Intro-Biomolecules

Statistical-Physics-Basics

Basics

Microstate:
M particles, N levels: $\Omega = M^N$
Macrostate:
Histogram of the number of particles per energy level
Macrostate{3, 1, 5}:

- 3 particles are in level 1
- 1 particle is in level 2
- 5 particles are in level 3

Fundamental concept of statistical Physics

- Describe a system only as a MACROSTATE = Histogram
- It is not relevant which individual particle is in what level
- Compared to the exact description of a system (MICROSTATE), information is lost. A histogram contains LESS information than the data set that generated it
- Cannot construct the exact(MICROSTATE) of a system from the MACROSTATE because the MACROSTATE is just a distribution
- The amount of the missing information is measureed by the statistical weight Ω of the Macrostate, or $\ln(\Omega)$

Stastical weight of a macrostate Ω

How many microstates belong to the macrostate
eg: {2,0,0,1,0} has 3 microstates

$\Omega = N!$(所有粒子能量均不相同)

Degeneracy

$1, 0, 0, 2 : \Omega = \frac{3!}{2!}$

Entropy

$$S = k_B \ln \Omega, \Omega = \frac{N!}{n_0! n_1! \cdots}$$

Stirling's theorem

$$N! \approx \frac{N^N}{e^N} \sqrt{2\pi N}$$

$$\ln N! \approx N \ln N - N$$

Entropy S is a property of a macrostate of a system, gives the level of disorder of that macrostate

Boltzman-Free-Energy

Boltzman

$$\ln \Omega = \ln \frac{N!}{\prod_i n_i!} = N \ln N - \sum_i (n_i \ln n_i)$$

Maximum of entropy occurs for $dS = d(k_B \ln \Omega) = 0$

$$d \ln \Omega = - \sum_i \ln n_i dn_i = 0$$

$\sum_i n_i = N, \sum_i dn_i = 0$

Use Lagrange's method of undertimined multipliers: $n_i = \frac{N}{M}$

Microcanonical ensemble

$$\sum_i \epsilon_i n_i = E$$

$n_i = A e^{-\beta \epsilon_i}, A = e^{-\lambda}$

$n_i = N \frac{e^{-\beta \epsilon_i}}{\sum_i e^{-\beta \epsilon_i}}$

$p_i = \frac{e^{-\beta \epsilon_i}}{\sum_i e^{-\beta \epsilon_i}}$

$Z = \sum_{i=1}^{M} e^{-\beta \epsilon_i}$

$T = 0, \beta = \infty, p_1 = 1, p_{i \geq 2} = 0$

$T = \infty, \beta = 0, p_i = \frac{1}{M}$

$E = \sum_i \epsilon_i n_i = N \sum_i \epsilon_i p_i = \frac{N}{Z} \sum_i \epsilon_i e^{-\beta \epsilon_i} = -N \frac{\partial \ln Z}{\partial \beta}$

Constant total energy of system depends on temperature

Connection

$dQ = TdS$

$$E = U = \sum_i \epsilon_i n_i$$

$$dU = \sum_i \epsilon_i dn_i + \sum_i n_i d\epsilon_i$$

因为$\ln \Omega$里面有dn_i，所以第一项指的是dQ，第二项是dW

Ensembles

$$S_{AB} = S_A + S_B$$

看看下面三个定义怎么推的

Temperature definition

$$\frac{1}{T} \equiv \frac{\partial S}{\partial E}$$

Pressure definition

$$\frac{P}{T} = \left(\frac{\partial S}{\partial V}\right)_E$$

Chemical potential definition

$$\frac{\mu}{T} = -\left(\frac{\partial S}{\partial N}\right)_{E,V}$$

Free energy

看ppt还有tutorial吧

Partition Function

Degeneracy

$$Z = e^{-\beta \epsilon_1} + 2e^{-\beta \epsilon_2}$$

In **equilibrium**, E,S and F are connected t Z by simple equations

$$S = \frac{E}{T} + Nk \ln Z$$
$$F = E - TS$$
$$S = Nk(\ln Z + T \frac{\ln Z}{\partial T})$$

Partition function of the system

$$Z_N = Z^N$$
$$Z_N = \sum_i e^{-\beta E_i}$$

Boltzmann Distribution derivation by system

$$p_i = \frac{1}{Z_N} e^{-\beta \epsilon_i}$$

Mixing-Osmosis

Mixing Entropy and dilute solutions

Lattice models: $N = N_W + N_S$

Entropy of Mixing

Polymer solutions-Mixing entropy

Polymer solutions

Entropy of mixing: $\Delta S_{mix} = -k(A \ln \frac{A}{A+B} + B \ln \frac{B}{A+B})$

