Molecular Biophysics

Instructor
Dr. Prem Chapagain
Office hrs: TuTh 5pm-6:15pm
Email: chapagap@fiu.edu
Phone: 305-348-6266

Textbooks / References
No formal required textbook, but the following are highly recommended

Molecular driving forces
Ken Dill, S. Bromberg

The Molecules of Life
J. Kurian et al.

Branden and Tooze – Introduction to Protein Structure
**Textbooks / References**

Thermodynamics Review  

or Google  
“Thermodynamics of Biomolecular Systems MIT”

Click ---→ **Download Course Material**

---

**Biological systems / Complexity**

A biological system is a complex of many small components (factories) working together

The components of a biological system must perform their necessary functions, e.g.

- Extract, store and transform energy
- Self-replicate (store and preserve the information from one generation to the next)
- Must be highly organized (complex macromolecular assemblies)
- Adapt to changing conditions: control of function and evolution

**Biophysics**: quantitative description of biological processes and phenomena, founded on fundamental physical laws.
Hierarchy of Complexity of Life

(Society)
Organism (Animal, Plant)
Specialized Organs
Specialized Tissues
Cells
Macromolecular Assemblies
Macromolecules
Simples Molecular Building Blocks

Central Dogma of Molecular Biology

by FRANCIS CRICK
MRC Laboratory of Molecular Biology,
Hills Road,
Cambridge CB2 2QH

The central dogma of molecular biology deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred from protein to either protein or nucleic acid.

"The central dogma, enunciated by Crick in 1958 and the keystone of molecular biology ever since, is likely to prove a considerable oversimplification."

This quotation is taken from the beginning of an unsigned article headed "Central dogma reversed", recounting the very important work of Dr Howard Temin and others showing that an RNA tumour virus can use viral RNA as a template for DNA synthesis. This is not the first time that the idea of the central dogma has been misunderstood, in one way or another. In this article I explain why the term was originally introduced, its true meaning, and state why I think that, properly understood, it is still an idea of fundamental importance.

analogous to thymine in DNA, thus giving four standard symbols for the components of nucleic acid.

The principal problem could then be stated as the formulation of the general rules for information transfer from one polymer with a defined alphabet to another. This could be compactly represented by the diagram of Fig. 1 (which was actually drawn at that time, though I am not sure that it was ever published) in which all possible simple transfers were represented by arrows. The arrows do not, of course, represent the flow of matter but the directional flow of detailed, residue-by-residue, sequence information from one polymer molecule to another.
Central Dogma of Molecular Biology

DNA → RNA → Proteins

Information is carried by the genes and expressed in proteins. Information flows from DNA → RNA → proteins; but not the reverse.

Exceptions and special cases: RNA → RNA
- Retroviruses (e.g. HIV-1), RNA → DNA
- Prions (e.g. BSE PrPc), Protein → Protein

Unknown Transfers

These are the three transfers which the central dogma postulates never occur:
- Protein → Protein
- Protein → DNA
- Protein → RNA

Stated in this way it is clear that the special transfers are those about which there is the most uncertainty. It might indeed have “profound implications for molecular biology” if any of these special transfers could be shown to be general, or—if not in all cells—at least to be widely distributed. So far, however, there is no evidence for the
Introduction: Biological Background

The Cell

Common Characteristics of Cellular Life

• Cell membrane to separate order and chaos
• Genetic material (DNA)
• Regulation of nutrients and waste in and out
• Reproduction
• Information Processing, signaling, apoptosis.
Introduction: Biological Background

The Cell

Prokaryotic
- Less Complex
- Primitive cell type

Eukaryotic
- More complex
- Evolved from Prokaryotic
- Higher degree of Organization
- Nucleus, Organelles

Bacterial Cell

E-Coli

David Goodsell, Scripps Research Institute
Animal Cell / Organelles

Cell Membrane
Thermodynamics

- Formalism to keep track of energies:
  e.g. Chem. Reaction: Initial conditions $\rightarrow$ Equilibrium

  Useful Energy (how much?)

