



University of Indonesia

**Nonlinear Dynamics and Statistical
Mechanics of Secondary Protein
Folding**

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Originality Declaration Page

This skripsi is my own work, and all the sources which are cited and referenced have been declared correctly.

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And when the prayer has been concluded, disperse within the land and seek from the bounty of Allah, and remember Allah often that you may succeed.

(Q. S. Al-Jumu'ah 10)

Science is simply common sense at its best.

Thomas Huxley

If it's green or wriggles, it's biology.

If it stinks, it's chemistry.

If it doesn't work, it's physics.

Handy Guide to Science

To be a great scientist, there are a lot of sacrifices that have to be made.

Max Planck, in Einstein and Eddington's Movie



Preface

A biophysicist talks physics to the biologists and biology to the physicists, but then he meets another biophysicist, they just discuss women.

Anonymous

At one time in the year 2010 (I forget the date and month) in the lab theory, Andi told me that there is someone who ask him about his skripsi; Ndi, why is your skripsi mathematics? And then Andi asked me; Why is your skripsi biology, Jan? We laughed uproariously at that time. We are in *Nuclear and Particle Physics Group* but we worked on the outside fields. Nevertheless, I still use the tools, such as; quantum relativistic, quantum field theory, theory group, and etc., which are only gotten in the group. I just applied those to explain the dynamics of bio-matters, such as protein, DNA, and etc. Hopefully it opens a new breakthrough in research of *Theoretical Biophysics*, so that the scientists can treat the cases from the different point of views.

Depok, June 2011



Moch. Januar

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Abstract

A model to describe the mechanism of conformational dynamics in protein based on matter interactions using lagrangian approach and imposing certain symmetry breaking is proposed. Both conformation changes of proteins and the injected non-linear sources are represented by the bosonic lagrangian with an additional ϕ^4 interaction for the sources. The path integral method is used to calculate its statistical mechanic properties.

Keywords: protein folding, model, nonlinear, path integral, ϕ^4 interaction
ix+77 pp.; appendices.

References: 32 (1965-2011)

Abstrak

Diajukan sebuah model yang menjelaskan mekanisme pembentukan gerak pada protein berdasarkan interaksi-interaksi materi dengan menggunakan pendekatan lagrangian dan perusakan simetri. Perubahan bentuk protein dan sumber non-linier yang disuntikan direpresentasikan oleh lagrangian boson dengan tambahan interaksi ϕ^4 sebagai sumber gangguan. Metode *path integral* digunakan untuk menghitung sifat mekanika statistik-nya.

Kata kunci: pelipatan protein, model, non-linier, path integral, interaksi ϕ^4
ix+77 hlm.; lamp.

Daftar Acuan: 32 (1965-2011)

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Chapter 1

Introduction

Has there (not) come upon man a period of time when he was not a thing (even) mentioned?

Indeed, We created man from a sperm-drop mixture that We may try him; and We made him hearing and seeing.

(Q. S. Al-Insan 1-2)

1.1 Background and Scope of Problem

Did you know about protein? Protein is a macro molecule that has essential role for living things. Organisms need protein in almost of all its activities. For example, the protein acts as a hormone that transmits information between cells and organs, serves as a defense against infections, controls the expression of genes, forms a large molecular organelles such as ribosome, and many other activities. Moreover, even the protective layer of a virus is also protein. In other words, every living organism cannot be separated from the protein [1].

To understand biological processes of an organism, the sequence of proteins must be known. From protein bio-synthesis, the pathway of proteins are determined by the sequences of its amino acid constituents, and this prediction has been known as the *protein folding problem* [2].

The research about protein folding mechanism is very important. It is known that the protein mis-folding has been identified as the main cause of several diseases like cancers and so on [3]. The mis-folding proteins cannot

function essentially in biological processes, or in other words, these proteins are broken. It will accumulate and form a new species which are toxic. Then can lead to genetic mutations, weakening of the immune system and also can cause many kind of diseases. The diseases that are caused by protein folding faulty have been classified in a group that was called *Protein Conformational Disorders* (PCDs). The various kinds of diseases in PCDs are including Alzheimer's disease (AD), haemolytic anemia, transmissible spongiform encephalopathies (TSEs), serpin-deficiency disorders, Huntington's disease (HD), cystic fibrosis, diabetes type II, amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), dialysis-related amyloidosis and more than 15 other diseases including cancers [4].

Unfortunately, our understanding on the underlying folding mechanism has not been at the satisfactory level. The main mechanism responsible for a structured folding pathway have not yet been identified at all. These lead the protein folding problem becomes one of the most important issues of modern science [2].

Seeing the above-mentioned importance cases, various models of the dynamics of protein folding have been made. Many approaches are done to describe the protein folding phenomenon. Recently, a toy model of protein folding that mediated by soliton has been proposed [5]. Further, Mingaleev *et.al.* have shown that the nonlinear excitations play an important role in conformational dynamics by decreasing the effective bending rigidity of a biopolymer chain leading to a buckling instability of the chain [6]. Following this understanding, a model to explain the transition of a protein from a metastable to its ground conformation induced by solitons has been proposed [7]. In the model the mediator of protein transition is the Davydov solitons propagating through the protein backbone. Moreover, using analogous style with the mentioned models, a lot of nonlinear models of DNA have been developed [8, 9].

At present, the most reliable theoretical explanation for this kind of the conformational dynamics of biomolecules is the so-called *ab initio* quantum chemistry approach. This however requires astronomical computational power to deal with realistic biological systems [10, 11]. In contrary, there are some

phenomenological model describing the folding pathway as a result of the interplay between the energy transfer from a solitary solution that travels along the protein backbone and string tension [12].

This work follows the later approach, but starting from the first principle using the lagrangian method to derive the responsible interactions and to clarify its origins. The folding pathway is modeled as consequence of existence of nonlinear sources (soliton) which are induced into the protein backbone. All the interactions among the nonlinear sources and protein backbone would be modeled by ϕ^4 self-interactions. Furthermore, its statistical mechanics properties would be obtained using path integral method [13]. The semi-classical expansions will be used in order to separate between the classical and quantum aspects of the fields [14].

Investigating the dynamical of protein folding hopefully can obtain knowledges which have good contribution to the health of the common society.

1.2 Research Aim

This research has main aim to review the nonlinear dynamics of secondary protein structure. This work is modeling the conformational changes of the backbone which leads transition process of protein from the unfolded state which looks like string into the secondary folded form which looks like a spiral (*alpha helix*). To support the model, its statistical mechanics properties would be shown by using path integral approach.

1.3 Research Method

This research is theoretics based on Lagrangian formulation [15]. The lagrangian is used to represent all the responsible interactions which is predicted by this model, and then certain symmetry breaking will be involved.

In the model, the involved interactions are imposing nonlinear terms that would produce nonlinear equation of motions (EOMs). So that, it is more convenient to solve it numerically using forward finite difference method [16,

17]. The numerical simulation will be obtained with the help of computational softwares, that is; MATLAB and Maple.

Furthermore, path integral method will be used in order to calculate the partition function of the system. This attempt is important to find statistical mechanics properties of occurred interactions in the folding process [18, 19].



Chapter 2

Fundamental Concepts

"You cannot teach a man anything; you can only help him find it within himself."

Galileo Galilei

2.1 Quantum Field Theory

Quantum field theory is a unification of special relativity and quantum mechanics. This theory formed the framework of the standard model in particle physics [15]. Mathematical foundation in quantum field theory is the formulation of *lagrangian*. One can observe a system by looking from its lagrangian. Afterwards, by using Euler-Lagrange equation, the relevant equation of motion of the system can be obtained. And many more works can be done from the lagrangian.

It will be cleared by considering properties of the lagrangian deeply. If the field $\phi(x)$ has a kinetic energy T and the potential V , then lagrangian is

$$L = T - V . \quad (2.1)$$

In the continuous case, actually it should be worked by using density of the lagrangian \mathcal{L}

$$L = T - V = \int d^3x \mathcal{L} . \quad (2.2)$$

Integration the lagrangian over the time gives a new important quantity

namely *action* S

$$S = \int dt L . \quad (2.3)$$

Action is functional because the action always takes functions as arguments and produces a number. Particles always take the path with the smallest action. To find the path, then the variation of the action should be minimized. This is done by describing the action as the minimum term and a variation term.

$$S \longrightarrow S + \delta S . \quad (2.4)$$

The action is minimum if satisfied

$$\delta S = 0 . \quad (2.5)$$

In quantum field theory, lagrangian density is used more often, then the equation for the action will be written as

$$S = \int d^4x \mathcal{L} . \quad (2.6)$$

For the sake of abbreviation, the lagrangian density \mathcal{L} is often called just *Lagrangian*.

This is an example of a lagrangian for a free scalar particle

$$\mathcal{L} = \frac{1}{2}(\partial_\mu \phi)(\partial^\mu \phi) - \frac{1}{2}m^2 \phi^2 . \quad (2.7)$$

The first term is the kinetic energy (containing $(\partial\phi)^2$) and the second one is the mass term of the field (containing ϕ^2).

2.1.1 U(1) Symmetry

In quantum field theory, one learned that any theory is built on a certain symmetry. The theory must be invariant against the transformation of *gauge* global and local levels of symmetry are built. If the theory is invariant, then all the produced physical quantities have value which does not depend on the inertial reference frame where it was measured.

The above statement implies that the lagrangian which is made in a theory must be invariant to a certain symmetry. In field theory, global and local gauge symmetry are often used to build a model. Global *gauge* transformation has form

$$\phi \rightarrow e^{i\theta} \phi, \quad (2.8)$$

where θ is constant.

Meanwhile local *gauge* has form

$$\phi \rightarrow e^{i\alpha(x)} \phi, \quad (2.9)$$

where $\alpha(x)$ is a space-time function.

To see the invariance of the two transformations above, consider the following lagrangian

$$\mathcal{L} = \frac{1}{2}(\partial_\mu \phi)(\partial^\mu \phi) - \frac{1}{2}m^2 \phi^2. \quad (2.10)$$

It was clear that the above lagrangian invariant against global transformation but not for local transformation. First term of the lagrangian is not invariant to local gauge transformation. To make the lagrangian invariant, the derivative operator ∂_μ must be modified become covariant derivative D_μ and a new gauge field should be introduced.

Unfortunately, the author wont explain this symmetry problem further, since it did not relevant to the our model. More details explanation can be seen in [15].

2.1.2 Spontaneous Symmetry Breaking

One of more interesting idea in quantum field theory is symmetry breaking. This concept can be related to the parity symmetry [15, 20]. Consider the lagrangian as follow

$$\mathcal{L} \equiv T - V = \frac{1}{2}(\partial\phi)^2 - \left(\frac{1}{2}\mu^2\phi^2 + \frac{1}{4}\lambda\phi^4\right), \quad (2.11)$$

with $\lambda > 0$. The lagrangian is invariant to the parity transformation ϕ to $-\phi$. to describe scalar field with mass μ . The ϕ^4 -term represents self-interaction of the field with a coupling constant λ .

The two possible potential has been shown in Fig. (2.1). The left figure (a) for $\mu^2 > 0$ Ground state (vacuum) is $\lambda = 0$. This state obeys parity symmetry of the lagrangian. Meanwhile, the more interesting case is located in the right side (b) for $\mu^2 < 0$. Now, the lagrangian in Eq. (2.11) has a mass term with the wrong sign for the field ϕ , as a sign of the relative term ϕ^2 by the kinetic energy T is a positive (it is should be negative). Unlike the case of (a), in case (b) the potential has two minimum values.

These minimum values satisfy

$$\frac{\partial V}{\partial \phi} = \phi(\mu^2 + \lambda\phi^2) = 0 \quad (2.12)$$

and is located on

$$\phi = \pm\nu \quad \text{with} \quad \nu = \sqrt{\frac{-\mu^2}{\lambda}} \quad (2.13)$$

Extreme value of $\phi = 0$ is not a state with minimum energy. $\phi = 0$ is an unstable situation (see Figure 2.1), the situation can be shifted to one of two other minimum conditions, where $\phi = +\nu$ or $\phi = -\nu$, which are the actual ground states. However, choosing one of these conditions would break the symmetry.

In the case of lagrangian (2.11), note that the actual minimum is at $\phi = \pm\nu$. The value $\phi = 0$ is not stable, then the perturbation expansion of this point is not convergent. Thus, perturbation expansion must be made to the $\phi = +\nu$ or $\phi = -\nu$. So that, $\phi(x)$ can be written as,

$$\phi(x) = \nu + \eta(x), \quad (2.14)$$

with $\eta(x)$ represents the quantum fluctuations to a minimum. In this case, $\phi = +\nu$ is chosen, but it wont lost its generality, since the $\phi = -\nu$ can

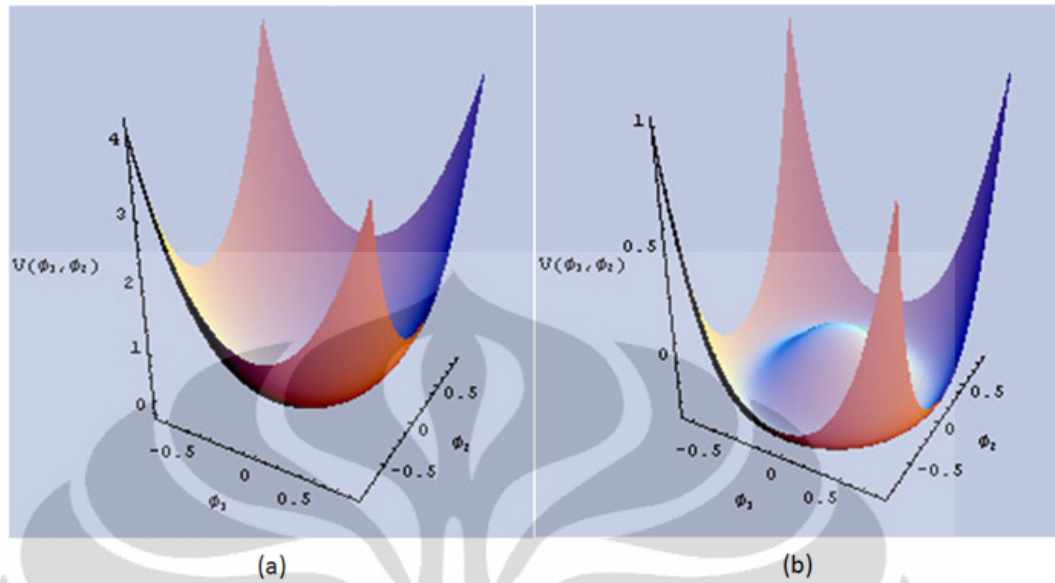


Figure 2.1: Potential $V(\phi) = \frac{1}{2}\mu^2\phi^2 + \frac{1}{4}\lambda\phi^4$ with $\lambda > 0$ for (a) $\mu^2 > 0$ and (b) $\mu^2 < 0$.

always be generated from the reflection symmetry. Substitution (2.14) into the lagrangian (2.11) obtains,

$$\mathcal{L}' = \frac{1}{2}(\partial\eta)^2 - \lambda\nu^2\eta^2 - \lambda\nu\eta^3 + \frac{1}{4}\lambda\eta^4 + const. \quad (2.15)$$

Field η has a mass term with the correct sign because the sign of the η^2 relative to the kinetic energy is negative. Comparing the first two terms in the lagrangian (2.7) will obtained,

$$m_\eta = \sqrt{2\lambda\nu^2} = \sqrt{-2\mu^2}. \quad (2.16)$$

Meanwhile, the higher order of η represents its self-interaction.

There is confusion here. Lagrangian \mathcal{L} of the Eq. (2.11) and \mathcal{L}' the Eq. (2.15) are equivalent. The transformation (2.14) is not possible to change the physical meaning. If the two Lagrangian can be solved exactly, they should produce identical physics. But in particle physics, the exact calculation is difficult, instead perturbation theory is usually used and the fluctuations is calculated around the minimum energy. If \mathcal{L} is used, perturbation series will not converge as the expansion is around the unstable point $\phi = 0$. So using

\mathcal{L}' and the expansion is done in η in the vicinity of the stable point $\phi = +\nu$. In perturbation theory, \mathcal{L}' give a true picture of physics, while \mathcal{L} is not. Thus, scalar particles (described by the Lagrangian \mathcal{L} and \mathcal{L}' are equivalent in principle) should be had a mass.

This method is often called "spontaneous symmetry breaking." In theory version of the \mathcal{L}' , the reflection symmetry of the Lagrangian has been damaged with a choice of ground state $\phi = +\nu$ (instead of $\phi = -\nu$). Often, this method is used to "arouse the mass" of a field.

2.2 Solitary Wave: Soliton

Besides of the quantum field theory and its symmetry, this work will obey some properties of soliton. The interactions are represented by bosonic ϕ^4 -interaction and Sine-Gordon potential which, of course, will produce sequences of nonlinear equation of motions. Its solutions can be approached using traveling solution. This solution benefits one of the properties of solitary wave (soliton).

In this section, some examples of finding the traveling solution of a nonlinear PDE can be explained briefly. It use some analogies with the Korteweg and deVries (KdV) method [21, 22].

2.2.1 Sine-Gordon EOM

Taking into consideration the Sine-Gordon equation of motion (EOM) as follows,

$$\begin{aligned} \square\phi + \frac{1}{b} \sin(b\phi) &= 0 \\ \phi_{tt} - \phi_{xx} + \frac{1}{b} \sin(b\phi) &= 0, \end{aligned} \quad (2.17)$$

where b is an arbitrary constant. To have a traveling solution, the two dimensional space and time coordinates should be reduced into one degree of

freedom with certain velocity,

$$\phi(x, t) = \phi(x - vt) = \phi(z) . \quad (2.18)$$

Then the derivatives can be written as,

$$\phi_t = \frac{\partial \phi}{\partial z} \frac{\partial z}{\partial t} = -v \phi_z , \quad (2.19)$$

$$\phi_{tt} = v^2 \phi_{zz}, \text{ and } \phi_{xx} = \phi_{zz} . \quad (2.20)$$

Thus, the PDE in Eq. (2.17) is changed into an ODE,

$$(v^2 - 1)\phi_{zz} + \frac{1}{b} \sin(b\phi) = 0 . \quad (2.21)$$

Assume $(v^2 - 1) = a$ for abbreviation the notation, and then times the equation with ϕ_z ,

$$\begin{aligned} a\phi_{zz}\phi_z + \frac{1}{b} \sin(b\phi)\phi_z &= 0 \\ \frac{a}{2} \frac{d\phi_z^2}{dz} - \frac{1}{b^2} \frac{d}{dz} (\cos(b\phi)) &= 0 \\ \frac{d}{dz} \left(\frac{a}{2} \phi_z^2 - \frac{1}{b^2} \cos(b\phi) \right) &= 0 . \end{aligned} \quad (2.22)$$

By integrating the last above equation in term of z , and assuming $\lim_{x \rightarrow 0} \phi = 0$ to vanish the integral constants, thus obtains,

$$\begin{aligned} \frac{a}{2} \phi_z^2 &= \frac{1}{b^2} \cos(b\phi) \\ \frac{d\phi}{dz} &= \sqrt{\frac{2}{ab^2} \cos(b\phi)} \\ \int \frac{d\phi}{\sqrt{\cos(b\phi)}} &= \sqrt{\frac{2}{ab^2}} \int dz . \end{aligned} \quad (2.23)$$

$$(2.24)$$

The left side integral can be solved by utilizing properties of the elliptic integral [23] from 0 to ϕ_0 , and the right one can be integrated directly from 0 to z . By integrating the both side integrals and inverting, the traveling solution for the

Sine-Gordon is obtained as [15],

$$\phi(x - vt) = \frac{4}{b} \arctan \left(\exp \left[\pm \left(\frac{\gamma}{\sqrt{b}} (x - vt) \right) \right] \right), \quad (2.25)$$

where $\gamma = (1 - v^2)^{-\frac{1}{2}}$. The positive sign in the solution is called *kink* soliton and the negative one is called *antikink* soliton.