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Osmosis

Entropy of mixing: $\Delta S_{mix} = -k(N_S \ln \frac{N_S}{N_S+N_W} + N_W \ln \frac{N_W}{N_S+N_W}) \approx -k(N_S \ln \frac{N_S}{N_W} - N_S)$

Solvation energy = contribution per solute molecule multiplied by the total number of such molecules.

$$dU = \epsilon_s dn_s$$

First law of thermodynamics

$\epsilon_s dN_s + \mu_W^0 dN_W = TdS + \mu_S dN_S + \mu_W dN_W$

分别令$dN_S, dN_W = 0$, 有$\mu_W = \ldots, \mu_S = \ldots$

使用ΔS_{mix}得到所需偏导

最后得到：$\mu_S = \epsilon_S + kT \ln \frac{n_S}{n_W}$

$$\mu_S = \mu_0 + kT \ln \frac{c}{c_0}, \ \ c = \frac{n_S}{V}, \ \ c_0 = \frac{n_W}{V}$$

Osmotic Pressure

$$\Delta P = cRT$$

$R = k_B N_A$

if equation contains kB, quantities relate to one particle, otherwise relate to one mole

$$\Delta P = cRT, \ \ c(mol/L)$$

$$\Delta P = ck_B T, \ \ c(个/m^3)$$

Revere Osmosis

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5. Binding

5.1 Equilibria Binding

Ligand-Receptor Binding

要看一下ppt和tutorial，推p_{bound}

Hill function

Reactions

$$K_{eq} \equiv \prod_i c_{i-eq}^{v_i}$$

$$\Delta G = \sum_i v_i \mu_i$$
$$\mu = \mu_0 + kT \ln \frac{c}{c_0}$$
$$\Delta G = 0$$

$$\Delta G_0 = -k_B T \ln K_{eq}$$

$$\Delta G = k_B T \ln \frac{K}{K_{eq}}$$

5.2 Protein folding

全是叙述，看一下ppt，不看也没问题

6. Grand-canonical-cooperativity

6.1 Gibbs-Ensemble

finding a given state of the system(charaterized by an energy E_A and nuber of particles N_A is **proportional to the number of states available to the reservoir R**) when the system is in this state

$$p_A = \frac{Z}{e^{-\beta(E_A - \mu N_A)}}$$

$$Z = \sum_i e^{-\beta(E_i - \mu N_i)}$$

看一下tutorial，怎么用公式

6.2 Cooperativity

使用上节公式，看一下tutorial，怎么用公式

7. Aminoacids-pKa-ATP-Phosphorylation

7.1 Aminoacids-pKa

Proteins, chirality, diversity, peptide bond formation, basic protein structure, from primary to quaternary structure, disease

$$K_W = [OH^-][H_3O^+], pH$$

$$pK_a = pH - \lg \frac{[A^-]}{[AH]}$$

得: $\frac{[A^-]}{AH} = \cdots$

$$p(A^-) = \frac{1}{1 + 10^{(pK_a - pH)}}$$

$$p(HA) = \frac{1}{1 + 10^{(pH - pK_a)}}$$

7.2 ATP

看一下tutorial ATP怎么算

7.3 Phosphorylation

看一下tutorial ATP怎么算

8. Diffusion

8.1 Mean Variance SEM

mean: $\overline{x} = \frac{1}{N} \sum_{i=1}^{N} x_i = \sum_i p_i x_i = \int_{-\infty}^{\infty} x p(x) dx$

σ : 三种形式

推一下ppt概率公式?

8.2 Diffusion

Divergence theorem: $\int_V \nabla \cdot \mathbf{E} dV = \oiint \mathbf{E} \cdot d\mathbf{A}$

Continuity equation: $\nabla \cdot \mathbf{j}(\mathbf{r}, t) = -\frac{\partial \rho(\mathbf{r}, t)}{\partial t}$

