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LIGAND CAPTURE BY RANDOMLY DISTRIBUTED TRAPS

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วิทยานิพนธ์ฉบับนี้ได้ศึกษาการสลายตัวของลิแกนด์ในระบบที่มีตัวจับกระจายแบบสุ่มโดยอาศัยความคล้ายคลึงกันของสมการชเรอดิงเงอร์และสมการการแพร่ของอนุภาคร่วมกับการอินทิเกรตตามวิถีแบบฟายน์แมน โดยสมมติว่าอันตรกิริยาระหว่างลิแกนด์และตัวจับเป็นศักย์แบบสุ่มซึ่งมีลักษณะฟังก์ชันแบบเกาส์เซียน ผลของการคำนวณทำให้ได้รูปแบบการสลายตัวเป็นฟังก์ชัน $exp(-t^m)$ ซึ่ง $1<m<2$

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In this thesis, the decay of ligands in randomly distributed traps is studied by using the analogy between the Schrödinger equation and the diffusion equation and Feynman path integration. We assume that the interaction between ligands and traps is the random potential whose form is the Gaussian function. The result shows that the form of decay is the function of $exp(-t^m)$ where $1 < m < 2$.

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Student's signature.....
Advisor's signature.....

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Chapter 1
Introduction

In many biological systems, ligand-receptor interaction is the heart of biological responses. Its understanding is fundamental to the study of all life sciences such as biochemistry, biophysics, and neurobiology. This will help us explain the nature of the biological signal and the biological outcome. Examples of ligand-receptor interaction are the detection of pheromones, chemotaxis, the immune system, and synaptic transmission.

This thesis embodies an analytical treatment of the important biological interactions using methods from physics and mathematics. The complexity of biological systems makes analytical modelling difficult, especially in situations of practical interest. However, physical principles can be applied to model biophysical systems if we can approximate them intelligently. This can reduce the complexity of systems with acceptable losses in accuracy. Our tool is the Feynman path integral [1]. Samathiyakanit [2] has used the Feynman path integration method to model an electron moving in a completely random system containing dense and weak scatterers, or equivalently in a Gaussian random potential. In the mean time, many biophysicists observe the motion of ligands in a completely random systems which contain a number of receptors in fixed position which is analogous to Samathiyakanit's model. Because of this, we apply the Feynman path integration method to solve the problem of the ligand-receptor interaction.

For the organization of this thesis, we review some important basic ideas about ligands and receptors in Chapter 2. In Chapter 3, we review Wiegel's model [3] which solves the diffusion equation to get the ligand population for ligands

moving in random traps. In Chapter 4, we present the Feynman path integration method approach to calculate the propagator of a ligand in a random potential and we use this propagator to calculate the probability of finding ligands. Finally, the discussion and conclusions are presented in Chapter 5.

Chapter 2
The biological aspects: ligand and receptor

This chapter provides the introduction about ligand and receptor by giving their definitions. We have to know what they are before we study them. Next, we present mostly the interaction which can occur between ligand and receptor. Finally, we give examples of chemoreception.

2.1 The definition of ligand and receptor

The ligand-receptor interaction is very important in biological system since it has a crucial role in the function of living organisms and is one method that the cell uses to interact with a variety of molecules. The function of all proteins is dependent upon their binding to other molecules. In the case of enzymes, these molecules, or ligands, are then transformed chemically. Many other proteins bind ligands in order to regulate gene expression or enzymic activity. To understand this in more detail, we would like to explain what we call "ligand" and "receptor". We shall generally define the smaller molecular weight partner in the binding interaction as "ligand". A ligand can be a nucleic acid, polysaccharide, lipid or even another protein. See Fig. (2.1)

Ligands bind to specific site on larger molecules, called receptors which is a protein, or a complex consisting of proteins and other biopolymers. The receptors are embedded usually in the outer membrane of the cell and they must interact only with appropriate ligands. Most of the receptors have just one binding site per polypeptide chain. In some cases, there may be more than one binding

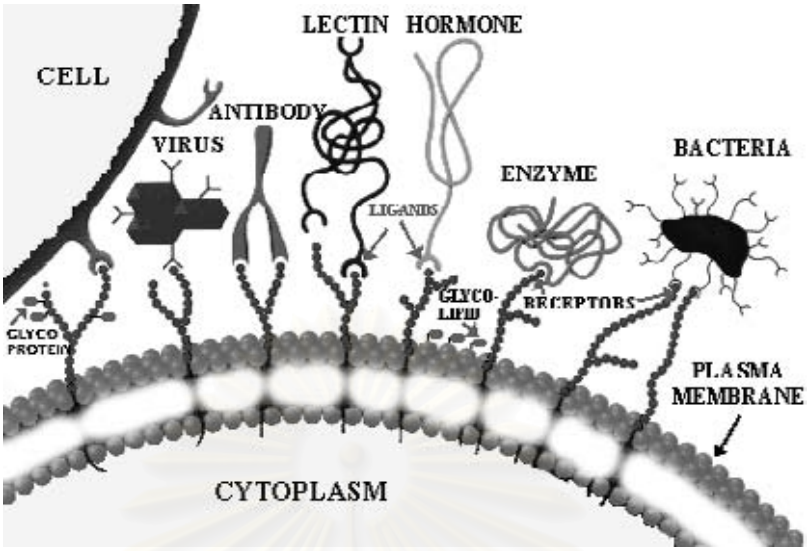


Figure 2.1: A typical cell contains a number of molecules exposed to the environment and in communication with it. These molecules act as the eyes, ears and noses of a cell and we show various kinds of ligands [4].

site on the receptor. Two different ligands or two similar ligands may be able to bind to the receptor at each binding site, such as hemoglobin binding to oxygen. Any binding of a ligand to a receptor is reversible and binding interactions show a high degree of specificity for size, shape, charge, and chemical properties. Fig. (2.2) illustrates some of these concepts.

After they have bound together, this complex acts usually in such a way that the ligand is rapidly transported through the membrane, which clears the receptor's binding site for its next catch. This process of a highly selective interaction of the cell with specific ligand is called "chemoreception." A key fitting into a lock is a good analogy for a ligand fitting into its binding site on a receptor. In addition to a precise fit, many keys will fit into a lock but only a few keys are capable of unlocking that lock. That is the ability of a ligand to bind to the receptor with high specificity is not enough, by itself, to produce the desired action.

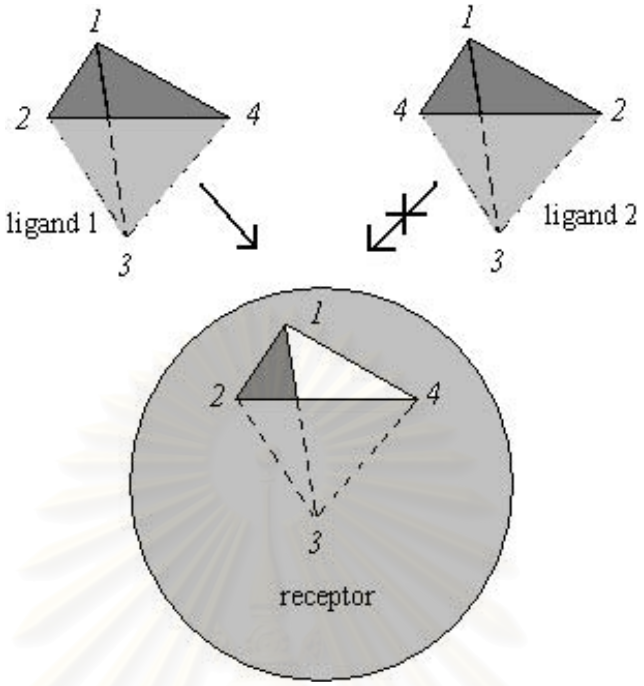


Figure 2.2: When the numbers on the shapes do not match those on the receptor, there are shape or chemical compatibility mismatches and the two structures will not fit together [5].

The ligand also must be capable of stimulating the receptor when it binds with its receptor. In other words, the ligand must have intrinsic activity. The highly selective interaction of a cell occurs from noncovalent interactions. The general principles of ligand-receptor interactions are generally similar to those seen within the protein. We can classify the interaction as strong (covalent) interaction or weak (noncovalent) interaction. Noncovalent interaction is of the order of $k_B T$ where k_B is the Boltzmann's constant and T is the absolute temperature. At our body temperature (310K), the thermal energy is 2.5×10^{-2} eV/particle which is less than the covalent interaction. The free energy associated with a covalent interaction is about $100-150\ k_B T$. In general, the common interaction occurring in the ligand receptor interaction is the noncovalent interaction [6,7].

2.2 Noncovalent interactions

There are many kinds of noncovalent interactions such as electrostatic interactions, Van der Waals interactions, hydrogen bonds, and hydrophobic interactions. Their names are derived from the condition in which the electrostatic forces are exerted on the molecules. Noncovalent interactions are important in the flexibility of macromolecules and they can interact reversibly.

2.2.1 Electrostatic Interactions

Molecules are collections of electrically charged particles. When two oppositely charged groups come into close proximity, they are attached to one another through a coulombic attractive force that is described by

$$F = \frac{q_1 q_2}{r^2 D} \tag{2.1}$$

where q_1 and q_2 are electric charges that are separated be the distance r and D is the dielectric constant of the medium in which the charges are immersed. Since D appears in the denominator, the attractive force is greatest in low dielectric solvents. Hence electrostatic forces are stronger in the hydrophobic interior of a protein than at the solvent-exposed surface. These attractive interactions referred to as ionic bonds, salt bridges, and ion pairs. If two atoms, oppositely charged or not, approach each other too closely, a repulsive force between the outer shell electrons on each atom will come into play.

2.2.2 Van der Waals Forces

The noncovalent associations between electrically neutral molecules are collectively known as "Van der Waals forces". They occur between ones where

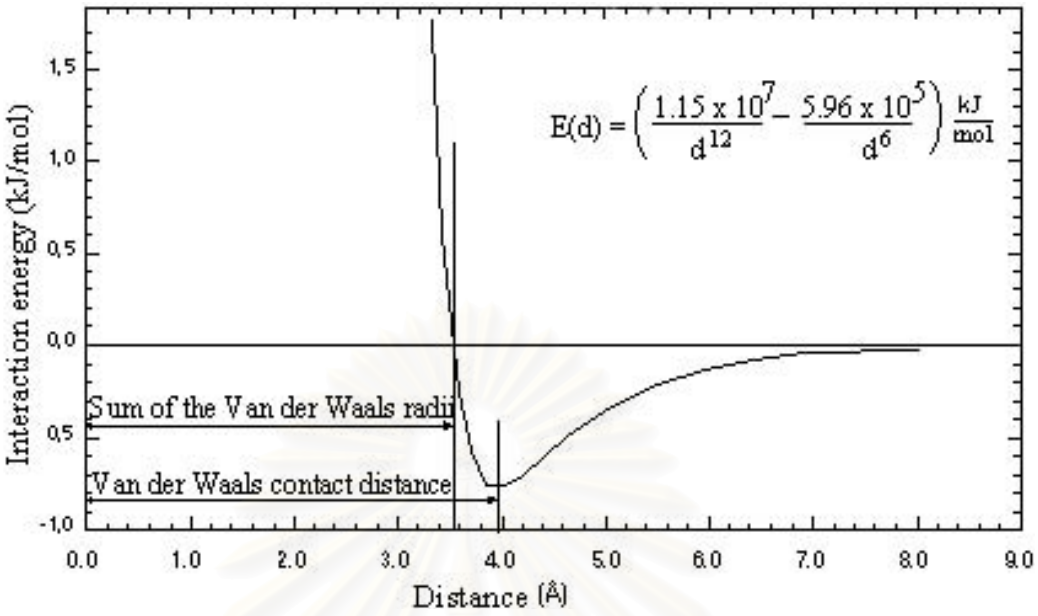


Figure 2.3: The Van der Waals energy for carbon-carbon interactions calculated as a Lennard-Jones 6,12 potential. The interaction energy is plotted as a function of distance between two atom centers. Note that the folding free energy is only between 15 to 50 kJ/mol for typical proteins - corresponding to a handful of optimal interactions, or a single close approach to 3 Å [8].

one or both molecules do not have a permanent dipole such as dipole-induced dipole interaction, and induced dipole-induced dipole interaction. A permanent dipole can be established by the symmetry of the distribution of the electron cloud around the positively charged nuclei. When atoms are close enough together, this symmetry of one atom can influence the electron distribution of neighboring atoms. Van der Waals forces may be attractive or repulsive, depending on the distance between the atoms involved. The attractive force between electron clouds increases as the two atoms approach each other but is counterbalanced by a repulsive force at a critical distance known as the Van der Waals contact distance Fig. (2.3).

A commonly used analytical form that lumps together all dipole-dipole

Atom	Radius(Å)
H	1.2
C	2.0
N	1.5
O	1.4
S	1.9
P	1.9

Table 2.1: Van der Waals radii for atoms in proteins

interactions and includes both the attractive and the repulsive terms is the Lennard-Jones potential where the repulsive term is approximated as having a $\frac{1}{r^{12}}$dependence:

$$U(r) = U_0 \left(\frac{r_0}{r}\right)^{12} - 2U_0 \left(\frac{r_0}{r}\right)^{6} \tag{2.2}$$

This form of the potential energy function has a minimum at $r = r_0$ with $U(r_0) = -U_0$.

Van der Waals bonds and surfaces can play an important role in establishing the specificity of interaction between ligand and receptor because of the differences in radii and the interplay between repulsive and attractive forces. See Table 2.1.

2.2.3 Hydrogen bonding

Hydrogen bond (H bond) forms when a hydrogen atom interacts with two electronegative atoms, called a proton donor group D−−−H and a proton acceptor atom A: D−−−H$\cdots$A. D−−−H is strongly polar, which means that electron density is primarily around the electronegative atom (examples, F−−−H, O−−−H, N−−−H, S−−−H in order of decreasing polarity). The acceptor atom A is also strongly electronegative and sometimes H$\cdots$A can be as strong as D−−−H. The

Bond Type	Typical Length(Å)
O–––H···O	2.70
O–––H···O^-	2.63
O–––H···N	2.88
N–––H···O	3.04
N^+–––H···O	2.93
N–––H···N	3.10

Table 2.2: Hydrogen bond lengths for H bonds found in proteins

hydrogen bond is strongest when the three atoms D, H, and A have a collinear geometry.

In biological systems, ligand and receptor can both be the highly electronegative nitrogen (N), oxygen (O), or sometimes sulfur (S) atom. Hydrogen bonds, which have bond energy between 2.5 and 8 kcal/mol, are weaker than covalent bonds. A distance is normally in the range 2.7 to 3.1 Å. See Table 2.2. Clearly, hydrogen bonding (Fig.(2.4))has a major influence on the structures of proteins and also contributes the binding energy of ligand to active sites on receptor.

2.2.4 Hydrophobic Interactions

When nonpolar molecules enter a polar solvent such as water, they coalesce into droplets in order to decrease their contact with water and prefer to cluster around each other. See Fig.(2.5). Hydrophobic interaction involves a number of water molecules which is different from other interactions that involve pairwise interactions between atoms and molecules. This process results from the solvent properties of water, not from the relatively weak attraction between the associating nonpolar molecules. Nonpolar molecules, such as hydrocarbons, are insoluble in water and are not good acceptors of the hydrogen bond. Therefore,

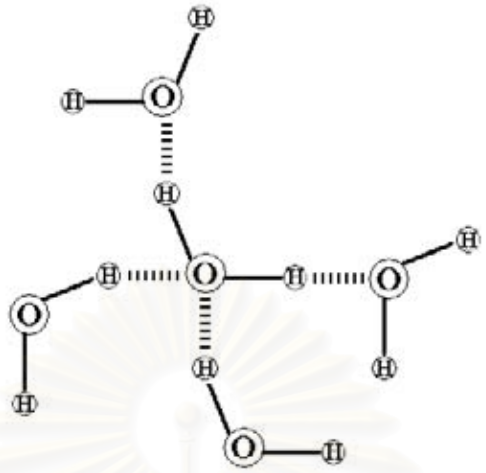


Figure 2.4: The hydrogen bond is weak attraction between an electronegative atom in one molecule and a hydrogen atom in other molecule. The hydrogen bonds between water molecules are represented by short parallel lines[9].

they will disrupt the hydrogen bonding network of water. The water molecules reorganize around the solute and attempt to form a cagelike structure in order to gain back the broken hydrogen bonds. This results in a loss in the configurational entropy of water and an increase in the free energy G. That is why nonpolar molecules try to cluster around each other for larger entropy, leading to a decrease in the free energy at equilibrium.