2.2.2 Nonlinear Klein-Gordon EOM

Supposing the Sine-Gordon EOM in Eq. (2.17) has infinitesimal b , such that it can be expanded using Taylor's expansion up to second order.

$$\begin{aligned} \square \phi + \frac{1}{b} \left(b\phi - \frac{(b\phi)^3}{3!} \right) &= 0 \\ \phi_{tt} - \phi_{xx} + \phi - \frac{b^2}{3!} \phi^3 &= 0, \end{aligned} \quad (2.26)$$

It is arrived to the massive nonlinear Klein-Gordon EOMs as follows [15],

$$\phi_{tt} - \phi_{xx} + m^2 \phi - \frac{\lambda}{3!} \phi^3 = 0. \quad (2.27)$$

where m stands for unit mass which is put by hand and $\lambda = b^2$ for the self-interaction coupling. Although the NKG equation can be derived from the Sine-Gordon equation, but it does not mean that both have the same solution. Nevertheless, the NKG also can be solve by using traveling solution method, same as above.

In the traveling solution scheme, same as before, the PDE in Eq. (2.27) should be changed into an ODE,

$$a\phi_{zz} + m^2\phi - \frac{\lambda}{3!}\phi^3 = 0. \quad (2.28)$$

where $a = (v^2 - 1)$. Using same mathematical tricks as earlier by timing the equation with ϕ_z and assuming $\lim_{x \rightarrow 0} \phi = 0$ to vanish the integral constants, obtains

$$a\phi_z\phi_{zz} + m^2\phi_z\phi - \frac{\lambda}{3!}\phi_z\phi^3 = 0$$

$$\begin{aligned}
\frac{a}{2} \frac{d\phi_z^2}{dz} + \frac{m^2}{2} \frac{d\phi^2}{dz} - \frac{\lambda}{4!} \frac{d\phi^4}{dz} &= 0 \\
\frac{d}{dz} \left(\frac{a}{2} \phi_z^2 + \frac{m^2}{2} \phi^2 - \frac{\lambda}{4!} \phi^4 \right) &= 0 \\
\frac{a}{2} \phi_z^2 + \frac{m^2}{2} \phi^2 - \frac{\lambda}{4!} \phi^4 &= 0 \\
-\frac{m^2}{a} \phi^2 + \frac{2\lambda}{a4!} \phi^4 &= \phi_z^2 \\
\sqrt{-\frac{m^2}{a} \phi^2 + \frac{2\lambda}{a4!} \phi^4} &= \frac{d\phi}{dz} \\
\int \frac{1}{\sqrt{\frac{2\lambda}{4!} \phi^4 - m^2 \phi^2}} d\phi &= \sqrt{\frac{1}{a}} \int dz .
\end{aligned} \tag{2.29}$$

Same as before, by utilizing the elliptic integral method, the soliton solution for the NKG equation can be obtained as follow,

$$\phi(x - vt) = \pm \frac{m}{\sqrt{\lambda}} \tanh\left(\frac{m}{\sqrt{2}}(x - vt)\right) . \tag{2.30}$$

Therefore, solitary wave solution for the Sine-Gordon and NKG equations can be investigated easily using this traveling approximation.

2.3 The Path Integral

The statistical mechanics for the models will be calculated using path integral method. At least, a brief introduction to the path integral calculation should be given as one of the preliminary requisites.

The calculation will be started from Huygen's Principles [15]

$$\psi(q_f, t_f) = \int K(q_f t_f, q_i t_i) \psi(q_i, t_i) dq_i . \tag{2.31}$$

The probability that is observed at q_f at time t_f is

$$P(q_f t_f; q_i t_i) = |K(q_f t_f; q_i t_i)|^2 . \tag{2.32}$$

Take as consideration the relation of eigenstate between Schrödinger picture

and Heisenberg picture.

$$\psi(q, t) = \langle q | \psi_t \rangle_S \rightarrow \text{Schrödinger picture} , \quad (2.33)$$

$$| \psi_t \rangle_S = e^{iHt/\hbar} | \psi \rangle_H \rightarrow \text{Heisenberg picture} . \quad (2.34)$$

Then, defining

$$\begin{aligned} |q_t\rangle &= e^{iHt/\hbar} |q\rangle \rightarrow |q\rangle = e^{-iHt/\hbar} |q_t\rangle , \\ \langle q| &= e^{iHt/\hbar} \langle q_t| e^{-iHt/\hbar} , \\ \langle q | \psi_t \rangle_S &= \langle q_t | e^{iHt/\hbar} e^{-iHt/\hbar} | \psi \rangle_H , \\ \psi(q, t) &= \langle q_t | \psi \rangle_H . \end{aligned} \quad (2.35)$$

Using completeness relation $\int |qt\rangle \langle qt| dq = 1$, obtains

$$\begin{aligned} \langle q_f t_f | \psi \rangle &= \int \langle q_f t_f | q_i t_i \rangle \langle q_i t_i | \psi \rangle dq_i , \\ \psi(q_f t_f) &= \int \langle q_f t_f | q_i t_i \rangle \psi(q_i t_i) dq_i . \end{aligned} \quad (2.36)$$

By using the Huygen's principles, thus

$$K(q_f t_f; q_i t_i) = \langle q_f t_f | q_i t_i \rangle . \quad (2.37)$$

The propagator K summaries the quantum mechanics of the system. It is given the solution directly. The idea now is to express the inner product $\langle q_f t_f | q_i t_i \rangle$ as a path integral. The integral is taken overall possible trajectories,

$$\langle q_f t_f | q_i t_i \rangle = \int \dots \int dq_1 dq_2 \dots dq_n \langle q_f t_f | q_n t_n \rangle \langle q_n t_n | q_{n-1} t_{n-1} \rangle \dots \langle q_i t_i | q_i t_i \rangle . \quad (2.38)$$

Considering small segment of the overall propagator. In the path integral, it will be as follow

$$\langle q_{j+1} t_{j+1} | q_j t_j \rangle = \langle q_{j+1} | e^{-iH\tau/\hbar} | q_j \rangle \quad (2.39)$$

$$= \langle q_{j+1} | 1 - \frac{i}{\hbar} H\tau + O(\tau^2) | q_j \rangle \quad (2.40)$$

$$= \langle q_{j+1} | q_j \rangle - \frac{i\tau}{\hbar} \langle q_{j+1} | H | q_j \rangle \quad (2.41)$$

$$= \delta(q_{j+1} - q_j) - \frac{i\tau}{\hbar} \langle q_{j+1} | H | q_j \rangle$$

$$= \frac{1}{2\pi\hbar} \int dp e^{ip(q_{j+1}-q_j)/\hbar} - \frac{i\tau}{\hbar} \langle q_{j+1}|H|q_j \rangle . \quad (2.42)$$

For special case, supposing a system with Hamiltonian as follow

$$H = \frac{p^2}{2\mu} + V(q) , \quad (2.43)$$

then the path integral calculation becomes

$$\begin{aligned} \langle q_{j+1}|H|q_j \rangle &= \langle q_{j+1}|\frac{p^2}{2\mu}|q_j \rangle + \langle q_{j+1}|V(q)|q_j \rangle \\ \langle q_{j+1}|\frac{p^2}{2\mu}|q_j \rangle &= \int dp' dp \langle q_{j+1}|p' \rangle \langle p'|\frac{p^2}{2\mu}|p \rangle \langle p|q_j \rangle . \end{aligned} \quad (2.44)$$

It is familiar to know that $\langle q_{j+1}|p' \rangle = (2\pi\hbar)^{-1/2} e^{ip'q_{j+1}/\hbar}$, then

$$\begin{aligned} \langle q_{j+1}|\frac{p'}{2\mu}|q_j \rangle &= \int \frac{dp' dp}{2\pi\hbar} e^{ip'q_{j+1}/\hbar} e^{-ipq_j/\hbar} \langle p'|\frac{p^2}{2\mu}|p \rangle \\ &= \int \frac{dp' dp}{2\pi\hbar} e^{i/\hbar(p'q_{j+1}-pq_j)} \frac{p^2}{2\mu} \delta(p' - p) \\ &= \frac{1}{2\pi\hbar} \int dp e^{\frac{ip}{\hbar}(q_{j+1}-q_j)} \frac{p^2}{2\mu} \\ &= \int \frac{dp}{h} \exp \left[\frac{ip}{\hbar}(q_{j+1} - q_j) \right] \frac{p^2}{2\mu} . \end{aligned} \quad (2.45)$$

Assuming the potential is local, then

$$\begin{aligned} \langle q_{j+1}|V(q)|q_j \rangle &= V \left(\frac{q_{j+1} + q_j}{2} \right) \langle q_{j+1}|q_j \rangle \\ &= V \left(\frac{q_{j+1} + q_j}{2} \right) \delta(q_{j+1} - q_j) \\ &= V \left(\frac{q_{j+1} + q_j}{2} \right) \int \frac{dp}{h} \exp \left[\frac{ip}{\hbar}(q_{j+1} - q_j) \right] . \end{aligned} \quad (2.46)$$

For abbreviation the notation, suppose

$$q_j = \frac{q_{j+1} + q_j}{2} , \quad (2.47)$$

$$\langle q_{j+1}|V(q)|q_j \rangle = V(q) \int \frac{dp}{h} \exp \left(\frac{ip}{\hbar}(q_{j+1} - q_j) \right) , \quad (2.48)$$

$$\langle q_{j+1}|H|q_j \rangle = \int \frac{dp}{h} \exp \left[\frac{ip}{\hbar}(q_{j+1} - q_j) \right] \left(\frac{p^2}{2\mu} + V_q \right) , \quad (2.49)$$

$$= \int \frac{dp}{h} \exp \left[\frac{ip}{h} (q_{j+1} - q_j) \right] H . \quad (2.50)$$

So that,

$$\langle q_{j+1} t_{j+1} | q_j t_j \rangle = \int \frac{dp_j}{h} \exp \left[\frac{ip_j}{h} (q_{j+1} - q_j) \right] \left(1 - \frac{i\tau}{h} H \right) \quad (2.51)$$

$$= \int \frac{dp_j}{h} \exp \left[\frac{ip_j}{h} (q_{j+1} - q_j) \right] \exp \left(\frac{-i}{h} \tau H \right) \quad (2.52)$$

$$= \int \frac{dp_j}{h} \exp \left[\frac{i}{h} p_j (q_{j+1} - q_j) - \tau H \right] , \quad (2.53)$$

where p_j is the momentum between t_j and t_{j+1} .

Therefore, the full propagator can be written as

$$\langle q_f t_f | q_i t_i \rangle = \lim_{n \rightarrow \infty} \int \prod_{j=1}^n dq_j \prod_{j=0}^n dp_j \exp \left\{ \frac{i}{h} \sum_{j=0}^n [p_j (q_{j+1} - q_j) - \tau H(p, \tilde{q})] \right\} . \quad (2.54)$$

There is another form for the transition amplitude, which holds when H is of the form Eq. (2.43), since in that case we can perform the p -integration. The above equation becomes,

$$\begin{aligned} \langle q_f t_f | q_i t_i \rangle &= \lim_{n \rightarrow \infty} \int \prod_1^n dq_j \prod_0^n \frac{dp_j}{h} \exp \left\{ \frac{i}{h} \sum_{j=0}^n [p_j (q_{j+1} - q_j) \tau \right. \\ &\quad \left. - \frac{p_j^2}{2\mu} - V(\tilde{q}_j) \tau] \right\} \\ &= \lim_{n \rightarrow \infty} \left(\frac{\mu}{ih\tau} \right)^{(n+1)/2} \int \prod_1^n dq_j \\ &\quad \times \exp \left\{ \frac{i\tau}{h} \sum_{j=0}^n \left[\frac{\mu}{2} \left(\frac{q_{j+1} - q_j}{\tau} \right)^2 - V \right] \right\} . \end{aligned} \quad (2.55)$$

In symbolic form it can be written as,

$$\langle q_f t_f | q_i t_i \rangle = N \int \mathcal{D}_q \exp \left[\frac{i}{h} \int_{t_i}^{t_f} L(q, \dot{q}) dt \right] . \quad (2.56)$$

The last equation will be used in partition function calculation later.

2.4 Functional Derivatives

2.4.1 Definition

Functional derivative method is very useful to outsmart the interaction terms in path integral calculation for the partition function. In this trick, the nonlinear fields and the interaction term in the lagrangian will be changed into functional derivative operators, then the partition function becomes linear and can be solved by plane wave approach. It will be clear in chapter 6. In this section, the definition and some example about functional derivative will be discussed.

In this case, the functional derivative means derivative of a functional integral. A functional integral is denoted by $F[f(x)]$ and it is usually called just *functional*. Derivative of the functional is defined by analogy with ordinary derivative [15], that is

$$\frac{\delta F[f(x)]}{\delta f(y)} = \lim_{\epsilon \rightarrow 0} \frac{F[f(x) + \epsilon \delta(x - y)] - F[f(x)]}{\epsilon}. \quad (2.57)$$

All of its properties are analogous with the ordinary derivatives.

2.4.2 Miscellaneous Functional Derivative

Some kind of functional derivatives that perhaps useful in path integral calculation will given.

Identity Functional

Considering the functional

$$F[f] = \int f(x) dx, \quad (2.58)$$

then derivative of the functional is

$$\begin{aligned} \frac{\delta F[f]}{\delta f(x)} &= \lim_{\epsilon \rightarrow 0} \frac{\int (f(x) + \epsilon \delta(x - y)) dx - \int f(x) dx}{\epsilon} \\ &= \lim_{\epsilon \rightarrow 0} \frac{\int f(x) dx + \int \epsilon \delta(x - y) dx - \int f(x) dx}{\epsilon} \end{aligned}$$

$$\begin{aligned}
&= \int \delta(x - y) dx \\
&= 1.
\end{aligned} \tag{2.59}$$

Parameter Function

Supposing $F_x[f] = \int G(x, y)f(y)dy$, where x in the left side is only a parameter. Then the derivative is

$$\begin{aligned}
\frac{\delta F_x[f]}{\delta f(z)} &= \lim_{\epsilon \rightarrow 0} \frac{\int G(x, y)(f(y) + \epsilon\delta(y - z))dy - \int G(x, y)f(y)dy}{\epsilon} \\
&= \lim_{\epsilon \rightarrow 0} \frac{\int G(x, y)f(y)dy + \int \epsilon G(x, y)\delta(y - z)dy - \int G(x, y)f(y)dy}{\epsilon} \\
&= \int G(x, y)\delta(y - z)dy \\
&= G(x, z).
\end{aligned} \tag{2.60}$$

Product

Supposing $F[f] = \int A[f(x)]B[f(x)]dx$. Then

$$\begin{aligned}
\frac{\delta F[f]}{\delta f(y)} &= \lim_{\epsilon \rightarrow 0} \frac{F[f(x) + \epsilon\delta(x - y)] - F[f(x)]}{\epsilon} \\
&= \lim_{\epsilon \rightarrow 0} \frac{1}{\epsilon} \left\{ \int (A[f(x) + \epsilon\delta(x - y)]B[f(x) + \epsilon\delta(x - y)]) dx \right. \\
&\quad \left. - \int A[f(x)]B[f(x)]dx \right\} \\
&= \lim_{\epsilon \rightarrow 0} \frac{1}{\epsilon} \left\{ \int (A[f(x) + \epsilon\delta(x - y)]B[f(x) + \epsilon\delta(x - y)] \right. \\
&\quad - A[f(x) + \epsilon\delta(x - y)]B[f(x)] + A[f(x) + \epsilon\delta(x - y)]B[f(x)] \\
&\quad \left. - A[f(x)]B[f(x)]) dx \right\} \\
&= \lim_{\epsilon \rightarrow 0} \int A[f(x) + \epsilon\delta(x - y)] \left(\frac{(B[f(x) + \epsilon\delta(x - y)] - B[f(x)])}{\epsilon} \right) dx \\
&\quad + \int \left(\frac{(A[f(x) + \epsilon\delta(x - y)] - A[f(x)])}{\epsilon} \right) B[f(x)] dx \\
&= \int \lim_{\epsilon \rightarrow 0} A[f(x) + \epsilon\delta(x - y)] \lim_{\epsilon \rightarrow 0} \left(\frac{(B[f(x) + \epsilon\delta(x - y)] - B[f(x)])}{\epsilon} \right) dx \\
&\quad + \int \lim_{\epsilon \rightarrow 0} \left(\frac{(A[f(x) + \epsilon\delta(x - y)] - A[f(x)])}{\epsilon} \right) B[f(x)] dx
\end{aligned}$$

$$= \int A[f(x)] \frac{\delta B[f(x)]}{\delta f(y)} dx + \int \frac{\delta A[f(x)]}{\delta f(y)} B[f(x)] dx . \quad (2.61)$$

Therefore, we have product rule of functional derivative

$$\frac{\delta F[f(x)]}{\delta f(y)} = \int A[f(x)] \frac{\delta B[f(x)]}{\delta f(y)} dx + \int \frac{\delta A[f(x)]}{\delta f(y)} B[f(x)] dx . \quad (2.62)$$