Flux: $\mathbf{j} \equiv \frac{Substance}{Area \times Time} = \rho \mathbf{v}$

Fick's First Law:

$$j = -D \frac{d\rho}{dx}, \ \ \mathbf{j} = -D \nabla \rho$$

Fick's Second Law:

$$\frac{\partial \rho}{\partial t} = D \nabla^2 \rho$$

Solution:

$$\rho(x,t) = \frac{\rho_0}{\sqrt{4\pi D t}} e^{-\frac{(x-x_0)^2}{4Dt}}$$

$$\rho(\mathbf{r},t) = \frac{\rho_0}{\sqrt{4\pi D t}} e^{-\frac{(\mathbf{r}-\mathbf{r_0})^2}{4Dt}}$$

mean: $\bar{x}(t) = 0$
variance: $\sigma_x^2 = 2Dt$

Brownain motion microscopic model: Random walk

$\overline{X} = 0$
But what counts is not the mean position, but the spread
$\sigma_x^2 = N(\overline{x^2} - \overline{x}^2) = N\overline{x^2} = Nl^2 = N\overline{v}l\tau = \overline{v}lt$
$\maltese$: $\sigma_x^2(t) = 2Dt$
$D = \frac{1}{2}\overline{v}l$
Different equations for different situations are in ppt

$$x = \sigma_x = \sqrt{2D}\sqrt{t}$$

Diffusion with external forces

$v_D = \mu F = \frac{1}{\gamma}mg$
Down-flux: $j_1 = \mu mg\rho$
Up-flux: $j_2 = -D\frac{d\rho}{dh}$
$j_1 = j_2$

$$\rho(h) = \rho_0 e^{(-\frac{\mu mg}{D}h)}$$

Compared to Boltzman distribution:

$$\rho(h) = \rho_0 e^{-\beta mgh}, \quad E = mgh$$

Einstein Relation:

$$D = \mu kT$$

Special case for Stoke's Law

Frictional force (drag force) exerted on spherical objects with very small Reynolds numbers (e.g., very small particles)in a continuous viscous fluid
Stoke's Law:

$$F = 6\pi R\eta v, \quad \mu = \frac{v}{F}$$

$$D = \frac{kT}{6\pi R\eta}$$

Flux with external force: $\mathbf{j} = -D\nabla\rho + \mu F\rho$
Diffusion equation with external force: $\frac{\partial \rho}{\partial T} = D\nabla^2\rho - \mu F\nabla\rho$

9. Electro

9.1 Poission-Boltzmann

Electronics for Salty Solutions

Magnetic fields play (almost) no role

$$\nabla \cdot \mathbf{E}(\mathbf{r}) = \frac{\rho(\mathbf{r})}{\varepsilon_0}$$

Poisson's equation: $\nabla^2\Phi(\mathbf{r}) = -\frac{\rho(\mathbf{r})}{\varepsilon_0}$
Laplace's equation: $\nabla^2\Phi(\mathbf{r}) = 0$

$p_{Ion}(\mathbf{r}) \propto e^{-\beta E(\mathbf{r})}, \quad E(\mathbf{r}) = q\Phi(\mathbf{r})$
Charge density of the ion cloud:

$$\rho_i(\mathbf{r}) = q_i n_i^\infty e^{-\beta q_i \Phi(\mathbf{r})}$$

total charge density:

$$\rho_{Ions}(\mathbf{r}) = \sum_i q_i n_i^\infty e^{-\beta q_i \Phi(\mathbf{r})}$$

Poisson-Boltzman equation

$$\nabla^2 \Phi(\mathbf{r}) = -\frac{e}{\varepsilon} \sum_{i=1}^{n} z_i c_{i,\infty} e^{-\beta z_i e \Phi(\mathbf{r})} - \frac{\rho(\mathbf{r})}{\varepsilon}$$

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9.2 Debye-Huckel theory

Bjerrum length

Balance the ekectrostatic interaction energy:

$$\frac{e^2}{4\pi\varepsilon_0 D l_B} = k_B T$$

$$l_B = \frac{e^2}{4\pi\varepsilon_0 D k_B T}$$

Debye-Huckel theory

Debye-Huckle equation:

$$\nabla^2 \Phi(\mathbf{r}) = \frac{e^2 \beta}{\varepsilon} \left(\sum_i z_i^2 n_i^{\infty} \right) \Phi(\mathbf{r})$$

Debye length

$$\lambda_D = \left(\frac{\varepsilon k_B T}{e^2 \sum_i z_i^2 n_i^{\infty}} \right)^{\frac{1}{2}}$$

Ionic strength

$$I \equiv \frac{1}{2} \sum_i z_i^2 n_i^{\infty}$$

$$\nabla^2 \Phi(\mathbf{r}) = \frac{1}{\lambda_D^2} \Phi(\mathbf{r})$$

看一下tutorial中公式怎么用的

10. Polymers-CentralLiit

10.1 Intro-Polymers

10.2 Binomial distribution

$$p(k) = C_n^k p^k (1-p)^{n-k}$$

Special case p=0.5

Expectation value:

If n=1, p(1)=p.
$\langle x \rangle = \sum_{i=1}^{1} 1 \cdot p = p$
$\langle x + y \rangle = \langle x \rangle \langle y \rangle$
therefore $\langle x \rangle = np$

Poisson limit theorem

n较大, p较小时，二项分布可以近似为泊松分布

10.3 Polymers-Random walk Central limit theorem

Atoms don't always matter.

