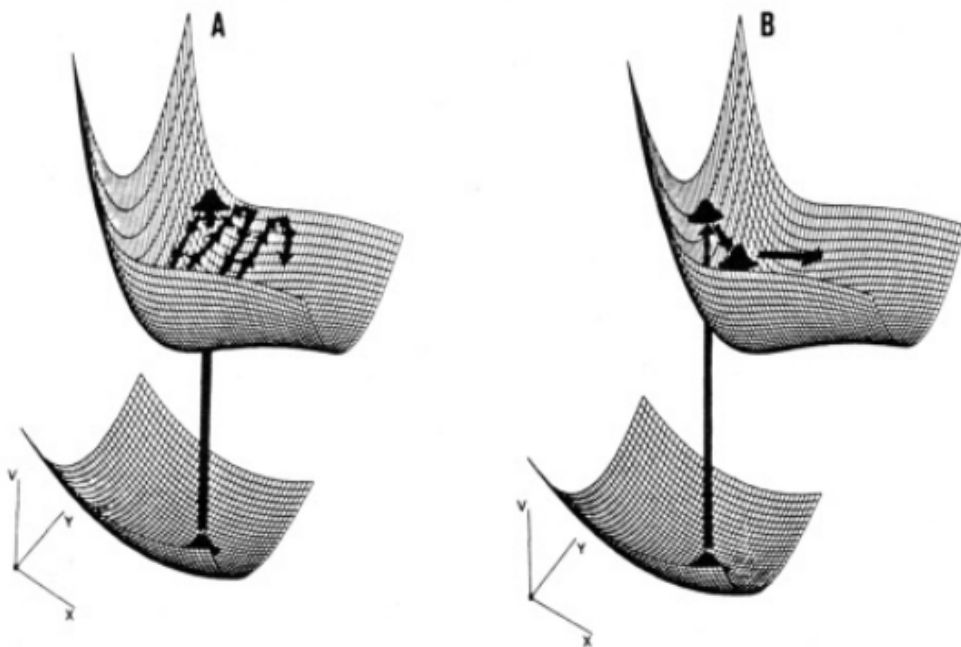
Redrawn from data of Sharp, T. E.,
Atomic Data, 2, 119 (1971)

Fig. 3 Photoelectron spectrum of the ionization of H_2

Semiclassical Theory of Molecular Spectroscopy

The Semiclassical Way to Molecular Spectroscopy,
Eric Heller, *Accounts of Chemical Research*, vol. 14, pg 368 (1981).

$$\sigma(\omega) = C\omega \int_{-\infty}^{\infty} \exp [i(\omega + E_0)t] \langle \phi | \phi(t) \rangle dt$$



Hessian Matrix and Vibrational Modes

Analysis of the PES:

- the number of geometrical configurations for a molecular system increases exponentially with the number of atoms.
- it is important to investigate the most representative configurations (stationary points of the PES: energy minima or transition states).

The **Hessian Matrix** ($3N \times 3N$) provides the necessary information

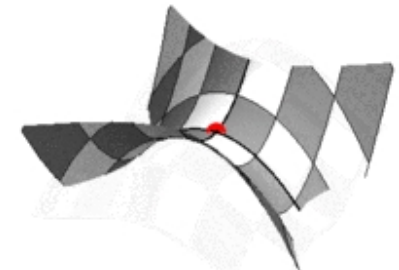
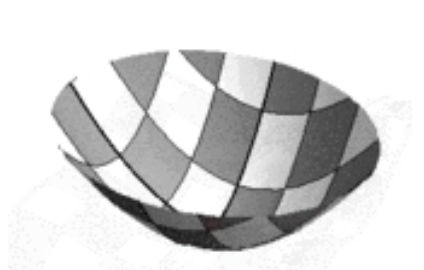
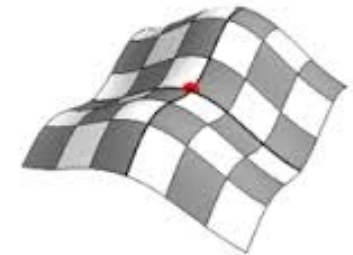
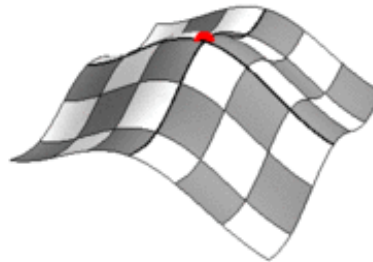
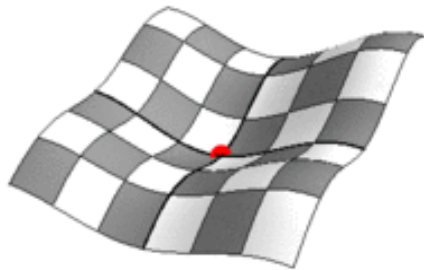
$$H_{ij} \equiv \frac{\partial^2 U(\{\mathbf{R}\})}{\partial \mathbf{R}_i \partial \mathbf{R}_j} = \begin{vmatrix} \frac{\partial^2 U}{\partial x_1^2} & \frac{\partial^2 U}{\partial x_1 \partial y_1} & \cdots & \frac{\partial^2 U}{\partial x_1 \partial z_N} \\ \frac{\partial^2 U}{\partial y_1 \partial x_1} & \frac{\partial^2 U}{\partial y_1^2} & \cdots & \frac{\partial^2 U}{\partial y_1 \partial z_N} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial^2 U}{\partial z_N \partial x_1} & \frac{\partial^2 U}{\partial z_N \partial y_1} & \cdots & \frac{\partial^2 U}{\partial z_N^2} \end{vmatrix}.$$

