Theoretical and Computational Chemistry in Biological Systems

王石嵘
Kuang Yaming Honors School

April 13, 2019

Contents

Two main schools of modern theoretical chemistry and physics

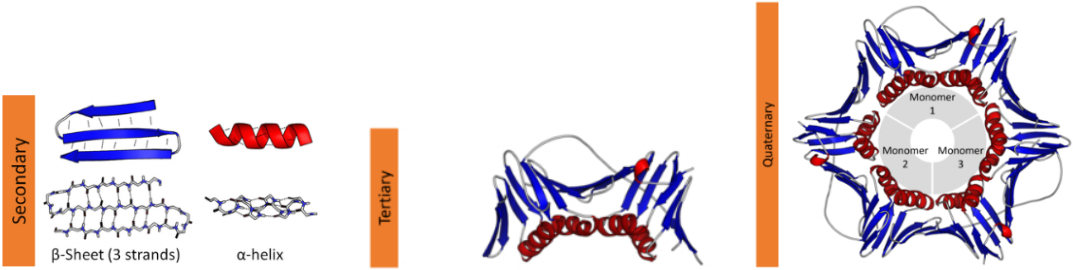
1. *ab initio* / empirical
2. deductive / inductive
3. *a priori* / *a posteriori*
4. ...

Motivations

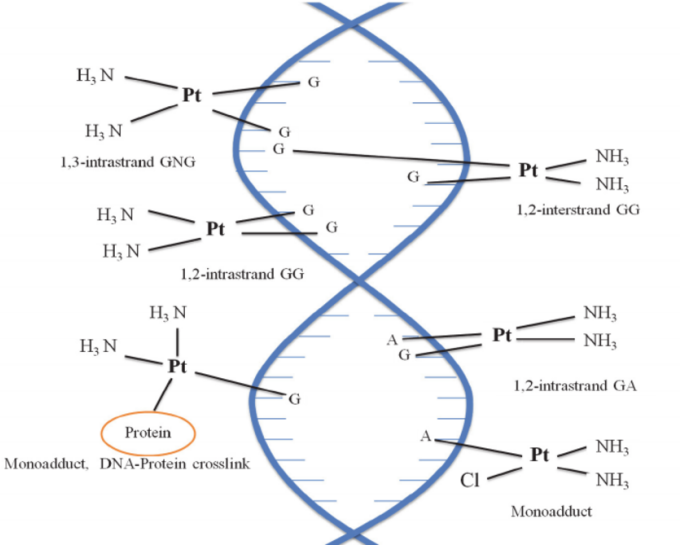
Contents in Brief

Questions:

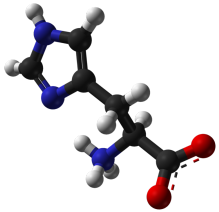
1. How to predict 2°, 3°, 4°structures of protein and DNA/RNA?
2. How to simulate protein/DNA/RNA folding?



3. How to explain or predict the mechanisms of biochemical reactions?



Basic Models



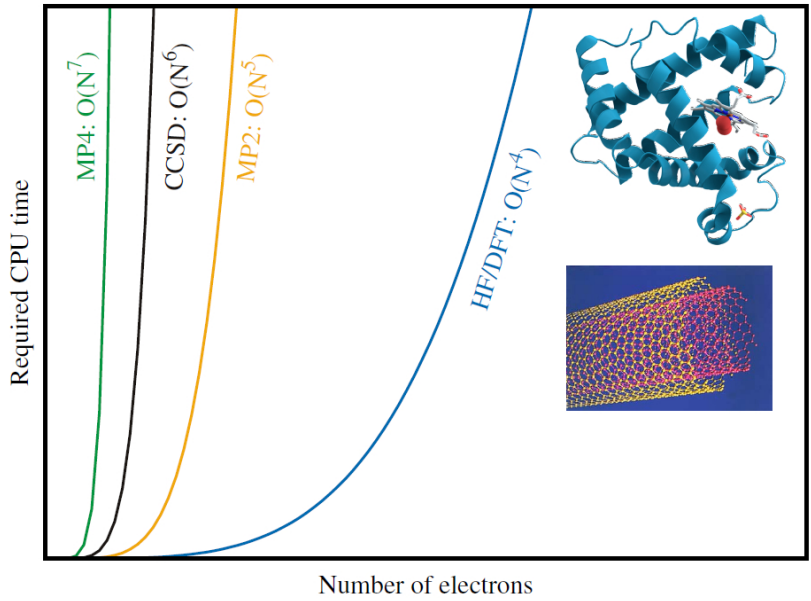
Molecules consist of nuclei and electrons.