Random walks: freely jointed chain (FJC)

几段等长的segment连接，每一段都可以是任意方向，each segment 的长度叫做 **Kuhn length (a)**

Chain: 1D random walks

The expected value of the walker's distance from the origin, R, after N steps is 0.
Similar to diffusion
mean = 0, variance = Na^2
R为end-to-end distance

Central limit theorem

For a set of N random variables {x_n} with finite mean and variance, the sum X of {x_n} will tend towards a **Gaussian** distribution *regardless of the distribution of x_n*

10.4 Polymers - Random walk

Sharpness of the Gause curve:

$$\sigma_x = \sqrt{N}$$

$$\frac{\sigma_x}{N} = \frac{1}{\sqrt{N}}$$

As N becomes larger, the RMS distance increases, but the relative (to N) RMS distance becomes tiny, so it is extremely unlikely to be far (as compared to N) from the pub door.

Polymer end-to-end vector (1D)

$$\langle x^2 \rangle = Na^2$$
$$p(x, N)\frac{1}{2\pi Na^2}e^{-\frac{x^2}{2Na^2}}$$

3D case

$$P(R; N) = P(R; N)(1Dcase)^3$$

Similar to diffusion

End-to-end distance R

$$P_{3d}(N, R)4\pi R^2 dR$$
3D Maximum of distribution NOT at zero! Different from the 1D case.

Limitation of Guassian model

Wrong for $R > Bb$

$P(R; N)$ is sharply peaked at R=0

11. FJC-Kuhn_Rg

11.1 FJC

$C_n = \frac{1}{n}\sum_{i=1}^{n} C_i'$: Flory's characteristic ratio
$\langle R^2 \rangle = l^2 \sum_{i=1}^{n} C_i' = C_n n l^2$

C_∞: Flory's characteristic ratio, for large chain

Freely rotating chain model (FRC)

different from FJC: θ is const. same for all

$$\langle R^2 \rangle = nl^2 + 2nl^2 \frac{\cos\theta}{1 - \cos\theta} = nl^2 \frac{1 + \cos\theta}{1 - \cos\theta}$$

$$C_\infty = \frac{1 + \cos\theta}{1 - \cos\theta}$$

Persistence length

$$s_p = -\frac{1}{\ln(\cos\theta)}$$

For rigid model: $L_p = a$

For Continuous model: tangent correlation function

$$\langle t(s) \cdot t(u) \rangle = e^{-|s-u|/\zeta_p}$$

For Worm-like chain(WLC) modle：DNA:

small $\theta, \ln(\cos\theta) \approx -\frac{\theta^2}{2}$

$$l_p = s_p l = l\frac{2}{\theta^2}$$

$$C_\infty = \frac{1 + \cos\theta}{1 - \cos\theta} \approx \frac{4}{\theta^2}$$

$$b = l\frac{C_\infty}{\cos(\frac{\theta}{2})} \approx l\frac{4}{\theta^2} = 2l_p$$

Kuhn lebgth b is twice the persistence length.

11.2 Polymers - Radius of Gyration(回转半径)

The radius of gyration is used because it can be easily measured experimentally.

Radisu of gyration determined via scattering experiments

Tutorial 证明
看一下tutorial中公式怎么用的

12. EntropicForce-AFM

12.1 Entropic Force

$$\Omega(N, x) \propto p(N, x), S = k_B \ln \Omega$$

$$\Delta S = -\frac{k_B}{2Na^2} x^2$$

$$\Delta G = \Delta U - T\Delta S$$

The ideal chain has no internal energy U

$$\therefore \Delta G = -\frac{k_B T}{2Na^2} x^2$$

$$f = \frac{\partial G(N, x)}{\partial x} = \frac{k_B T}{Na^2} x$$

Hooke's law:

entropic spring constant

$$k = \frac{k_B T}{Na^2}$$

It's easier to stretch polymers with:

- large numbers of monomers N
- large monomer size a
- at lower temperature T

The entropic nature of elasticity in polymers distinguishes them from other materials.