Hessian Matrix and Vibrational Modes

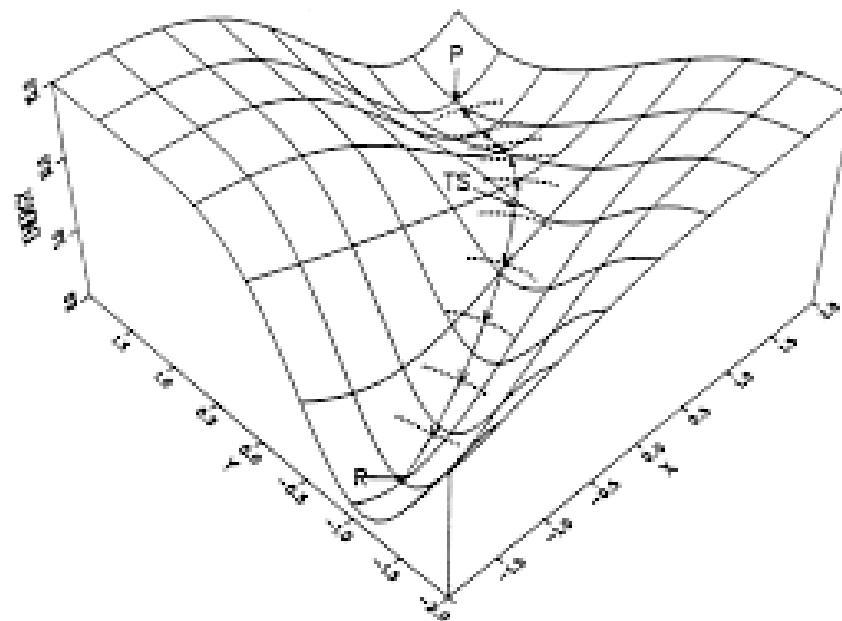
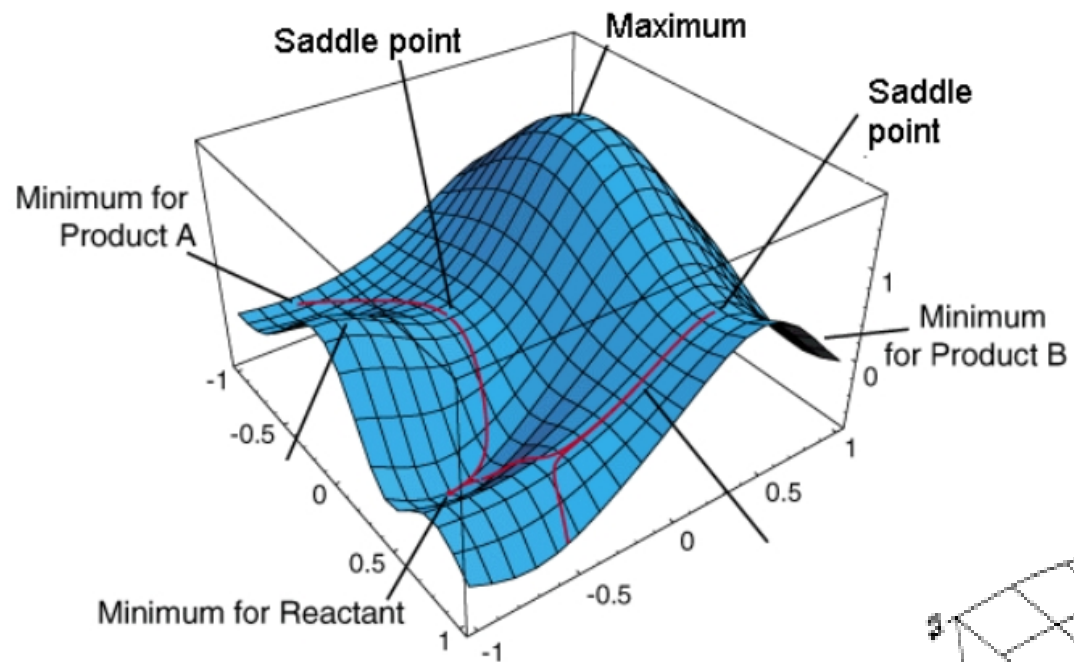
The Hessian is a symmetric matrix: $\frac{\partial}{\partial x_i} \frac{\partial U}{\partial x_j} = \frac{\partial}{\partial x_j} \frac{\partial U}{\partial x_i}$, with real eigenvalues.