Hydrophobic interactions are found in the core of the folded protein molecules, where they are shielded from the polar solvent. Likewise, in the active sites of receptors, hydrophobic regions of the proteins tend to stabilize the binding of hydrophobic molecules.

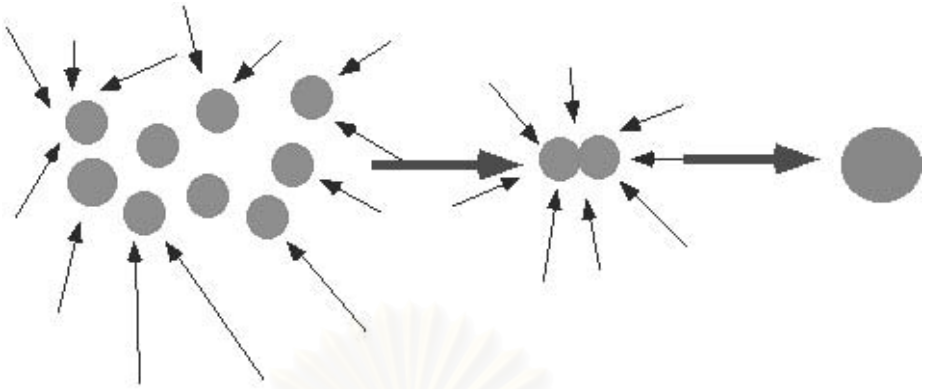


Figure 2.5: Hydrophobic interactions between water and nonpolar molecules. It looks like the oil molecules (circle particles), are avoiding the water (arrow) [10].

2.3 Examples of chemoreception

Multicellular organisms, especially the higher animals, are stimulated by the environment through the sensory system or through chemoreception. In this section, we will list several examples [1] of chemoreception and follow the historical development of the various attempts at theoretical modelling

2.3.1 Detecting of pheromones

A pheromone is a substance which is secreted to the environment by an organism and perceived by a second organism of the same species which changes its behavior consequently. "Bombykol" is a kind of sex attractive pheromone which is released into the air by the female silkworm moth Bombyx mori. In this case, Bombykol molecule is the ligand and a sensory cell in the antennae system of the male of this species detecting this ligand is receptor. This system was modeled theoretically by Adam and Delbrück[11]. They calculate the number of ligands which are absorbed by the detecting cell per unit of time. They recognize that

chemoreception might occur in steps in which geometrical objects of decreasing dimensionality play a role. Because of roughly cylindical shape of the sensory cell in Bombyx mori, Murray [12] use a cylindrical geometry rather than the spherical geometry.

2.3.2 Chemotaxis

Chemotaxis is the phenomenon which most unicellular microorganisms will move towards certain chemicals and away from others. Chemotaxis has been studied mostly in the bacteria Escherichia coli and Salmonella typhimurium [13, 14]. These bacteria perform a three-dimensional random walk[15]. Berg and Purcell [16] developed the theory to describe the rate of capture of ligands by a large number of receptors which are distributed uniformly over the cell membrane.

2.3.3 The immune system

All organisms are continually subject to attack by other organisms. In response to predators, animals have developed the variety of defensive strategies. The important strategy is the immune system. The immune response is triggered by the presence of foreign macromolecules, virus, cell, tissue, nucleic acid and carbohydrates, known as "antigens". The receptors are antibody molecules embedded in the outer membrane of certain cells of the immune system. The total weight of all the cells which together form the immune system is roughly 5% of the total weight of body. The immune system is remarkable in many respects. It can distinguish "itself" from "foreign" with a very high accuracy, memorize the previous infections, and react more appropriately in the next infections. The interested reader in the theoretical work is referred to monographs by Delisi [17], and by Perelson, Delisi and Wiegel [18].

2.3.4 Synaptic transmission

The nerve cell releases the specific substance known as a neurotransmitter to other cell by passing the junctions, synapses. This process, synaptic transmission, involves four stages. First, the signal travels down to presynaptic axon and reaches the presynaptic knob. If the threshold action potential is reached, the neurotransmitter is recreated by the presynaptic cell. Second, the molecules of neurotransmitter diffuse across the cleft and binds to their corresponding receptors on the postsynaptic membrane. Third, neurotransmitter binding induces a change in the biochemical properties of the post synaptic membrane in such a way that this membrane becomes selectively permeable to certain ions. Last, the influx of these ions causes a change in the difference of the electrical potential between the outside and the inside of the postsynaptic neuron. When this difference exceeds a threshold, a new signal originates in the vicinity of postsynaptic membrane and travels down to postsynaptic axon. The second step involves the basis event of chemoreception and ligands are the neurotransmitters. There are various neurotransmitters such as acetylcholine, glutamic acid and others.

2.3.5 Vision

In the case of vision, the ligand is the photon, a quantum mechanical particle. Chemoreception for vision can be found in most living organisms such as vertebrate animals, plants, some algae, some bacteria and also the clusters of cells found on the surface of worms and molluscs. Some bacteria have a light-sensitive receptors in their outer membrane which they use to orient themselves with respect to the sun. It is believed that this sensitivity to light appeared in the primitive life-forms on Earth about 3.7×10^9 years ago.

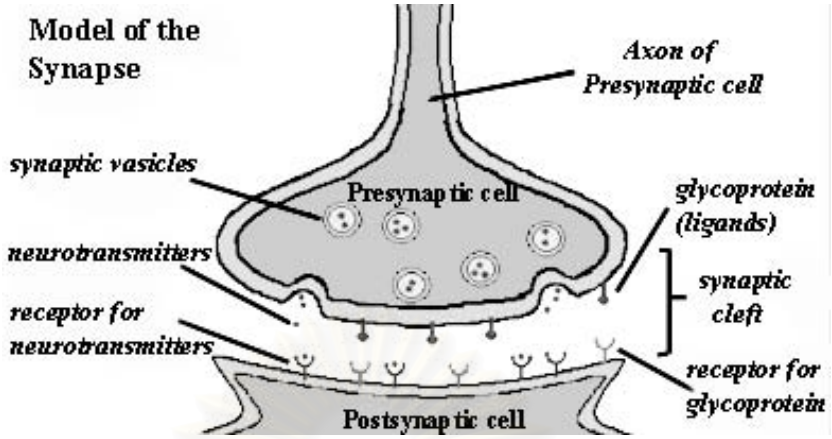


Figure 2.6: The transmission of nerve impluses across a synaptic cleft whose width mostly is more than 200 Å. The neurotransmitter such as Acetylcholine, Ach, is sequestered in 400 Å-diameter synaptic vescicles, which contain $\sim 10^4$molecules each [9].

These are only some important examples which show the idea how we can use physics to explain biological systems.

Chapter 3
Ligand with randomly distributed traps

In this chapter, we review Wiegel's method [3] which is used to explain a ligand captured by a system of many receptors. His model is a rough calculation but it provides useful guidelines for the further work. Generally, ligands can move from a cell to another cell by means of Brownian motion, hydrodynamic convection, electromagnetic fields, and other processes. These cells have the properties as in Table (3.1). These cells monitor certain molecules, ligands, which are in their vicinity and capture them by means of receptors, or traps

3.1 The coarse-grained description of a system of absorbing traps

In the tissues of a living organism, the cells involved with chemoreception will occur in great numbers. Therefore, we can consider chemoreception in the way that it consists of identical receptors. Next, we call receptors as traps. These traps are distributed in space with number density $m(\mathbf{r}, t)$. Wiegel treats this problem simply by considering the distance between cells which is larger than the

Property	Value
1. Shape	sphere
2. Radius	5 μm
3. Volume	5.24×10^{-16} m^3
4. Density	1.03×10^{3} kgm^{-3}
5. Mass	5.40×10^{-13} kg

Table 3.1: Average values of cell properties.

size of cells. Therefore

$$mR^3 \ll 1 \tag{3.1}$$

with spherical cells of radius R. He can set the differential equation by considering the following equation.

$$\frac{\partial C}{\partial t} = -\overrightarrow{\bigtriangledown} \cdot \mathbf{J} \tag{3.2}$$

where C is the coarse-grained concentration and $\mathbf{J}$ is the total ligand current. If there are the external force $\mathbf{F}$ and the fluid flow field, $\mathbf{J}$ will be consists of three terms.

$$\mathbf{J} = -D_T \overrightarrow{\bigtriangledown} C + \frac{C}{f_T}\mathbf{F} + C\mathbf{v} + \mathbf{J}_N \tag{3.3}$$

where D_T is diffusion coefficient ($D_T = \frac{k_B T}{6\pi\eta a}$ where k_B is Boltzmann's constant, T is the absolute temperature, η is viscosity of fluid, and a is the radius of spherical ligand), f_T is the friction coefficient of a ligand, $\mathbf{v}$ is the velocity of the fluid flow field and $\mathbf{J}_N$ is the ligand current assimilated by the perfectly absorbing cell . For the case of no external force and fluid flow field, we obtain

$$\mathbf{J} = -D_T \overrightarrow{\bigtriangledown} C + \mathbf{J}_N \tag{3.4}$$

Consider the term of $\mathbf{J}_N$;

$$\frac{\partial C_N}{\partial t} = -\overrightarrow{\bigtriangledown} \cdot \mathbf{J}_N \tag{3.5}$$

For spherical case, Eq.(3.5) can be rewritten as

$$\frac{\partial C_N}{\partial t} = D_T \left(\frac{\partial^2 C_N}{\partial r^2} + \frac{2}{r}\frac{\partial C_N}{\partial r} \right) \tag{3.6}$$

In stationary state, $\frac{\partial C_N}{\partial t} = 0$. Now we have

$$\frac{1}{r^2}\frac{d}{dr}\left(r^2 \frac{dC_N}{dr} \right) = 0 \tag{3.7}$$

Hence

$$\begin{aligned} r^2\frac{dC_N}{dr} &= A \\ \frac{dC_N}{dr} &= \frac{A}{r^2} \end{aligned} \tag{3.8}$$

where A is a constant. We use the fact that the ligand current should be the same through surface around the cell. Then we get

$$\left(D_T\frac{dC_N}{dr}\right)4\pi r^2 = J_N \tag{3.9}$$

Substitute Eq.(3.8) into Eq.(3.9). This give

$$A = \frac{J_N}{4\pi D_T} \tag{3.10}$$

The general solution of Eq.(3.8) at $r = R$ is

$$\begin{aligned} C_N(R) &= C_N(\infty) - A\int_R^\infty \frac{1}{\rho^2}d\rho \\ &= C_N(\infty) - \frac{A}{R} \end{aligned} \tag{3.11}$$

Use the condition that $s << R$ where s is the binding site. We have

$$\begin{aligned} D_T\frac{dC_N}{dR} &= \alpha v D_T s C_N(R) \\ \frac{dC_N}{dR} &= \alpha v s C_N(R) \end{aligned} \tag{3.12}$$

where α is a constant and v is the number of binding sites per unit area. Substitute Eq.(3.11) into Eq.(3.12).

$$A = \frac{\alpha R^2 v s C_N(\infty)}{1 + \alpha R v s} \tag{3.13}$$

Therefore

$$\begin{aligned} J_N &= \frac{4\pi D_T \alpha R^2 v s C_N(\infty)}{1 + \alpha R v s} \\ &= 4\pi R D_T C_N(\infty)\beta \end{aligned} \tag{3.14}$$

where $\beta = \frac{Ns}{\pi R + Ns}$. Substitute this equation into Eq.(3.4) and use the boundary condition $c(R) = 0$. We have

$$\frac{\partial C}{\partial t} = D_T \triangle C - 4\pi R D_T \beta m C \tag{3.15}$$

where $\triangle$ is the Laplacian operator and β depends on the model ($\beta = 1$ for a perfectly absorbing cell). The diffusion coefficient and R is the radius of receptor. From Eq.(3.15), the distribution of ligands can be solved under the approximate initial and boundary condition. Here we consider only one dimension and assume that m is constant m_0 through out the tissue.

3.1.1 In the case of stationary state of ligand

Eq.(3.15) becomes

$$\frac{d^2 C}{dx^2} = 4\pi R \beta m_0 C \tag{3.16}$$

and its solution is

$$C(x) = C(0) \exp\left(-x\sqrt{4\pi R \beta m_0}\right) \tag{3.17}$$

where $C(0)$ is the concentration of ligands at the position $x = 0$. Then $C(x)$ is independent on the diffusion coefficient. Ligands penetrate the tissue over a distance of the order of magnitude $(4\pi R \beta m_0)^{-1/2}$.

3.1.2 In the case of uniform ligand

Eq.(3.15) becomes

$$\frac{dC}{dt} = -4\pi R D_T \beta m_0 C \tag{3.18}$$

Its solution is

$$C(t) = C(0) \exp\left(-4\pi R D_T \beta m_0 t\right) \tag{3.19}$$

where $C(0)$ is the concentration of ligands at time $t = 0$. Eq.(3.19) interprets that ligands decay on a time scale of the order magnitude $(4\pi R D_T \beta m_0)^{-1}$.

3.2 Examples of time-dependent problems

The study of ligand populations is popular in biophysical and biochemical experiments. One observes the decay of ligand population captured by a system of traps in different dimension as the following:

3.2.1 In one-dimensional system

One observed the time dependence of the number of bound repressor molecules. A number of repressor diffuses along a single DNA molecule which is followed by their binding to the corresponding operators.

3.2.2 In two-dimensional system

A population of membrane proteins is captured by a system of traps. These traps are fixed randomly in the membrane. The membrane protein can diffuse laterally in this membrane and be captured when it hits the trap.

3.2.3 In three-dimensional system

One observed the population of antigens is reduced by binding to macrophages a type of white blood cell that ingest and, if possible, destroy a variety of foreign substances. The examples of antigens are foreign macromolecules, proteins, carbohydrates, and nuclei acids. These antigens trigger the immune response which leads to the destruction of offending cells.

In many experimental aspects, the decay of ligand population is assumed that the total number $N(t)$ of free ligands will decay as a "pure" exponential function of the form

$$N(t) \cong N_0 \exp\left[-\frac{t}{\tau_0}\right] \tag{3.20}$$

at the long-time behavior of the decay where N_0 is a dimensionless constant and τ_0 is a relaxation time. The decay form of Eq.(3.20) is granted by most authors. But it is argued that it might be another form, stretch exponential form [19,20,21]. Donsker and Varadhan [20] presented the mathematical model of Brownian motion between random traps. They proved that the exponent is proportional to $t^{d/(d+2)}$ in d dimensions. Grassberger and Procacica [21] also investigate the long time behavior of particle moving in the randomly distributed traps. They found that the particle population decays slower than any exponential. This is the effect of the existence of large trap-free regions. They also can prove that the ligand population has the form

$$N(t) \sim \exp(-c\, t^{d/(d+2)}) \tag{3.21}$$

where c is a constant and d is the dimension of system. We will show how they can get this form in three dimension system.