- Describes macroscopic properties of equilibrium systems

- Built upon 4 universal laws:

  $0^{th}$ Law $\rightarrow$ Defines Temp (T);
  $1^{st}$ Law: Defines Energy (E)

  $2^{nd}$ Law $\rightarrow$ Defines Entropy (S);
  $3^{rd}$ Law $\rightarrow$ value of (S)
System: Finite portion of the Universe

Isolated: $Q=0$, $W=0$, $\Delta n=0$
- No mass, no energy transfer

Open: $Q \neq 0$, $\Delta n \neq 0$, $W \neq 0$
- Mass and energy transfer

Adiabatic: $Q=0$, $\Delta n=0$, $W \neq 0$

For any system, a state $S_j$ is characterized by specific values of macroscopic states variables:

$$V, P, T, n_i, \vec{B}, \ldots$$

These state variables are connected by macroscopic equation of state

$$f(V, P, T, n_i, \vec{B}, \ldots) = 0$$

Independent of the History of the System

(only depends on state variables, not on history of approach to the present state)
State Function:
only depends on state variables,
not on history of approach to present state

\[ \Delta f = \int_{1}^{2} df = f(V_2, P_2, T_2, n_{i2}) - f(V_1, P_1, T_1, n_{i1}) \]

Examples:
The Ideal Gas Law: \[ pV = nRT \]
The van der Waals equation of state:

\[
\left( p + \frac{a}{V^2} \right)(V - b) = RT
\]

Biological Conditions

- Isothermic \( T = \) constant
- Isobaric \( P = \) constant
- Isochoric \( V = \) constant
First Law

Work and Heat

Expansion Work

\[ W = F \cdot l = (-p_{ext} A) l = -p_{ext} \Delta V \]

\[ \delta W = -p \Delta V \]

\[ W = -\int_{1}^{2} p \, dV \]

Let's see if it depends on path ...

Consider a reversible process so that \( p(\text{ext}) = p \):

Consider two paths:
1: first change \( V \) and then \( p \)
2: first change \( P \) and then \( V \)
For a cyclic process, change of state can occur for
\[ \oint \delta W \neq 0 \]
Similarly, Heat (Q) is also a function of path.

State can change from
\[(P_1, V_1, T_1) \rightarrow (P_2, V_2, T_2)\]

adiabatically (no heat transfer, \(Q=0\)) or nonadiabatically

Work (W) and Heat (Q) each depend on path!

Equivalence of work and heat:

(1840's) Joule showed that it's possible to raise the temperature of H₂O

(a) with only heat \[T_1 \rightarrow T_2\]

(b) with only work (weight falls & churns propeller) \[T_1 \rightarrow T_2\]
Experimentally it was found that
\[ \int (\delta W + \delta Q) = 0 \]

→ The sum \((W + Q)\) is independent of path

→ Implies that there is a state function whose differential is \(\delta W + \delta Q\)

Define it as the “Internal Energy” \(E\) (or \(U\))

\[ dE = \delta W + \delta Q \]

First law

\[ dE = \delta W + \delta Q \]

- Exact differential
- Incomplete, non-integrable differential of non state function

For a cyclic process \[ \int dE = 0 \]

For a change from State 1 to State 2

\[ \Delta E = \int_{1}^{2} dE = E_2 - E_1 = Q + W \]
Energy Conservation

Internal Energy E is the total energy content of a system.

\[ \Delta E = Q + W \]

Heat up the system \( E \uparrow \)  
Cool-off the system \( E \downarrow \)

Do work on the system  
Extract work from the system

\[ W = \begin{cases} -PV' & \text{path} \\ w' & \text{v} \end{cases} \]

For a fixed \( n \), we just need to know two properties, e.g. (T,V) to fully describe the system, i.e. \( E = E(T,V) \)

\[ dE(T,V) = \left( \frac{\partial E}{\partial T} \right)_V dT + \left( \frac{\partial E}{\partial V} \right)_T dV \]

Heat Capacity (C)

----> Connects heat with temperature

\[ \delta Q = C_{\text{path}} dT \quad \rightarrow \quad C_{\text{path}} = \left( \frac{\delta Q}{dT} \right)_{\text{path}} \]

\[ dE = \delta W + \delta Q \]

\[ \rightarrow \quad dE = C_{\text{path}} dT - p_{\text{ext}} dV \]