Analysis of the PES via the Hessian matrix:

- 1) If all eigenvalues of H are positive, the stationary point is a relative (or local) minimum; ***stable or metastable configuration***.
- 2) If all eigenvalues of H are negative, the stationary point is a relative (or local) maximum; ***unstable configuration***.
- 3) If H has both positive and negative eigenvalues, the stationary point is a saddle point.



Hessian Matrix and Transition States



The nuclear problem in molecular structures

Classical Regime, the Molecular Dynamics solution:

Because of the heavy mass of the nuclei one can assume that they behave like classical particles in some conditions, such as:

- above cryogenic temperatures,
- solutions,
- long time dynamics, and so on.

The Schrödinger equation is substituted by the classical dynamical equations

$$\sum_n \frac{P_n^2}{2M_n} \nabla_n^2 + U_a(R) = E$$
$$U_a(R) = \varepsilon_a(R) - V_{NN}$$

The harmonic approximation can be dropped.

The classical equations of motion can be written as

$$M_n \frac{d^2 \vec{R}_n}{dt^2} = -\vec{\nabla}_n U_a(R)$$

still assuming the electron-nuclear problem decoupled in the adiabatic approximation!

It is necessary to calculate the forces acting on the nuclei: $\vec{F}_n = -\vec{\nabla}_n U_a(R)$

The nuclear problem in molecular structures

For the “ab-initio” molecular dynamics one calculates the nuclear forces from the PES obtained from first principles methods (DFT, for instance) by using the Hellmann-Feynman principle.

Obs: for practical applications this method has to be modified by including the Pulay force terms.

$$\vec{F}_n = -\vec{\nabla}_n U_a(R)$$

The Hellmann-Feynman Theorem:

consider the hamiltonian of some arbitrary many-atom (many-electron) system which depends on some external parameters, for instance the positions of the nuclei

$$\hat{H}_{el}(r; R)$$

so that the time-independent Schrödinger equation reads:

$$\hat{H}_{el}(r; R)\psi(r; R) = \varepsilon(R)\psi(r; R)$$

we want to calculate the derivative of one of its eigenvalues: $\frac{\partial \varepsilon(R)}{\partial R_n}$

The Hellmann-Feynman Theorem

Consider the hamiltonian of some arbitrary many-atom (many-electron) system which depends on some external parameters, for instance the positions of the nuclei

$$\hat{H}_{el}(r; R) ,$$

so that the time-independent Schrödinger equation reads:

$$\hat{H}_{el}(r; R)\psi(r; R) = \varepsilon(R)\psi(r; R)$$

We want to calculate the derivative of one of its eigenvalues: $\partial\varepsilon(R)/\partial R_n \equiv \partial_n\varepsilon(R)$

$$\begin{aligned} \frac{\partial\varepsilon(R)}{\partial R_n} &= \frac{\partial}{\partial R_n} \langle \psi(R) | \hat{H}(R) | \psi(R) \rangle \\ &= \langle \partial_n \psi(R) | \hat{H}(R) | \psi(R) \rangle + \langle \psi(R) | \hat{H}(R) | \partial_n \psi(R) \rangle + \langle \psi(R) | \frac{\partial \hat{H}(R)}{\partial R_n} | \psi(R) \rangle \\ &= \varepsilon(R) [\langle \partial_n \psi(R) | \psi(R) \rangle + \langle \psi(R) | \partial_n \psi(R) \rangle] + \langle \psi(R) | \frac{\partial \hat{H}(R)}{\partial R_n} | \psi(R) \rangle \\ &= \varepsilon(R) \int \left[\frac{\partial \psi^*}{\partial R_n} \psi + \psi^* \frac{\partial \psi}{\partial R_n} \right] d\tau + \langle \psi(R) | \frac{\partial \hat{H}(R)}{\partial R_n} | \psi(R) \rangle \\ &= \langle \psi(R) | \frac{\partial \hat{H}(R)}{\partial R_n} | \psi(R) \rangle \end{aligned}$$

because the normalized eigenstates satisfy: $\frac{\partial}{\partial R_n} \langle \psi(R) | \psi(R) \rangle = 0$

The Hellmann-Feynman Theorem

$$\frac{\partial \varepsilon(R)}{\partial R_n} = \langle \psi(R) | \frac{\partial \hat{H}(R)}{\partial R_n} | \psi(R) \rangle$$

In principle it is much more practical to calculate the RHS than the LHS of this equation; numerically, the LHS requires two diagonalizations per cartesian axis.