The ideal chain can be thought of as an entropic spring and obeys Hooke's law for elongations much smaller than the maximum elogation.
可以把上面那个x换成end-to-end vector R

等会看ppt吧，写不下去了

12.2 DNA Properties and genetics

structure and packing
Polymerase chain reaction

13. DNA-Genetics-Bending

13.1 DNA-Genetics

GENETICS NETWORKS:
DOING THE RIGHT THING AT RIGHT TIME
maybe 再看一下ppt上概率那一张

13.1 Bending

Three modes of deformation of a beam:

- stretching
- bending
- twisting

if a bond stretches by Δa, the beam stretches by $\Delta L = \frac{L_0}{a_0} \Delta a$

$$\epsilon = \frac{\Delta L}{L_0} = \frac{\Delta a}{a_0}$$

看ppt上公式吧，还有tutorial

14. DNA-Looping-packing-Viruses

14.1 DNA-Looping

$$E_{bend} = \frac{EIL}{2R^2}, L = 2\pi R$$

$$\therefore E_{loop} = \frac{\pi EI}{R} = \frac{2\pi^2 EI}{L}, \zeta_p / x_p = \frac{EI}{k_B T}$$

$$E_{loop} = k_B T 2\pi^2 \frac{x_p^2}{L} = k_B T 2\pi^2 \frac{x_p^2}{d \cdot N_{bp}}, L = d \cdot N_{bp}$$

$$\Delta S_{loop} = k_B \ln p_o = k_B(-\frac{3}{2} \ln N_{bp} + const)$$

p_o is the probability of loop formation, $p_o \propto N_{bp}^{-\frac{3}{2}}$

$$\Delta G_{loop} = \Delta E_{loop} - T\Delta S_{loop}$$

14.2 DNA packing, Viruses

Viruses as Charged Spheres
$q = -2e$ per base pair

$$U_{el} = \int dU = \int_0^R V(r) dq$$

DNA in solution: λ_D
DNA in capsid

$$W = NkT \ln(\frac{V_{cloud}}{V_{capsid}})$$

ppt上单分子技术

15. Reactions

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Some examples

Cytoskeleton polymerization

$$\frac{dn}{dt} = k_{on}(c_) - \frac{Mn(t)}{V} - k_{off}$$

16. Membrane-Surfaces

16.1 Membranes-Intro

- 2D fluid: Lateral diffusion
- MP can also diffuse
- Lipid flip-flop

Lipids self assemble

The effective shape of a lipid molucule is described by a packing parameter:

$$P = \frac{v}{al}$$

Membrane Permeability

$$j = P\Delta c$$

P为Permeability coefficient

All membranes indergo spontaneous shape changes and fluctuations due to thermal energy or application of external forces

Membrane fusion and budding

16.2 Surfaces Math Background

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$$dE_{surface} = [\frac{\kappa}{2}(\frac{1}{R_1} + \frac{1}{R_2} - \frac{2}{R_0})^2 + \frac{\kappa G}{R_1 R_2}]dA$$

16.3 Membrane deformation and curvature

bending
curvature: height function

$$\kappa = \frac{1}{R} = \frac{\partial^2 h}{\partial x^2}$$

对角化Hessian matrix, 本征值即为两个方向上的曲率

$$G_{bend} = \frac{K_b}{2} \int da[\kappa_1 + \kappa_2]^2$$

$$G_{thickness} = \frac{K_t}{2} \int (\frac{w - w_0}{w_0})^2 da$$

$$G_{stretch} = \frac{K_a}{2} \int (\frac{\Delta a}{a_0})^2 da$$

17. Membrane-Potential

17.1 MPs

Membrane proteins

MP structure determination

17.2 Membrane Potential

$$c(x) \sim e^{\beta E(x)} = e^{-\beta z e V(x)}$$

$$\Delta V = V_2 - V_1 = \frac{k_B T}{ze} \ln \frac{c_1}{c_2}$$

$$\Delta \epsilon = \Delta \epsilon_{conf} - p \frac{V_{mem}}{d}$$

$$p_{open} = \frac{e^{-\beta \Delta \epsilon}}{1 + e^{-\beta \Delta \epsilon}}$$

Nerst equation relates chemical potential to electric potential

18. Membrane-PatchClamp

18.1 Vesicles

For a vesicle of radius R:

$$GG_{bend} = 8\pi K_b$$

For a Cylinder:

$$G_{bend} = K_b \pi \frac{L}{R}$$

18.2 Surface Tension

表面处: $E = -\frac{z}{2}\epsilon$

内部: $E = -z\epsilon$

$$\Delta E = +\frac{z}{2}\epsilon$$

Surface tension γ: Energy per unit area of the surface = surface energy density

$$\gamma = \frac{F}{2L} = \frac{dW}{dA}$$

dA is total area change, 2 sides

Laplace-Young law:

$$\Delta P = \frac{2\gamma}{R}$$

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18.3 Membranes: Patch clamp

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