At constant volume, \( W = 0 \Rightarrow dE = \delta Q = C_V dT \)

Also, \[ dE = \left( \frac{\partial E}{\partial T} \right)_V dT + \left( \frac{\partial E}{\partial V} \right)_T dV \]

important result \[ C_V = \left( \frac{\partial E}{\partial T} \right)_V \]
**Enthalpy (H)**

Important State Function

\[ H = E + PV \]

Useful under isobaric conditions \( dP = 0 \)

\[ \Delta H = \Delta E + P\Delta V + \dot{V}\Delta P \]

\[ Q - P\Delta V + w' \]

At constant pressure \( \Rightarrow \) \( \Delta P = 0 \)

Only P-V work involved \( \Rightarrow \) \( w' = 0 \)

\[ \Delta H = Q \]

At constant \( P \), \( \Delta H \) in a process is = amount of heat exchanged in the process by the system.

\[ \Delta H = Q \]

Enthalpy of process = Heat \iff \( \Delta P = 0 \)

Endothermic: Heat absorbing \( \Rightarrow \) \( \Delta H = Q > 0 \)

Exothermic: Heat releasing \( \Rightarrow \) \( \Delta H = Q < 0 \)
Example: Photosynthesis

\[ 6CO_2 + 6H_2O \rightarrow C_6H_{12}O_6 + 6O_2 \]

\[ \Delta H^0 = Q = +2801 \text{ kJ/mol} = 673 \text{ kCal/mol} \]

Since \( \Delta H > 0 \), heat is consumed (Endothermic)

The reverse process, oxidation of glucose in cells, is exothermic \( \Rightarrow \Delta H < 0 \)

\[ H = E + PV \Rightarrow \Delta H = \Delta E + P\Delta V + V\Delta P \]

In biological systems \( \Delta P = 0 \)
\( \Delta V \approx 0 \)

\( \Rightarrow \Delta H \approx \Delta E \)

Energy is stored in the system:
1) As kinetic energy of the molecules. In isothermal processes (i.e. \( \Delta T = 0 \)), this KE does not change.

2) As energy stored in chemical bonds and interactions. This “potential” energy could be released or increased in chemical reactions
Molar Heat Capacities

\[ C = \frac{\delta Q}{dT} \]

Isobaric: \[ \overline{C}_p(T) = \left( \frac{\partial H}{\partial T} \right)_p \]

\[ \Delta H_p = n \int_{T_1}^{T_2} \overline{C}_p(T)\,dT \]

Isochoric: \[ dV = 0 \Rightarrow dE = \delta Q \]

\[ \Delta E_v = n \int_{T_1}^{T_2} \overline{C}_v(T)\,dT \]

Calculating Q, W, \( \Delta E \), and \( \Delta H \) for various conditions:

\[ dE = \delta W + \delta Q \]

Isothermal, Reversible process:

Isothermal: T constant, so \( \Delta T = 0 \)

\[ \Delta E = nC_v \Delta T = 0 \]

Reversible: system always in equilibrium

\[ p = p_{ext} \]

\[ W = -\int_{V_1}^{V_2} pdV \]

use PV = nRT

Adiabatic: Q = 0, \( \Delta E = Q + W = W \).

\[ W = -P \Delta V \]

You can also calculate final temperature using

\[ \Delta E = nC_v \Delta T \]
Energy conservation is NOT a criterion to decide if a process will occur or not.

Second Law

This process occurs because the final state with $p = p_{\text{max}}$ is the most probable state of the system.

Same is true with this:

Example:

All permutations of tossing 4 coins:

Macroscopic states...

1 way to obtain 4 heads, 0 tail
4 ways to obtain 3 heads, 1 tail
6 ways to obtain 2 heads, 2 tails
4 ways to obtain 1 head, 3 tails
1 way to obtain 0 head, 4 tails

$\Omega(N, r) = \frac{N!}{r!(N-r)!}$

$\Omega = \frac{4!}{2!2!} = 6$

$2H, 2T$ is the most probable which is also most disordered!