For the electronic hamiltonian

$$\left(\hat{T}_e(r) + V_{ee}(r) + V_{eN}(r, R) \right) \psi_a(r; R) = (\varepsilon_a - V_{NN}) \psi_a(r; R)$$

only the following potentials depend on R

$$V_{eN} = - \sum_{j,n} \frac{Z_n e^2}{|\vec{r}_j - \vec{R}_n|} \quad V_{NN} = \frac{1}{2} \sum_{n \neq m} \frac{Z_n Z_m e^2}{|\vec{R}_n - \vec{R}_m|}$$

so that the force on the n^{th} atom along the cartesian direction α is

$$\begin{aligned} F_{n\alpha} &= - \frac{\partial V_{NN}}{\partial R_{n\alpha}} - e^2 Z_n \int \frac{(\vec{r} - \vec{R}_n)}{|\vec{r} - \vec{R}_n|^3} \rho(\vec{r}) d\vec{r} \\ &= - \frac{\partial V_{NN}}{\partial R_{n\alpha}} + e \int \frac{V_{eN}(r, R)}{\partial R_{n\alpha}} \rho(\vec{r}) d\vec{r} \end{aligned}$$

only the electronic density is required $\rho(r) = \int |\psi(r; R)|^2 dr_2 \cdots dr_{N_e}$

The Hellmann-Feynman-Pulay forces

For variational methods using a set of basis functions the plain Hellmann-Feynman method is unreliable !

If the eigenstates are written as a linear combination of localized basis states:

$$\psi_a(r; R) = \sum_{\lambda} c_{a\lambda} \phi_{\lambda}(r; R)$$

The eigenvalue equation that results from the time-independent Schrödinger equation in the Hilbert space of the basis set is

$$\sum_{\lambda} \{H_{\nu\lambda}(R) - \varepsilon_a(R) S_{\nu\lambda}(R_n, R_m)\} c_{a\lambda} = 0$$

the overlap matrix: $S_{\nu\lambda}(R_n, R_m) = \langle \phi_{\nu}(R_n) | \phi_{\lambda}(R_m) \rangle$

The coefficients $c_{a\lambda}$ are determined so that they minimize the total energy for a given molecular conformation $\varepsilon_a(R) = \langle \psi_a | \hat{H}_{el}(R) | \psi_a \rangle$. The variational principle.

Therefore
$$\frac{d\varepsilon_a}{dR_{n\alpha}} = \sum_{\lambda} \frac{\cancel{\partial\varepsilon_a}}{\cancel{\partial c_{a\lambda}}} \frac{\partial c_{a\lambda}}{\partial R_{n\alpha}} + \frac{\partial\varepsilon_a}{\partial R_{n\alpha}} = \frac{\partial\varepsilon_a}{\partial R_{n\alpha}}$$

Nevertheless
$$F_{n\alpha} = -\frac{d\varepsilon_a}{dR_{n\alpha}} = -\langle \psi_a | \frac{\partial \hat{H}_{el}}{\partial R_{n\alpha}} | \psi_a \rangle - 2\langle \partial_{n\alpha} \psi_a | \hat{H}_{el} | \psi_a \rangle$$

(assuming real wavefunctions, which is possible in the stationary case in the absence of magnetic fields)

The Hellmann-Feynman-Pulay forces

$$F_{n\alpha} = -\frac{d\varepsilon_a}{dR_{n\alpha}} = -\langle\psi_a|\frac{\partial\hat{H}_{el}}{\partial R_{n\alpha}}|\psi_a\rangle - 2\langle\partial_{n\alpha}\psi_a|\hat{H}_{el}|\psi_a\rangle$$

- the first term is the usual Hellmann-Feynman term
- the second term is due to Pulay, which he called the wavefunction force

In general terms, we finally obtain for the total force on the n^{th} atom:

$$F_{n\alpha} = -\frac{\partial V_{NN}}{\partial R_{n\alpha}} + 2\sum_a^{\text{occ}}\sum_{\nu\lambda}c_{a\nu}\left[\frac{\partial H_{\nu\lambda}}{\partial R_{n\alpha}} - \varepsilon_a\frac{\partial S_{\nu\lambda}}{\partial R_{n\alpha}}\right]c_{a\lambda}$$