3.3 Fractional exponential decay

The system consists of M traps in volume V. The traps are assumed to be perfectly absorbing spheres of radius a and completely random. At the initial time $t = 0$, the number of ligands $N(0)$ distributed uniformly throughout V. There are some regions where have no traps at all, called "holes". These holes have various shapes and sizes, see Fig.(3.1)

In order to calculate the probability $H(s)\,ds$ to find a hole in volume V, the Boltzmann factor $\exp(-E/k_BT)$ is used with E the amount of work needed to create a hole. From thermodynamics,

$$E = Pv \tag{3.22}$$

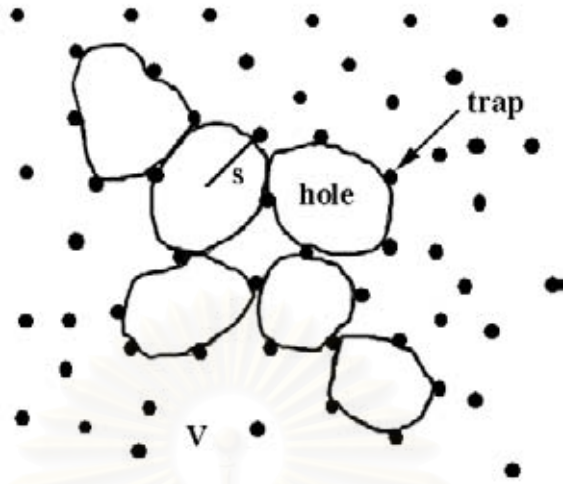


Figure 3.1: A system in volume V consisting of a number of randomly distributed traps, radius a, and holes which have an average radius s.

where $P = \frac{M}{V}k_BT$ and v is the volume of spherical hole, $\frac{4\pi s^3}{3}$. Thus the total number $H(s)\,ds$ of holes with radius between s and $s + ds$ is

$$H(s) = H_0 \frac{4\pi M}{V} s^3 \exp\left[-\frac{4\pi M}{3V} s^3\right] \tag{3.23}$$

where the specific value of H_0 depends on the precise definition of a hole.

3.3.1 Decay of ligand concentration

For $t = 0$, the ligand concentration is constant c_0 inside a hole of radius s, and vanishes outside the hole since ligands are surrounding by traps at density m.

For $t > 0$, the ligand concentration is denoted by $c(r,t)$ and we use the spherical coordinates to solve the diffusion equation

$$\frac{\partial c}{\partial t} = D_T \Delta c \qquad \text{for } 0 < r < s \tag{3.24}$$

$$\frac{\partial c}{\partial t} = D_T \Delta c - 4\pi a D_T m c \qquad \text{for } r > s \tag{3.25}$$

where a is βR as defined in the Eq.(3.15)

The general solution of diffusion equation has the form of an eigenfunction expansion. If the hole is large enough to be the ground state, the long-time behavior of solution is

$$c(r,t) \cong d_0 \psi_0(r) \exp(-\lambda_0 t) \qquad \text{for } t \gg \frac{1}{\lambda_0} \tag{3.26}$$

with d_0 is a constant, ψ_0 denotes the ground state and λ_0 is the eigenvalue. Thus, the ligand population $N(s,t)$ becomes

$$N(s,t) \cong N_0(s) \exp[-\lambda_0(s)\, t] \qquad \text{for } t \gg \frac{1}{\lambda_0} \tag{3.27}$$

where

$$N_0(s) \cong 4\pi d_0 \int_0^\infty \psi_0(r)\, r^2 dr \tag{3.28}$$

Calculating the ground state eigenvalue by substituting Eq.(3.26) into (3.24) and (3.25), the result is

$$D_T \left(\frac{d^2}{dr^2} + \frac{2}{r}\frac{d}{dr} \right) \psi_0 + \lambda_0 \psi_0 = 0 \quad \text{for } 0 < r < s \tag{3.29}$$

$$D_T \left(\frac{d^2}{dr^2} + \frac{2}{r}\frac{d}{dr} \right) \psi_0 - (4\pi a m D_T - \lambda_0)\, \psi_0 = 0 \quad \text{for } r > s \tag{3.30}$$

Note: this problem is similar to the mathematical problem of finite spherical quantum well.

Now we replace

$$\psi_0 = \frac{\psi}{r} \tag{3.31}$$

to Eq.(3.29) and Eq.(3.30), gives

$$\frac{d^2\psi}{dr^2} + \frac{\lambda_0}{D_T}\psi = 0 \quad \text{for } 0 < r < s \tag{3.32}$$

$$\frac{d^2\psi}{dr^2} - \left(4\pi a m - \frac{\lambda_0}{D_T} \right) \psi = 0 \quad \text{for } r > s \tag{3.33}$$

with the boundary condition as

$r = 0 \Rightarrow \psi/r$ **is required to be finite,**

Hence

$$\psi(r) = A \sin \sqrt{\frac{\lambda_0}{D_T}} r \quad for 0 < r < s \tag{3.34}$$

$r \to \infty \Rightarrow \psi/r$ **is close to zero**

Hence

$$\psi(r) = B \exp \left[-\sqrt{4\pi am - \frac{\lambda_0}{D_T}} \cdot r \right] \quad \text{for } r > s \tag{3.35}$$

$r = s \Rightarrow \psi$ **and** $\frac{d}{dr}\psi$ **must be continuous**

These give

$$A \sin \sqrt{\frac{\lambda_0}{D_T}} s = B \exp \left[-\sqrt{4\pi am - \frac{\lambda_0}{D_T}} \cdot s \right] \tag{3.36}$$

and

$$A \sqrt{\frac{\lambda_0}{D_T}} \cos \sqrt{\frac{\lambda_0}{D_T}} s = -B \sqrt{4\pi am - \frac{\lambda_0}{D_T}} \exp \left(-\sqrt{4\pi am - \frac{\lambda_0}{D_T}} \cdot s \right) \tag{3.37}$$

dividing Eq.(3.37) by Eq.(3.36) and changing variable $\sqrt{\frac{\lambda_0}{D_T}} s$ to k, we obtain

$$k \cot k = -\sqrt{4\pi ams^2 - k^2} \tag{3.38}$$

Plotting both sides of this equation as the function of k. See Fig. (3.2). We get the lowest bound state which is

$$k \cong \pi \quad \text{for} \quad ams^2 \gg \frac{\pi}{16} \tag{3.39}$$

inserting k into

$$\lambda_0 = \frac{k^2}{s^2} D_T \cong \frac{\pi^2}{s^2} D_T \tag{3.40}$$

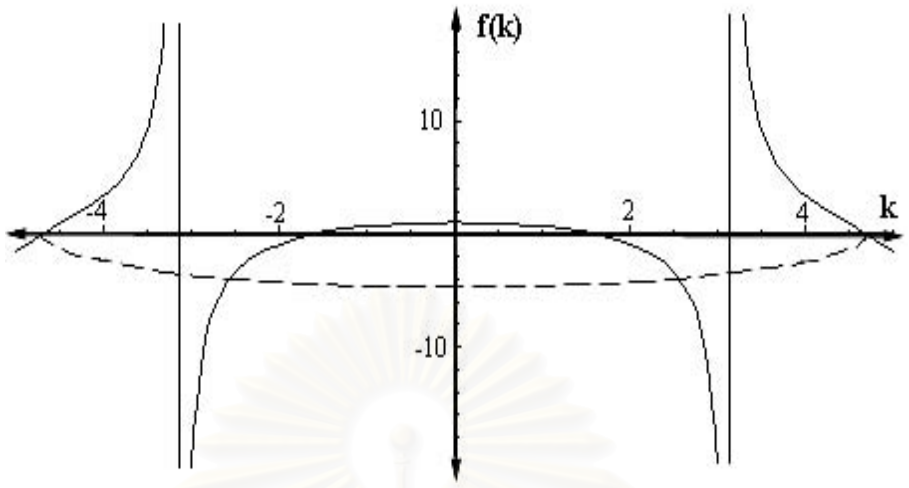


Figure 3.2: Plot $f(k)$ versus k where the solid line is $k\cot k$ and the dashed line is $-\sqrt{4\pi ams^2-k^2}$.

Now we consider all ligands being in holes at time $t=0$ with radii

$$s > s_0 \equiv \sqrt{\frac{\pi}{16am}} \tag{3.41}$$

therefore, the ligand population is

$$N(s,t) \cong \frac{4}{3}\pi s^3 c_0 \exp\left[-\frac{\pi^2 D_T t}{s^2}\right] \tag{3.42}$$

and in the holes large enough to have a bound state. This population consists of ligands

$$N_h(t) = \int_{s_0}^{\infty} N(s,t)\, H(s)\, ds \tag{3.43}$$

Replacing Eq.(3.23) into Eq.(3.43), we have

$$N_h(t) \cong \frac{1}{3}(4\pi)^2 c_0 m H_0 \int_{s_0}^{\infty} s^5 \exp\left[-\frac{4\pi}{3}ms^3 - \pi^2 t\frac{D_T}{s^2}\right] ds \tag{3.44}$$

We change the integration variable to

$$x = t^{-1/5} s_0 \tag{3.45}$$

then, we get

$$N_h(t) \cong \frac{16}{3}\pi^2 c_0 m H_0 t^{6/5} \int_{s_0 t^{-1/5}}^{\infty} x^5 \exp\left[-t^{3/5} f(x)\right] dx \tag{3.46}$$

where

$$f(x) = \frac{4\pi}{3} m x^3 + \pi^2 D_T x^{-2} \tag{3.47}$$

For $t \to \infty$, we can approximate Eq.(3.46) by using the steepest descent method. Find the minimum point

$$\left.\frac{df(x)}{dt}\right|_{x_0} = 4\pi m x_0^2 - 2\pi^2 D_T x_0^{-3} = 0 \tag{3.48}$$

$$x_0^5 = \frac{\pi D_T}{2m} \tag{3.49}$$

$$x_0 = \left[\frac{\pi D_T}{2m}\right]^{1/5} \tag{3.50}$$

We expand $f(x)$ in Taylor's series by keeping only up to second term and $f'(x) = 0$

$$f(x) = f(x_0) + \frac{f''(x_0)(x - x_0)^2}{2!} \tag{3.51}$$

where $f(x_0) = \frac{10}{3}\pi m \left(\frac{\pi D_T}{2m}\right)^{3/5}$

$$\frac{d^2 f(x)}{dx^2} = 8\pi m x + 6\pi^2 D_T x^{-4}$$

$$\left.\frac{d^2 f(x)}{dx^2}\right|_{x_0} = 20\pi m \left[\frac{\pi D_T}{2m}\right]^{1/5} \tag{3.52}$$

Substituting Eq.(3.51) into Eq.(3.46)

$$\begin{aligned} N_h(t) &\cong \frac{16}{3}\pi^2 c_0 m H_0 t^{6/5}\left(\frac{\pi D_T}{2m}\right)\int_0^\infty \exp\left\{-t^{3/5}\left[\frac{10}{3}\pi m\left(\frac{D_T\pi}{2m}\right)^{3/5}\right.\right. \\ &\quad \left.\left. +10\pi m\left(\frac{D_T\pi}{2m}\right)^{1/5}(x-x_0)^2\right]\right\}dx \\ &= \frac{16}{3}\pi^2 c_0 m H_0 t^{6/5}\pi D_T \exp\left\{-t^{3/5}\left[\frac{10}{3}\pi m\left(\frac{D_T\pi}{2m}\right)^{3/5}\right]\right\} \\ &\quad \times\int_0^\infty \exp\left[-t^{3/5}10\pi m\left(\frac{D_T\pi}{2m}\right)^{1/5}(x-x_0)^2\right]dx \\ &= \alpha' c_0 H_0 m^{-2/5} D_T^{9/10} t^{9/10}\exp\left[-\beta' m^{2/5} D_T^{3/5} t^{3/5}\right] \end{aligned} \tag{3.53}$$

where

$$\alpha' = \frac{8}{3}\cdot 2^{-5/2}\cdot 5^{-1/2}\pi^{29/30} \tag{3.54}$$

$$\beta' = \frac{10}{3}\cdot 2^{-3/5}\pi^{8/5} \tag{3.55}$$

Since

$$N_h(t) \approx N_0 t^{9/10}\exp\left(-t^{3/5}\right) \tag{3.56}$$

for a three dimensional system. The ligand population decays slower than the pure exponential function. See Fig. (3.3)

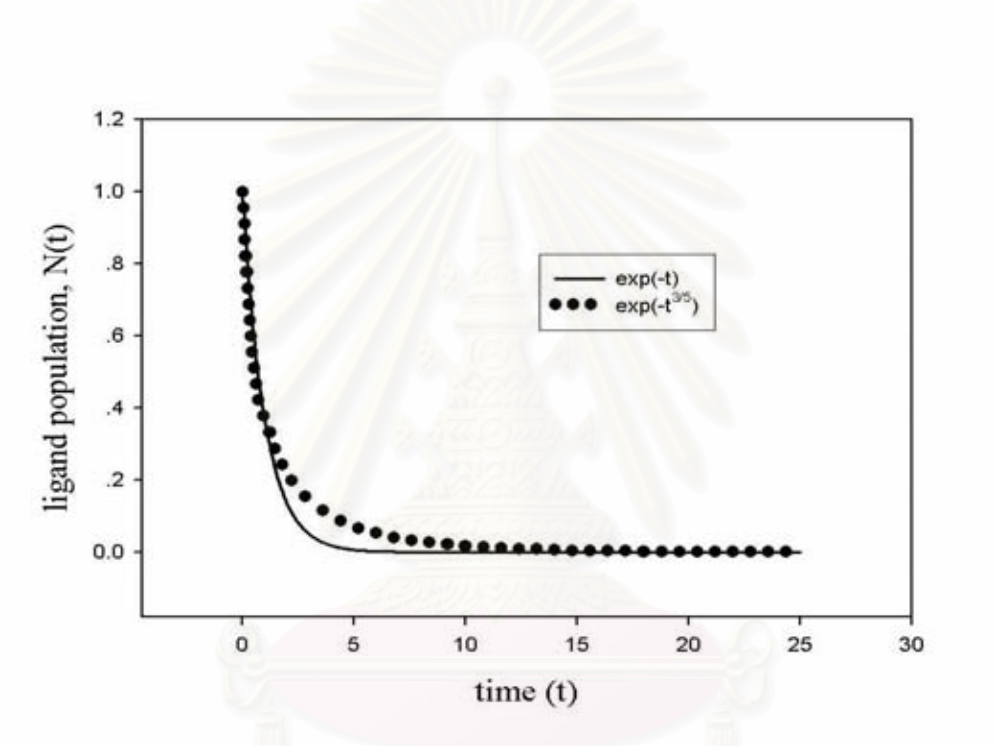


Figure 3.3: Plot of the ligand population as function $\exp(-t^n)$ versus the time t for ligands moving in the randomly distribution traps.

Chapter 4
Path Integral Representation

The path integral method of Feynman [22] provides us an approach to solve quantum mechanical problem . The Feynman method is based on the Lagrangian which gives us easy generalization from non-relativistic to relativistic problem. The main concept of Feynman path integral is the propagator which contains all the informations about system. The propagator, $G(\mathbf{x}_2, t_2 : \mathbf{x}_1, t_1)$, represents the quantum mechanical transition amplitude for a particle to be found at position $\mathbf{x}_2$ at time t_2 by the particle was at position $\mathbf{x}_1$ at an earlier time t_1. For more detail in the concept of Feynman path integral, the interested reader is referred to see the book of Feynman and Hibbs [1].

Because of the advantages of propagator, it is used to solve the problem about the motion of particles in a random environment, where path integral give an accurate answer. Edward [23] studied the electron moving in a completely random system containing dense and weak scatterer, or equivalently an electron in a Gaussian random potential. In addition to Samathiyakanit's trial action [2], we can apply both of them to describe the system of a ligand moving in the randomly distributed receptors. This trial action is non-local harmonic trial action which has the term of the memory effects for the system in the interaction with a larger system. Path integration of this action involves only Gaussian integrals and can be performed exactly [24].

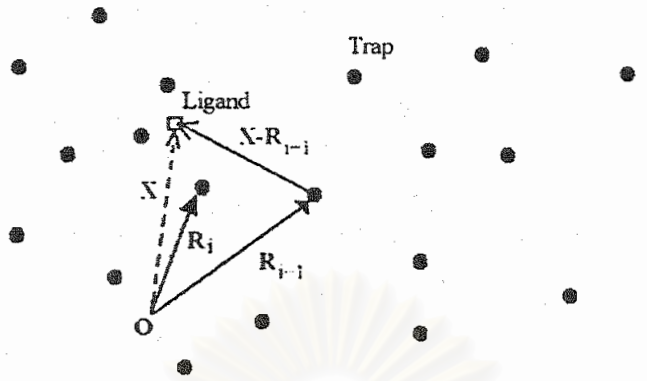


Figure 4.1: Ligand at position x moves in the system which consists of traps randomly distributed in position R_i, R_{i+1}, and so on.

