

# Theoretical and Computational Chemistry in Biological Systems

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# Contents

- 1 Introduction
- 2 Motivations
- 3 Basic Models
  - Ab Initio
  - Molecular Mechanics Force Field
  - QM/MM, or ONIOM
  - Semi-empirical
    - Neural Network

## Two main schools of modern theoretical chemistry and physics

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

# Motivations

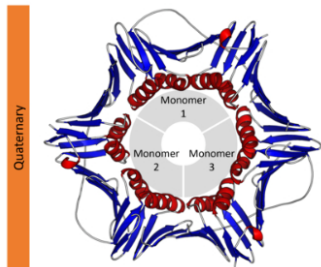
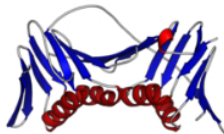
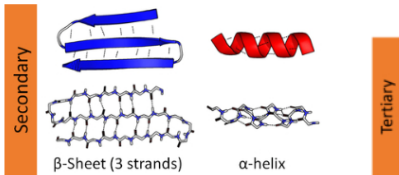
## Contents in Brief

<i>Preface</i>	<i>viii</i>
1 The Foundations of Biochemistry	1
<b>I STRUCTURE AND CATALYSIS</b>	<b>41</b>
2 Water	43
3 Amino Acids, Peptides, and Proteins	71
4 The Three-Dimensional Structure of Proteins	113
5 Protein Function	153
6 Enzymes	183
7 Carbohydrates and Glycobiology	235
8 Nucleotides and Nucleic Acids	271
9 DNA-Based Information Technologies	303
10 Lipids	343
11 Biological Membranes and Transport	371
12 Biosignaling	417

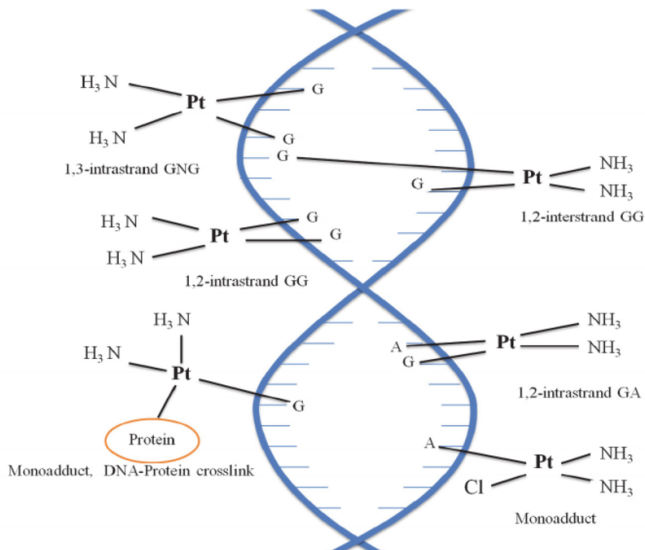
<b>II BIOENERGETICS AND METABOLISM</b>	<b>485</b>
13 Bioenergetics and Biochemical Reaction Types	489
14 Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway	527
15 Principles of Metabolic Regulation	569
16 The Citric Acid Cycle	615
17 Fatty Acid Catabolism	647
18 Amino Acid Oxidation and the Production of Urea	673
19 Oxidative Phosphorylation and Photophosphorylation	707
20 Carbohydrate Biosynthesis in Plants and Bacteria	773
21 Lipid Biosynthesis	805
22 Biosynthesis of Amino Acids, Nucleotides, and Related Molecules	851
23 Hormonal Regulation and Integration of Mammalian Metabolism	901
<b>III INFORMATION PATHWAYS</b>	<b>945</b>
24 Genes and Chromosomes	947
25 DNA Metabolism	975
26 RNA Metabolism	1021
27 Protein Metabolism	1065
28 Regulation of Gene Expression	1115

## Questions:

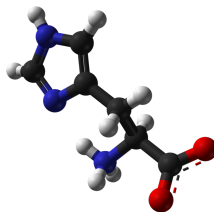
- 1 How to predict 2°, 3°, 4° structures of protein and DNA/RNA?
- 2 How to simulate protein/DNA/RNA folding?