Thus the dynamics of the nuclei can be calculated with

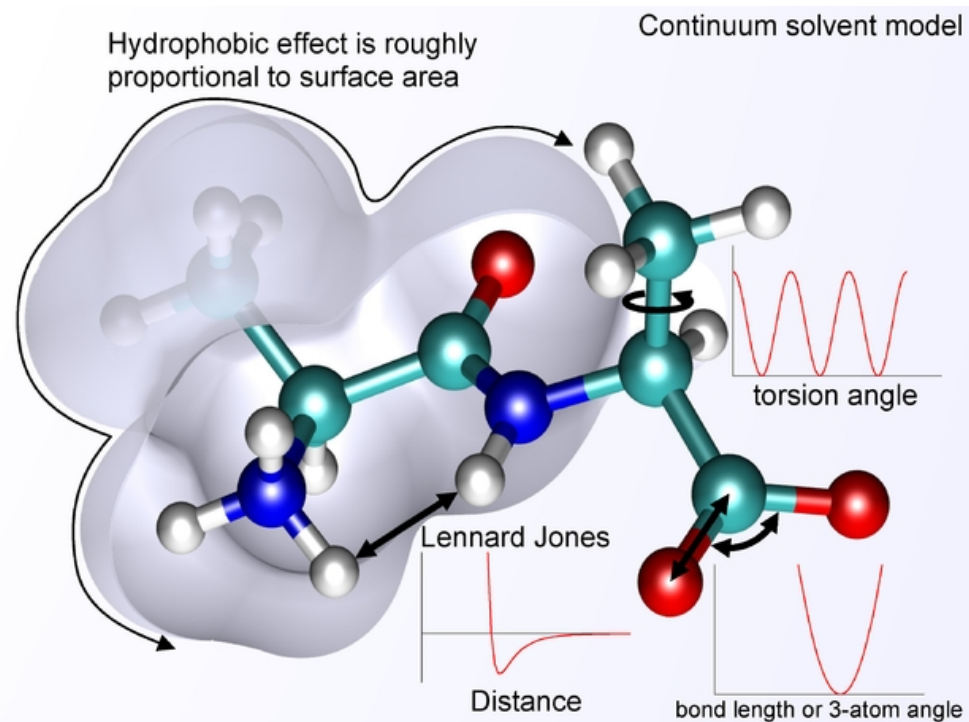
$$M_n\frac{d^2R_{n\alpha}}{dt^2} = F_{n\alpha}$$

Generally, ab-initio molecular dynamics is used for:

- ***usually restricted to the ground state PES***
- usually geometry optimization, for systems comprised of hundreds of atoms (exceptionally up to a few thousand, depending on the numerical methods);
- for dynamics calculations: a few hundred atoms in the system;
- time range of ab-initio dynamics simulations are in picosecond time scale
- alternative for bigger systems: classical molecular dynamics (Molecular Mechanics)

Classical Force Fields

$$\begin{aligned}
 V^{FF} &= V_{short\ R} + V_{long\ R} \\
 &= V_{bonded} + V_{nonbonded}
 \end{aligned}$$



$$V_{bonded}^{FF} = \sum_{bonds} K_b (R - R_o)^2 + \sum_{angles} K_\theta (\theta - \theta_o)^2 + \sum_{torsions} \sum_{n=0}^5 C_n (\cos\phi)^n$$

$$V_{nonbonded}^{FF} = \sum_{i,j \neq i} 4\epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{R_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{R_{ij}} \right)^6 \right] + \sum_{i,j \neq i} \frac{q_j q_i}{4\pi\epsilon_o R_{ij}}$$

FF parameters: $K, R_0, K_\theta, \theta_0, C_n, \epsilon_{ij}, \sigma_{ij}, q$

Many other force fields exist and can be defined.

Molecular Dynamics with Classical Force Fields

Molecular mechanics used to study small molecules as well as large biological systems or material assemblies with many thousands to millions of atoms.

Characteristics:

- Each atom is simulated as a single particle; electrons are disregarded;
- Each particle is assigned a radius (typically the van der Waals radius), polarizability, and a constant net charge (generally derived from quantum calculations and/or experiment);
- generally restricted to systems in the electronic ground state;
- very fast from the computational point of view;
- The FF parameters of the energy functions can be derived from experimental work
- (for instance, free energies of solvation, lattice energies, density functions) and quantum mechanical calculations;
- does not describe charge transfer processes adequately, particularly electron transfer reactions;
- does not describe quantum effects;
- able to simulate the dynamics of very large systems (tens of thousands of atoms) for very long times (microseconds);
- easy to parallelize;
- the hybrid QMMM (Quantum Mechanical-Molecular Mechanics) methods are a powerful simulation technique used in biophysics for various applications, including drug discovery.
- Force fields are difficult to use and develop.