4.1 The analogy of diffusion equation and Schrödinger equation

In order to apply the path integral techniques for heavily doped semiconductor to diffusion equation, we would like to present our model. See Fig. (4.1)

We can write the diffusion equation for this system as

$$\frac{\partial C(\mathbf{x},t)}{\partial t} = D_T \nabla^2 C(\mathbf{x},t) - \sum_{i=1}^{N} v\left(\mathbf{x}-\mathbf{R}_i\right) C(\mathbf{x},t) \tag{4.1}$$

where $C(\mathbf{x},t)$ is the concentration of ligands, D_T is the diffusion coefficient depending on temperature T, and $v\left(\mathbf{x}-\mathbf{R}_i\right)$ is the interaction between ligand and traps. We assume that $v\left(\mathbf{x}-\mathbf{R}_i\right)$ is the Gaussian interaction.

$$v\left(\mathbf{x}-\mathbf{R}_i\right) = u(\pi l^2)^{\frac{-3}{2}} \exp(|\mathbf{x}-\mathbf{R}_i|/l^2) \tag{4.2}$$

where l is the correlation length. We can rewrite the Eq. (4.1) as

$$\frac{\partial C(\mathbf{x},t)}{\partial t} = \hat{L} C(\mathbf{x},t) \tag{4.3}$$

where $\hat{L}$,the operator ,is $D_T \nabla^2 - \sum_{i=1}^{N} v\left(\mathbf{x}-\mathbf{R}_i\right)$.

Now let consider the schrödinger equation in heavily doped semiconductor [2].

$$i\hbar\frac{\partial\Psi}{\partial t} = -\frac{\hbar^2}{2m}\nabla^2\Psi + \sum_{i=1}^{N} v\left(\mathbf{x}-\mathbf{R}_i\right)\Psi \tag{4.4}$$

We will change parameters in Eq. (4.4) to the following diagram.

$t \Rightarrow -is$

$\frac{\hbar}{2m} \Rightarrow D_T$

$\sum_{i=1}^{N} v\left(\mathbf{x}-\mathbf{R}_i\right)/\hbar \Rightarrow V_c$

$\Psi(\mathbf{x},t) = C(\mathbf{x},t)$

Now we obtain

$$\frac{\partial C(\mathbf{x},t)}{\partial s} = D_T\nabla^2 C(\mathbf{x},t) - V_c C(\mathbf{x},t) \tag{4.5}$$

From this analogy, we apply the path integral techniques to solve this problem.

4.2 Edward's model

We consider a ligand moving in the presence of a set of N receptors, confined within a volume V, and having a density $\rho = \frac{N}{V}$. Let $v\left(\mathbf{x}-\mathbf{R}_i\right)$ is the ligand-receptor interaction, where $\mathbf{x}$ and $\mathbf{R}_i$ are the position of receptors on cell and a ligand respectively. Then the one ligand Hamiltonian is

$$H = -\frac{\hbar^2}{2m}\nabla^2 + \sum_{i=1}^{N} v\left(\mathbf{x}-\mathbf{R}_i\right) \tag{4.6}$$

where m is the ligand mass. This Hamiltonian obviously depends on the position of the stationary receptors. Therefore we will consider the simplest model of disordered system to eliminate the need for extraneous mathematical approximation by letting the scattering centers are taken distributed randomly. The probability

distribution of the scattering potential is

$$P\left[\mathrm{R}\right] d\left(\left[\mathrm{R}\right]\right) = \frac{d\mathrm{R}_1 d\mathrm{R}_2 ... d\mathrm{R}_N}{V^N} \tag{4.7}$$

This is satisfactory in the analogous consideration of heavily doped semiconductors with short-range electron scatterer interaction where the correlation scatterers can be ignored safely [24]. Here, we neglect the ligand-ligand interaction for simplified model that is why we can use the analogy with the one electron approximation instead of the many-body one. For a given configuration of the receptors, the propagator $g\left(\mathrm{x}_2, \mathrm{x}_1; t, [v]\right)$ of this system satisfies the usual equation

$$\left[i\hbar\frac{\partial}{\partial t} - H\left([v]\right)\right] g\left(\mathrm{x}_2, \mathrm{x}_1; t, [v]\right) = \delta\left(\mathrm{x} - [\mathrm{R}]\right)\delta\left(t\right) \tag{4.8}$$

which can expressed in the path integral representation as

$$g\left(\mathrm{x}_2, \mathrm{x}_1; t, [v]\right) = \int D\mathrm{x}\left(t\right) \exp\left\{\frac{i}{\hbar}\int_0^t d\tau \left[\frac{m}{2}\dot{\mathrm{x}}^2 - v\left(\mathrm{x} - [\mathrm{R}]\right)\right]\right\} \tag{4.9}$$

where $D\mathrm{x}\left(t\right)$ denotes the path integral to be carried out with the boundary conditions $\mathrm{x}\left(0\right) = \mathrm{x}_1$ and $\mathrm{x}\left(t\right) = \mathrm{x}_2$ and

$$v\left(\mathrm{x} - [\mathrm{R}]\right) = \sum_{i=1}^{N} v\left(\mathrm{x} - \mathrm{R}_i\right) \tag{4.10}$$

Now we consider the properties of the identically prepared system. Therefore, the measured properties are averaged over all configurations of expression

(4.9) and it can be perform exactly by Edwards and Gulyaev [25].

$$\begin{aligned} G(\mathbf{x}_2,\mathbf{x}_1;t) &= \int P[\mathrm{R}]\, d([\mathrm{R}])\, g(\mathbf{x}_2,\mathbf{x}_1;t,[v]) \\ &= \int D\mathbf{x}(t) \exp\left\{\frac{i}{\hbar}\int_0^t d\tau \left[\frac{m}{2}\dot{\mathbf{x}}^2\right]\right\} \\ &\quad \cdot \int \frac{d\mathrm{R}_1 d\mathrm{R}_2 ... d\mathrm{R}_N}{V^N} \exp\left\{-\frac{i}{\hbar}\int_0^t d\tau \left[\sum_{i=1}^{N} v(\mathbf{x}-\mathrm{R}_i)\right]\right\} \\ &= \int D\mathbf{x}(t) \exp\left\{\frac{i}{\hbar}\int_0^t d\tau \left[\frac{m}{2}\dot{\mathbf{x}}^2\right]\right\} \\ &\quad \cdot \left\{\int \frac{d\mathrm{R}}{V} \exp\left[-\frac{i}{\hbar}\int_0^t d\tau\, v(\mathbf{x}-\mathrm{R}_i)\right]\right\}^N \end{aligned} \tag{4.11}$$

$G(\mathbf{x}_2,\mathbf{x}_1;t)$ describes the motion of an average ligand which moves in the average system. Next, we consider only the term by assuming $a << V$ and using the identity

$$\{1+\frac{a}{V}\}^N = \exp[\frac{aN}{V}] \tag{4.12}$$

then we have

$$\begin{aligned} &\left\{\int \frac{d\mathrm{R}}{V} \exp\left[-\frac{i}{\hbar}\int_0^t d\tau\, v(\mathbf{x}-\mathrm{R}_i)\right]\right\}^N \\ &= \left\{1+\int \frac{d\mathrm{R}}{V}\left(\exp\left[-\frac{i}{\hbar}\int_0^t d\tau\, v(\mathbf{x}-\mathrm{R}_i)\right]-1\right)\right\}^N \\ &= \exp\left\{\rho\int d\mathrm{R}\left(\exp\left[-\frac{i}{\hbar}\int_0^t d\tau\, v(\mathbf{x}-\mathrm{R}_i)\right]-1\right)\right\} \end{aligned} \tag{4.13}$$

Then expanding the exponential exponent in Taylor series and considering the system in the limits of receptor concentration is very large ($\rho \to \infty$) and the ligand-receptor interaction is weak ($v \to 0$) so that ρv^2 is finite. Since $\rho v^2 >> \rho v^3$, we truncate the expansion after quadratic term in $v(\mathbf{x}-\mathrm{R})$. In this limit, it allows us completely to describe the system by the first and second moments of the potential. The distribution can be the Gaussian distribution which means

that a system of a ligand moving in weak and dense receptors is equivalent to moving in the Gaussian random potential. See Fig. (4.2). We obtain

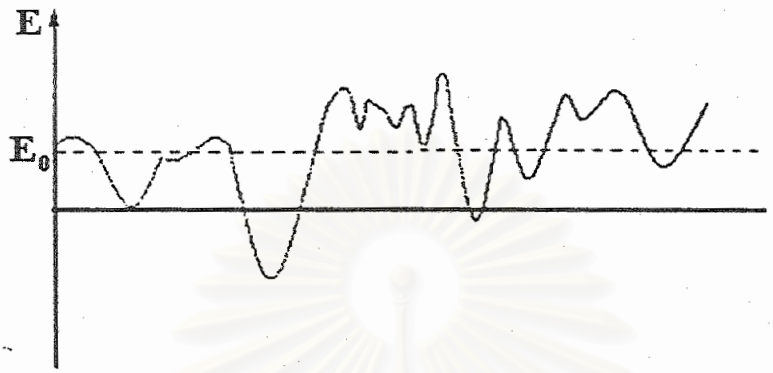


Figure 4.2: Sketch of the random potential (the solid line). The dashed line denotes the average potential of the system, E_0.

$$G(\mathbf{x}_2,\mathbf{x}_1;t)=\int D\mathbf{x}(t)\exp\left\{\frac{i}{\hbar}\left[\begin{array}{c}\int_0^t d\tau\frac{m}{2}\dot{\mathbf{x}}^2-\rho\int_0^t d\tau\int d\mathbf{R}v(\mathbf{x}-\mathbf{R}_i)\\+\frac{i\rho}{2\hbar}\int_0^t d\tau\int_0^t d\sigma\int d\mathbf{R}\,v(\mathbf{x}(\tau)-\mathbf{R})\,v(\mathbf{x}(\sigma)-\mathbf{R})\end{array}\right]\right\} \tag{4.14}$$

Here we have taken the average potential energy to be

$$E_0=\int d\mathbf{R}v(\mathbf{x}-\mathbf{R}_i) \tag{4.15}$$

and the auto-correlation function define as

$$W(\mathbf{x}(\tau)-\mathbf{x}(\sigma))=\int d\mathbf{R}v(\mathbf{x}(\tau)-\mathbf{R})\,v(\mathbf{x}(\sigma)-\mathbf{R}) \tag{4.16}$$

The auto-correlation function tells us the effect of a potential at one point on a potential to another point. By using these two functions, the average propagator can be written as

$$G(\mathbf{x}_2,\mathbf{x}_1;t)=\int D\mathbf{x}(\tau)\exp\left\{\frac{i}{\hbar}S[\mathbf{x}(\tau)]\right\} \tag{4.17}$$

where $S[\mathbf{x}(\tau)]$ is defined by

$$S[\mathbf{x}(\tau)] = \int_0^t d\tau \left[\frac{m}{2}\dot{\mathbf{x}}^2 - nE_0 + \frac{i\rho}{2\hbar}\int_0^t d\sigma W(\mathbf{x}(\tau) - \mathbf{x}(\sigma))\right] \tag{4.18}$$

In the form of $S[\mathbf{x}(\tau)]$, it seems that the system can be viewed as a ligand moving in the average potential with a "memory effect". In our case, we use the Gaussian potential

$$v(\mathbf{x}(\tau) - \mathbf{R}) = u(\pi l^2)^{-3/2} \exp\left(\frac{|\mathbf{x}(\tau) - \mathbf{R}|^2}{l^2}\right) \tag{4.19}$$

where u is a parameter to take care the dimension of system. An analytical expression

$$W(\mathbf{x}(\tau) - \mathbf{x}(\sigma)) = u^2(\pi L^2)^{-3/2} \exp\left(\frac{|\mathbf{x}(\tau) - \mathbf{x}(\sigma)|^2}{L^2}\right) \tag{4.20}$$

is obtained (see appendix A), where L is the new Gaussian correlation length of the random system, $L^2 = 2l^2$. We substitute Eq. (4.20) into Eq. (4.18), then we have

$$G(\mathbf{x}_2, \mathbf{x}_1; t) = \int D\mathbf{x}(t) \exp\left\{\frac{i}{\hbar}\int_0^t d\tau \left[\frac{m}{2}\dot{\mathbf{x}}^2 - nE_0 + \frac{i\xi}{2\hbar}\int_0^t d\sigma \exp\left(\frac{|\mathbf{x}(\tau) - \mathbf{x}(\sigma)|^2}{L^2}\right)\right]\right\} \tag{4.21}$$

where $\xi = \frac{u^2\rho}{(\pi L^2)^{3/2}}$ has the dimension of E^2.

4.3 The approximate propagator

In general, a lot of path integrals can not be integrated out and our problem is one of them. Therefore an approximation method is needed. In our problem, we use the variational method which we can adjust the appropriate trial action with parameter. In this investigation, we follow the method given in Samathiyakanit [2], which is similar to Feynman [26] used in the polaron problem by introducing

a non-local harmonic trial action

$$S_0(\omega) = \int_0^t d\tau \left[\frac{m}{2}\dot{\mathbf{x}}^2(\tau) - \frac{\omega^2}{2t}\int_0^t d\sigma\, |\mathbf{x}(\tau) - \mathbf{x}(\sigma)|^2\right] \tag{4.22}$$

where ω is an unknown parameter to be determined. $S_0(\omega)$ is chosen to be translationally invariant since we are not considering the localized states. The average propagator is written as

$$G_1(\mathbf{x}_2, \mathbf{x}_1; t) = G_0(\mathbf{x}_2, \mathbf{x}_1; t, \omega) \left\langle \exp\left[\frac{i}{\hbar}(S - S_0(\omega))\right]\right\rangle_{S_0(\omega)} \tag{4.23}$$

where nonlocal harmonic oscillator propagator

$$G_0(\mathbf{x}_2, \mathbf{x}_1; t, \omega) = \int D(\mathbf{x}(\tau)) \exp\left(\frac{i}{\hbar} S_0[\mathbf{x}(\tau)]\right) \tag{4.24}$$

and the average $\langle\ \ \rangle_{S_0(\omega)}$ is defined as

$$\langle O\rangle_{S_0(\omega)} = \frac{\int D(\mathbf{x}(\tau)) O \exp\left(\frac{i}{\hbar} S_0[\mathbf{x}(\tau)]\right)}{\int D(\mathbf{x}(\tau)) \exp\left(\frac{i}{\hbar} S_0[\mathbf{x}(\tau)]\right)} \tag{4.25}$$

where O denotes a function to be averaged. Consequently, we approximate Eq. (4.23) by using the first order cumulant expansion [27].

$$\langle \exp[a]\rangle = \exp\left[\langle a\rangle + \frac{1}{2}(\langle a^2\rangle - \langle a\rangle^2) - \ldots\right] \tag{4.26}$$

and we keep only the first order.

$$G_1(\mathbf{x}_2, \mathbf{x}_1; t, \omega) = G_0(\mathbf{x}_2, \mathbf{x}_1; t, \omega) \exp\left[\frac{i}{\hbar}\langle S - S_0(\omega)\rangle_{S_0(\omega)}\right] \tag{4.27}$$

where the index 1 denotes the first order approximation. To obtain $G_1(\mathbf{x}_2, \mathbf{x}_1; t; \omega)$ we have to find $G_0(\mathbf{x}_2, \mathbf{x}_1; t, \omega)$ and $\langle S - S_0(\omega)\rangle_{S_0(\omega)}$ which is defined as $\langle S' - S_0'(\omega)\rangle_{S_0(\omega)}$ since their kinetic term are identical and always cancel each other. The prime symbol in both actions means excluding the kinetic energy term. Fortunately, $G_0(\mathbf{x}_2, \mathbf{x}_1; t, \omega)$ has been already carried out by Samathiyakanit [2].