Quotient

Considering $F[f] = \int \frac{A[f(x)]}{B[f(x)]} dx$. Then

$$\begin{aligned} \frac{\delta F[f]}{\delta f(y)} &= \lim_{\epsilon \rightarrow 0} \frac{F[f(x) + \epsilon \delta(x-y)] - F[f(x)]}{\epsilon} \\ &= \lim_{\epsilon \rightarrow 0} \frac{1}{\epsilon} \left\{ \int \left(\frac{A[f(x) + \epsilon \delta(x-y)]}{B[f(x) + \epsilon \delta(x-y)]} \right) dx - \int \frac{A[f(x)]}{B[f(x)]} dx \right\} \\ &= \lim_{\epsilon \rightarrow 0} \frac{1}{\epsilon} \left\{ \int \frac{A[f(x) + \epsilon \delta(x-y)] B[f(x)]}{B[f(x) + \epsilon \delta(x-y)] B[f(x)]} dx \right. \\ &\quad \left. - \int \frac{B[f(x) + \epsilon \delta(x-y)] A[f(x)]}{B[f(x) + \epsilon \delta(x-y)] B[f(x)]} dx \right\} \\ &= \lim_{\epsilon \rightarrow 0} \frac{1}{\epsilon} \left\{ \int \frac{A[f(x) + \epsilon \delta(x-y)] B[f(x)] - A[f(x)] B[f(x)]}{B[f(x) + \epsilon \delta(x-y)] B[f(x)]} dx \right. \\ &\quad \left. + \int \frac{A[f(x)] B[f(x)] - B[f(x) + \epsilon \delta(x-y)] A[f(x)]}{B[f(x) + \epsilon \delta(x-y)] B[f(x)]} dx \right\} \\ &= \int \left\{ \left(\lim_{\epsilon \rightarrow 0} \frac{(A[f(x) + \epsilon \delta(x-y)] - A[f(x)])}{\epsilon} B[f(x)] \right. \right. \\ &\quad \left. \left. - A[f(x)] \lim_{\epsilon \rightarrow 0} \frac{(B[f(x) + \epsilon \delta(x-y)] - B[f(x)])}{\epsilon} \right) \right. \\ &\quad \left. \times \lim_{\epsilon \rightarrow 0} \frac{1}{B[f(x) + \epsilon \delta(x-y)] B[f(x)]} \right\} dx \\ &= \int \frac{\frac{\delta A[f(x)]}{\delta f(y)} B[f(x)] - A[f(x)] \frac{\delta B[f(x)]}{\delta f(y)}}{B[f(x)] B[f(x)]} dx . \quad (2.63) \end{aligned}$$

Therefore, the quotient rule of functional derivative has been obtained as

$$\frac{\delta F[f]}{\delta f(y)} = \int \frac{\frac{\delta A[f(x)]}{\delta f(y)} B[f(x)] - A[f(x)] \frac{\delta B[f(x)]}{\delta f(y)}}{B[f(x)] B[f(x)]} dx . \quad (2.64)$$

Exponential

Solving the derivative of exponential functional is most important. It appears frequently in a lot of path integral cases. Let $F[f] = e^{\int G(x,y)f(x)dx}$.

$$\begin{aligned} \frac{\delta F[f]}{\delta f(z)} &= \lim_{\epsilon \rightarrow 0} \frac{e^{\int G(x,y)(f(x)+\epsilon\delta(x-z))dx} - e^{\int G(x,y)f(x)dx}}{\epsilon} \\ &= \lim_{\epsilon \rightarrow 0} \frac{e^{\int G(x,y)f(x)dx} e^{\int \epsilon G(x,y)\delta(x-z)dx} - e^{\int G(x,y)f(x)dx}}{\epsilon} \\ &= \lim_{\epsilon \rightarrow 0} \frac{e^{\int G(x,y)f(x)dx} (e^{\int \epsilon G(x,y)\delta(x-z)dx} - 1)}{\epsilon}, \end{aligned} \quad (2.65)$$

$e^{\int \epsilon G(x,y)\delta(x-z)dx}$ can be expanded using Taylor's expansion. Because of ϵ is very small, this expansion can be approached only first two terms.

$$e^{\int \epsilon G(x,y)\delta(x-z)dx} \approx 1 + \int \epsilon G(x,y)\delta(x-z)dx. \quad (2.66)$$

Therefore, the derivative becomes

$$\begin{aligned} \frac{\delta F[f]}{\delta f(z)} &= \lim_{\epsilon \rightarrow 0} \frac{e^{\int G(x,y)f(x)dx} (1 + \int \epsilon G(x,y)\delta(x-z)dx - 1)}{\epsilon} \\ &= e^{\int G(x,y)f(x)dx} \int G(x,y)\delta(x-z)dx \\ &= e^{\int G(x,y)f(x)dx} G(z,y). \end{aligned} \quad (2.67)$$

Then, the exponential functional derivative is

$$\frac{\delta F[f]}{\delta f(z)} = G(z,y) e^{\int G(x,y)f(x)dx}. \quad (2.68)$$

Hopefully this derivation will help calculations in this work.

Chapter 3

Secondary Protein Folding

*Recite in the name of your Lord who created -
Created man from a clinging substance.
(Q.S. Al-'Alaq 1-2)*

3.1 Global Pictures

The protein folding problem is a prediction of the structure of proteins from the knowledge of their amino acid sequences. There are many stages structure of protein, namely primary structure, secondary and so on, depend on how its amino acids are composed.

The primary is a state when the protein constituent amino acids which held together by covalent or peptide bonds. The amino acids did not interact with each other, so that the protein looks like a string.

Meanwhile, the secondary structure consists of the shape representing each segment of a polypeptide tied by hydrogen bonds, Van Der Waals forces, electrostatic interaction and hydrophobic effects [24]. It is moreover formed around a group of amino acids considered as the ground state. Then it is extended to include adjacent amino acids till the blocking amino acids are reached, and the whole protein chain along the polypeptide adopted its preferred secondary structure. The famous secondary protein structures are *alpha helix* and *beta sheet*.

The amino acids which are assembling the protein sequences change the

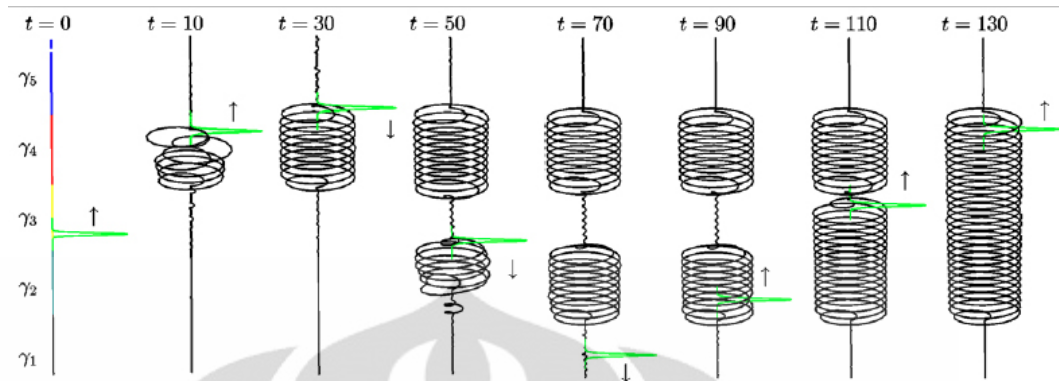


Figure 3.1: (Color online.) Time snapshots of the secondary folding of a toy protein consisting of five regions where the local potential energy functional is constant with $\gamma_1 = \gamma_5 = 0.9$, $\gamma_2 = \gamma_4 = 0.1$, and $\gamma_3 = 0.55$. The regions with different values of assigned γ_i are shown in different colours (shadings) along the initial ($t = 0$) state. Initially the solitary wave is $\psi(t = 0) = 2\text{sech}[2(x - 40)]\exp[i(x - 40)]$ and $\phi = 0$. The coefficients in (6)(8) are $\zeta = 0.1$, $\Gamma = 0.1$, $m = 0.5$, $C = 2$, $\Lambda = 0.5$. The position of the solitary wave is shown in green (light Grey) and the arrows indicate the direction of its motion.

protein shape from the primary to the secondary and subsequent structures. Some models have then been proposed to explain such protein transition [5, 7, 10, 11, 12, 25, 26, 27]. This work is also modeling conformational dynamics of secondary structure of protein.

3.2 Toy Ad-Hoc Model

This work actually reproduces toy ad-hoc model which has been made by Berloff [12]. In this section, the toy model will be described briefly.

The model produces such nonlinear equations of motion by defining the lagrangian as follow,

$$\mathcal{L} = i\psi^*\partial_t\psi - |\partial_x\psi|^2 + |\psi|^4 + \frac{1}{2}m(\partial_t\phi)^2 - V(\phi) - U(|\psi|, \phi) - T(\phi) - |\partial_x\phi|^2 \quad (3.1)$$

The first three terms are the lagrangian of nonlinear Schrödinger equation, while U is the potential interaction between solitons with protein backbone, V describes the local potential that represents the shape of the body proteins,

and T is the strain potential between the peptide building blocks of protein. Those potentials are written as follows,

$$\begin{aligned} U(|\psi|, \phi) &= \Lambda |\psi|^2 (\phi - \frac{1}{2})^2, \\ V(\phi) &= C (\phi - \gamma(x))^2 (\gamma(x)^2 + 2\gamma(x)(\phi - 1) + \phi(3\phi - 4)), \\ T(\phi(x)) &= \eta [(\phi(x) - \phi(x - l_i))^2 + (\phi(x) - \phi(x + l_i))^2] \end{aligned} \quad (3.2)$$

By using Euler-Lagrange equation, one can obtain two coupled nonlinear EOMs as follows,

$$i\partial_t \psi = -\psi_{xx} + \left[\Lambda (\phi - \frac{1}{2})^2 - 2|\psi|^2 \right] \psi, \quad (3.3)$$

$$\begin{aligned} m\partial_{tt} \phi &= -12C\phi(\phi - 1)(\phi - \gamma(x)) - 2\Lambda |\psi|^2 (\phi - \frac{1}{2}) + \phi_{xx} \\ &\quad - 2\zeta(\phi - \phi(x - l_i)) - 2\zeta(\phi - \phi(x + l_i)) - \Gamma \partial_t \phi. \end{aligned} \quad (3.4)$$

The strain potential term T in the above EOMs has been ignored for the sake of simplicity.

Berloff was succeed reproduce nonlinear EOMs which can describe the non-linear dynamics of secondary protein folding. As can be seen in Fig. (3.1), the numerical result of the EOMs shows either how a protein chain can fold from primary to the secondary forms. Nevertheless, the model is not built from first principle. The interaction terms are adding just put by hand.

Chapter 4

The Models

Our imagination is stretched to the utmost, not, as in fiction, to imagine things which are not really there, but just to comprehend those things which 'are' there.

Richard Feynman

This chapter is the core of my work. The first principle models of secondary protein folding will be constructed with two approximations, namely *linear conformation* and *nonlinear conformation* [28, 29]. The difference of the both approaches are only in the initial stage assumptions, that is linear and nonlinear initial protein backbone forms.

4.1 Linear Conformation Model

4.1.1 Construction of the Lagrangian

The model is an extension of the toy model proposed in [5]. More than considering a self-interaction mechanism as proposed in [5] and subsequently developed in [7, 12], more realistic model is introduced. In this model, the dynamics of amino acids forming proteins is initially considered as a free and linear system of bosonic matters. Further, external nonlinear sources, like laser or light bunch, are introduced. The sources which propagate through the protein backbone interact each other with the amino acids to induce conformation changes.

The model describes the conformation changes as the dynamics of amino acids using a free and massive (relativistic) bosonic lagrangian as below,

$$\mathcal{L}_c = \frac{1}{2} (\partial_\mu \phi)^\dagger (\partial^\mu \phi) + \frac{1}{2} m_\phi^2 \phi^\dagger \phi, \quad (4.1)$$

where ϕ represents the conformation field and $\phi^\dagger \equiv (\phi^*)^T$ is the hermitian conjugate for a general complex field ϕ . On the other hand, the nonlinear sources represented by the field ψ are also governed by a massless bosonic lagrangian,

$$\mathcal{L}_s = \frac{1}{2} (\partial_\mu \psi)^\dagger (\partial^\mu \psi) + V(\psi), \quad (4.2)$$

with an additional potential $V(\psi)$ taking the typical ϕ^4 - self-interaction,

$$V(\psi) = \frac{\lambda_\psi}{4!} (\psi^\dagger \psi)^2, \quad (4.3)$$

where λ_ψ is the coupling constant. It should be noted that both scalar fields, $\phi = \phi(t, x)$ denotes the local curvature of the conformation at position x with $\phi(x) = 1$ or 0 for α or β -helix.

The choice of interactions in Eqs. (4.1) and (4.2) are justified by the following considerations,

- The conformation changes are assumed to be linear. It is actually not necessarily massive. Although one can put by hand the mass term $m_\phi^2 \phi^\dagger \phi$ in the lagrangian as written above, the massive conformational field could also be generated dynamically through certain symmetry breaking as shown later.
- The source is assumed to be massless concerning the laser or light source injected to the protein chains to induce the foldings.
- Its non-linearity is realized by introducing the ψ self-interaction which leads to the non-linear EOM.
- For the sake of simplicity, the lagrangian is imposed to be symmetry under certain transformations, for instance in the present case is time

and parity symmetry, *i.e.* $\phi(t, x) \rightarrow -\phi(-t, -x)$ for one-dimensional space.

We should remark here that the model is although written in a relativistic form, after deriving relevant EOMs one can take its non-relativistic limits to obtain final EOMs describing the desired dynamics. Secondly, instead of using the vector electromagnetic field A_μ to represent the nonlinear sources, like laser for instance, it is more convenient to consider the nonlinear source as a bunch of light or laser such that one might represent it in a 'macroscopic' scalar field ψ .

Considering the dimensional counting and the invariance on time-parity symmetry, the most general interaction between the conformation field and nonlinear sources is,

$$\mathcal{L}_{\text{int}} = -\Lambda (\phi^\dagger \phi)(\psi^\dagger \psi) , \quad (4.4)$$

with Λ denotes the strength of the interaction. Eqs. (4.3) and (4.4) lead to the total potential in the model,

$$V_{\text{tot}} = \frac{\lambda_\psi}{4!} (\psi^\dagger \psi)^2 - \Lambda (\phi^\dagger \phi)(\psi^\dagger \psi) . \quad (4.5)$$

Eqs. (4.1), (4.2) and (4.5) provide the underlying interactions in the model.

4.1.2 Symmetry Breaking for the Nonlinear Source

Concerning the minima of the total potential in term of nonlinear source field, that is

$$\left. \frac{\partial V_{\text{tot}}}{\partial \psi} \right|_{\langle \psi \rangle, \langle \phi \rangle} = 0 , \quad (4.6)$$

$$\begin{aligned} \frac{\lambda_\psi}{6} \langle \psi \rangle^3 - 2\Lambda \langle \phi \rangle^2 \langle \psi \rangle &= 0 \\ (\lambda_\psi \langle \psi \rangle^2 - 12\Lambda \langle \phi \rangle^2) \langle \psi \rangle &= 0 . \end{aligned} \quad (4.7)$$

Since the fields are a fluctuated wave, then the minima should be fixed in an value. So that, we take the expectation value of their minima. At the vacuum

expectation values (VEV) of the fields yields the non-trivial solutions,

$$\langle \psi \rangle = 0, \quad \text{and} \quad \langle \psi \rangle = \pm \sqrt{\frac{12\Lambda}{\lambda_\psi}} \langle \phi \rangle. \quad (4.8)$$

Imposing certain local symmetry, namely the phase or U(1) symmetry to the above total lagrangian, the VEV in Eq. (4.8) obviously breaks the symmetry.

Considering the mixed lagrangian Eqs. (4.1) and (4.4),

$$\mathcal{L}_c = \frac{1}{2} (\partial_\mu \phi)^\dagger (\partial^\mu \phi) + \frac{1}{2} m_\phi^2 \phi^\dagger \phi - \Lambda (\psi^\dagger \psi) (\phi^\dagger \phi), \quad (4.9)$$

then substituting the VEV in Eq. (4.8) into the lagrangian.

$$\begin{aligned} \mathcal{L}_c &= \frac{1}{2} (\partial_\mu \phi)^\dagger (\partial^\mu \phi) + \frac{1}{2} m_\phi^2 \phi^\dagger \phi - \Lambda \left(\sqrt{\frac{12\Lambda}{\lambda_\psi}} \langle \phi \rangle \right)^2 (\phi^\dagger \phi) \\ &= \frac{1}{2} (\partial_\mu \phi)^\dagger (\partial^\mu \phi) + \frac{1}{2} \left(m_\phi^2 - \frac{24\Lambda^2}{\lambda_\psi} \langle \phi \rangle^2 \right) \phi^\dagger \phi. \end{aligned} \quad (4.10)$$

The symmetry breaking at the same time shifts the mass term for ϕ as follow,

$$m_\phi^2 \rightarrow \bar{m}_\phi^2 \equiv m_\phi^2 - \frac{24\Lambda^2}{\lambda_\psi} \langle \phi \rangle^2. \quad (4.11)$$

Estimate, the both values of $\langle \phi \rangle$ and m_ϕ are in same order. Then one can derive a constrain to the constants of the lagrangian.

$$1 - \frac{24\Lambda^2}{\lambda_\psi} > 0 \quad \text{or} \quad 24\Lambda^2 < \lambda_\psi \quad (4.12)$$

On the other hand, Eq. (4.8) induces the 'tension force' which plays an important role to enable folded pathway in the present model. This will be discussed in the following section.

4.1.3 EOMs and its Behaviours

Having the total lagrangian at hand, one can derive the EOM's using the Euler-Lagrange equation,

$$\frac{\partial \mathcal{L}_{\text{tot}}}{\partial |\phi|} - \partial_{\mu} \frac{\partial \mathcal{L}_{\text{tot}}}{\partial (\partial_{\mu} \phi)} = 0, \quad (4.13)$$

where $\mathcal{L}_{\text{tot}} = \mathcal{L}_c + \mathcal{L}_s + \mathcal{L}_{\text{int}}$.

Substituting Eqs. (4.1), (4.2) and (4.4) into Eq. (4.13) in term of ϕ and ψ , one immediately obtains a set of EOMs,

$$\left(\frac{\partial^2}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2}{\partial t^2} - \frac{m_{\phi}^2}{\hbar^2 c^2} + 2\Lambda |\psi|^2 \right) |\phi| = 0, \quad (4.14)$$

$$\left(\frac{\partial^2}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2}{\partial t^2} + 2\Lambda |\phi|^2 - \frac{\lambda_{\psi}}{6} |\psi|^2 \right) |\psi| = 0. \quad (4.15)$$

Here the natural unit is restored to make the light velocity c and \hbar reappear in the equation. Actually, taking the absolute value for the both fields is not a compulsion. Since there is no exclusion providing the EOMs in complex form. It was doing just for the sake of simplicity.

The last term in Eq. (4.15) determines the non-linearity of the EOM of source. One should also put an attention in the last term of Eq. (4.14), *i.e.* $\sim k \phi$ with $k \sim 2\Lambda \langle \psi \rangle^2$. This actually induces the tension force in the dynamics of conformational field enabling the folded pathway as expected.