Multiscale Models for Complex Chemical Systems

The Nobel Prize in Chemistry 2013



Martin Karplus



Michael Levitt



Arieh Warshel

Awarded jointly "for the development of multiscale models for complex chemical systems".

Methods use both classical and quantum mechanical theory:

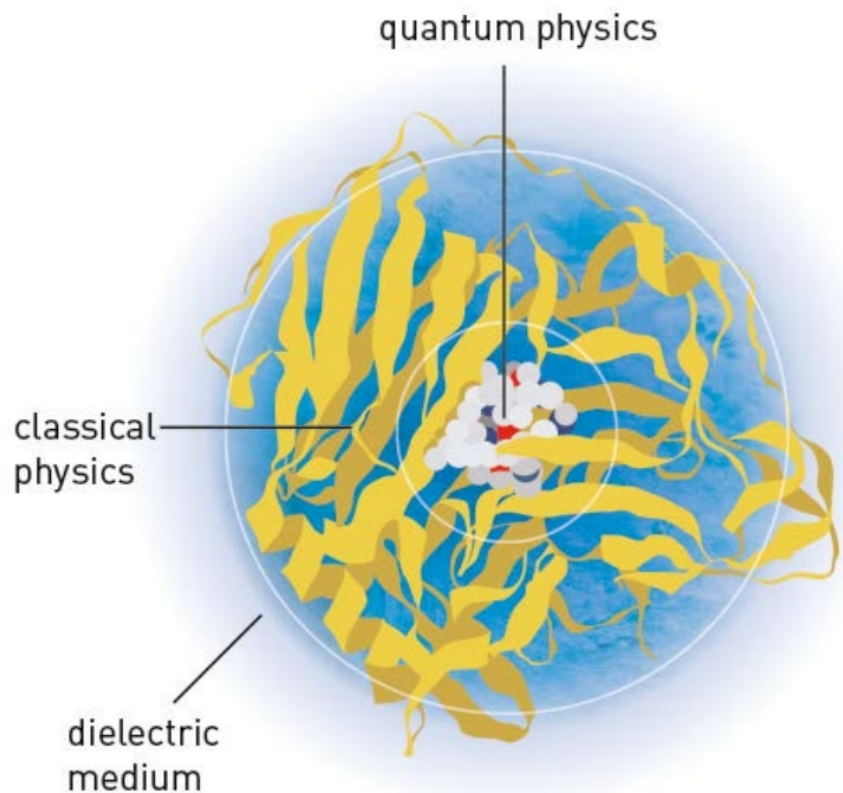
- hybrid methods that combine the advantages of classical and quantum methods to describe complex chemical systems;
- opened up a fruitful cooperation between theory and experiment that has made many otherwise unsolvable problems solvable.
- particularly, to study complex processes in organic chemistry and biochemistry.

Multiscale Models for Complex Chemical Systems

QMMM = Quantum Mechanical / Molecular Mechanics

QMMM uses (first principles) quantum mechanical models for the central part of the system (reaction center) whereas the surrounding (environment) is described by classical models.

Frequently the entire system is embedded in a dielectric continuum.



A crucial point is to make the two models (QM-MM) interact in a physically meaningful way.