$$G_0(\mathbf{x}_1, \mathbf{x}_2; t, \omega) = \left(\frac{m}{2\pi i\hbar t}\right)^{3/2} \left(\frac{t}{2\sin\frac{\omega t}{2}}\right)^3 \tag{4.28}$$

From

$$\langle S' - S'_0(\omega)\rangle_{S_0(\omega)} = \langle S'\rangle_{S_0(\omega)} - \langle S'_0(\omega)\rangle_{S_0(\omega)} \tag{4.29}$$

Therefore, we can rewrite

$$G_1(\mathbf{x}_1,\mathbf{x}_2;t,\omega) = G_0(\mathbf{x}_1,\mathbf{x}_2;t,\omega)\exp\left[\frac{i}{\hbar}(\langle S'\rangle_{S_0(\omega)} - \langle S'_0\rangle_{S_0(\omega)})\right] \tag{4.30}$$

we will consider $\langle S'\rangle_{S_0(\omega)}$ by substitute S from Eq.(4.18)

$$\langle S'\rangle_{S_0(\omega)} = -nE_0t + \frac{i}{2\hbar}\rho\int_0^t d\tau\int_0^t d\sigma\,\langle W(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\rangle_{S_0(\omega)} \tag{4.31}$$

where $W(\mathbf{x}(z)-\mathbf{x}(\sigma))$ is given by Eq.(4.20) for Gaussian potentials. This average is difficult so that we use its Fourier transform.

$$W(\mathbf{x}(z)-\mathbf{x}(\sigma)) = \int\frac{d\mathbf{k}}{(2\pi)^3}W(\mathbf{k})\exp[i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma)] \tag{4.32}$$

where

$$W(\mathbf{k}) = u^2\exp\left[-\frac{L^2}{4}\mathbf{k}^2\right] \tag{4.33}$$

(See appendix B) and u is the parameter introduced in order to the take care of dimension of the system (see appendix A). Thus we can rewrite $\langle S'\rangle_{S_0(\omega)}$as

$$\begin{aligned}\langle S'\rangle_{S_0(\omega)} &= -nE_0t + \frac{i}{2\hbar}\rho\int_0^t d\tau\int_0^t d\sigma\int\frac{d\mathbf{k}}{(2\pi)^3}W(\mathbf{k})\langle\exp[i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma))]\rangle_{S_0(\omega)}\\ &= -nE_0t + \frac{i}{2\hbar}\rho\int_0^t d\tau\int_0^t d\sigma\int\frac{d\mathbf{k}}{(2\pi)^3}W(\mathbf{k})\exp(a_1+a_2)\end{aligned} \tag{4.34}$$

Using cumulant expansions.

$$a_1 = i\mathbf{k}\cdot\langle\mathbf{x}(\tau)-\mathbf{x}(\sigma)\rangle_{S_0(\omega)} \tag{4.35}$$

$$a_2 = -\frac{i}{2}\mathbf{k}^2\left[\frac{1}{3}\left\langle(\mathbf{x}(\tau)-\mathbf{x}(\sigma))^2\right\rangle_{S_0(\omega)} - \langle x(\tau)-x(\sigma)\rangle^2_{S_0(\omega)}\right] \tag{4.36}$$

where $x(\tau)-x(\sigma) = x_x(\tau)-x_x(\sigma) = x_y(\tau)-x_y(\sigma) = x_z(\tau)-x_z(\sigma)$.See appendix C for more detail. Inserting $W(\mathbf{k})$ into Eq. (4.34) and performing the k-integration,

we obtain

$$\langle S' \rangle_{S_0(\omega)} = -nE_0 t + \frac{i}{2\hbar}\rho \int_0^t d\tau \int_0^t d\sigma \left(\frac{1}{4\pi}\right)^{3/2} A^{-3/2} \exp\left[\frac{-\mathrm{B}^2}{4A}\right] \tag{4.37}$$

where

$$A = \frac{1}{4}L^2 + \frac{1}{2}\left[\frac{1}{3}\left\langle (\mathrm{x}(\tau) - \mathrm{x}(\sigma))^2 \right\rangle_{S_0(\omega)} - \langle x(\tau) - x(\sigma) \rangle^2_{S_0(\omega)}\right] \tag{4.38}$$

and

$$\mathrm{B} = \langle \mathrm{x}(\tau) - \mathrm{x}(\sigma) \rangle_{S_0(\omega)} \tag{4.39}$$

Next we consider the average of the trial action $\langle S_0'(\omega) \rangle_{S_0(\omega)}$ which is written as

$$\langle S_0'(\omega) \rangle_{S_0(\omega)} = -\frac{m}{2}\frac{\omega^2}{2t} \int_0^t d\tau \int_0^t d\sigma \left\langle ((\mathrm{x}(\tau) - \mathrm{x}(\sigma))^2 \right\rangle_{S_0(\omega)} \tag{4.40}$$

Eq. (4.37) and Eq. (4.40) can be expressed in terms of the following averages $\langle \mathrm{x}(\tau) \rangle_{S_0(\omega)}$and $\langle (\mathrm{x}(\tau) - \mathrm{x}(\sigma) \rangle_{S_0(\omega)}$. Such averages can be obtained from a characteristic functional of $\left\langle \exp(\frac{i}{\hbar}\int_0^t d\tau \mathrm{f}(\tau) \cdot \mathrm{x}(\tau)) \right\rangle_{S_0(\omega)}$.

4.4 Detailed calculations

From Feynman and Hibbs[1], we can rewrite the characteristic functional as

$$\left\langle \exp\left(\frac{i}{\hbar}\int_0^t d\tau \mathrm{f}(\tau) \cdot \mathrm{x}(\tau)\right) \right\rangle_{S_0(\omega)} = \exp\left(\frac{i}{\hbar}\left[S^f_{0,cl} - S_{0,cl}\right]\right) \tag{4.41}$$

where $S^f_{0,cl}, S_{0,cl}$ are the forced classical trial action and classical trial action respectively and we have derived from appendix D, by defining

$$S^f_0 = S_0 + \int_0^t d\tau \mathrm{f}(\tau) \cdot \mathrm{x}(\tau) \tag{4.42}$$

Both $S^f_{0,cl}$ and $S_{0,cl}$ are Gaussian. To obtain the forced classical action $S^f_{0,cl}$, we need to find the classical path which can be obtained by making a variation on $S^f_0(\omega)$.

$$S^f_0 = \int_0^t d\tau L(\dot{\mathrm{x}}, \mathrm{x}, t) + \int_0^t d\tau \mathrm{f}(\tau) \cdot \mathrm{x}(\tau) \tag{4.43}$$

From Eq. (4.41), we differentiate it with respect to $\mathrm{f}(\tau)$. The result is

$$\left\langle \mathrm{x}(\tau) \exp\left[\frac{i}{\hbar}\int \mathrm{f}(\tau)\cdot\mathrm{x}(\tau)d\tau\right]\right\rangle = \frac{\delta S'_{0,cl}}{\delta \mathrm{f}(\tau)}\left\{\exp\left[\frac{i}{\hbar}\left(S^f_{0,cl}-S_{0,cl}\right)\right]\right\} \tag{4.44}$$

therefore, by evaluating both sides at $\mathrm{f}(\tau)=0$, we obtain

$$\langle \mathrm{x}(\tau)\rangle = \left.\frac{\delta S^f_{0,cl}}{\delta \mathrm{f}(\tau)}\right|_{\mathrm{f}(\tau)=0} \tag{4.45}$$

and continue differentiating Eq. (4.41) to get the second derivative as

$$\langle \mathrm{x}(\tau)\cdot\mathrm{x}(\sigma)\rangle = \left.\left[\frac{\hbar}{i}\frac{\delta^2 S^f_{0,cl}}{\delta \mathrm{f}(\tau)\cdot\delta \mathrm{f}(\sigma)}+\frac{\delta S^f_{0,cl}}{\delta \mathrm{f}(\tau)}\cdot\frac{\delta S^f_{0,cl}}{\delta \mathrm{f}(\sigma)}\right]\right|_{\mathrm{f}(\tau)=0} \tag{4.46}$$

Using Eq.(4.34), (4.38),(4.39),(4.45) ,(4.46)and (C.10). The first and second functional derivatives can be evaluated and we can get A, and B for $\tau>\sigma$.

$$\begin{aligned}\langle \mathrm{x}(\tau)\rangle_{S(0)} &= \left.\frac{\delta S^f_{0,cl}}{\delta \mathrm{f}(\tau)}\right|_{\mathrm{f}(\tau)=0} \\ &= \frac{m\omega}{2\sin\omega t}\left[\begin{array}{c}\frac{2\mathrm{x}_2}{m\omega}\left(\sin\omega\tau-2\sin\frac{\omega\tau}{2}\sin\frac{\omega}{2}(t-\tau)\sin\frac{\omega t}{2}\right)\\ +\frac{2\mathrm{x}_1}{m\omega}\left(\sin\omega(t-\tau)-2\sin\frac{\omega\tau}{2}\sin\omega\frac{(t-\tau)}{2}\sin\frac{\omega t}{2}\right)\end{array}\right]\end{aligned} \tag{4.47}$$

and

$$\begin{aligned}\langle \mathrm{x}(\tau)\mathrm{x}(\sigma)\rangle_{S_0(\omega)} &= \frac{\delta^2 S^f_{0,cl}}{\delta \mathrm{f}(\tau)\cdot\delta \mathrm{f}(\sigma)} \\ &= \frac{3\hbar}{im\omega\sin\omega t}\left[\begin{array}{c}\sin\omega(t-\tau)\sin\omega\sigma\\ -4\sin\frac{\omega\sigma}{2}\sin\omega\frac{(t-\tau)}{2}\sin\frac{\omega\tau}{2}\sin\omega\frac{(t-\tau)}{2}\end{array}\right]\end{aligned} \tag{4.48}$$

substituting Eq.(4.47) and (4.48) into (4.38) and (4.39)

$$A\equiv A(t,\tau-\sigma;\omega)=\left(\frac{L^2}{4}+\frac{i\hbar}{m\omega}\frac{\sin\frac{\omega}{2}(\tau-\sigma)\sin\frac{\omega}{2}(t-(\tau-\sigma))}{\sin\frac{\omega t}{2}}\right) \tag{4.49}$$

and

$$\mathrm{B}\equiv \mathrm{B}(\mathrm{x}_2-\mathrm{x}_1;t;\tau,\sigma;\omega)=\frac{\sin\frac{\omega}{2}(\tau-\sigma)\cos\frac{\omega}{2}(t-(\tau+\sigma))}{\sin\frac{\omega t}{2}}(\mathrm{x}_2-\mathrm{x}_1) \tag{4.50}$$

Using Eq.(4.40), (4.47), and (4.48), we get

$$\langle S_0'(\omega)\rangle_{S_0(\omega)} = \frac{3}{2}i\hbar(\frac{\omega t}{2}\cot\frac{\omega t}{2} - 1) + \frac{m}{2}\left[\frac{\omega t}{2}\cot\frac{\omega t}{2} - \left(\frac{\omega t}{2}\csc\frac{\omega t}{2}\right)^2\right]\frac{|\mathbf{x}_2 - \mathbf{x}_1|^2}{2t} \tag{4.51}$$

substituting Eq.(4.37),(4.38),(4.39), and (4.51) into (4.30),we get

$$\begin{aligned} G_1(\mathbf{x}_1, \mathbf{x}_2; t, \omega) &= (\frac{m}{2\pi i\hbar t})^{\frac{3}{2}}\left(\frac{\omega t}{2\sin\frac{\omega t}{2}}\right)^3 \\ &\cdot\exp\left[\begin{array}{l} \frac{3}{2}(\frac{\omega t}{2}\cot\frac{\omega t}{2} - 1) - \frac{mi}{4\hbar}\left[\frac{\omega t}{2}\cot\frac{\omega t}{2} + \left(\frac{\omega t}{2}\csc\frac{\omega t}{2}\right)^2\right]\frac{|\mathbf{x}_2-\mathbf{x}_1|^2}{t} \\ -\frac{\varsigma}{2\hbar^2}\left(\frac{L^2}{4}\right)^{\frac{3}{2}}\int_0^t d\tau\int_0^t d\sigma\left(\frac{1}{4\pi}\right)^{3/2}A^{-3/2}(t, \tau-\sigma;\omega)\exp\left[\frac{-\mathrm{B}^2}{4A}\right] \end{array}\right] \end{aligned} \tag{4.52}$$

where A and B are Eq. (4.49) and Eq. (4.50) respectively.

This is the average propagator in the first order cumulant expansion. It describes the motion of single electron in randomly distributed scatterers. The propagator is defined as

$$G_1(\mathbf{x}_1, \mathbf{x}_2; t, \omega) = \sum_{n=1}^{\infty}\phi_n(\mathbf{x}_2)\phi_n^*(\mathbf{x}_1)e^{-\frac{i}{\hbar}E_n(t_2-t_1)} \tag{4.53}$$

The electron moves from a point $\mathbf{x}_1$ to the point $\mathbf{x}_2$ with the time $t_2 - t_1 = t$ where $t_2 > t_1$. This is the probability amplitude which sums over all contribution. Now we use the analogy of Eq.(4.4) and Eq.(4.5) and convert $t \Rightarrow -is$ and $\frac{E_n}{\hbar} \Rightarrow \lambda_n$. We obtain

$$P(\mathbf{x}_1, \mathbf{x}_2; s, \omega) = \sum_{n=1}^{\infty}\phi_n(\mathbf{x}_2)\phi_n^*(\mathbf{x}_1)e^{-\lambda_n(s_2-s_1)} \tag{4.54}$$

and consider $\mathbf{x}_1 = \mathbf{x}_2 = \mathbf{x}$. We can interpret $P(\mathbf{x}, \mathbf{x}; s, \omega)$ as the probability of ligands at location $\mathbf{x}$ and consider the asymptotic behavior of the probability at large time. After we set $\mathbf{x}_1 = \mathbf{x}_2 = \mathbf{x}$, this propagator is determined as the returning probability amplitude. We will use $G_1(\mathbf{x}, \mathbf{x}; t, \omega)$ to find $P(\mathbf{x}, \mathbf{x}; s, \omega)$. Beside, we still have to determine the unknown parameter (ω) in $G_1(\mathbf{x}_1, \mathbf{x}_2; t, \omega)$

by minimizing the density of states $n(E)$. This process gives us the optimal ω for our system. Before we continue to the next process, we have to prove that the density of states of the capture rate, $n(\lambda)$, has the same function as the density of the state.

$$n(E) = \sum_{n=1}^{\infty} \delta(E - E_n) \tag{4.55}$$

From the definition

$$2\,\mathrm{Re}\,G(\mathbf{x}, \mathbf{x}; t, \omega) = \int_0^{\infty} n(E) e^{-\frac{i}{\hbar}Et} dE \tag{4.56}$$

and convert the variables, $t \Rightarrow -is$ and $\frac{E}{\hbar} \Rightarrow \lambda$. We have to convert $n(E)$ to $n(\lambda)$ by using the following expression.

$$n(E)dE = n(\lambda)d(\lambda) \tag{4.57}$$

$$n(E) = n(\lambda)\frac{d(\lambda)}{dE} = \frac{n(\lambda)}{\hbar} \tag{4.58}$$

Now we get

$$2P(\mathbf{x}, \mathbf{x}; s, \omega) = \int_0^{\infty} n(\lambda) e^{-\lambda s} d\lambda \tag{4.59}$$

Therefore,

$$P(\mathbf{x}, \mathbf{x}; s, \omega) = \frac{1}{2} L\{n(\lambda)\} \tag{4.60}$$

where $L\{n(\lambda)\}$ is the Laplace transform of $n(\lambda)$. Since

$$\mathrm{Tr}P(\mathbf{x}, \mathbf{x}; s, \omega) = VP(\mathbf{x}, \mathbf{x}; s, \omega) \tag{4.61}$$

where V is the volume of system and

$$\mathrm{Tr}P(\mathbf{x}, \mathbf{x}; s, \omega) = \frac{e^{-\alpha s}}{2} \tag{4.62}$$

where α is the gound state energy of decay rate. Then we have

$$P(\mathbf{x}, \mathbf{x}; s, \omega) = \frac{e^{-\alpha s}}{2V} \tag{4.63}$$

Substitute Eq.(4.63) into Eq.(4.60). We get

$$L\{n(\lambda)\} = \frac{e^{-\alpha s}}{V} \tag{4.64}$$

Now we know

$$n(\alpha) = L^{-1}\{\frac{e^{-\alpha s}}{V}\} = \sum_{n=1}^{\infty} \frac{1}{V}\delta(\alpha - \alpha_n) \tag{4.65}$$

This expression is similar to Eq.(4.55). This show us that we can use the same method to find the minimizing energy for finding the density of state.