4.2 Nonlinear Conformation Model

To investigate that the folded pathways are really induced and dominated by the injected nonlinear sources or not, take as consideration a similar model but has different conformation changes field. In this approach, the contribution of the initial condition to the folding mechanism will be observed.

4.2.1 Construction of the Lagrangian

This approximation is only an extension of the above linear model. In contrast with the previous model which assumes the initial conformational state is

linear, now the protein is initially assumed to be nonlinear likes Sine-Gordon soliton [29],

$$\mathcal{L}_c = \frac{1}{2} (\partial_\mu \phi)^\dagger (\partial^\mu \phi) + \frac{m_\phi^4}{\lambda_\phi} \left[1 - \cos \left(\frac{\sqrt{\lambda_\phi}}{m_\phi} |\phi| \right) \right]. \quad (4.16)$$

However, the sources injected into the backbone remain nonlinear and massless. Then, same as before the nonlinear sources are modeled by ψ^4 self-interaction.

$$\mathcal{L}_s = \frac{1}{2} (\partial_\mu \psi)^\dagger (\partial^\mu \psi) + \frac{\lambda_\psi}{4!} (\psi^\dagger \psi)^2. \quad (4.17)$$

The interaction term between both is described by,

$$\mathcal{L}_{int} = -\Lambda (\phi^\dagger \phi) (\psi^\dagger \psi). \quad (4.18)$$

All of them provide the underlying model in the paper with total potential,

$$V_{tot}(\psi, \phi) = \frac{m_\phi^4}{\lambda_\phi} \left[1 - \cos \left(\frac{\sqrt{\lambda_\phi}}{m_\phi} |\phi| \right) \right] + \frac{\lambda_\psi}{4!} (\psi^\dagger \psi)^2 - \Lambda (\phi^\dagger \phi) (\psi^\dagger \psi). \quad (4.19)$$

4.2.2 Limit to the Berloff's Model

Now, throughout the paper let us assume that λ_ϕ is small enough, that is approximately at the same order with λ_ψ . In this case, the first term can be expanded in term of $\sqrt{\lambda_\psi}$,

$$V_{tot}(\psi, \phi) \approx \frac{m_\phi^2}{2} \phi^\dagger \phi - \frac{\lambda_\phi}{4!} (\phi^\dagger \phi)^2 + \frac{\lambda_\psi}{4!} (\psi^\dagger \psi)^2 - \Lambda (\phi^\dagger \phi) (\psi^\dagger \psi). \quad (4.20)$$

up to the second order accuracy. If $\lambda_\phi = 0$, the result coincides to the linear case [28]. Besides of that, the above total potential is reduced to the potential in Berloff's model [12]. Nonetheless, the kinetic term of this model is relativistic Klein-Gordon. It is contrast with the Berloff's model which was deploying nonlinear Schrödinger as the injected soliton.

One can derive easily the Schödinger equation from the Klein-Gordon equation by taking its non-relativistic limit. So that to reproduce the Berloff's model totally, it should be taken the non-relativistic limit for the kinetic term

of the nonlinear source field. It will be done conveniently in equation of motion form.

Considering the free linear Klein-Gordon EOM as follow,

$$\frac{\partial^2 \psi}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2 \psi}{\partial t^2} - \frac{m^2}{\hbar^2 c^2} \psi = 0 . \quad (4.21)$$

In the non-relativistic limit, the velocity is very small relative to its mass, then one can write $E \approx m$. Furthermore, the fact shows us that $\psi \rightarrow e^{-iEt}$. Using these motivations, the solution of the EOM can be defined as follow,

$$\psi \equiv \exp \left\{ -\frac{im}{\hbar} t \right\} \bar{\psi}(x, t) , \quad (4.22)$$

where the field $\psi(x, t)$ oscillates much slower in time. Plugging this into the EOM gives

$$\frac{\hbar^2}{2m} \frac{\partial^2 \bar{\psi}}{\partial x^2} + i\hbar \frac{\partial \bar{\psi}}{\partial t} - \frac{\hbar^2}{2mc^2} \frac{\partial^2 \bar{\psi}}{\partial t^2} = 0 . \quad (4.23)$$

The second time derivatives on ψ is infinitesimal relative to the other terms, since it is divided by c^2 which has large value, then it can be neglected. Therefore we get the Schrödinger equation back.

So that by using those above approaches we can reproduce complete form of the Berloff's model. Therefore this nonlinear conformational model can be said as generalization for the previous models.

4.2.3 Symmetry Breaking for the Both Fields

Imposing namely local U(1) symmetry breaking to the total lagrangian makes the vacuum expectation value (VEV) of the fields yields the non-trivial solutions. Same as with the linear one, the 'tension force' which plays an important role to enable folded pathway can be appeared naturally by concerning the minima of total potential in term of source field [28].

$$\begin{aligned} \frac{\partial V_{\text{tot}}}{\partial \psi} \Big|_{\langle \psi \rangle, \langle \phi \rangle} &= 0 , \\ \frac{\lambda_\psi}{6} \langle \psi \rangle^3 - 2\Lambda \langle \phi \rangle^2 \langle \psi \rangle &= 0 \end{aligned} \quad (4.24)$$

$$\begin{aligned}
(\lambda_\psi \langle \psi \rangle^2 - 12\Lambda \langle \phi \rangle^2) \langle \psi \rangle &= 0 \\
\langle \psi \rangle = 0, \text{ and } \langle \psi \rangle &= \pm \sqrt{\frac{12\Lambda}{\lambda_\psi}} \langle \phi \rangle.
\end{aligned} \tag{4.25}$$

Something new from this approach is nontrivial VEV in term of conformation changes field is also occurred, that is,

$$\begin{aligned}
\left. \frac{\partial V_{\text{tot}}}{\partial \phi} \right|_{\langle \psi \rangle, \langle \phi \rangle} &= 0, \\
m_\phi^2 \langle \phi \rangle - \frac{\lambda_\psi}{6} \langle \phi \rangle^3 - 2\Lambda \langle \psi \rangle^2 \langle \phi \rangle &= 0 \\
(6m_\phi^2 - \lambda_\phi \langle \phi \rangle^2 - 12\Lambda \langle \psi \rangle^2) \langle \phi \rangle &= 0 \\
\langle \phi \rangle = 0, \text{ and } \langle \phi \rangle &= \pm \sqrt{\frac{6m_\phi^2 - 12\Lambda \langle \psi \rangle^2}{\lambda_\phi}}.
\end{aligned} \tag{4.26}$$

It shows that the existence of Sine-Gordon potential makes the early stable ground state of conformational field turns out to be metastable. In other words, the non trivial VEV in Eq. (4.27) constitutes new more stable ground state of the conformational field. Transition between metastable into stable state breaks the symmetry of the vacuum spontaneously, while the conformational field should be nonlinear even though the external nonlinear source has not been instilled. Therefore the protein backbone should be in nonlinear form at the initial stage.

Same as before, the symmetry breaking also shifts the mass term of ϕ as follow,

$$m_\phi^2 \rightarrow \bar{m}_\phi^2 \equiv m_\phi^2 - \frac{24\Lambda^2}{\lambda_\psi} \langle \phi \rangle^2. \tag{4.28}$$

Nevertheless, the nonlinear source field is set being massless, since it represents a bunch of light source like laser. Thus, the broken symmetry of conformational field should not be considered to introduce its mass.

4.2.4 The EOMs

Same as before, having the total lagrangian at hand, one can derive the EOM using the Euler-Lagrange equations,

$$\frac{\partial \mathcal{L}_{\text{tot}}}{\partial |\phi|} - \partial_\mu \frac{\partial \mathcal{L}_{\text{tot}}}{\partial (|\partial_\mu \phi|)} = 0 \quad \text{and} \quad \frac{\partial \mathcal{L}_{\text{tot}}}{\partial |\psi|} - \partial_\mu \frac{\partial \mathcal{L}_{\text{tot}}}{\partial (|\partial_\mu \psi|)} = 0, \quad (4.29)$$

where $\mathcal{L}_{\text{tot}} = \mathcal{L}_c + \mathcal{L}_s + \mathcal{L}_{\text{int}}$ in Eqs. (4.16), (4.17) and (4.18) respectively.

Substituting Eqs. (4.16), (4.17) and (4.18) into Eq. (4.29), one immediately obtains a set of EOMs,

$$\frac{\partial^2 |\phi|}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2 |\phi|}{\partial t^2} + 2\Lambda |\phi| |\psi|^2 - \frac{m_\phi^3 c^3}{\hbar^3 \sqrt{\lambda_\phi}} \sin \left(\frac{\sqrt{\lambda_\phi}}{m_\phi} |\phi| \right) = 0, \quad (4.30)$$

$$\frac{\partial^2 |\psi|}{\partial x^2} - \frac{1}{c^2} \frac{\partial^2 |\psi|}{\partial t^2} + 2\Lambda |\psi| |\phi|^2 - \frac{\lambda_\psi}{6} |\psi|^3 = 0. \quad (4.31)$$

The last terms in Eqs. (4.30) and (4.31) determine the non-linearity of backbone and source respectively. Also, the protein mass term is melted in the Sine-Gordon potential. One should put an attention in the second last term of Eq. (4.30), *i.e.* $\sim k\phi$ with $k \sim 2\Lambda \langle \psi \rangle^2$. This actually induces the tension force which is responsible for the dynamics of conformational field and enabling the folded pathway as expected.

Hence, solving EOMs in Eqs. (4.30) and (4.31) simultaneously would provide the contour of conformational changes in term of time and one-dimensional space components for the nonlinear model. Meanwhile, solving EOMs in Eqs. (4.14) and (4.15) simultaneously would provide the contour the linear one. All of the EOMs will be solved numerically using forward finite difference method [28, 29, 16].

Chapter 5

Numerical Analysis

All theoretical chemistry is really physics; and all theoretical chemists know it.

Richard Feynman

This chapter contains the calculation for the EOMs of our models. Since the under consideration EOMs of the both models are involving non-linear terms, one should solve them numerically. The numerical analysis and simulation of the model are done using the finite difference method [28, 29, 16]. In this section, the procedure will be explained in details. Its results hopefully can show us the dynamical simulation for the folding pathway of the protein backbone from unfolded state into the alpha helix folded state. It will be discussed in chapter 7.

The both linear and nonlinear conformation models are imposing the non-linear terms. The different among the models only in choosing the EOMs for the conformational field, that is LKG and Sine-Gordon EOMs. Meanwhile, the injected nonlinear sources for the both model are same, using bosonic lagrangian with addition ϕ^4 interaction. It consequences that the calculation of the EOMs for the both models should be similar. So that, all of the EOMs can be solved with just one method.

First, the numerical calculation for the EOMs of the linear conformation model will be given in details. Furthermore, the nonlinear one will be explained briefly in the same method.

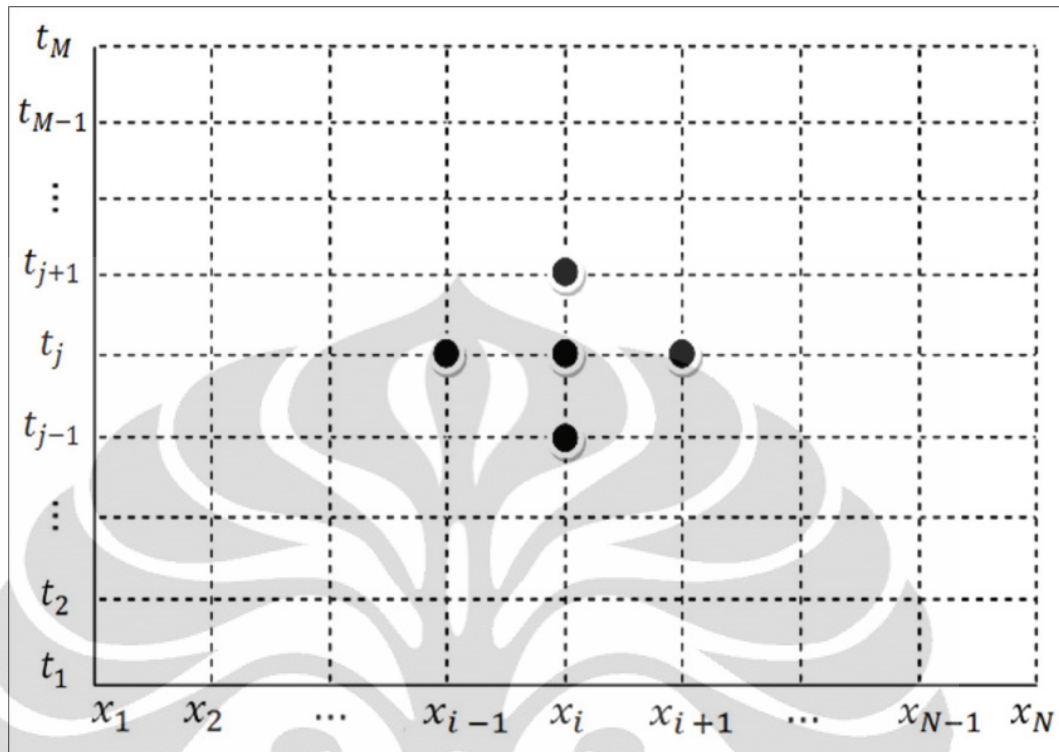


Figure 5.1: The discretized grid for solving the EOMs over the coordinate space R .

5.1 The Linear Conformation Model

The numerical analysis will be calculated using forward explicit scheme of finite difference method. Consider the coordinate space $R = \{(x, t) : 0 \leq x \leq L, 0 \leq t \leq b\}$ discretized on a grid consisting of $(N-1) \times (M-1)$ rectangles with side length $\Delta x = \delta$ and $\Delta t = \epsilon$ shown in Fig. (5.1). Throughout numerical works, non-relativistic limit $v = \partial x / \partial t \ll c$ and the following boundary conditions for both fields are deployed,

$$\begin{aligned}
 \psi(0, t) = \psi(L, t) = 0 \quad \text{and} \quad \phi(0, t) = \phi(L, t) = 0 \quad & \text{for } 0 \leq t \leq b, \\
 \psi(x, 0) = f(x) \quad \text{and} \quad \phi(x, 0) = p(x) \quad & \text{for } 0 \leq x \leq L, \\
 \frac{\partial \psi(x, 0)}{\partial t} = g(x) \quad \text{and} \quad \frac{\partial \phi(x, 0)}{\partial t} = q(x) \quad & \text{for } 0 < x < L,
 \end{aligned} \tag{5.1}$$

with $f(x)$, $p(x)$, $g(x)$ and $q(x)$ are newly introduced auxiliary functions. Solving the equations over the grid with all the boundary conditions gives us the desired numerical solutions.

The EOMs in Eqs. (4.14) and (4.15) are necessary writing in explicit form in second time derivatives to apply the forward finite difference method.

$$\phi_{tt} = c^2 \left(\phi_{xx} - \frac{c^2}{\hbar^2} m_\phi^2 \phi + 2\Lambda \psi^2 \phi \right), \quad (5.2)$$

$$\psi_{tt} = c^2 \left(\psi_{xx} + 2\Lambda \phi^2 \psi - \lambda \psi^3 \right). \quad (5.3)$$

It is more convenient to replace ψ and ϕ with u and w respectively, and rewrite them in discrete forms using the following relations

$$u_{tt} = \frac{u_{i,j+1} - 2u_{i,j} + u_{i,j-1}}{\epsilon^2}, \text{ and } u_{xx} = \frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\delta^2}. \quad (5.4)$$

Thus the EOMs can be written as

$$u_{i,j+1} - 2u_{i,j} + u_{i,j-1} = c^2 \epsilon^2 \left(\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\delta^2} + 2\Lambda w_{i,j}^2 u_{i,j} - \frac{\lambda}{6} u_{i,j}^3 \right), \quad (5.5)$$

$$w_{i,j+1} - 2w_{i,j} + w_{i,j-1} = c^2 \epsilon^2 \left(\frac{w_{i+1,j} - 2w_{i,j} + w_{i-1,j}}{\delta^2} + 2\Lambda u_{i,j}^2 w_{i,j} - \frac{c^2}{\hbar^2} m_\phi^2 w_{i,j} \right). \quad (5.6)$$

To get the forward time solutions, then the both coupled EOMs are rewritten in explicit discrete forms as follows,

$$u_{i,j+1} = 2u_{i,j} - u_{i,j-1} + c^2 \epsilon^2 \left(\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\delta^2} + 2\Lambda w_{i,j}^2 u_{i,j} - \frac{\lambda}{6} u_{i,j}^3 \right), \quad (5.7)$$

$$w_{i,j+1} = 2w_{i,j} - w_{i,j-1} + c^2 \epsilon^2 \left(\frac{w_{i+1,j} - 2w_{i,j} + w_{i-1,j}}{\delta^2} + 2\Lambda u_{i,j}^2 w_{i,j} - \frac{c^2}{\hbar^2} m_\phi^2 w_{i,j} \right), \quad (5.8)$$

for $i = 2, 3, \dots, N - 1$ and $j = 2, 3, \dots, M - 1$.

In order to calculate all values of Eqs. (5.7) and (5.8), the initial values for two lowest rows in Fig. (5.1) must be given. On the other hand, the value at t_1 is fixed by the boundary conditions in Eq. (5.1). The values in the second

row can be determined using the second order Taylor expansion as following

$$u(x, \epsilon) = u(x, 0) + u_t(x, 0)\epsilon + u_{tt}(x, 0)\frac{\epsilon^2}{2}, \quad (5.9)$$

$$w(x, \epsilon) = w(x, 0) + w_t(x, 0)\epsilon + w_{tt}(x, 0)\frac{\epsilon^2}{2}. \quad (5.10)$$

where the values of $u(x, 0)$, $w(x, 0)$, $u_t(x, 0)$, $w_t(x, 0)$, $u_{tt}(x, 0)$, and $w_{tt}(x, 0)$ has been determined in the boundary conditions Eq. (5.1) and the explicit time derivatives of EOMs Eqs. (5.2) and (5.3) respectively.

Furthermore, substituting all the values which has been known and rewriting it in discrete form. Therefore, the values at t_2 are determined by,

$$u_{i,2} = f_i - \epsilon g_i + \frac{c^2 \epsilon^2}{2} \left(\frac{f_{i+1} - 2f_i + f_{i-1}}{\delta^2} + 2\Lambda p_i^2 f_i - \frac{\lambda}{6} f_i^3 \right), \quad (5.11)$$

$$w_{i,2} = p_i - \epsilon q_i + \frac{c^2 \epsilon^2}{2} \left(\frac{p_{i+1} - 2p_i + p_{i-1}}{\delta^2} + 2\Lambda f_i^2 p_i - \frac{c^2}{\hbar^2} m_\phi^2 p_i \right), \quad (5.12)$$

for $i = 2, 3, \dots, N - 1$.