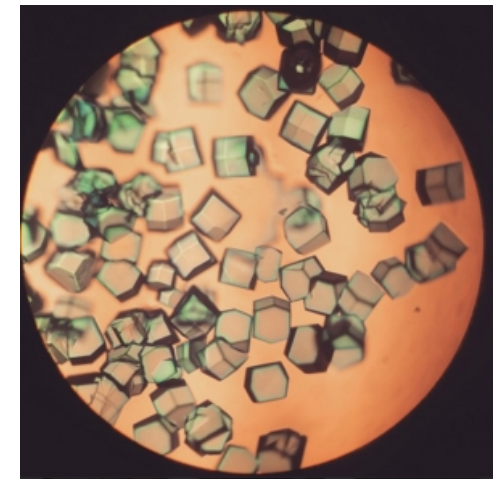
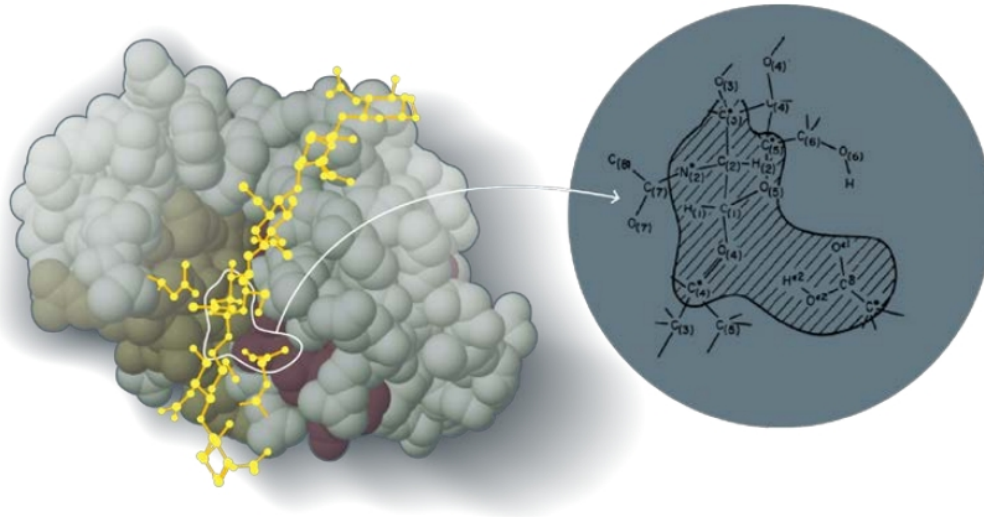
Multi-copper-oxidase embedded in water

Multiscale Models for Complex Chemical Systems

QMMM = Quantum Mechanical / Molecular Mechanics

glycoside chain cleavage in lysozyme enzyme:

model only the relevant parts of the system with QM, while most of the surrounding may be treated using MM or a continuum model.