4.5 The density of states

The density of states per unit volume is related to the diagonal part of the average propagator as

$$n(E) = \frac{1}{2\pi\hbar}\int_{-\infty}^{\infty} dt\, G(\mathbf{x},\mathbf{x};t)\exp\left[\frac{i}{\hbar}Et\right] \tag{4.66}$$

where

$$\begin{aligned} G_1(\mathbf{o},\mathbf{o};t) &= \left(\frac{m}{2\pi i\hbar t}\right)^{3/2}\left(\frac{\omega t}{2\sin(\omega t/2)}\right)^3 \exp\left[\frac{3}{2}\left(\frac{1}{2}\omega t\cot\frac{\omega t}{2}-1\right)-\frac{i}{\hbar}E_0 t\right. \\ &\left. -\frac{\xi}{2\hbar^2}\left(\frac{L^2}{4}\right)^{3/2}\int_0^t d\tau\int_0^t d\sigma A^{-3/2}(t,\tau,\sigma;\omega)\right] \end{aligned} \tag{4.67}$$

Now we use the property

$$A(t,\tau,\sigma;\omega) = A(t,t-(\tau-\sigma);\omega) \tag{4.68}$$

thus the integral in Eq.(4.67) can be reduced to

$$\int_0^t d\tau\int_0^t d\sigma A^{-3/2}(t,\tau,\sigma;\omega) = t\int_0^t dx A^{-3/2}(t,x;\omega) \tag{4.69}$$

where

$$A(t,x;\omega) = \frac{L^2}{4} + \frac{i\hbar}{m\omega}\frac{\sin(\omega x/2)\sin(\omega(t-x)/2)}{\sin(\omega t/2)} \tag{4.70}$$

Besides, we consider the system at large times, $t \Rightarrow -is$ and $s \rightarrow \infty$. We can make the following approximation:

$$\lim_{t\to\infty} \sin\frac{\omega t}{2} \Longrightarrow \lim_{s\to\infty} \sin\frac{\omega(-is)}{2} = \frac{1}{2i}e^{\omega s/2} \tag{4.71}$$

$$\lim_{t\to\infty} \cot\frac{\omega t}{2} \Longrightarrow \lim_{s\to\infty} \cot\frac{\omega(-is)}{2} = i \tag{4.72}$$

$$\lim_{t\to\infty} \frac{\sin(\omega x/2)\sin(\omega(t-x)/2)}{\sin(\omega t/2)} \Longrightarrow \lim_{s\to\infty} \frac{\sin\omega(-ix')/2\sin\omega(-i)(s-x')/2}{\sin\omega(-is)/2} = \frac{1}{2i} \tag{4.73}$$

Therefore, the average propagator can be rewritten as

$$\lim_{t\to\infty} G_1(\mathbf{x},\mathbf{x};t,\omega) = \left(\frac{m}{2\pi i\hbar t}\right)^{3/2}(i\omega t)^3 \exp\left[-\frac{3}{4}i\omega t - \frac{iE_0 t}{\hbar} - \frac{\xi t^2}{2\hbar^2}\left(1+\frac{4\hbar}{2m\omega L^2}\right)^{-3/2}\right] \tag{4.74}$$

putting Eq.(4.74) 1into Eq.(4.66), we obtain

$$\begin{aligned} n(E) &= \frac{1}{2\pi\hbar}\int_{-\infty}^{\infty} dt \left(\frac{m}{2\pi i\hbar t}\right)^{3/2}(i\omega t)^3 \exp\left[-\frac{3}{4}i\omega t - \frac{iE_0 t}{\hbar} + \frac{iEt}{\hbar}\right. \\ &\quad \left. -\frac{\xi t^2}{2\hbar^2}\left(1+\frac{4\hbar}{2m\omega L^2}\right)^{-3/2}\right] \end{aligned} \tag{4.75}$$

This integration can be integrated by using a formula [28]

$$\int_{-\infty}^{\infty} dt\,(it)^p \exp\left[-\beta^2 t^2 - iqt\right] = 2^{-p/2}\sqrt{\pi}\beta^{-p-1}\exp\left[\frac{-q^2}{8\beta^2}\right] D_p\left(\frac{q}{\beta\sqrt{2}}\right) \tag{4.76}$$

we can get the density of states in the following equation

$$n(E) = \frac{1}{4}\left(\frac{\sqrt{2}}{\pi}\right)^{1/2}\omega^3\left(\frac{m}{2\pi i\hbar}\right)^{3/2}\beta^{-5/2}\exp\left[\frac{-q^2}{8\beta^2}\right] D_{3/2}\left(\frac{q}{\beta\sqrt{2}}\right) \tag{4.77}$$

where $q = \frac{1}{\hbar}\left(\frac{3}{4}E_\omega + E_0 - E\right)$, $\beta^2 = \frac{1}{2\hbar^2}\xi\left(1+4\frac{E_L}{E_\omega}\right)$, $E_L = \frac{\hbar^2}{2mL^2}$, $E_\omega = \hbar\omega$ and $D_p(z)$ is the parabolic cylinder function. As asymptotic expansions [28]. If $|z| \gg 1$, then

$$D_p(z) \sim e^{-z^2/4}z^p\left(1 - \frac{p(p-1)}{2z^2} + \ldots\right) \tag{4.78}$$

Now we will consider the system that the magnitude of the potential fluctuation ξ is close to 0. By using this consideration,

$$\lim_{\xi \to 0} \left(\frac{q}{\beta\sqrt{2}} \right) \to \infty \tag{4.79}$$

thus

$$\lim_{z \to 0} D_p(z) = e^{-z^2/4} z^p \tag{4.80}$$

Then the density of states becomes

$$n(E) = \left[\left(\frac{E_L}{L} \right)^3 \frac{1}{\xi^2} \right] a(\nu, \chi) \exp\left[-\frac{E_L^2 b(\nu, \chi)}{2\xi} \right] \tag{4.81}$$

where

$$a(\nu, \chi) = \frac{\left(\frac{3}{4}\chi + \nu\right)^{3/2} (4+\chi)^3}{8\sqrt{2}\pi^2} \tag{4.82}$$

and

$$b(\nu, \chi) = \left(\frac{3}{4}\chi + \nu \right)^2 \left(1 + \frac{4}{\chi} \right)^{3/2} \tag{4.83}$$

with $\chi = \frac{E_\omega}{E_L}$ and $\nu = \frac{E_0 - E}{E_L}$. To determine ω, we have to choose χ which maximize the density of states. From (4.81), the exponential term is sensitive to χ. We will maximize this term

$$\frac{\partial b(\nu, \chi)}{\partial \chi} = 0 \tag{4.84}$$

which satisfies equivalently with the following expression.

$$\chi^2 - \chi - 4\nu = 0 \tag{4.85}$$

The solution of Eq.(4.85) thus two roots. Since χ is the ratio of the energy associated with the harmonic oscillator and the energy of fluctuation [29]. We choose only the positive one, $\chi = \left(\sqrt{1+16\nu} - 1\right)/2$. We substitute this root to Eq.(4.82) and Eq.(4.83), so that we have

$$a(\nu) = \frac{1}{2^{12}\sqrt{2}\pi^2}\left(\sqrt{1+16\nu}-1\right)^{3/2}\left(\sqrt{1+16\nu}+7\right)^{9/2} \tag{4.86}$$

$$b(\nu) = \frac{1}{2^8}\left(\sqrt{1+16\nu}-1\right)^{1/2}\left(\sqrt{1+16\nu}+7\right)^{7/2} \tag{4.87}$$

and the density of states

$$n(E) = \left[\left(\frac{E_L}{L}\right)^3 \frac{1}{\xi^2}\right] a(\nu) \exp\left[-\frac{E_L^2\, b(\nu)}{2\xi}\right] \tag{4.88}$$

is obtained.

4.6 The probability of finding ligands

Since we have already determine the parameter (ω) through the density of states, we can evaluate the probability amplitude $G_1(\mathbf{x},\mathbf{x};t)$ by doing the Fourier transforms of $n(E)$

$$G_1(\mathbf{x},\mathbf{x};t) = \int_{-\infty}^{\infty} n(E)\ \exp\left[-\frac{i}{\hbar}Et\right] dE \tag{4.89}$$

Substituting Eq.(4.88) into Eq.(4.89), and setting $\nu = (E_0 - E)/E_L$, we get

$$G_1(\mathbf{x},\mathbf{x};t) = \int_{-\infty}^{\infty} \left[\left(\frac{E_L}{L}\right)^3 \frac{1}{\xi^2}\right] a(\nu) \exp\left[-E_L^2\, b(\nu) - \frac{i}{\hbar}Et\right] dE \tag{4.90}$$

Now letting $\xi'_L = \xi/E_L^2$ and $t' = tE_L/\hbar$. These two parameters are dimensionless. The propagator can be rewritten as

$$G_1(\mathbf{x},\mathbf{x};t) = \frac{1}{L^2}\xi_L'^2 \int_{-\infty}^{\infty} a(\nu) \exp\left[-\frac{b(\nu)}{2\xi'_L} + i\nu t'\right] d\nu \tag{4.91}$$

where $a(\nu)$and $b(\nu)$ are Eq.(4.86) and Eq.(4.87) respectively.

Since Eq.(4.91) can not be integrated analytically, we have to approximate it by using the steepest descent method [17,18].

4.6.1 The steepest descent method

This method is used to determine such asymptotic behavior when the considered function can be expressed as an integral of the general form

$$I(s) = \int_C g(z)\ e^{sf(z)} dz \tag{4.92}$$

where $|s|$ is large compared to 1 and $f(z)$ and $g(z)$ are analytic in the contour C.Redefining $f(z)$, we have

$$f(z) = u(x,y) + iv(x,y) \tag{4.93}$$

We expect that the exponential will be large at the maximum of $u(x,y)$. Next, we deform contour which passes through a point z_c at which $u(x,y)$ is maximum. Since the imaginary term $v(x,y)$ make the contribution of real part small, we

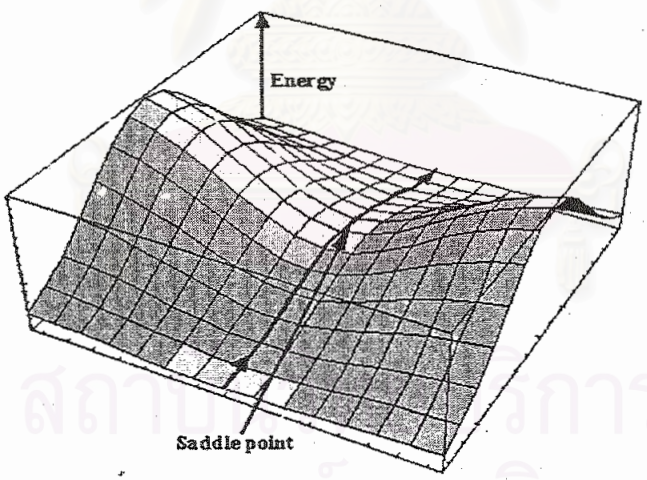


Figure 4.3: The real part and the imaginary part of an analytic function have not the absolute maximum and minimum at saddle point, z_0.

can have

$$\frac{\partial u}{\partial x} + i\frac{\partial v}{\partial x} \equiv \left.\frac{df}{dz}\right|_{z_0} = 0 \tag{4.94}$$

and we can find the saddle point from this equation. This leads to

$$f(z) = f(z_0) + \frac{1}{2}(z - z_0)^2 f''(z_0) \tag{4.95}$$

Finally, Eq.(4.92) can be rewritten as

$$\begin{aligned} I(s) &= \int_C g(z) \exp\left[s\left\{f(z_0) + \frac{1}{2}(z - z_0)^2 f''(z_0)\right\}\right] dz \\ &= \exp[sf(z_0)] \int_C g(z) \exp\left[\frac{s}{2}(z - z_0)^2 f''(z_0)\, dz\right] \end{aligned} \tag{4.96}$$

we use Eq.(4.96) to approximate our result. Before we continue the approximation, we have set $\xi'_L = 1$ for calculating simply. Using these for Eq.(4.91), we get

$$G_1(\mathbf{x}, \mathbf{x}; t) = \frac{1}{L^2} \int_0^\infty a(\nu) \exp\left[\frac{-b(\nu)}{2} + i\nu t'\right] d\nu \tag{4.97}$$

we rewrite it to

$$G_1(\mathbf{x}, \mathbf{x}; t) = \frac{1}{L^2} \int_0^\infty \exp\left[t'\left(\frac{\ln a(\nu)}{t'} - \frac{b(\nu)}{2t'} + i\nu\right)\right] d\nu \tag{4.98}$$

where $t'$is large since we consider our system in large time. Now we have

$$f(\nu) = \frac{\ln a(\nu)}{t'} - \frac{b(\nu)}{2t'} + i\nu \tag{4.99}$$

Find the first derivation of $f(\nu)$

$$f'(\nu) = \frac{1}{t'a(\nu)} \frac{da(\nu)}{d\nu} - \frac{1}{2t'} \frac{db(\nu)}{d\nu} + i \tag{4.100}$$

Find the second derivation of $f(\nu)$

$$f''(\nu) = \frac{1}{t'}\left(\frac{1}{a(\nu)} \frac{d^2a(\nu)}{d\nu^2} - \frac{1}{a^2(\nu)} \frac{da(\nu)}{d\nu}\right) - \frac{1}{2t'} \frac{d^2b(\nu)}{d\nu^2} \tag{4.101}$$

Using Eq.(4.96) and replacing Eq.(4.100) and Eq. (4.101) around the saddle point ν_0, we obtain

$$G_1(\mathbf{x},\mathbf{x};t) = \frac{1}{L^2}\exp\left[\ln a(\nu_0) - \frac{b(\nu_0)}{2} + i\nu_0 t'\right]\int_0^\infty \exp\left[\frac{f''(\nu_0)(\nu-\nu_0)^2 t'}{2}\right]d\nu \tag{4.102}$$

and we consider only the dominant term at large time which is the exponential term so that we get

$$G_1(\mathbf{x},\mathbf{x};t) \approx \frac{1}{L^2}\exp\left[\ln a(\nu_0) - \frac{b(\nu_0)}{2} + i\nu_0 t'\right] \tag{4.103}$$

Now using Eq.(4.94) and Eq.(4.100), we can get ν_0 from the following equation

$$\frac{1}{t'a(\nu)}\frac{da(\nu)}{d\nu} - \frac{1}{2t'}\frac{db(\nu)}{d\nu} + i = 0 \tag{4.104}$$

multiplying t' to Eq.(4.104), we have

$$\frac{1}{a(\nu)}\frac{da(\nu)}{d\nu} - \frac{1}{2}\frac{db(v)}{d\nu} + it' = 0 \tag{4.105}$$

and letting $t'' = it'$, thus

$$-\frac{1}{a(\nu)}\frac{da(\nu)}{d\nu} + \frac{1}{2}\frac{db(v)}{d\nu} = t'' \tag{4.106}$$