For the initial stage, suppose the nonlinear sources has a particular form $f(x) = 2\text{sech}(2x) e^{i2x}$ and $g(x) = 1$ to generate the α -helix, while $g(x) = q(x) = 0$ for the sake of simplicity. Then, one can obtain the initial values in this case using Eqs. (5.11) and (5.12). The subsequent values are generated by substituting the preceding values into Eqs. (5.7) and (5.8). The higher order values can be obtained using iterative procedure.

In this case, the values of the constants in the protein folding simulation are chosen as follows (in natural units)

$$\begin{aligned} m &= 0.08 \text{ eV} \equiv 1.42 \times 10^{-37} \text{ kg}, \\ L &= 12 \text{ eV}^{-1} \equiv 2,364 \text{ nm}, \\ \Lambda &= 2.83 \times 10^{-3}, \\ \lambda &= 3 \times 10^{-4}. \end{aligned} \quad (5.13)$$

Although the constants was chosen arbitrarily, but it must be satisfied into

the constrains in Eq. (4.12).

5.2 The Nonlinear Conformation Model

Same as with the linear one, the EOMs in Eqs. (4.30) and (4.31) will be solved using forward finite difference method. In the scheme, with same procedures as above, it is more convenient to replace ψ and ϕ with u and w respectively and rewritten it in explicit discrete forms as follows,

$$u_{i,j+1} = 2u_{i,j} - u_{i,j-1} + c^2 \epsilon^2 \left(\frac{u_{i+1,j} - 2u_{i,j} + u_{i-1,j}}{\delta^2} + 2\Lambda w_{i,j}^2 u_{i,j} - \frac{\lambda_\psi}{6} u_{i,j}^3 \right), \quad (5.14)$$

$$w_{i,j+1} = 2w_{i,j} - w_{i,j-1} + c^2 \epsilon^2 \left(\frac{w_{i+1,j} - 2w_{i,j} + w_{i-1,j}}{\delta^2} + 2\Lambda u_{i,j}^2 w_{i,j} - \frac{m_\phi^3 c^3}{\hbar^3 \sqrt{\lambda_\phi}} \sin \left(\frac{\sqrt{\lambda_\phi}}{m_\phi} w_{i,j} \right) \right), \quad (5.15)$$

for $i = 2, 3, \dots, N-1$ and $j = 2, 3, \dots, M-1$. Forward iterative procedure of the discrete EOMs can be performed if the two lowest time values are known.

First, the value at t_1 is fixed by the following boundary conditions,

$$\begin{aligned} \psi(0, t) = \psi(L, t) = 0 \quad \text{and} \quad \phi(0, t) = \phi(L, t) = 0 & \quad \text{for} \quad 0 \leq t \leq b, \\ \psi(x, 0) = f(x) \quad \text{and} \quad \phi(x, 0) = p(x) & \quad \text{for} \quad 0 \leq x \leq L, \\ \frac{\partial \psi(x, 0)}{\partial t} = g(x) \quad \text{and} \quad \frac{\partial \phi(x, 0)}{\partial t} = q(x) & \quad \text{for} \quad 0 < x < L, \end{aligned} \quad (5.16)$$

with $f(x)$, $p(x)$, $g(x)$ and $q(x)$ are newly introduced auxiliary functions. Secondly, the values at t_2 can be determined using second order Taylor expansion,

$$u_{i,2} = f_i - \epsilon g_i + \frac{c^2 \epsilon^2}{2} \left(\frac{f_{i+1} - 2f_i + f_{i-1}}{\delta^2} + 2\Lambda p_i^2 f_i - \frac{\lambda_\psi}{6} f_i^3 \right), \quad (5.17)$$

$$w_{i,2} = p_i - \epsilon q_i + \frac{c^2 \epsilon^2}{2} \left(\frac{p_{i+1} - 2p_i + p_{i-1}}{\delta^2} + 2\Lambda f_i^2 p_i - \frac{m_\phi^3 c^3}{\hbar^3 \sqrt{\lambda_\phi}} \sin \left(\frac{\sqrt{\lambda_\phi}}{m_\phi} p_i \right) \right), \quad (5.18)$$

for $i = 2, 3, \dots, N - 1$. $\delta = \Delta x$ and $\epsilon = \Delta t$ constitutes the side length between the discretized value.

At the initial stage, suppose the nonlinear source and conformation fields have particular form of $f(x) = 2\text{sech}(2x)e^{i2x}$ and $g(x) = \arctan[\exp(4x - 10)]$, while $g(x) = q(x) = 0$ for the sake of simplicity. Furthermore, the numerical solutions can be obtained by iterative procedure against Eqs. (5.14) and (5.15) using the results in Eqs. (5.17) and (5.18) with the boundary conditions in Eq. (5.16).

The numerical script programs that have been used to solve the EOMs for the both models with applying this finite difference method can be seen in appendix B. The script was made in MATLAB R2009a's program. And remember that results for this simulation will be given in chapter 7.

Chapter 6

Statistical Mechanics

The laws of thermodynamics may easily be obtained from the principles of statistical mechanics, of which they are the incomplete expression.

Gibbs

Investigating some physical quantities in the model in order to compare with the already available results are very important. The relevant observables, such as; free energy, heat capacity, and etc., can be conveniently seen from its statistical mechanics properties which is started by considering the partition function. It will be calculated using path integral method with perturbation approach directly from the lagrangian [30, 15, 14].

In statistical mechanics, the partition function usually is written as,

$$Z = \sum_j e^{-\beta E_j} , \quad (6.1)$$

where $\beta = \frac{1}{k_B T}$ and E_j is the energy of the state $|j\rangle$ which obeys,

$$H|j\rangle = E_j|j\rangle . \quad (6.2)$$

Thus, Z can be written in eigenstate form as follow,

$$Z = \sum_j \langle j | e^{-\beta H} | j \rangle . \quad (6.3)$$

In this work, the partition function will be solved using path integral method. Meanwhile, the path integral derivation are absolutely independent to statistical mechanics and vice versa. So that, the relation between Z and the path integral calculation should be found. It will be done by starting from the definition of the propagator [30],

$$K(q', T; q, 0) = \langle q' | e^{-iTH} | q \rangle . \quad (6.4)$$

where T will be considered to be pure imaginary, that is $T = i\beta$ with β is real. Thus the propagator can be written as,

$$K(q', -i\beta; q, 0) = \langle q' | e^{-i(-i\beta)H} | q \rangle . \quad (6.5)$$

Using an ordinary discrete completeness relation $\sum_j |j\rangle\langle j| = 1$ [31], the propagator can be simplified as follows,

$$\begin{aligned} K(q', -i\beta; q, 0) &= \langle q' | e^{-\beta H} \sum_j |j\rangle\langle j| q \rangle \\ &= \sum_j \langle q' | e^{-\beta H} |j\rangle\langle j| q \rangle \\ &= \sum_j e^{-\beta E_j} \langle q' | j \rangle \langle j | q \rangle \\ &= \sum_j e^{-\beta E_j} \langle j | q \rangle \langle q' | j \rangle . \end{aligned} \quad (6.6)$$

Integrating it in term of canonical space q , and using continuous completeness relation $\int dq |q\rangle\langle q|$, obtains

$$\begin{aligned} \int dq K(q, -i\beta; q, 0) &= \int dq \sum_j e^{-\beta E_j} \langle j | q \rangle \langle q | j \rangle \\ &= \sum_j e^{-\beta E_j} . \end{aligned} \quad (6.7)$$

Thus it is arrive at the form of the partition function Z ,

$$\int dq K(q, -i\beta; q, 0) = Z . \quad (6.8)$$

Therefore the partition function can be formed in the path integral scheme.

Employing the above properties and the propagator form in chapter 2, the generating functional for scalar fields can be defined as [15]

$$Z = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ i \int d^2x \mathcal{L}_{tot}(\phi, \psi) \right\} \propto \langle 0, \infty | 0, -\infty \rangle, \quad (6.9)$$

where \mathcal{L} is an interacting lagrangian density of the system. The partition function can be obtained from the generating functional by implementing a Wick rotation of the real axis [19]. Define imaginary time $it = \tau$ and limiting the range between $0 \rightarrow \beta$ to perform periodicity condition of the field ($\phi(0,0) = \phi(L,\beta)$). In this case, L is a fixed boundary of one dimensional space of protein backbone. In other word, the integration of the field becomes finite. This is specifically leads to the finite temperature case in Euclidean coordinates.

$$Z = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int_0^\beta \int_0^L d\tau dx \mathcal{L}_{tot}(\phi, \psi) \right\}. \quad (6.10)$$

The partition function of the system can be obtained by substituting the total lagrangian from the both models into this generating functional.

6.1 The Linear Conformation Model

The aspect of the system that has a physical meaning is represented in real component of the field. There is no physical interpretation in the imaginary term yet. Assuming the fields are hermitian, then the real term of the generating functional for the linear model can be written as follow,

$$Z_{LCM} = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x \left(\frac{1}{2} \partial_\mu \phi \partial^\mu \phi + \frac{1}{2} m_\phi^2 \phi^2 + \frac{1}{2} \partial_\mu \psi \partial^\mu \psi + \frac{\lambda}{4!} \psi^4 - \Lambda \phi^2 \psi^2 \right) \right\}. \quad (6.11)$$

where $\int d^2x$ stands for $\int_0^\beta d\tau \int_0^L dx$ in case of abbreviation the notation. Label LCM in Z stands for the linear conformational model. It used to differentiate with the nonlinear one, since its partition function will be calculated in the

next chapter.

The lagrangian of the system has nonlinear terms, its so hard to solve directly. Some mathematical trick would be attempted to seek a way the interactions become functional derivatives in respect to external source. Furthermore, the lagrangian remains linear and can be solved by using Fourier's representation.

Considering the vacuum transition amplitude in the presence of current $J(x)$. In this case, the interactions formed as a linear form of the source. Actually, this method is involving the behaviour of Gaussian integral.

$$Z_0[J_\psi(x), J_\phi(x)] = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x [\mathcal{L}_0(\phi, \psi) + J_\phi(x)\phi(x) + J_\psi(x)\psi(x)] \right\}, \quad (6.12)$$

where $\mathcal{L}_0(\phi, \psi) = \frac{1}{2}\partial_\mu\phi\partial^\mu\phi + \frac{1}{2}m_\phi^2\phi^2 + \frac{1}{2}\partial_\mu\psi\partial^\mu\psi$. The generating functional will be simplified become derivatives of the linear vacuum transition in Eq. (6.12). But remember of course this system does not involve the external current J . To fulfill it, takes $J = 0$ at the end of the calculations.

The functional derivative of the transition respect to J_ψ is

$$\begin{aligned} \left. \frac{\delta Z_0[J(x)]}{\delta J_\psi(y)} \right|_{J_\phi=0, J_\psi=0} &= \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x [\mathcal{L}_0 + J_\phi(x)\phi(x)] \right\} \\ &\quad \times \frac{\delta}{\delta J_\psi(y)} \exp \left\{ \int d^2x [J_\psi(x)\psi(x)] \right\} \\ &= \lim_{\epsilon \rightarrow 0} \frac{1}{\epsilon} \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x [\mathcal{L}_0 + J_\phi(x)\phi(x)] \right\} \\ &\quad \times \left(\exp \left\{ \int d^2x [(J_\psi(x) + \epsilon\delta(x-y))\psi(x)] \right\} \right. \\ &\quad \left. - \exp \left\{ \int d^2x [J_\psi(x)\psi(x)] \right\} \right) \\ &= \lim_{\epsilon \rightarrow 0} \frac{Z_0}{\epsilon} \left(\exp \left\{ \int d^2x \epsilon\delta(x-y)\psi(x) \right\} - 1 \right). \quad (6.13) \end{aligned}$$

The term of $\exp \left\{ \int d^2x \epsilon\delta(x-y)\psi(x) \right\}$ can be expanded using Taylor's expansion. Because of ϵ is very small, this expansion can be approached only first

two terms.

$$\exp \left\{ \int d^2x \epsilon \delta(x-y) \psi(x) \right\} \approx 1 + \int d^2x \epsilon \delta(x-y) \psi(x) . \quad (6.14)$$

Then the derivative becomes

$$\begin{aligned} \left. \frac{\delta Z_0}{\delta J_\psi} \right|_{J_\phi=0, J_\psi=0} &= \lim_{\epsilon \rightarrow 0} \frac{Z_0}{\epsilon} \left(1 + \int d^2x \epsilon \delta(x-y) \psi(x) - 1 \right) \\ &= \lim_{\epsilon \rightarrow 0} \frac{Z_0}{\epsilon} \epsilon \psi(y) \\ &= Z_0 \psi(y) . \end{aligned} \quad (6.15)$$

Therefore, the fourth derivatives in respect to $J_\psi(x)$ can be obtained as

$$\left. \frac{\delta^4 Z_0}{\delta J_\psi^4(x)} \right|_{J_\phi=0, J_\psi=0} = Z_0 \psi^4(x) . \quad (6.16)$$

Put by hand a constant $\frac{\lambda}{4!}$ in front of the derivative and integration it about x ,

$$\left(\int d^2x \frac{\lambda}{4!} \frac{\delta^4}{\delta J_\psi^4} \right) Z_0 = Z_0 \left(\int d^2x \frac{\lambda}{4!} \psi^4 \right) . \quad (6.17)$$

The higher order derivatives will be gotten in the similar way. Further adding Eqs. (6.12) and (6.17), and then the higher order derivatives, will obtain

$$\begin{aligned} \left(1 + \frac{\lambda}{4} \int d^2x \frac{\delta^4}{\delta J_\psi^4} + \dots \right) Z_0 &= Z_0 \left(1 + \int dx \frac{\lambda}{4} \psi^4 + \dots \right) \\ \exp \left\{ \frac{\lambda}{4} \int d^2x \frac{\delta^4}{\delta J_\psi^4} \right\} Z_0 &= Z_0 \exp \left\{ \int d^2x \frac{\lambda}{4!} \psi^4 \right\} \\ &= \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x [\mathcal{L}_0 + J_\phi \phi \right. \\ &\quad \left. + J_\psi \psi + \frac{\lambda}{4!} \psi^4] \right\} . \end{aligned} \quad (6.18)$$

Remember that the external current must be vanished ($J_\phi, J_\psi = 0$). Therefore

$$\exp \left\{ \frac{\lambda}{4!} \int d^2x \frac{\delta^4}{\delta J_\psi^4} \Big|_{J_\phi=0, J_\psi=0} \right\} Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x \left[\mathcal{L}_0 + \frac{\lambda}{4!} \psi^4 \right] \right\} . \quad (6.19)$$

One of the interacting fields has been changed into functional derivatives form. But this work is not finish yet. There is remaining a coupled-interaction that has not changed into functional derivative form yet. In the same way with before, the interaction can be found by functional derivative trick. Since the remain interaction is involving two fields, the functional derivatives must do to the both external currents. By using the same way as the derivation of Eq. (6.16), the forth derivatives of Z_0 respect to both J_ϕ and J_ψ can be obtained as,

$$\frac{\delta^4 Z_0}{\delta J_\phi^2 \delta J_\psi^2} \Big|_{J_\phi=0, J_\psi=0} = Z_0 \phi^2 \psi^2 . \quad (6.20)$$

Mix up the higher derivatives until yield an exponential form same as before. Put a coupling constant Λ and integration it over space-time x . We have

$$\exp \left\{ \Lambda \int d^2x \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \Big|_{J_\phi=0, J_\psi=0} \right\} Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x \left[\mathcal{L}_0 + \Lambda \phi^2 \psi^2 \right] \right\} . \quad (6.21)$$

As can be seen in Eqs. (6.19) and (6.21), it can be concluded that the fields have been constructed into functional derivative operators form as follows

$$\psi^4 \rightarrow \frac{\delta^4}{\delta J_\psi^4} \Big|_{J_\phi=0, J_\psi=0} , \quad (6.22)$$

$$\phi^2 \psi^2 \rightarrow \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \Big|_{J_\phi=0, J_\psi=0} . \quad (6.23)$$

If we add them inside the exponential functional and do it into Z_0 , then the result back to the complete form of the generating functional as in Eq. (6.11) that has been desired before. The generating functional becomes the functional derivatives exponentially from a linear lagrangian respect to the sources.