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



# Basic Models



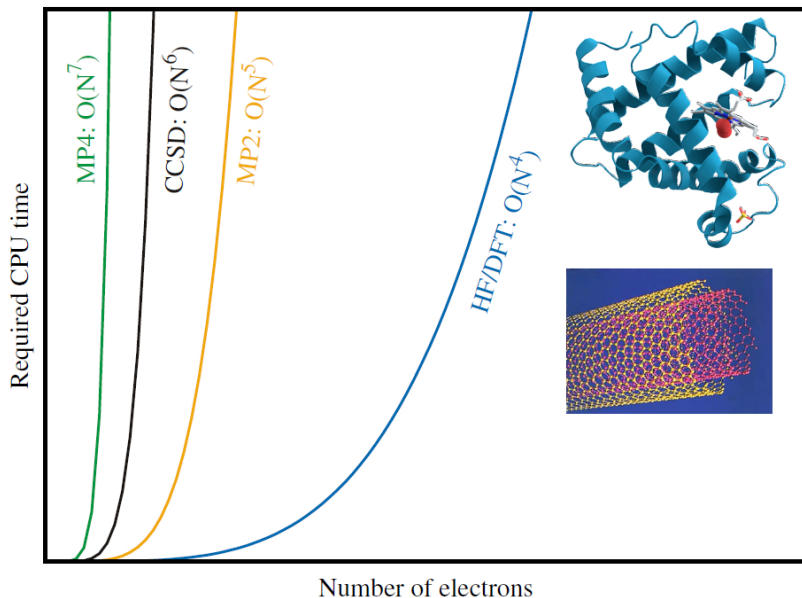
Molecules consist of nuclei and electrons.

$$E = E_N + E_e + E_{NN} + E_{Ne} + E_{ee} \quad (3.1)$$

Born-Oppenheimer Approximation:

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

# Ab Initio Methods





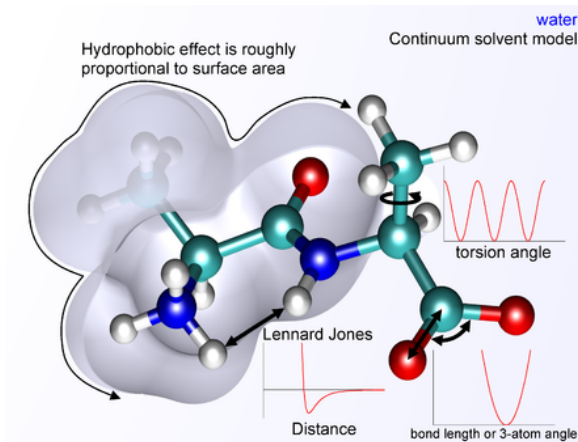
$$\hat{H}\Psi = E\Psi \quad \Psi_i = \sum_{ij} c_{ij}\chi_j \quad (3.3)$$

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

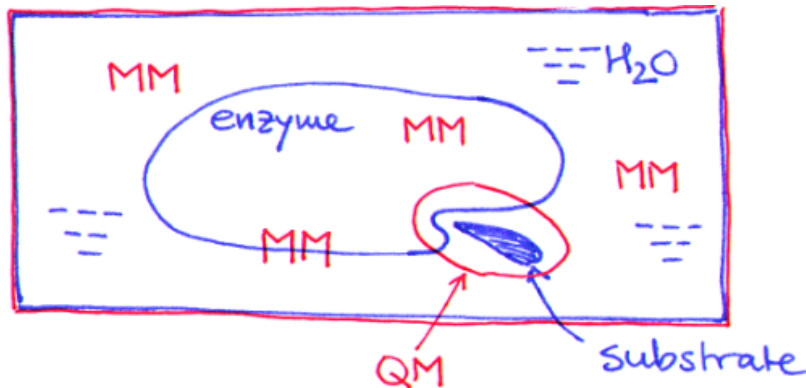
$$\begin{aligned} & + \sum_{A=1}^M \sum_{B>A}^M \frac{Z_A Z_B}{R_{AB}} \\ E_{\text{XC}} = & E_{\text{XC}}[\rho] \end{aligned} \quad (3.5)$$

# Molecular Mechanics Force Field

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



## 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

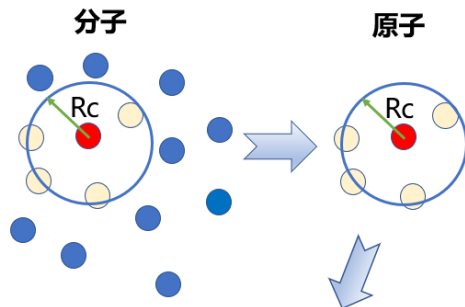


# Descriptor

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

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

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



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

对称函数