We consider $\frac{da(\nu)}{d\nu}$ and $\frac{db(\nu)}{d\nu}$ by using Eq.(4.91) and (4.92)

$$\frac{da(\nu)}{d\nu} = \frac{3\left(\sqrt{1+16\nu}-1\right)^{1/2}\left(7+\sqrt{1+16\nu}\right)^{7/2}}{256\pi\sqrt{2+32\nu}} \tag{4.107}$$

and

$$\begin{aligned}\frac{db(\nu)}{d\nu} &= \frac{7\left(\sqrt{1+16\nu}-1\right)^{1/2}\left(7+\sqrt{1+16\nu}\right)^{5/2}}{64\sqrt{1+16\nu}} \\ &\quad + \frac{\left(7+\sqrt{1+16\nu}\right)^{7/2}}{64\sqrt{1+16\nu}\left(\sqrt{1+16\nu}-1\right)^{1/2}} \\ &= \frac{\left(25+8\nu+7\sqrt{1+16\nu}\right)(-3+\nu)}{2\sqrt{\left(2+4\nu-2\sqrt{1+16\nu}\right)(-3+\nu)}}\end{aligned} \tag{4.108}$$

If we insert Eq.(4.107) and Eq.(4.108) into Eq.(4.106), we have

$$t'' = -\frac{48\sqrt{2}\left(1+\sqrt{1+16\nu}\right)}{\sqrt{2+32\nu}\left(\sqrt{1+16\nu}-1\right)\left(\sqrt{1+16\nu}+7\right)} + \frac{\left(25+8\nu+7\sqrt{1+16\nu}\right)(-3+\nu)}{4\sqrt{\left(2+4\nu-2\sqrt{1+16\nu}\right)(-3+\nu)}} \tag{4.109}$$

Taking the limit of ν

Next we take Eq.(4.109) into two limits as the following:

i) $\nu \ll 1$ Using

$$(1+x)^n = 1 + nx + \frac{n(n-1)}{2!}x^2 + ... \tag{4.110}$$

and keeping only up to the second term. Therefore we have

$$-\frac{3(1+4\nu)}{2\nu(1+8\nu)(1+\nu)} + \frac{(25+8\nu+7(1+8\nu))(-3+\nu)}{4\left((2+4\nu-2(1+8\nu))(-3+\nu)\right)^{\frac{1}{2}}} = t'' \tag{4.111}$$

This equation can be reduced to

$$-\frac{3}{2\nu} + \frac{32(-3)}{4(36\nu)^{1/2}} = t'' \tag{4.112}$$

and we rewrite it again

$$-3 - 8\nu^{1/2} = 2t''\nu \tag{4.113}$$

Let $x = \nu^{1/2}$. Now we have

$$2t''x^2 + 8x + 3 = 0 \tag{4.114}$$

$$x = -2t''^{-1} \pm \frac{\sqrt{16-6t''}}{2t''} \tag{4.115}$$

For large t'', we have

$$\nu^{1/2} \approx -2t''^{-1} \pm \frac{\sqrt{3}}{2}it''^{-1/2} \tag{4.116}$$

We insert Eq.(4.116) into Eq.(4.103) , use the limiting values of $a(\nu) = \frac{32\sqrt{2}\nu^{3/2}}{\pi^2}$ and $b(\nu) = 16\nu^{1/2}$, and consider only real part of propagator. We obtain

$$\mathrm{Re}\, G_1(\mathbf{x},\mathbf{x};t'') \approx \frac{t''^{-2}}{L^2} \exp\left[12t''^{-1}\right] \tag{4.117}$$

and we change variable t'' back to t', $t'' = it'$.

$$\mathrm{Re}\, G_1(\mathbf{x},\mathbf{x};t') \approx \frac{(it')^{-2}}{L^2} \exp\left[12\,(it')^{-1}\right] \tag{4.118}$$

Then the probability is

$$P(\mathbf{x},\mathbf{x},s) \approx \frac{s^{-2}}{L^2} \exp\left[12s^{-1}\right] \tag{4.119}$$

This probability decays as the function s^{-2} at large time.

ii) $\nu \gg 1$ From Eq.(4.109), we obtain

$$t'' = -\frac{48\sqrt{2}\cdot 4\nu^{1/2}}{4\sqrt{2}\nu^{1/2}\cdot 4\nu^{1/2}\cdot 4\nu^{1/2}} + \frac{8\nu^2}{4\sqrt{(4\nu - 8\nu^{1/2})\nu}} \tag{4.120}$$

This equation is reduced to

$$-\frac{3}{\nu} + \nu = t'' \tag{4.121}$$

and we rewrite to

$$\nu^2 - \nu t'' - 3 = 0 \tag{4.122}$$

There are two solutions which are

$$\nu_0 = \begin{cases} \left(t'' + \sqrt{t''^2 + 12}\right)/2 \\ \left(t'' - \sqrt{t''^2 + 12}\right)/2 \end{cases} \tag{4.123}$$

$$\nu_0 \approx t'' \tag{4.124}$$

We insert Eq.(4.124) into Eq.(4.103) and use the limiting values of $a(\nu) = \frac{\sqrt{2}\nu^3}{\pi^2}$ and $b(\nu) = \nu^2$, then our propagator becomes

$$G_1(\mathbf{x},\mathbf{x};t'') \approx \frac{1}{L^2} t''^3 \exp\left[-\frac{t''^2}{2} - t''^2\right] \tag{4.125}$$

and we change variable t'' back to t', $t'' = it'$.

$$G_1(\mathbf{x},\mathbf{x};t') \approx \frac{-it'^3}{L^2}\exp\left[-\frac{3(it')^2}{2}\right] \tag{4.126}$$

Then the probability is

$$\begin{aligned} P(\mathbf{x},\mathbf{x};s) &\approx \frac{-i(-is)^3}{L^2}\exp\left[-\frac{3(s)^2}{2}\right] \\ &= \frac{s^3}{L^2}\exp(-\frac{3s^2}{2}) \end{aligned} \tag{4.127}$$

After we consider the limit of propagator at $\nu << 1$ and $\nu >> 1$, we have the probabilities which depend on the exponential function of time, s^{-2} and $\exp(-s^2)$ respectively.

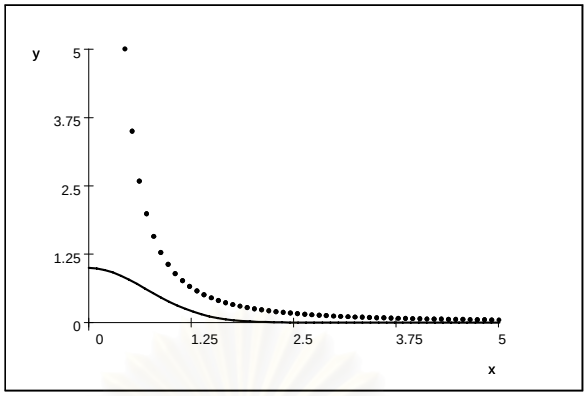
Chapter 5
Disscussion and Conclusion

The problem of a particle moving in randomly distributed traps has been studied in both its theoretical and experimental aspects. Most experimental researchers find the population of substances such as protein and antigen and they know the behavior of the molecules in the biological system. In the mean time, the theoretical researchers try to explain these problems by using different models. Most models come from the diffusion equations which describe the problem classically. Here we tried to find the probability of finding ligand in the system containing randomly distributed traps by using the Feynman path integral method.

Firstly, we gave an introduction about ligand and receptor. This showed how to apply our model with a simple system. Secondly, we reviewed one of the diffusion equation methods (Wiegel's model) to find the population of ligand at large times. This model assumes that ligands must be in the hold (the region without traps) at time $t = 0$ and then they will diffuse to neighboring regions at later times. When they collide with the traps, they will be trapped immediately. From this model, we know that ligands decay according to a fractional exponential function and this is the result for the existence of a large hole, unlike the system having regularly distributed traps. The population in the latter system will decay exponentially. However, many experimental researchers assume that all systems will behave as the latter system.

Next, we used the analogous relation between Schrödinger equation and diffusion equation and applied the Feynman Path Integral method to find the

population of ligands at large times. We assume that the ligands are identical. Therefore, we can study only one ligand in this simple model. In addition, we use the Gaussian random potential to model the real interactions of the system. In addition to Samathiyakanit's trial action, we obtain the average propagator for our system. This propagator, $G(\mathsf{x}_1, \mathsf{x}_2; t)$,means the probability amplitude of the electron moving in randomly distributed traps. In this problem, we have to change some parameters in the propagator in order to get the probability of finding ligands at position x, $P(\mathsf{x}, \mathsf{x}; s)$,for the diffusion equation. These parameters came from the analogous equations. At limit $\nu << 1$, the probability depends on the function, s^{-2} and at the limit $\nu >> 1$, the probability depends on the exponential function, $\exp(-s^{\mathsf{m}})$ which has the exponent $m = 2$. The last limit has the same form of decay as Wiegel [3] but it decays faster than his model. At limit $\nu << 1$, the correlation length, L, is short. This shows that it has the short range potential. It decreases slower than the case which $\nu >> 1$. Therefore we can describe that ligands moving in the short range random potential have the probability to avoid capture by the traps more than the case of long correlation length,$\nu >> 1$. It has a longer time to stay in the system without trapping.



The graph shows the relation between the probability of finding ligand, $P(\mathsf{x}, \mathsf{x}, s)$, versus time, s where the solid line is $\exp(-s^2)$ and the dotted line is s^{-2}.

I have suggestion for the future work. This model can be improved later by changing the interaction to the real one. It depends on the kind of interaction force. Besides, it might be better if we try to use other trial actions. Then we may get the full propagator. In fact, this problem involves both quantum mechanics and statistical mechanics so that it may be explained by using the quantum-statistical method.

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Appendices

Appendix A:
Find correlation function

We define the correlation function $W(\mathrm{x}(\tau)-\mathrm{x}(\sigma))$ as

$$W(\mathrm{x}(\tau)-\mathrm{x}(\sigma)) = \int d\mathrm{R}\; v(\mathrm{x}(\tau)-\mathrm{R})\, v(\mathrm{x}(\sigma)-\mathrm{R}) \qquad \text{(A.1)}$$

where the interaction, $v(\mathrm{x}(\sigma)-\mathrm{R})$, is the Gaussian potential of the following form :

$$v(\mathrm{x}(\tau)-\mathrm{R}) = u\left(\pi l^2\right)^{-3/2} \int d\mathrm{R} \exp\left[-\frac{|\mathrm{x}(\tau)-\mathrm{R}|^2}{l^2}\right] \qquad \text{(A.2)}$$

Thus we can write

$$\begin{aligned} W(\mathrm{x}(\tau)-\mathrm{x}(\sigma)) &= u^2\left(\pi l^2\right)^{-3} \int d\mathrm{R} \exp\left[\frac{-|\mathrm{x}(\tau)-\mathrm{R}|^2-|\mathrm{x}(\sigma)-\mathrm{R}|^2}{l^2}\right] \\ &= u^2\left(\pi l^2\right)^{-3} \exp\left[\frac{-|\mathrm{x}(\tau)|^2-|\mathrm{x}(\sigma)|^2}{l^2}\right] \\ &\quad \times \int d\mathrm{R} \exp\left[\frac{2\mathrm{R}\cdot\mathrm{x}(\tau)+2\mathrm{R}\cdot\mathrm{x}(\sigma)-2\mathrm{R}\cdot\mathrm{R}}{l^2}\right] \qquad \text{(A.3)} \end{aligned}$$

considering the integral term

$$\begin{aligned} &\int_0^{2\pi} d\phi \int_0^{\pi} d\theta \sin\theta \int_0^{\infty} dR\; R^2 \exp\left[\frac{2\mathrm{R}(\mathrm{x}(\tau)+\mathrm{x}(\sigma)-\mathrm{R})}{l^2}\right] \\ &= \int_0^{2\pi} d\phi \int_0^{\infty} dR\; R^2 \exp\left[\frac{-2R^2}{l^2}\right] \int_0^{\pi} d\theta \sin\theta \exp\left[\frac{2|\mathrm{R}|\,|\mathrm{x}(\tau)+\mathrm{x}(\sigma)|\cos\theta}{l^2}\right] \\ &= \frac{\pi l^2}{|\mathrm{x}(\tau)+\mathrm{x}(\sigma)|} \int_0^{\infty} dR\; R \exp\left[\frac{-2R^2}{l^2}\right] \left\{ \begin{array}{c} \exp\left[\frac{2|\mathrm{R}||\mathrm{x}(\tau)+\mathrm{x}(\sigma)|}{l^2}\right] \\ -\exp\left[\frac{-2|\mathrm{R}||\mathrm{x}(\tau)+\mathrm{x}(\sigma)|}{l^2}\right] \end{array} \right\} \\ &= \frac{\pi l^2}{|\mathrm{x}(\tau)+\mathrm{x}(\sigma)|} \int_{-\infty}^{\infty} dR\; R \exp\left[\frac{-2R^2}{l^2}+\frac{2R}{l^2}|\mathrm{x}(\tau)+\mathrm{x}(\sigma)|\right] \qquad \text{(A.4)} \end{aligned}$$

Let

$$y = \frac{2R^2}{l^2} - \frac{2R}{l^2}\left|x(\tau) + x(\sigma)\right|$$

$$dy = \frac{4R}{l^2}dR - \frac{2}{l^2}\left|x(\tau) + x(\sigma)\right| dR$$

$$RdR = \frac{l^2}{4}dy + \frac{1}{2}\left|x(\tau) + x(\sigma)\right| dR \qquad \text{(A.5)}$$

Therefore, we obtain

$$\int_{-\infty}^{\infty} dR\, R \exp\left[\frac{-2R^2}{l^2} + \frac{2R}{l^2}\left|x(\tau) + x(\sigma)\right|\right]$$

$$= \int_{-\infty}^{\infty} \exp[-u]\frac{l^2}{4}dy + \int_{-\infty}^{\infty} dR\frac{1}{2}\left|x(\tau) + x(\sigma)\right| \exp\left[\frac{-2R^2}{l^2} + \frac{2R}{l^2}\left|x(\tau) + x(\sigma)\right|\right]$$

$$= \frac{\left|x(\tau) + x(\sigma)\right|}{2} \exp\left[\frac{\left|x(\tau) + x(\sigma)\right|^2}{2l^2}\right]\sqrt{\frac{\pi l^2}{2}} \qquad \text{(A.6)}$$

substituting Eq.(A.6) into Eq. (A.3), then we get

$$W(x(\tau) - x(\sigma)) = \frac{u^2}{(\pi L^2)^{3/2}} \exp\left[-\frac{\left|x(\tau) + x(\sigma)\right|^2}{L^2}\right] \qquad \text{(A.7)}$$

where $L^2 = 2l^2$

Appendix B:
Fourier Transform of W(x(τ)-x(σ))

We consider the fourier transform of

$$W(\mathrm{x}(\tau)-\mathrm{x}(\sigma)) = u^2\left(\pi L^2\right)^{-\frac{3}{2}}\exp\left(\frac{|\mathrm{x}(\tau)-\mathrm{x}(\sigma)|^2}{L^2}\right) \tag{B.1}$$

and we rewrite it as

$$W(\mathrm{r}) = u^2\left(\pi L^2\right)^{-\frac{3}{2}}\exp\left(\frac{\mathrm{r}^2}{L^2}\right) \tag{B.2}$$

where r is $(\mathrm{x}(\tau)-\mathrm{x}(\sigma))$. Hence

$$\begin{aligned} W(\mathrm{k}) &= \frac{1}{(2\pi)^{\frac{3}{2}}}\frac{u^2}{(\pi L^2)^{\frac{3}{2}}}\int_{-\infty}^{\infty} W(\mathrm{r})\exp(-i\mathrm{k}.\mathrm{r})\,d\mathrm{r} \\ &= \frac{2\pi u^2}{(2\pi^2L^2)^{\frac{3}{2}}}\int_0^{\infty} dr\; r^2 W(\mathrm{r})\exp\left(-\frac{r^2}{L^2}\right)\int_0^{\pi} d\theta\sin\theta\exp(-ikr\cos\theta) \\ &= \frac{2\pi u^2}{(2\pi^2L^2)^{\frac{3}{2}}}\int_0^{\infty} dr\; r\exp\left(-\frac{r^2}{L^2}\right)\left(\frac{\exp(-ikr)-\exp(ikr)}{-ik}\right) \end{aligned} \tag{B.3}$$