Therefore, the form of Z looks simpler.

$$Z_{LCM} = \exp \left\{ \int d^2x \left(\frac{\lambda}{4!} \frac{\delta^4}{\delta J_\psi^4} + \Lambda \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \right) \Big|_{J_\phi=0, J_\psi=0} \right\} Z_0[J_\phi, J_\psi]. \quad (6.24)$$

6.1.1 Calculation of the Vacuum Transition Amplitude

To complete the calculation, the form of the vacuum transition amplitude Z_0 in term of current J should be found. The lagrangian density in Z_0 is linear, then it can be evaluated by using Fourier representation of Green's function. It just seems like a generating functional for ordinary free bosonic particle with external current. Simplifying the expression $\partial_\mu \phi \partial^\mu \phi$ and $\partial_\mu \psi \partial^\mu \psi$ in the \mathcal{L}_0 by evaluate this [15]

$$\partial_\mu (\phi \partial^\mu \phi) = \partial_\mu \phi \partial^\mu \phi + \phi \partial_\mu \partial^\mu \phi \quad (6.25)$$

where $\partial_\mu \partial^\mu$ can be written as D'Alembertian. Exchange the position, so we have

$$\partial_\mu \phi \partial^\mu \phi = \partial_\mu (\phi \partial^\mu \phi) - \phi \square \phi \quad (6.26)$$

The first term of right side can be vanished by taking $\phi \rightarrow 0$ at infinity. Then, also for ψ in the same way, we will be obtained

$$\partial_\mu \phi \partial^\mu \phi = -\phi \square \phi, \text{ and } \partial_\mu \psi \partial^\mu \psi = -\psi \square \psi. \quad (6.27)$$

Remembering that the system only contains one dimensional space and an imaginary time, then D'Alembertian stands only for

$$\square \equiv -\frac{\partial^2}{\partial t^2} - \frac{\partial^2}{\partial x^2}. \quad (6.28)$$

Substituting this result into \mathcal{L}_0 . Thus

$$Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int d^2x \left(-\frac{1}{2} \phi (\square + m_\phi^2) \phi - \frac{1}{2} \psi \square \psi + J_\phi \phi + J_\psi \psi \right) \right\} \quad (6.29)$$

In this work, the fields will be approached more simple. The wave function of the system is approximately has a mean value that corresponding to classical

trajectory and a fluctuation value around of the mean value. In other words, there are combines quantum and classical aspect in the system. Therefore, the fields in the lagrangian can be expanded as [14]

$$\begin{aligned}\phi &\rightarrow \bar{\phi}(x) \\ \psi &\rightarrow \bar{\psi}(x) + \psi'(x)\end{aligned}\quad (6.30)$$

where $\bar{\phi}$ and $\bar{\psi}$ are the mean fields of the classical path while ψ' is the dispersion of the solution. Variational of the conformational field ϕ' does not give a significant contribution into the system. This leads us to the fact that the protein is a classical matter that has an infinitesimal dispersion relative to the mean value, then the quantum aspect of the field can be ignored ($\phi' = 0$). Beside of that, the classical path must be satisfied with the classical equation of motions that obtained from the lagrangian. Then the linear terms could be vanished in the integration over all the path [30]. The expression of the vacuum generating functional Eq. (6.29) becomes

$$\begin{aligned}Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ - \int d^2x \left(\frac{1}{2} \bar{\phi} (\square + m_\phi^2) \bar{\phi} - J \bar{\phi} + \frac{1}{2} \bar{\psi} \square \bar{\psi} \right. \right. \\ \left. \left. + \frac{1}{2} \bar{\psi} \square \psi' + \frac{1}{2} \psi' \square \bar{\psi} + \frac{1}{2} \psi' \square \psi' - J \bar{\psi} - J \psi' \right) \right\},\end{aligned}\quad (6.31)$$

Use analogous argument that was obtaining Eq. (6.27) obtains relation as

$$\int \bar{\psi} \square \psi' d^2x = \int \psi' \square \bar{\psi} d^2x ,\quad (6.32)$$

then we have

$$\begin{aligned}Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ - \int d^2x \left(\frac{1}{2} \bar{\phi} (\square + m_\phi^2) \bar{\phi} - J \bar{\phi} + \frac{1}{2} \bar{\psi} \square \bar{\psi} \right. \right. \\ \left. \left. + \psi' \square \bar{\psi} + \frac{1}{2} \psi' \square \psi' - J \bar{\psi} - J \psi' \right) \right\},\end{aligned}\quad (6.33)$$

The lagrangian has been changed to the linear form, and then taking the solution of $\bar{\phi}$ and $\bar{\psi}$ by the Fourier representations [15],

$$\bar{\psi}(x) \rightarrow \square \bar{\psi}(x) = J(x) ,$$

$$\bar{\phi}(x) \rightarrow (\square + m_\phi^2) \bar{\phi}(x) = J(x) . \quad (6.34)$$

These equations have solutions in Fourier representations, that is

$$\begin{aligned} \bar{\psi}(x) &= - \int \Delta_\psi(x-y) J_\psi(y) d^2y , \\ \bar{\phi}(x) &= - \int \Delta_\phi(x-y) J_\phi(y) d^2y , \end{aligned} \quad (6.35)$$

where $\Delta(x-y)$ is called Feynman propagator. Substituting Eq. (6.34) to Eq. (6.33) obtains

$$Z_0 = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ - \int d^2x \left(-\frac{1}{2} \bar{\phi} J_\phi - \frac{1}{2} \bar{\psi} J_\psi + \frac{1}{2} \psi' \square \psi' \right) \right\} , \quad (6.36)$$

And then substituting Eq. (6.35) into the result, will obtain Z_0 in term of J as follow

$$\begin{aligned} Z_0 &= \exp \left\{ -\frac{1}{2} \int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right\} \\ &\times \int \mathcal{D}\psi' \exp \left\{ - \int d^2x \frac{1}{2} \psi' \square \psi' \right\} . \end{aligned} \quad (6.37)$$

Under this approximation, only ψ' that can be hold in the path integral. Suppose N is the path integral result for the fluctuation field term. By defining the ψ as a Fourier's series, the value of N can be obtained as [30],

$$N = \frac{1}{4\pi \sinh(\frac{k\beta}{2})} . \quad (6.38)$$

Furthermore, let us calculate the vacuum transition amplitude by expanding the Eq. (6.37) using Taylor's expansion.

$$\begin{aligned} Z_0 &= N \left\{ 1 - \frac{1}{2} \int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right. \\ &\quad + \frac{1}{2!} \left(\frac{1}{2} \right)^2 \left(\int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) \right. \\ &\quad \left. \left. + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right)^2 + \dots \right\} . \end{aligned} \quad (6.39)$$

First term of the expansion of the both fields are irrelevant to involve in the

calculation, because it will be vanished if given the fourth functional derivatives in respect to J . The term that can be possible to describe the ϕ^4 interaction is only the quadratic term. The higher order term will be vanished by setting $J = 0$ [30].

$$Z_0 \approx \frac{1}{2!} \left(\frac{1}{2}\right)^2 N \left(\int d^2x d^2y [J_\phi(x) \Delta_\phi(x-y) J_\phi(y) + J_\psi(x) \Delta_\psi(x-y) J_\psi(y)] \right)^2 . \quad (6.40)$$

The Taylor's expansion will be used to expand Eq. (6.24), and then do it into the Eq. (6.40). Then we have

$$Z_{LCM} = N \exp \left\{ \int d^2x \left(\frac{\lambda}{4!} \frac{\delta^4}{\delta J_\psi^4(x)} + \Lambda \frac{\delta^4}{\delta J_\phi^2(x) \delta J_\psi^2(x)} \right) \right\} \\ \times \frac{1}{2!} \left(\frac{1}{2}\right)^2 \left(\int d^2x_1 d^2x_2 [J_\phi(x_1) \Delta_\phi(x_1-x_2) J_\phi(x_2) + J_\psi(x_1) \Delta_\psi(x_1-x_2) J_\psi(x_2)] \right)^2 . \quad (6.41)$$

This derivatives will be taken approximately from the first term in the Taylor's expansion of Eq. (6.41). Exponential functional of the first term has been represented all the terms of the derivatives. In the case of abbreviation the notation let us define

$$\zeta = \int d^2x \left(\frac{\lambda}{4!} \frac{\delta^4}{\delta J_\psi^4(x)} + \Lambda \frac{\delta^4}{\delta J_\phi^2(x) \delta J_\psi^2(x)} \right) , \\ \kappa = \int d^2x_1 d^2x_2 [J_\phi(x_1) \Delta_\phi(x_1-x_2) J_\phi(x_2) + J_\psi(x_1) \Delta_\psi(x_1-x_2) J_\psi(x_2)] , \\ \dot{\kappa}_\psi = \frac{\delta \kappa}{\delta J_\psi(x)} = \int d^2x_2 \Delta_\psi(x-x_2) J_\psi(x_2) + \int d^2x_1 J_\psi(x_1) \Delta_\psi(x_1-x) , \\ \dot{\kappa}_\phi = \frac{\delta \kappa}{\delta J_\phi(x)} = \int d^2x_2 \Delta_\phi(x-x_2) J_\phi(x_2) + \int d^2x_1 J_\phi(x_1) \Delta_\phi(x_1-x) , \\ \ddot{\kappa}_\psi = \frac{\delta^2 \kappa}{\delta J_\psi^2(x)} = 2\Delta_\psi(0) , \\ \ddot{\kappa}_\phi = \frac{\delta^2 \kappa}{\delta J_\phi^2(x)} = 2\Delta_\phi(0) . \quad (6.42)$$

Then the generating functional can be written in more compact form

$$Z_{LCM} = N \exp \left\{ \zeta \right\} \frac{1}{2!} \left(\frac{1}{2} \right)^2 \kappa^2. \quad (6.43)$$

In this abbreviate notations, let us evaluate

$$\begin{aligned} \zeta \kappa^2 &= \int d^2x \left\{ \frac{\lambda}{4!} \frac{\delta^4 \kappa^2}{\delta J_\psi^4(x)} + \Lambda \frac{\delta^4 \kappa^2}{\delta J_\phi^2(x) \delta J_\psi^2(x)} \right\} \\ &= \int d^2x \left\{ \frac{2\lambda}{4!} \frac{\delta^3}{\delta J_\psi^3(x)} [\kappa \dot{\kappa}_\psi] + 2\Lambda \frac{\delta^3}{\delta J_\phi^2(x) \delta J_\psi(x)} [\kappa \dot{\kappa}_\psi] \right\} \\ &= \int d^2x \left\{ \frac{2\lambda}{4!} \frac{\delta^2}{\delta J_\psi^2(x)} [\dot{\kappa}_\psi^2 + 2\Delta_\psi(0)\kappa] + 2\Lambda \frac{\delta^2}{\delta J_\phi^2(x)} [\dot{\kappa}_\psi^2 + 2\Delta_\psi(0)\kappa] \right\} \\ &= \int d^2x \left\{ \frac{2\lambda}{4!} \frac{\delta}{\delta J_\psi(x)} [4\dot{\kappa}_\psi \Delta_\psi(0) + 2\Delta_\psi(0)\dot{\kappa}_\psi] + 2\Lambda \frac{\delta}{\delta J_\phi(x)} [2\Delta_\psi(0)\dot{\kappa}_\phi] \right\} \\ &= \int d^2x \left\{ \frac{24}{4!} \lambda \Delta_\psi^2(0) + 8\Lambda \Delta_\phi(0) \Delta_\psi(0) \right\}. \end{aligned} \quad (6.44)$$

The value is valid only for the fourth derivative term. The result for all the terms are the exponential function of this value. Therefore the generating functional can be obtained as

$$Z_{LCM} = N \exp \left\{ \int_0^\beta d\tau \int_0^L dx \left[\frac{3}{4!} \lambda \Delta_\psi^2(0) + \Lambda \Delta_\phi(0) \Delta_\psi(0) \right] \right\}, \quad (6.45)$$

This is the partition function form that we are looking for.

In the next section, the partition function for the nonlinear conformational model will be calculated.

6.2 The Nonlinear Conformation Model

Actually, this calculation will be similar with the above preceding model [32]. The difference only lies in the additional nonlinear conformational term. The partition function will be also calculated from the bosonic generating functional using perturbation approach [30] and takes the non-relativistic limit by implementing a Wick rotation of the real axis [19]. Same as before, these are analogous to the finite temperature case in Euclidean coordinates.

The partition function of the system can be obtained by solving the total lagrangian from the nonlinear conformation model from the section 4.2 into the generating functional as follows,

$$Z_{NCM} = \int \mathcal{D}\phi \mathcal{D}\psi \exp \left\{ \int_0^\beta d\tau \int_0^L dx \left(\frac{1}{2} \partial_\mu \phi \partial^\mu \phi + \frac{m_\phi^2}{2} \phi^2 - \frac{\lambda_\phi}{4!} \phi^4 + \frac{1}{2} \partial_\mu \psi \partial^\mu \psi + \frac{\lambda_\psi}{4!} \psi^4 - \Lambda \phi^2 \psi^2 \right) \right\}, \quad (6.46)$$

where τ is an imaginary time with the limited integral range between $-\frac{\beta}{2} \rightarrow \frac{\beta}{2}$ to perform periodicity condition of the field ($\phi(0, -\frac{\beta}{2}) = \phi(L, \frac{\beta}{2})$), and L is a fixed boundary of one dimensional space of protein backbone. In this case, the fields are assuming to be hermitian $\phi^\dagger = \phi$. Therefore the integration of the lagrangian becomes finite and constitutes its non-relativistic limit.

The lagrangian of the model is involving nonlinear and interaction terms. So that, the integral will be calculated by involving the properties of Gaussian integral. This is important to simplify the interaction terms in the lagrangian become sequences of functional derivatives in term of external current $J(x)$. Furthermore, the lagrangian remains linear and can be solved by using Fourier's plane wave approach.

Same as before, by utilizing functional derivative properties to the vacuum transition amplitude in the presence of external current Eq. (6.12), the partition function Eq. (6.46) can be linearized. But remember of course all the currents J should be taken equal zero at the end of the calculation to fulfill the fact that there are no external currents J in the model.

After linearization, the interaction terms in the lagrangian will be constructed become functional derivative operators as previously done [32],

$$\begin{aligned} \phi^4 &= \left. \frac{\delta^4}{\delta J_\phi^4} \right|_{J_\phi=0, J_\psi=0}, \quad \psi^4 = \left. \frac{\delta^4}{\delta J_\psi^4} \right|_{J_\phi=0, J_\psi=0}, \quad \text{and} \\ \phi^2 \psi^2 &= \left. \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \right|_{J_\phi=0, J_\psi=0}. \end{aligned} \quad (6.47)$$

Therefore Z can be written in functional derivatives form,

$$Z_{NCM} = \exp \left\{ \int d^2x \left(\frac{\lambda_\phi}{4!} \frac{\delta^4}{\delta J_\phi^4} + \frac{\lambda_\psi}{4!} \frac{\delta^4}{\delta J_\psi^4} + \Lambda \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \right) \Big|_{J_\phi=0, J_\psi=0} \right\} Z_0[J_\phi, J_\psi]. \quad (6.48)$$

In contrast with the our preceding model, there is one additional functional derivative term in the exponential. This is important to investigate the contribution of the new term to show that the folded pathways are really induced and dominated by the nonlinear sources or not.

The lagrangian of Z_0 has been evaluated in our previous section by using Fourier's representative with the underlying assumptions as follows [32, 15, 30, 14],

$$\begin{aligned} \phi, \psi &\rightarrow 0 \text{ at infinity, then } \partial_\mu \phi \partial^\mu \phi = -\phi \square \phi \text{ and } \partial_\mu \psi \partial^\mu \psi = -\psi \square \psi. \\ \phi &\rightarrow \bar{\phi}(x), \text{ where } \bar{\phi}(x) = \int \Delta_\phi(x-y) J_\phi(y) d^2y. \\ \psi &\rightarrow \bar{\psi}(x) + \psi'(x), \text{ where } \bar{\psi}(x) = \int \Delta_\psi(x-y) J_\psi(y) d^2y. \end{aligned} \quad (6.49)$$

where $\bar{\phi}$ and $\bar{\psi}$ are the mean fields of the classical path, while ψ' is the dispersion of the solution. In this model, D'Alembertian \square only contains one dimensional space and an imaginary time,

$$\square \equiv -\frac{\partial^2}{\partial t^2} - \frac{\partial^2}{\partial x^2}. \quad (6.50)$$

From the our previous section, Z_0 can be written

$$Z_0 = N \exp \left\{ \frac{1}{2} \int d^2x_1 d^2x_2 [J_\phi(x_1) \Delta_\phi(x_1-x_2) J_\phi(x_2) + J_\psi(x_1) \Delta_\psi(x_1-x_2) J_\psi(x_2)] \right\}, \quad (6.51)$$

where $\int d^2x$ and N stand for $\int_0^\beta d\tau \int_0^L dx$ and $\int \mathcal{D}\psi' \exp \left\{ -\int d^2x_1 \frac{1}{2} \psi' \square \psi' \right\}$ respectively.

Considering the Taylor's expansion of Z_0 , only quadratic term which can be possible to be exist. The lower order term of the expansions will be vanished

if given the fourth functional derivatives in term of J , meanwhile the higher order term will be vanished by setting $J = 0$ [30]. Therefore the partition function in Eq. (6.48) can be written as follow,

$$\begin{aligned}
Z_{NCM} = & N \exp \left\{ \int d^2x \left(\frac{\lambda_\phi}{4!} \frac{\delta^4}{\delta J_\phi^4} + \frac{\lambda_\psi}{4!} \frac{\delta^4}{\delta J_\psi^4} + \Lambda \frac{\delta^4}{\delta J_\phi^2 \delta J_\psi^2} \right) \Big|_{J_\phi=0, J_\psi=0} \right\} \\
& \times \frac{1}{2!} \left(\frac{1}{2} \right)^2 \left(\int d^2x_1 d^2x_2 [J_\phi(x_1) \Delta_\phi(x_1 - x_2) J_\phi(x_2) \right. \\
& \left. + J_\psi(x_1) \Delta_\psi(x_1 - x_2) J_\psi(x_2)] \right)^2 . \tag{6.52}
\end{aligned}$$

The exponential derivatives will be solved by taking approximately from the second order term in the Taylor's expansion of Eq. (6.52). Exponential functional of the term has been represented for all the terms of the derivatives. Then the partition function for the nonlinear conformational model can be obtained as

$$\begin{aligned}
Z_{NCM} = & N \exp \left\{ \int_0^\beta d\tau \int_0^L dx \left[\frac{3}{4!} \lambda_\phi \Delta_\phi^2(0) + \frac{3}{4!} \lambda_\psi \Delta_\psi^2(0) \right. \right. \\
& \left. \left. + \Lambda \Delta_\phi(0) \Delta_\psi(0) \right] \right\} . \tag{6.53}
\end{aligned}$$

Having the partition function for the both models at hand, one can obtain some thermodynamics quantities, such as; free energy, heat capacity and etc. The result will be shown in chapter 7.

Chapter 7

Results and Discussions

Physicists like to think that all you have to do is say, these are the conditions, now what happens next?.

Richard Feynman

As can be seen in the two previous chapters, the results for our models embraced numerical simulation and statistical mechanics properties, have been obtained. In this chapter, discussions for the results will be given. Some comparison about the both models also will be discussed.

7.1 The Numerical Simulations

The numerical procedure for the linear conformational model has been done as can be seen Fig. (7.1). The left figure in each box describes the propagation of nonlinear sources in protein backbone, while the right one shows how the protein is folded. As can be seen in the figure, the protein backbone is initially linear before the nonlinear source injection. As the soliton started propagating over the backbone, the conformational changes appear. It generates the folding pathway from primary unfolded state to the secondary alpha helix state.

Furthermore, the numerical analysis for the nonlinear conformation model has been performed and the results are given in Fig. (7.2). Same as previous, the left figures in each box describe the propagation of nonlinear sources in protein backbone, while the right ones show how the protein is folded according

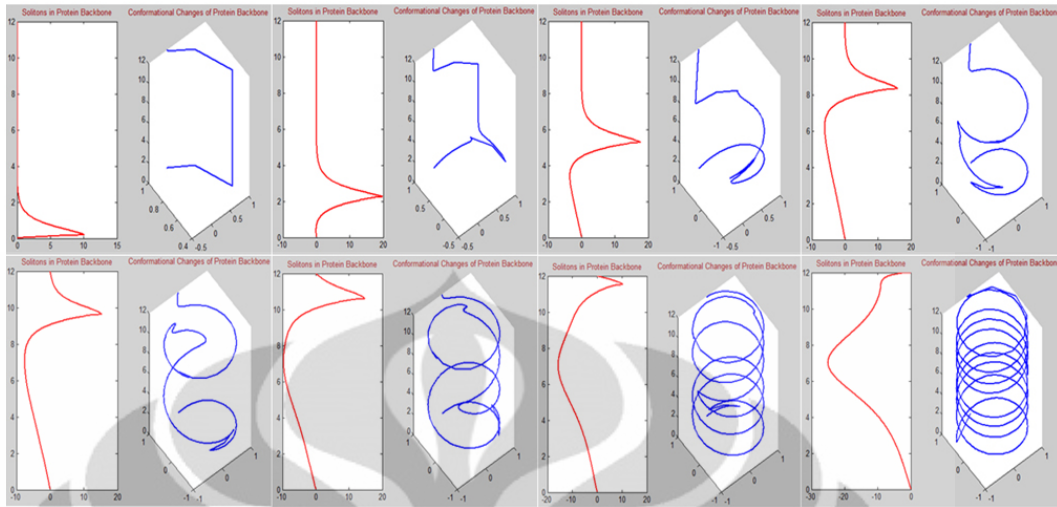


Figure 7.1: The soliton propagations and conformational changes on the protein backbone inducing protein folding. The vertical axis in soliton evolution denotes time in second, while the horizontal axis denotes its amplitude. The conformational changes are on the (x, y, z) plane. The constants of the simulation are chosen as $m = 0.08 \text{ eV} \equiv 1.42 \times 10^{-37} \text{ kg}$, $L = 12 \text{ eV}^{-1} \equiv 2,364 \text{ nm}$, $\Lambda = 2.83 \times 10^{-3}$, $\lambda = 3 \times 10^{-3}$, and $\hbar = c = 1$.

to the time evolution. From the figure, differ with the linear one, it is clear that the protein backbone is infinitesimally bending at the initial stage before the nonlinear source injection. The bending constitutes the contribution of Sine-Gordon potential into the conformation field. However, this bending is too small to generate folding pathway, then the backbone still remains unfolded.