A. Warshel and M. Levitt, J. Mol. Biol. 103, 227-249, 1976.

Lysozyme crystals

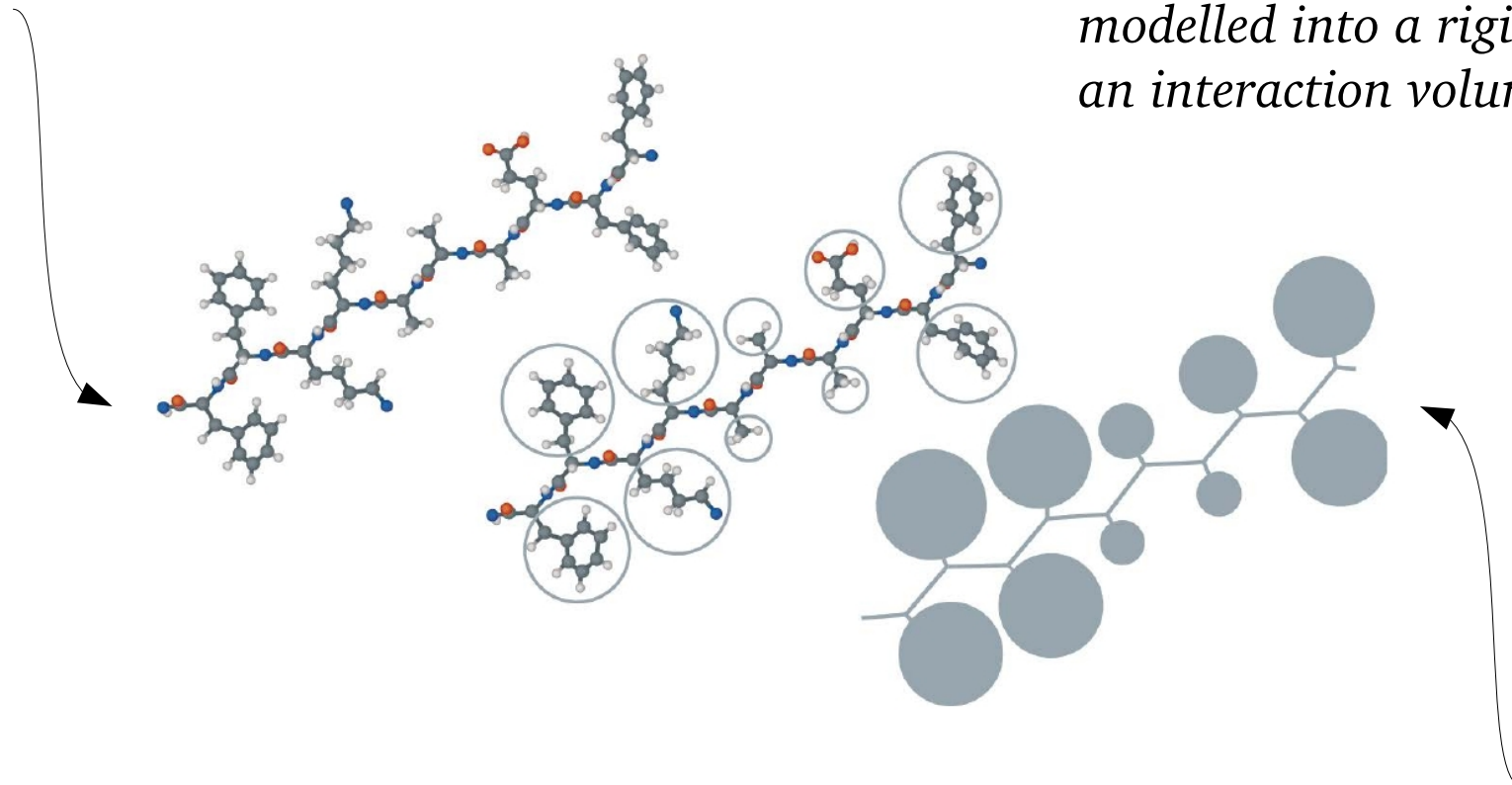
wikipedia

Multiscale Models for Complex Chemical Systems

Coarse Grained Molecular Dynamics:

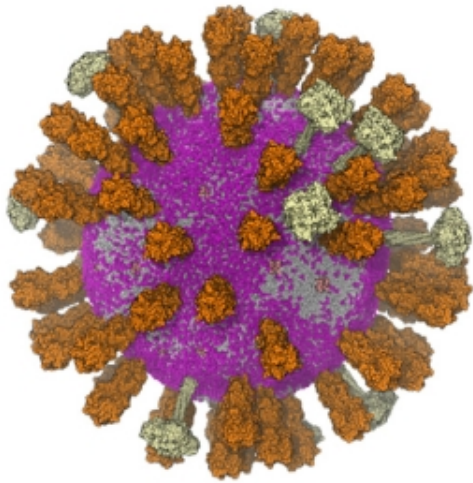
detailed structure of a polypeptide chain

each amino acid residue is modelled into a rigid unit with an interaction volume

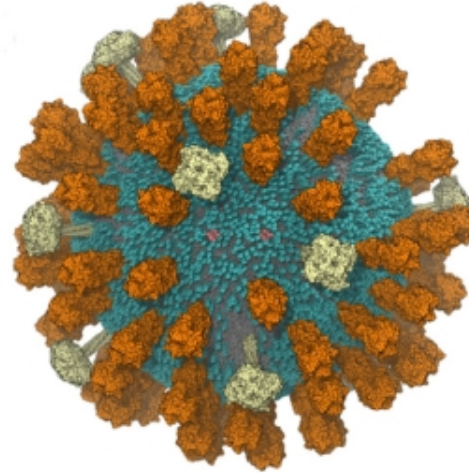


string-of-pearls like structure

(-) Forssman Glycolipid



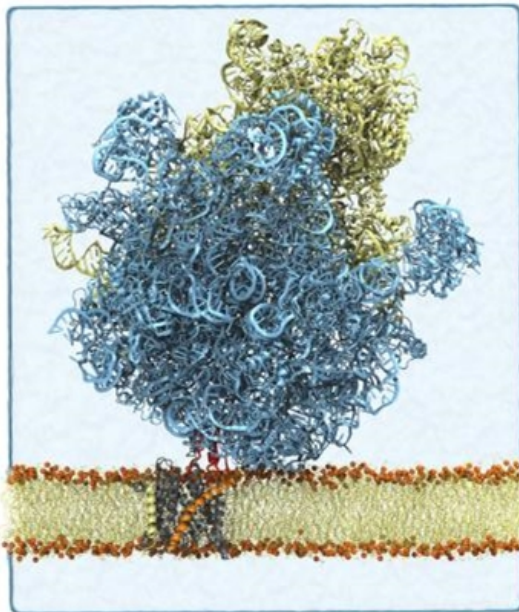
(+) Forssman Glycolipid



“Nothing to Sneeze At: A Dynamic and Integrative Computational Model of an Influenza A Virion”

the first microsecond timescale coarse-grained molecular dynamics simulations of enveloped virions in explicit solvent. The simulated properties of the influenza A virion were consistent with experimental measurements, and revealed that the Forssman glycolipid affects several biophysical characteristics of the virion.

Structure 23, 584–597, March 3, 2015



A molecular dynamics flexible fitting (MDFF) method

Gumbart J, Trabuco LG, Schreiner E, Villa E, Schulten K. *“Regulation of the protein-conducting channel by a bound ribosome”*. Structure. 2009;17(11):1453-1464