Considering the integral term

$$\int_0^{\infty} drr\exp\left(-\frac{r^2}{L^2}-ikr\right) = \int_0^{\infty} dr\; r\exp\left[-\frac{1}{L}\left(r+\frac{ikL^2}{2}\right)^2-\frac{k^2L^2}{4}\right]dr \tag{B.4}$$

giving

$$y = \left(r+\frac{ikL^2}{2}\right)\frac{1}{L} \tag{B.5}$$

and $dr = Ldy$. Thus we obtain

$$\begin{aligned} &\int_0^{\infty} dyL\left(Ly-\frac{ikL^2}{2}\right)\exp\left[-y^2-\frac{k^2L^2}{4}\right] \\ &= L\exp\left[-\frac{k^2L^2}{4}\right]\int_0^{\infty}\left(Lye^{-y^2}-\frac{ikL^2}{2}e^{-y^2}\right)dy \\ &= \exp\left[-\frac{k^2L^2}{4}\right]\left[\frac{L^2}{2}-\frac{ikL^3\sqrt{\pi}}{4}\right] \end{aligned} \tag{B.6}$$

and

$$\int_0^\infty dr\ r \exp\left(-\frac{r^2}{L^2} + ikr\right) = \exp\left[-\frac{k^2L^2}{4}\right]\left[\frac{L^2}{2} + \frac{ikL^3\sqrt{\pi}}{4}\right] \qquad \text{(B.7)}$$

If we change variable r to $-r$, we will get

$$\begin{aligned}\int_0^{-\infty} dr\ (-r) \exp\left(-\frac{r^2}{L^2} - ikr\right) &= \int_{-\infty}^0 dr\ r \exp\left(-\frac{r^2}{L^2} - ikr\right) \\ &= \exp\left[-\frac{k^2L^2}{4}\right]\left[\frac{L^2}{2} + \frac{ikL^3\sqrt{\pi}}{4}\right] \qquad \text{(B.8)}\end{aligned}$$

We combine Eq.(B.6) and Eq. (B.8). Then we have

$$W(k) = \frac{u^2}{(2\pi)^{\frac{3}{2}}} \exp\left[-\frac{k^2L^2}{4}\right] \qquad \text{(B.9)}$$

Appendix C:
Cumulant Expansion

We approximate $\langle \exp[i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma))]\rangle_{S_\theta(\omega)}$ by using cumulant expansion,

$$\langle \exp[a]\rangle = \exp\left[\langle a\rangle + \frac{1}{2!}\left(\langle a^2\rangle - \langle a\rangle^2\right) + \frac{1}{3!}[\ldots] + \ldots\right] \tag{C.1}$$

Considering only up to the second order, we therefore have

$$\begin{aligned}\langle \exp[i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma))]\rangle \;=\; \exp\Big[&\langle i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\rangle + \frac{1}{2!}\left\{\left\langle (i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma)))^2\right\rangle\right. \\ &\left.-\langle i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\rangle^2\right\}\Big]\end{aligned} \tag{C.2}$$

We seperate (C.2) into 3 terms and consider firstly in the first term

$$a_1 = \langle i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\rangle = i\mathbf{k}\cdot\langle(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\rangle \tag{C.3}$$

and

$$\begin{aligned}\left\langle (i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma)))^2\right\rangle \;=\; &-\frac{\mathbf{k}^2}{3}\left\langle(\mathbf{x}(\tau)-\mathbf{x}(\sigma))^2\right\rangle \\ &-2k_xk_y\left\langle(x_x(\tau)-x_x(\sigma))\,(x_y(\tau)-x_y(\sigma))\right\rangle \\ &-2k_xk_z\left\langle(x_x(\tau)-x_x(\sigma))\,(x_z(\tau)-x_z(\sigma))\right\rangle \\ &-2k_yk_z\left\langle(x_y(\tau)-x_y(\sigma))\,(x_z(\tau)-x_z(\sigma))\right\rangle\end{aligned} \tag{C.4}$$

and the last term is

$$\begin{aligned}\langle(i\mathbf{k}\cdot(\mathbf{x}(\tau)-\mathbf{x}(\sigma)))\rangle^2 \;=\; &-\mathbf{k}^2\langle\mathbf{x}(\tau)-\mathbf{x}(\sigma)\rangle^2 \\ &+2k_xk_y\left\langle x_x(\tau)-x_x(\sigma)\right\rangle\left\langle x_y(\tau)-x_y(\sigma)\right\rangle \\ &+2k_xk_z\left\langle x_x(\tau)-x_x(\sigma)\right\rangle\left\langle x_z(\tau)-x_z(\sigma)\right\rangle \\ &+2k_yk_z\left\langle x_y(\tau)-x_y(\sigma)\right\rangle\left\langle x_z(\tau)-x_z(\sigma)\right\rangle\end{aligned} \tag{C.5}$$

From (C.3) and (C.4), we give

$$C_x = x_x(\tau) - x_x(\sigma) \tag{C.6}$$

$$C_y = x_y(\tau) - x_y(\sigma) \tag{C.7}$$

$$C_Z = x_z(\tau) - x_z(\sigma) \tag{C.8}$$

Therefore, we have

$$\begin{aligned} & \left\langle (i\mathbf{k}\cdot(\mathbf{x}(\tau) - \mathbf{x}(\sigma)))^2 \right\rangle - \left\langle (i\mathbf{k}\cdot(\mathbf{x}(\tau) - \mathbf{x}(\sigma))) \right\rangle^2 \\ = & -\frac{\mathbf{k}^2}{3}\left\langle (\mathbf{x}(\tau) - \mathbf{x}(\sigma))^2 \right\rangle + \mathbf{k}^2 \left\langle x(\tau) - x(\sigma) \right\rangle^2 - 2k_x k_y \left[\langle C_x C_y \rangle - \langle C_x \rangle \langle C_y \rangle\right] \\ & -2k_x k_z \left[\langle C_x C_z \rangle - \langle C_x \rangle \langle C_z \rangle\right] - 2k_y k_z \left[\langle C_y C_z \rangle - \langle C_y \rangle \langle C_z \rangle\right] \\ = & -\frac{\mathbf{k}^2}{3}\left\langle (\mathbf{x}(\tau) - \mathbf{x}(\sigma))^2 \right\rangle + \mathbf{k}^2 \left\langle x(\tau) - x(\sigma) \right\rangle^2 \end{aligned} \tag{C.9a}$$

where

$$\langle C_x C_y \rangle = \langle C_x C_z \rangle = \langle C_y C_z \rangle = 0 \tag{C.10}$$

See Feynman and Hibbs (p.178)[1]. Hence we have

$$a_2 = -\frac{1}{2}\mathbf{k}^2 \left[\frac{1}{3}\left\langle (\mathbf{x}(\tau) - \mathbf{x}(\sigma))^2 \right\rangle - \left\langle x(\tau) - x(\sigma) \right\rangle^2\right] \tag{C.11}$$

Appendix D:
Find trial action

In this appendix, we find $S_{0,cl}^{f}$ and $S_{0,cl}$ which are used to evaluate $\langle \mathbf{x}(\tau)\rangle_{S(0)}$ and $\langle \mathbf{x}(\tau)\mathbf{x}(\sigma)\rangle_{S_0(\omega)}$. In order to obtain $S_{0,cl}^{f}$ and $S_{0,cl}$, we have to find the classical path by working a variation on $S_0^f(\omega)$

$$\begin{aligned} S_0^f(\omega) &= \int_0^t d\tau\ L(\dot{\mathbf{x}}(\tau), \mathbf{x}(\tau), t) + \int_0^t \mathbf{f}(\tau)\cdot\mathbf{x}(\tau)\,d\tau \\ &= \int_0^t d\tau \left[\frac{m}{2}\dot{\mathbf{x}}^2(\tau) - \frac{m}{2}\left(\frac{\omega^2}{2t}\right)\int_0^t d\sigma\,|\mathbf{x}(\tau)-\mathbf{x}(\sigma)|^2 + \mathbf{f}(\tau)\cdot\mathbf{x}(\tau)\right] \end{aligned} \tag{D.1}$$

At the extremum point,

$$\begin{aligned} \delta S_0^f(\omega) &= \int_0^t d\tau \left[m\dot{\mathbf{x}}(\tau)\,\delta\dot{\mathbf{x}}(\tau) + \mathbf{f}(\tau)\cdot\delta\mathbf{x}(\tau)\right. \\ &\qquad \left. -\frac{m\omega^2}{2t}\int_0^t d\sigma\,(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\cdot\delta(\mathbf{x}(\tau)-\mathbf{x}(\sigma))\right] \end{aligned} \tag{D.2}$$

where $\delta\dot{\mathbf{x}}(\tau) = \delta\left[\frac{d\mathbf{x}(\tau)}{dt}\right] = \frac{d\delta\mathbf{x}(\tau)}{dt}$ and $\delta\mathbf{x}(t) = \delta\mathbf{x}(0) = 0$. Thus

$$\delta S_0^f(\omega) = -\int_0^t d\tau \left[m\ddot{\mathbf{x}}(\tau) + \frac{m\omega^2}{t}\int_0^t d\sigma\,(\mathbf{x}(\tau)-\mathbf{x}(\sigma)) - \mathbf{f}(\tau)\right]\cdot\delta\mathbf{x}(\tau) = 0 \tag{D.3}$$

Therefore, we can obtain a classical equation

$$\ddot{\mathbf{x}}_c(\tau) + \omega^2\mathbf{x}_c(\tau) = \frac{\omega^2}{t}\int_0^t d\sigma\mathbf{x}_c(\sigma) + \frac{\mathbf{f}(\tau)}{m} \tag{D.4}$$

and we can solve Eq.(D.4) by using the Green function

$$g(\tau,\sigma) = -\frac{1}{\omega \sin \omega t}\left[\sin\omega(t-z)\sin\omega\sigma\ \Theta(\tau-\sigma) + \sin\omega(t-\sigma)\sin\omega\tau\ \Theta(\sigma-\tau)\right] \tag{D.5}$$

where Θ is the Heaviside step function and we use the boundary condition $x(0) = x_1$and $x(t) = x_2$. From Eq.(D.4), we use Eq.(D.5) and get

$$x_c(\tau) = x_h(\tau) + \int_0^t \left[\frac{\omega^2}{t}\int_0^t d\sigma' x_c(\sigma') + \frac{f(\sigma')}{m}\right] g(\tau,\sigma)\, d\sigma \tag{D.6}$$

where $x_h(\tau)$ is the homogenous solution of Eq.(D.4). Integrating both sides of Eq.(D.6) and adding the same term together, we obtain

$$\int_0^t d\sigma x_c(\tau) = \frac{1}{1-\frac{\omega^2}{t}\int_0^t d\tau\int_0^t d\sigma g(\tau,\sigma)}\left[\int_0^t x_h(\tau)\,d\tau + \int_0^t d\sigma\int_0^t d\tau\frac{f(\sigma)}{m}g(\tau,\sigma)\right] \tag{D.7}$$

$$= \frac{t}{2\sin\omega t/2}\left[(x_1+x_2)\sin\frac{\omega t}{2} + \frac{2}{m\omega}\int_0^t f(\sigma)\left(\sin\frac{\omega\sigma}{2}\sin\frac{\omega(\sigma-\tau)}{2}\right)d\sigma\right] \tag{D.8}$$

and

$$\int_0^t d\sigma\int_0^t d\tau\frac{f(\sigma)}{m}g(\tau,\sigma) = \frac{2}{m\omega^2\cos\omega t/2}\int_0^t d\sigma f(\sigma)\left(\sin\frac{\omega\sigma}{2}\sin\frac{\omega(\sigma-\tau)}{2}\right) \tag{D.9}$$

Substituting Eq.(D.8) and Eq.(D.9) into Eq.(D.6), we have

$$\begin{aligned} x_c(\tau) &= \frac{1}{\sin\omega t}\left(x_2\sin\omega\tau + x_1\sin\omega(t-\tau)\right) - \frac{2}{\sin\omega t}\left(\sin\frac{\omega\tau}{2}\sin\frac{\omega(t-\tau)}{2}\right) \\ &\quad\times\left[(x_2+x_1)\sin\frac{\omega t}{2} - \frac{2}{m\omega}\int_0^t d\sigma f(\sigma)\left(\sin\frac{\omega\sigma}{2}\sin\frac{\omega(\tau-\sigma)}{2}\right)\right] \\ &\quad+\int_0^t \frac{f(\sigma)}{m}g(\sigma,\tau)\,d\sigma \end{aligned} \tag{D.10}$$

The forced classical trial action $S^f_{s,cl}(\mathbf{x}_2, \mathbf{x}_1; t, \omega)$ is obtained by substituting Eq.(D.10) into the expression

$$S^f_{0,cl}(\mathbf{x}_2, \mathbf{x}_1; t, \omega) = S_{0,cl}(\mathbf{x}_2, \mathbf{x}_1; t, \omega) + \int_0^t d\tau\ \mathbf{f}(\tau)\, \mathbf{x}_c(\tau) \qquad \text{(D.11)}$$

which we have

$$\begin{aligned} S^f_{0,cl}(\mathbf{x}_2, \mathbf{x}_1; t, \omega) &= \frac{m}{2}\left[\int_0^t d\tau\ \dot{\mathbf{x}}_c^2(\tau) - \frac{\omega^2}{2t}\int_0^t d\tau \int_0^t d\sigma\, |\mathbf{x}(\tau) - \mathbf{x}(\sigma)|^2 \right. \\ &\quad \left. + \int_0^t d\tau\ \mathbf{f}(\tau)\, \mathbf{x}_c(\tau)\right] \\ &= \frac{m}{2}\left[\dot{\mathbf{x}}_c(\tau)\, \mathbf{x}_c(\tau) - \dot{\mathbf{x}}_c(0)\, \mathbf{x}_c(0)\right] + +\frac{1}{2}\int_0^t d\tau\ \mathbf{f}(\tau)\, \mathbf{x}_c(\tau) \end{aligned} \qquad \text{(D.12)}$$

Thus, we get

$$\begin{aligned} S^f_{0,cl}(\mathbf{x}_2, \mathbf{x}_1; t, \omega) &= \frac{m\omega}{4}\cot\frac{\omega t}{2}\,|\mathbf{x}_2 - \mathbf{x}_1|^2 \\ &\quad + \frac{m\omega}{2\sin\omega t}\left[\frac{2\mathbf{x}_2}{m\omega}\int_0^t d\tau\ \mathbf{f}(\tau)\left(\sin\omega\tau - 2\sin\frac{\omega t}{2}\sin\frac{\omega}{2}(t-\tau)\sin\frac{\omega\tau}{2}\right)\right. \\ &\quad + \frac{2x_1}{m\omega}\int_0^t d\tau\ \mathbf{f}(\tau)\left(\sin\omega(t-\tau) - 2\sin\frac{\omega t}{2}\sin\frac{\omega}{2}(t-\tau)\sin\frac{\omega\tau}{2}\right) \\ &\quad - \frac{2}{m^2\omega^2}\int_0^t d\tau\int_0^t d\sigma \mathbf{f}(\tau)\,\mathbf{f}(\sigma)\left\{\sin\omega(t-\tau)\sin\omega\sigma\right. \\ &\quad \left.\left. -4\sin\frac{\omega}{2}(t-\tau)\sin\frac{\omega\tau}{2}\sin\frac{\omega}{2}(t-\sigma)\sin\frac{\omega\sigma}{2}\right\}\right] \end{aligned} \qquad \text{(D.13)}$$

By means of Eq.(D.11), the classical trial action $S_{0,cl}$ can be obtained if we set $\mathbf{f}(\tau)$ equals zero. Hence, we find

$$S_{0,cl}(\mathbf{x}_2, \mathbf{x}_1; t, \omega) = \frac{1}{2}m\omega\cot\frac{\omega t}{2}\,|\mathbf{x}_2 - \mathbf{x}_1|^2 \qquad \text{(D.14)}$$

Vitae

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