The conformation changes which generate the folding pathway start appearing as the soliton starts propagating over the backbone. The result is surprisingly, even slightly, different with the earlier work. The folding processes are slower than the linear conformation case. It might be considered as an effect of the nonlinear conformational field. One may conclude here that the effect is destructive against the nonlinearity of nonlinear sources. It can also be recognized from Eq. (4.20) that the nonlinear terms of both fields have opposite sign.

It should be remarked that the results for the both numerical calculations are obtained up to the second order accuracy in Taylor expansion. In order to guarantee that the numerical solutions contain no large amount of truncation

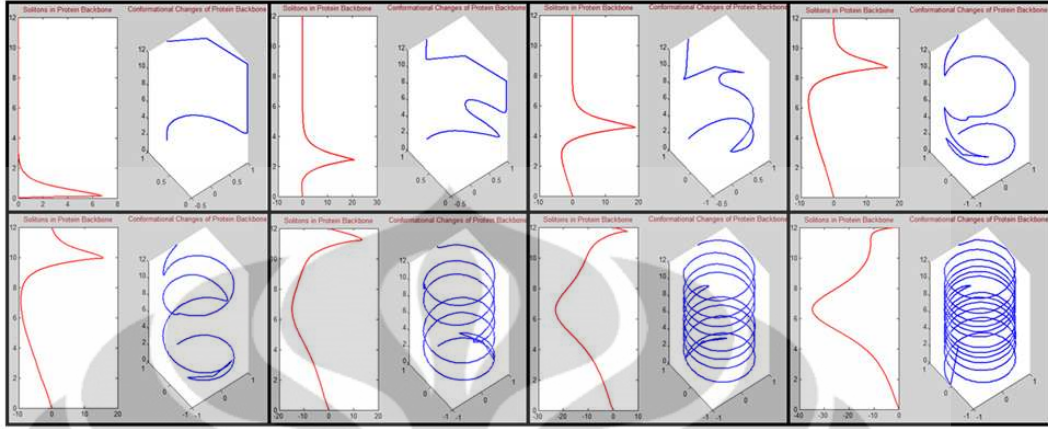


Figure 7.2: The soliton propagations and conformational changes on the protein backbone inducing protein folding. The vertical axis in soliton evolution denotes time in second, while the horizontal axis denotes its amplitude. The conformational changes are on the (x, y, z) plane. The constants of the simulation are chosen as $m = 0.008 \text{ eV} \equiv 1.42 \times 10^{-38} \text{ kg}$, $L = 12 \text{ eV}^{-1} \equiv 2,364 \text{ nm}$, $\Lambda = 2.83 \times 10^{-3}$, $\lambda_\psi = 5 \times 10^{-3}$, $\lambda_\phi = 6 \times 10^{-3}$, and $\hbar = c = 1$.

errors, the step sizes δ and ϵ are kept small enough. Nevertheless, the present method should still be good approximation to describe visually the mechanism of secondary protein folding.

7.2 The Statistical Mechanics Properties

In the chapter 6, in order to enlighten the physical consequences of the underlying interactions from the models to the folding process, the partition function has been calculated. From the partition function, one can evaluate some thermodynamics quantities, such as free energy, internal energy, heat capacity, and etc. It is important to relate the internal dynamics with the external observables, particularly its properties according to temperature. Since the quantities describe same system, then it is unnecessary to calculate all of them. In this case, however heat capacity is well chosen to verify with experiment.

The heat capacity of constant volume can be evaluated directly from the

partition function by using relation bellow,

$$C_V = \beta^2 \left(\frac{\partial^2 \ln Z}{\partial \beta^2} \right)_V . \quad (7.1)$$

Since the propagators $\Delta(0)$ behave for the case of τ and x are zero, then those should be independent to τ and x . Thus the heat capacity for the LCM is

$$C_V^{LCM} = \beta^2 \frac{\partial^2}{\partial \beta^2} \left(\ln N + \beta L \left[\frac{3}{4!} \lambda \Delta_\psi^2(0) + \Lambda \Delta_\phi(0) \Delta_\psi(0) \right] \right)_V . \quad (7.2)$$

It is also important to compare the result with the nonlinear one. Similar with the linear one, the heat capacity for NCM can be found as

$$C_V^{NCM} = \beta^2 \frac{\partial^2}{\partial \beta^2} \left(\ln N + \beta L \left[\frac{3}{4!} \lambda_\phi \Delta_\phi^2(0) + \frac{3}{4!} \lambda_\psi \Delta_\psi^2(0) + \Lambda \Delta_\phi(0) \Delta_\psi(0) \right] \right)_V . \quad (7.3)$$

The second term of the derivatives will not vanish such as those which seen, because the result for the both $\Delta_\psi(0)$ and $\Delta_\phi(0)$ are the function of β . It will clear later.

To calculate the both above derivatives, the solution for the Green's functions $\Delta(x)$ should be find out. The propagators are obeying,

$$\begin{aligned} \left(-\frac{\partial^2}{\partial \tau^2} - \frac{\partial^2}{\partial x^2} \right) \Delta_\psi(x, \tau) &= \delta(x) \delta(\tau) , \\ \left(-\frac{\partial^2}{\partial \tau^2} - \frac{\partial^2}{\partial x^2} + m_\phi^2 \right) \Delta_\phi(x, \tau) &= \delta(x) \delta(\tau) . \end{aligned} \quad (7.4)$$

Take as consideration that the Fourier representation of the Green's functions are [18]

$$\begin{aligned} \Delta_\psi(x, \tau) &= \int \frac{dk}{2\pi} e^{ikx} \Delta_\psi(\tau, k) , \\ \Delta_\phi(x, \tau) &= \int \frac{dq}{2\pi} e^{iqx} \Delta_\phi(\tau, q) . \end{aligned} \quad (7.5)$$

Afterwards, the imaginary-time propagators $\Delta(\tau, k)$ should be satisfied the following differential equations,

$$\begin{aligned} \left(-\frac{\partial^2}{\partial \tau^2} + k^2 \right) \Delta_\psi(\tau, k) &= \delta(\tau) \delta(k) , \\ \left(-\frac{\partial^2}{\partial \tau^2} + q^2 + m_\phi^2 \right) \Delta_\phi(\tau, k) &= \delta(\tau) \delta(k) , \end{aligned} \quad (7.6)$$

and the Dirichlet periodic boundary conditions,

$$\begin{aligned}\Delta_\psi(-\frac{\beta}{2}, \tau) &= \Delta_\psi(\frac{\beta}{2}, \tau) \text{ and } \Delta_\psi(\tau, -\frac{\beta}{2}) = \Delta_\psi(\tau, \frac{\beta}{2}), \\ \Delta_\phi(-\frac{\beta}{2}, \tau) &= \Delta_\phi(\frac{\beta}{2}, \tau) \text{ and } \Delta_\phi(\tau, -\frac{\beta}{2}) = \Delta_\phi(\tau, \frac{\beta}{2}).\end{aligned}\quad (7.7)$$

Obeying Eq. (7.6) and the boundary conditions Eq. (7.7), the form of imaginary-time propagators has been obtained as [13]

$$\Delta_\psi(\tau, k) = \frac{\cosh(k(\frac{\beta}{2} - \tau))}{2k \sinh(\frac{k\beta}{2})}, \quad (7.8)$$

$$\Delta_\phi(\tau, q) = \frac{\cosh(\sqrt{q^2 + m^2}(\frac{\beta}{2} - \tau))}{2\sqrt{q^2 + m^2} \sinh(\frac{\beta\sqrt{q^2 + m^2}}{2})}. \quad (7.9)$$

Therefore the Fourier representation of Green's function can be written as

$$\Delta_\psi(x, \tau) = \int \frac{dk}{2\pi} \frac{\exp(ikx) \cosh(k(\frac{\beta}{2} - \tau))}{2k \sinh(\frac{k\beta}{2})}, \quad (7.10)$$

$$\Delta_\phi(x, \tau) = \int \frac{dq}{2\pi} \frac{\exp(iqx) \cosh(\sqrt{q^2 + m^2}(\frac{\beta}{2} - \tau))}{2\sqrt{q^2 + m^2} \sinh(\frac{\beta\sqrt{q^2 + m^2}}{2})}. \quad (7.11)$$

It is clear that the $\Delta(x, \tau)$ is the function of β , even x and τ are zero.

It has been showed that from Eq. (7.11) the propagator $\Delta_\phi(x, \tau)$ is involving nontrivial term $\sqrt{q^2 + m_\phi^2}$, then it will hard to solve analytically. Therefore the integral should be calculated numerically. By evaluating the integrals in Eqs. (7.10) and (7.11), then substituting the results into Eqs. (7.2) and (7.3), the volume constant heat capacity can be obtained numerically as can be shown in Figs. (7.3) and (7.4). The numerical scripts can be seen in appendix C.

From Fig. (7.3), the properties of the folding processes according to the temperature changes can be shown. The temperature changes in this case are equivalent with the time. In other words, injected soliton makes the temperature is raising. As can be seen from the figure, in the low temperatures that is less than 0.002 eV, we can see that the heat capacity is linear. It shows that the transferred energy from the soliton has not capable making the protein folds

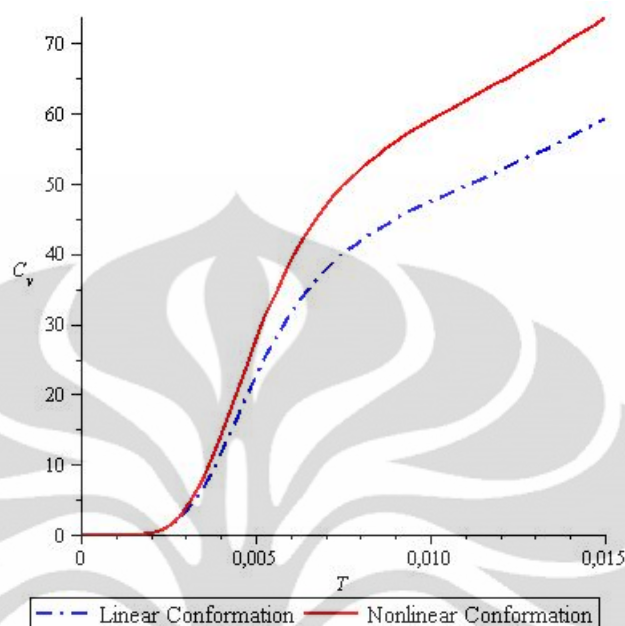


Figure 7.3: Heat capacity v.s temperature, comparing the both conformational model.

spontaneously. The soliton still need a lot of effort to build conformational changes in the protein backbone. The system is approaching its equilibrium state in temperature about 0.002 eV. In temperature higher than 0.002 eV, the energy from the soliton is started enough to excite to folding process. The conformational changes is raising rapidly along with increasing temperature. So that, one can say that the protein which induced by nonlinear source is always folding spontaneously at high temperatures.

From the figure also can be seen that the nonlinear conformation has higher heat capacity in same temperature with the linear one. This is indicates that the existence of the Sine-Gordon potential makes the backbone is harder to fold. Fortunately, this fact agree with the numerical analysis that shows the nonlinear conformation folding more slows than the linear one.

Alteration of the heat capacity for the both model with quantum fluctuation (N) variations according to the temperature changes can be investigated

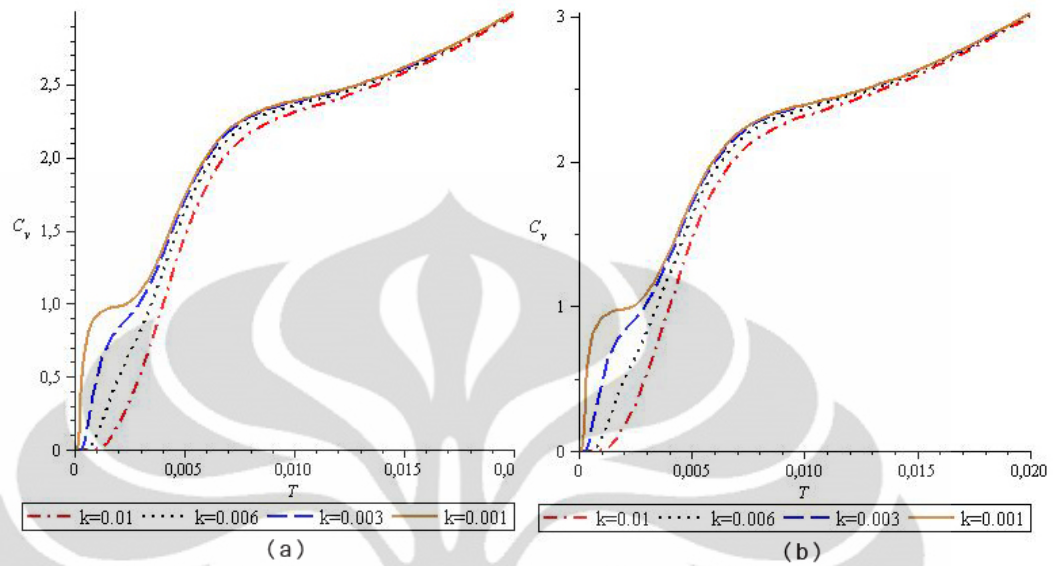


Figure 7.4: Heat capacity v.s temperature with quantum fluctuation term variations $N = \frac{1}{4\pi \sinh(\frac{k\beta}{2})}$, where (a) linear conformation model and (b) nonlinear conformational model.

from Fig. (7.4). The form of N has been shown in Eq. (6.38) as,

$$N = \frac{1}{4\pi \sinh(\frac{k\beta}{2})}. \quad (7.12)$$

Varying N surprisingly indicates an anomaly in low temperature. The quantum fluctuation term helps the folding process go on more easy. In very small value of N ($k = 0.01$), as has been explained on Fig. (7.3), the soliton hard to transfer its energy to the backbone. Meanwhile, in very large N ($k = 0.01$) the energy of soliton is high enough to build conformation changes on the backbone. Although it seems can quick the folding process, however, the quantum fluctuation contribution is very small comparing to the other terms which are classical aspect of the system. This has been showed in the simulation, that the backbone has only small bending when the soliton started propagating. The folding is occurred as the injected soliton propagates in adequately long standing.

Chapter 8

Conclusion

The scientist is not a person who gives the right answers, he's one who asks the right questions.

Claude Lévi-Strauss, *Le Cru et le cuit*, 1964

The extension of phenomenological model describing the conformational dynamics of secondary proteins are proposed. The model based on the matter interactions among the relevant constituents, namely the conformational field; with linear and nonlinear approaches, and the nonlinear sources represented as the bosonic fields ϕ and ψ . It has been shown that from the relativistic bosonic lagrangian with ψ^4 self-interaction, the nonlinear and tension force terms appear naturally as expected in some previous works [12].

However, the present model has different contour since the EOMs governing the whole dynamics are the linear and nonlinear Klein-Gordon equations. Note that the original model by Berloff deployed the linear Klein-Gordon and nonlinear Schrödinger equations.

Besides of that, from the nonlinear conformation approach, the folding process is getting slower since the EOMs governing the whole dynamics are the nonlinear Sine-Gordon and nonlinear Klein-Gordon equations. It is argued that the nonlinearity of the both fields are against each other. Note that the Sine-Gordon potential generalizes the earlier models which deployed both linear, or the linear and nonlinear equations.

Moreover, the present model has inhomogeneous tension force, in contrast

with the homogeneous tension force in the Berloff's model, due to simultaneous solutions of Eqs. (4.14) and (4.15). These lead to wriggling folded pathways as shown in Figs. (7.1) and (7.2) which should be more natural than the homogeneous one.

The heat capacity that has been obtained from the model give us the temperature regions when the protein folding process can be occurred. It has been shown from Figs. (7.3) and (7.4) that the protein backbone which under influenced of nonlinear source are folding spontaneously almost at the all temperatures, except at the infinitesimal critical regions at very low temperatures less than 0.002 eV. In the critical temperature, soliton needs more energy to excite the conformational changes. Although has small contribution, the critical region shows a quantum fluctuation anomaly which can make the folding more easy go on. Fortunately, this statistical mechanics result is agree with the spontaneous symmetry breaking that has been proposed early as one of the main trigger that causes the folding pathway can be occurred.

References

- [1] Protein, <http://en.wikipedia.org/wiki/Protein>.
- [2] P. Echenique, *Contemporary Physics* **48**, p. 81 (2008).
- [3] C. M. Dobson, *Nature* **426**, p. 884 (2003).
- [4] C. Soto, *FEBS Letters* **498**, p. 204 (2001).
- [5] S. Caspi and E. Ben-Jacob, *Europhys. Lett.* **47**, p. 522 (1999).
- [6] S. F. Mingaleev, Y. B. Gaididei, P. L. Christiansen and Y. S. Kivshar, *Europhys. Lett.* **59**, p. 403 (2002).
- [7] S. Caspi and E. Ben-Jacob, *Phys. Lett. A* **272**, p. 124 (2000).
- [8] L. V. Yakushevich, *Nonlinear Physics of DNA* (Wiley-VCH, 2003).
- [9] A. C. Scott, *Phys. Rev. A* **31**, p. 3518 (1985).
- [10] A. G. Garcia and J. N. Onuchi, *Proc. Natl. Acad. Sci. USA* **100**, p. 13898 (2003).
- [11] J. N. Onuchi and P. G. Wolynes, *Curr. Opin. Struct. Biol.* **14**, p. 70 (2004).
- [12] N. G. Berloff, *Phys. Lett. A* **337**, p. 391 (2005).
- [13] R. Rattazzi, *The Path Integral Approach to Quantum Mechanics* (EPFL, 2009).
- [14] R. P. Feynman and A. R. Hibbs, *Quantum Mechanics and Path Integrals* (McGraw-Hill, 1965).