$$E = E_N + E_e + E_{NN} + E_{Ne} + E_{ee} \tag{3.1}$$

Born-Oppenheimer Approximation:

$$\text{Nuclei don't move.} \Rightarrow E_N = 0 \tag{3.2}$$

Ab Initio Methods



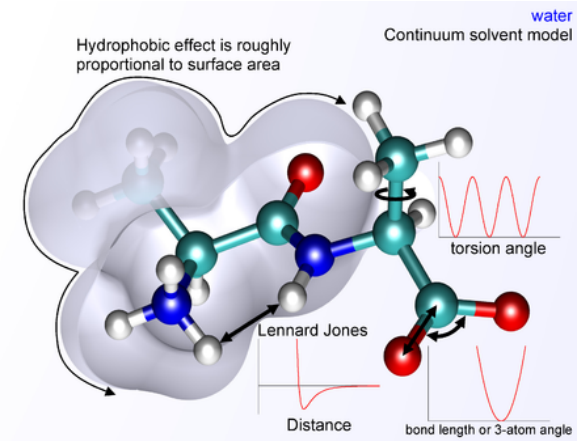
$$\hat{\mathbf{H}}\,\Psi = E\Psi \qquad \Psi_i = \sum_{ij} c_{ij}\chi_j \tag{3.3}$$

$$\begin{aligned} E_{\mathrm{HF}} = &\sum_{\mu\nu} P_{\nu\mu} \left\langle \mu \left| -\frac{1}{2}\nabla^2 - \sum_{A=1}^{M} \frac{Z_A}{|r - R_A|} \right| \nu \right\rangle \\ &+ \frac{1}{2} \sum_{\mu\nu} P_{\nu\mu} \sum_{\lambda\sigma} P_{\sigma\lambda} \left[(\mu\nu|\lambda\sigma) - \frac{1}{2}(\mu\sigma|\lambda\nu) \right] \\ &+ \sum_{A=1}^{M} \sum_{B>A}^{M} \frac{Z_A Z_B}{R_{AB}} \end{aligned} \tag{3.4}$$

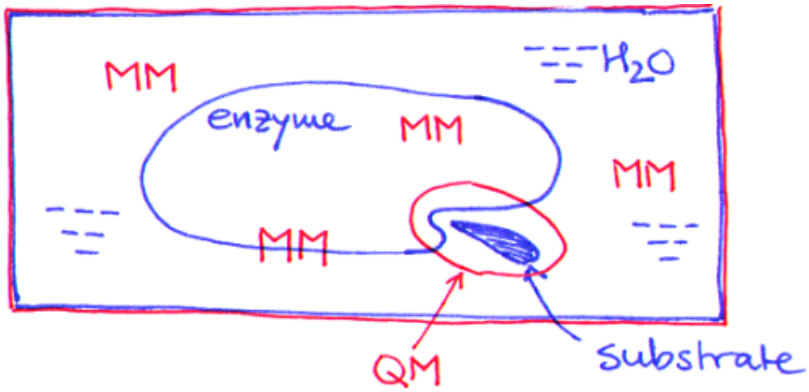
$$E_{\mathrm{XC}} = E_{\mathrm{XC}}[\rho] \tag{3.5}$$

Molecular Mechanics Force Field

$$V = V_{\text{bond}} + V_{\text{angle}} + V_{\text{dihedral}} + V_{\text{electrostatic}} + V_{\text{van der Waals}} \tag{3.6}$$



QM/MM, by Martin Karplus

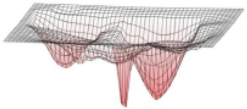


ONIOM (Our own N-layered Integrated molecular Orbital and molecular Mechanics), by Morokuma Keiji (諸熊 奎治)

Semi-empirical

1. PM7
2. GFN2-xTB
3. NN

Neural Network



训练集构型采集

神经网络结构

构型从头算计算

低维势能面

高维势能面

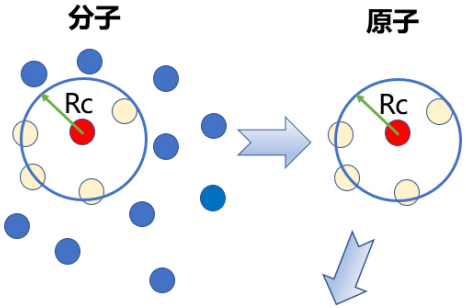
神经网络输入描述符 → 平移旋转不变性（函数对应法则）

Descriptor

$$G_i^{rad} = \sum_j Z_j e^{-\eta(R_{ij}-\mu)^2} \bullet f_c(R_{ij})$$

$$G_i^{ang} = 2^{1-\zeta} \sum_{j,k\neq i} Z_j Z_k (1+\lambda\cos\theta_{ijk})^{\zeta} e^{-\eta(R_{ij}^2+R_{ik}^2+R_{jk}^2)} \bullet f_c(R_{ij}) f_c(R_{ik}) f_c(R_{jk})$$

$$f_c(R_{ij}) = \begin{cases} 0.5(\cos\frac{\pi R_{ij}}{R_c}+1) & R<R_c \\ 0 & R>R_c \end{cases}$$



$$\{G_i^{rad}, G_i^{ang}\}$$

对称函数