- [15] L. H. Ryder, *Quantum Field Theory 2nd Ed.* (Cambridge University Press, 1996).
- [16] J. H. Mathews and K. D. Fink, *Numerical Methods using Matlab 4th Ed.* (Prentice-Hall, 2004).
- [17] S. Suparno, *Komputasi untuk Sains dan Teknik 3rd Ed.* (Departemen Fisika, Universitas Indonesia, 2008).
- [18] M. L. Bellac, *Thermal Field Theory* (Cambridge University Press, 1996).
- [19] J. I. Kapusta and C. Gale, *Finite-Temperature Field Theory: Principles and Applications 2nd Ed.* (Cambridge University Press, 2006).
- [20] A. Zee, *Quantum Field Theory in a Nutshell* (Princeton University Press, 2003).
- [21] D. J. Korteweg and G. deVries, *Phil. Mag.* **39**, p. 422 (1895).
- [22] A. D. Scott, F. Y. F. Che and D. W. McLaughlin, *Proceeding of The IEEE* (1973).
- [23] G. B. Arfken and H. J. Weber, *Mathematical Methods for Physicists 5th Ed.* (Harcourt Academic Press, 2001).
- [24] Protein structure, http://en.wikipedia.org/wiki/Protein_structure.
- [25] A. Sulaiman and L. T. Handoko, *J. Compt. Theor. Nanoscience* **in press** (2010).
- [26] A. Sulaiman, F. P. Zen, H. Alatas and L. T. Handoko, *Phys. Rev. E* **in press** (2010).
- [27] A. Sulaiman, F. P. Zen, H. Alatas and L. T. Handoko, Statistical mechanics of davydov-scott's protein model in thermal bath, in *Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity, Proceeding of the Conference in Honour of Murray Gell-Mann's*

80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity 2011.

- [28] M. Januar, A. Sulaiman and L. T. Handoko, Conformational changes and protein folding induced by ϕ^4 interaction, in *Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity, Proceeding of the Conference in Honour of Murray Gell-Mann's 80th Birthday : Quantum Mechanics, Elementary Particles, Quantum Cosmology and Complexity* 2011.
- [29] M. Januar, A. Sulaiman and L. T. Handoko, Nonlinear conformation of secondary protein folding, in *Proceedings of the International Conference on Mathematical and Computational Biology 2011, International Journal of Modern Physics: Conference Series* 2011.
- [30] R. MacKenzie, *arXiv:quant-ph/0004090v1* , p. 28 (2000).
- [31] J. J. Sakurai, *Modern Quantum Mechanics* (Addison-Wesley Publishing Company, 1994).
- [32] M. Januar, A. Sulaiman and L. T. Handoko, *Physica D* **submitted** (2011).

Appendix A

Notations

The system of units that have been used in the above calculations are natural system of units, which is defined $\hbar = c = k = 1$ and dimensionless. In this manner, energy, mass, length and temperature, all have same dimension with energy, i.e, with eV unit. Thus, the dimensions of length and area respectively becomes energy⁻¹ and energy⁻². To get the value and returning the dimensions of a quantity, use the following conversions:

$$1eV^{-1} \text{ of length} = 1.97 \times 10^{-7} m = (1eV^{-1})\hbar c \quad (\text{A.1})$$

$$1eV \text{ of mass} = 1.78 \times 10^{-36} kg = \frac{1eV}{c^2} \quad (\text{A.2})$$

$$1eV^{-1} \text{ of time} = 6.58 \times 10^{-16} s = (1eV^{-1})\hbar \quad (\text{A.3})$$

$$1eV \text{ of temperature} = 1.16 \times 10^4 K = \frac{(1eV)}{k_B} \quad (\text{A.4})$$

Appendix B

The MATLAB's Scripts for Solving EOMs of the Model

B.1 The Linear Conformation Model

```
% Finite Difference Method for Coupled EOMs of Protein Folding
% Linear Conformational Model
% By: Moch. Januar, 0606068442
% Department of Physics, University of Indonesia

clear all;
clc;
close all;
format long
a=0; % initial boundary of one dimensional space-interval x
b=12; % end boundary of one dimensional space-interval x
c=0; % initial boundary of time-interval t
d=12; % end boundary of time-interval t
N=631; % positive integer
M=631; % positive integer
h=(b-a)/N;% step-size value for x
k=(d-c)/M;% step-size value for t
sc=0.000000001; % stopping criteria
```

```



```



```

end
for i=2:N-1
    u(2,i) = u(1,i) + (v^2*k^2)/2*((u(1,i+1)-2*u(1,i) + u(1,i-1))/(h^2)
    + 2*L*w(1,i)^2*u(1,i) - 3*l*u(1,i)^3));
end
% For t_3 and higher
% If one of the equations are disappear, the iteration to the other
equation can not be occurred.
% Therefore, it was proving that the both equations are coupled in
above scripts.
for j=2:M-1
    for i=2:N-1
        u(j+1,i) = 2*u(j,i)-u(j-1,i) + v^2*k^2*((u(j,i+1)-2*u(j,i)
        + u(j,i-1))/(h^2) + 2*L*w(j,i)^2*u(j,i)-3*l*u(j,i)^3);
        w(j+1,i) = 2*w(j,i)-w(j-1,i) + v^2*k^2*((w(j,i+1)-2*w(j,i)
        + w(j,i-1))/(h^2)+ 2*L*u(j,i)^2*w(j,i)-(v^2/q^2)*m^2*w(j,i));
    end
end
%-----
% checking the stability/convergence of the each iteration solutions
s=0;
o=0;
for j=1:M-1
    for i=1:N
        s=s+(u(j+1,i)-u(1,i))^2;
        o=o+(w(j+1,i)-w(1,i))^2;
    end
end
epsilon1=sqrt(s);
epsilon2=sqrt(o);
% checking the stopping criteria
u(1,i)=u(j+1,i);

```

```

w(1,i)=w(j+1,i);
if epsilon1 && epsilon2 < sc
u(:,:)=u(j+1,i);
w(:,:)=w(j+1,i);
break
end
end

%-----Animations (Plotting)-----
%r=1; % Radius of Polar Coordinates
%Record the movie
for j=1:M
% Plotting for the Nonlinear Source field
subplot(1,2,1);
plot(u(j,:),x);
set(findobj(gca,'Type','line','Color',[0 0 1]),...
'Color','red',...
'LineWidth',1.5) %setting the color, type & line width.
title('Solitons in Protein Backbone','Color',[.6 0 0])
% 3D Plotting for the Conformational Changes field using Polar Coordinates
subplot(1,2,2);
plot3(sin(w(j,:)),cos(w(j,:)),x); %Polar Coordinates
set(findobj(gca,'Type','line','Color',[0 0 1]),...
'Color','blue',...
'LineWidth',1.5) %setting the color, type & line width.
title('Conformational Changes of Protein Backbone',
'Color',[.6 0 0])
F(j)=getframe;
end

```

B.2 The Nonlinear Conformation Model

```

% Finite Difference Method for Coupled EOMs of Protein Folding
% Nonlinear Conformational Model
% By: Moch. Januar, 0606068442
% Department of Physics, University of Indonesia

clear all;
clc;
close all;
format long
a=0; % initial boundary of one dimensional space-interval x
b=12; % end boundary of one dimensional space-interval x
c=0; % initial boundary of time-interval t
d=12; % end boundary of time-interval t
N=631; % positive integer
M=631; % positive integer
h=(b-a)/N;% step-size value for x
k=(d-c)/M;% step-size value for t
sc=0.000000001; % stopping criteria
%input
L=0.00283; % coupling interaction constant
l=0.005; % nonlinear source term constant
e=0.006; % nonlinear conformation term constant m=0.008; % protein
mass
v=1; % light velocity
q=1; % Planck's constant
% boundary conditions
u(:,1)=0;
w(:,1)=0;
u(:,N)=0;
w(:,N)=0;

```

```

%-----The Model (Iteration Process)-----
% u: Nonlinear Source (Solitons)
% w: Conformational Changes
for i=1:N
    x(i)=a+i*h;
end
% Begin Iteration
itermax=100;
for iterasi=1:itermax
% initial condition at t_1=0
for i=2:N-1
    u(1,i)=2*sech(2*x(i))*exp(imag(2*x(i)));
end
for i=2:N-1
    w(1,i)=atan(exp(4*x(i)-10));
end
% at t_2=k
for i=2:N-1
    u(2,i) = u(1,i) + (v^2*k^2)/2*((u(1,i+1)-2*u(1,i) + u(1,i-1))/(h^2)
    + 2*L*w(1,i)^2*u(1,i) - 1/6*u(1,i)^3));
end
for i=2:N-1
    w(2,i) = w(1,i) + (v^2*k^2)/2*((w(1,i+1)-2*w(1,i) + w(1,i-1))/(h^2)
    + 2*L*u(1,i)^2*w(1,i) + (v/q)^3*(m^3/sqrt(e))*sin((sqrt(e)/m)*w(1,i)));
end
% For t_3 and higher
% If one of the equations are disappear, the iteration to the other
equation can not be occurred.
% Therefore, it was proving that the both equations are coupled in
above scripts.
for j=2:M-1

```

```

for i=2:N-1
    u(j+1,i) = 2*u(j,i)-u(j-1,i) + v^2*k^2*((u(j,i+1)-2*u(j,i)
    + u(j,i-1))/(h^2) + 2*L*w(j,i)^2*u(j,i)-1/6*u(j,i)^3);
    w(j+1,i) = 2*w(j,i)-w(j-1,i) + v^2*k^2*((w(j,i+1)-2*w(j,i)
    + w(j,i-1))/(h^2)+ 2*L*u(j,i)^2*w(j,i)
    +(v/q)^3*(m^3/sqrt(e))*sin((sqrt(e)/m)*w(j,i)));
end
end
%-----
% checking the stability/convergence of the each iteration solutions
s=0;
o=0;
for j=1:M-1
    for i=1:N
        s=s+(u(j+1,i)-u(1,i))^2;
        o=o+(w(j+1,i)-w(1,i))^2;
    end
end
epsilon1=sqrt(s);
epsilon2=sqrt(o);
% checking the stopping criteria
u(1,i)=u(j+1,i);
w(1,i)=w(j+1,i);
if epsilon1 && epsilon2 < sc
    u(:,:)=u(j+1,i);
    w(:,:)=w(j+1,i);
    break
end
end
%-----Animations (Plotting)-----
%r=1; % Radius of Polar Coordinates

```

```
%Record the movie
for j=1:M
% Plotting for the Nonlinear Source field
    subplot(1,2,1);
    plot(u(j,:),x);
    set(findobj(gca,'Type','line'),'Color',[0 0 1]),...
        'Color','red',...
        'LineWidth',1.5) %setting the color, type & line width.
    title('Solitons in Protein Backbone','Color',[.6 0 0])
% 3D Plotting for the Conformational Changes field using Polar Coordinates
    subplot(1,2,2);
    plot3(sin(w(j,:)),cos(w(j,:)),x); %Polar Coordinates
    set(findobj(gca,'Type','line'),'Color',[0 0 1]),...
        'Color','blue',...
        'LineWidth',1.5) %setting the color, type & line width.
    title('Conformational Changes of Protein Backbone',
        'Color',[.6 0 0])
    F(j)=getframe;
end
```

Appendix C

The Maple's Script for the Statistical Mechanics Calculation

C.1 Heat Capacity v.s Temperature: The Both Conformational Models

```
restart;
m := 0.08; #Protein Mass
L := 12; #Protein length
λ1 := 0.007; #Nonlinear source constant
λ2 := 0.006; #Nonlinear conformation constant
Λ := 0.00283; #Coupling constant
a := 0.028;
ω := 12.028;
N :=  $\frac{1}{4 \cdot \pi \cdot \sinh\left(\frac{0.01\beta}{2}\right)}$ ;
with(student):
u := simpson  $\left( \frac{e^{I \cdot k \cdot x}}{4 \cdot \pi \cdot k} \cdot \frac{\cosh\left(k \cdot \left(\frac{\beta}{2} - \tau\right)\right)}{\sinh\left(k \cdot \frac{\beta}{2}\right)} \right)$ ;
w := simpson  $\left( \frac{e^{I \cdot \sqrt{q^2 + m^2} \cdot x}}{4 \cdot \pi \cdot \sqrt{q^2 + m^2}} \cdot \frac{\cosh\left(\sqrt{q^2 + m^2} \cdot \left(\frac{\beta}{2} - \tau\right)\right)}{\sinh\left(\sqrt{q^2 + m^2} \cdot \frac{\beta}{2}\right)} \right)$ ;
x := 0;
τ := 0;
```

```

U1 := - $\frac{d}{d\beta}$  (ln(N) +  $\beta \cdot (\frac{3}{24} \cdot \lambda1 \cdot u \cdot u + \Lambda \cdot u \cdot w)$ );
U2 := - $\frac{d}{d\beta}$  (ln(N) +  $\beta \cdot (\frac{3}{24} \cdot \lambda1 \cdot u \cdot u + \frac{3}{24} \cdot \lambda2 \cdot w \cdot w + \Lambda \cdot u \cdot w)$ );
 $\beta := \frac{1}{T}$ ;
Cv1 :=  $\frac{d}{dT}$ (U1);
Cv2 :=  $\frac{d}{dT}$ (U2);
plot([Cv1, Cv2], T = 0 .. 0.02, color = [red, blue], labels = ["T",
"Cv"], legend = ["Linear Conformation", "Nonlinear Conformation"]);

```

C.2 Heat Capacity v.s Temperature: Quantum Fluctuation Variations in the Linear Conformational Models

```

restart;
m := 0.08; #Protein Mass
L := 12; #Protein length
 $\lambda1 := 0.007$ ; #Nonlinear source constant
 $\Lambda := 0.00283$ ; #Coupling constant
a := 0.028;
 $\omega := 12.028$ ;
N1 :=  $\frac{1}{4 \cdot \pi \cdot \sinh(\frac{0.01\beta}{2})}$ ;
N2 :=  $\frac{1}{4 \cdot \pi \cdot \sinh(\frac{0.006\beta}{2})}$ ;
N3 :=  $\frac{1}{4 \cdot \pi \cdot \sinh(\frac{0.003\beta}{2})}$ ;
N4 :=  $\frac{1}{4 \cdot \pi \cdot \sinh(\frac{0.001\beta}{2})}$ ;
with(student):
u := simpson  $\left( \frac{e^{I \cdot k \cdot x}}{4 \cdot \pi \cdot k} \cdot \frac{\cosh(k \cdot (\frac{\beta}{2} - \tau))}{\sinh(k \cdot \frac{\beta}{2})} \right)$ ;
w := simpson  $\left( \frac{e^{I \cdot \sqrt{q^2 + m^2} \cdot x}}{4 \cdot \pi \cdot \sqrt{q^2 + m^2}} \cdot \frac{\cosh(\sqrt{q^2 + m^2} \cdot (\frac{\beta}{2} - \tau))}{\sinh(\sqrt{q^2 + m^2} \cdot \frac{\beta}{2})} \right)$ ;
x := 0;
 $\tau := 0$ ;
U1 := - $\frac{d}{d\beta}$  (ln(N1) +  $\beta \cdot (\frac{3}{24} \cdot \lambda1 \cdot u \cdot u + \Lambda \cdot u \cdot w)$ );
U2 := - $\frac{d}{d\beta}$  (ln(N2) +  $\beta \cdot (\frac{3}{24} \cdot \lambda1 \cdot u \cdot u + \Lambda \cdot u \cdot w)$ );

```



```

U3 := -d/dβ (ln(N3) + β · (3/24 · λ1 · u · u + Λ · u · w));
U4 := -d/dβ (ln(N4) + β · (3/24 · λ1 · u · u + Λ · u · w));
β := 1/T;
Cv1 := d/dT(U1);
Cv2 := d/dT(U2);
Cv3 := d/dT(U3);
Cv4 := d/dT(U4);
plot([Cv1, Cv2,Cv3,Cv4], T = 0 .. 0.02, color = [red, black, blue,
gold], labels = ["T", "Cv"], legend = ["k=0.01", "k=0.006", "k=0.003",
"k=0.001"]);

```

C.3 Heat Capacity v.s Temperature: Quantum Fluctuation Variations in the Non-linear Conformational Models

```

restart;
m := 0.08; #Protein Mass
L := 12; #Protein length
λ1 := 0.007; #Nonlinear source constant
λ2 := 0.006; #Nonlinear conformation constant
Λ := 0.00283; #Coupling constant
a := 0.028;
ω := 12.028;
N1 := 1/(4*π*sinh(0.01β/2));
N2 := 1/(4*π*sinh(0.006β/2));
N3 := 1/(4*π*sinh(0.003β/2));
N4 := 1/(4*π*sinh(0.001β/2));
with(student):
u := simpson ( e^{I·k·x} · cosh(k·(β/2-τ)) / (4·π·k · sinh(k·β/2)) );
w := simpson ( e^{I·√{q^2+m^2}·x} · cosh(√{q^2+m^2}·(β/2-τ)) / (4·π·√{q^2+m^2} · sinh(√{q^2+m^2}·β/2)) );

```

```

x := 0;
τ := 0;
U1 := - $\frac{d}{d\beta}$  (ln(N1) + β · ( $\frac{3}{24}$  · λ1 · u · u +  $\frac{3}{24}$  · λ2 · w · w + Λ · u · w));
U2 := - $\frac{d}{d\beta}$  (ln(N2) + β · ( $\frac{3}{24}$  · λ1 · u · u +  $\frac{3}{24}$  · λ2 · w · w + Λ · u · w));
U3 := - $\frac{d}{d\beta}$  (ln(N3) + β · ( $\frac{3}{24}$  · λ1 · u · u +  $\frac{3}{24}$  · λ2 · w · w + Λ · u · w));
U4 := - $\frac{d}{d\beta}$  (ln(N4) + β · ( $\frac{3}{24}$  · λ1 · u · u +  $\frac{3}{24}$  · λ2 · w · w + Λ · u · w));
β :=  $\frac{1}{T}$ ;
Cv1 :=  $\frac{d}{dT}$ (U1);
Cv2 :=  $\frac{d}{dT}$ (U2);
Cv3 :=  $\frac{d}{dT}$ (U3);
Cv4 :=  $\frac{d}{dT}$ (U4);
plot([Cv1, Cv2,Cv3,Cv4], T = 0 .. 0.02, color = [red, black, blue,
gold], labels = ["T", "Cv"], legend = ["k=0.01", "k=0.006", "k=0.003",
"k=0.001"]);
    
```