

A model of nonlinear DNA-protein interaction system with Cornell potential and its stability

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Abstract: The purpose of this study was to determine the model of a interaction system between the DNA with protein. The interaction system consisted of a molecule of protein bound with a single chain of DNA. The interaction between DNA chain, especially adenine and thymine, and DNA-protein bound to glutamine and adenine. The forms of these bonds are adapted from the hydrogen bonds. The Cornell potential was used to describe both of the interactions. We proposed the Hamiltonian equation to describe the general model of interaction. Interaction system is divided into three parts. The interaction model is satisfied when a protein molecule triggers pulses on a DNA chain. An initial shift in position of protein x_m should trigger the shift in position of DNA y_m , or alter the state. However, an initial shift in DNA, y_n , should not alter the state of a rest protein (i.e. $x_m = 0$), otherwise, the protein would not steadily bind. We also investigated the stability of the model from the DNA-protein interaction with Lyapunov function. The stability of system can be determined when we obtained the equilibrium point.

Keywords: DNA; protein; Cornell potential; Hamiltonian equation; Lyapunov function.

1. Introduction

The study of the existence of the nucleic acid was first performed by Fredrich Miescher in 1869. Than Yuwono (2005) explains that in the nucleus are called nucleic phosphate containing compounds. As technology develops, in the 19th century has been successfully carried out the separation of DNA (deoxyribonucleic acid) and RNA (Ribonucleic Acid) of proteins that attaches to cells. The molecular structure of DNA was first articulated double helix (Watson and Crick, 1953; Watson, 1976). Various studies and methods have been conducted to illustrate the dynamics of motion as well as the system of interaction of DNA. The depiction of the dynamics of motion of the DNA is a form of dynamic linear and nonlinear dynamics (Yakushevich, 1998). The nonlinear effect might play an important role in DNA dynamic that was suggested by Englander et al (1980).

There are several models of interaction are quite famous presented to illustrate the dynamics of DNA (Peyrard and Bhisop, 1989; Yakushevich, 1998). Solomon (2012), in

her study, to learn about the dynamics of motion and thermal effects models Peyrard-Bhisop (PB) associated with external potential. Research on the longitudinal motion non harmonic and nonlinear excitation DNA also began modeled (Pthasne, 2016). The dynamics of the transcription bubble in DNA is studied by using a nonlinear model in which torsional and longitudinal conformations of the biomolecule are coupled. In the absence of forcing and dissipation the torsional dynamics is described by a perturbed kink of the Sine-Gordon DNA model, while the longitudinal conformational energy propagate as phonons (Garbo, 2016).

DNA dynamics of the system cannot be separated by the DNA molecule interaction with molecules in the surrounding area, both with adjacent DNA molecules, and proteins. The interaction that occurs in these molecules is generally a no covalent interaction, divided into hydrogen bonding, ionic bonding, Van der Waals interactions and interactions Hydrophobic (Tom, 2011). From these interactions, hydrogen bonding interactions are most easily observed interaction. Signal transmission is obtained from the experiments on the interaction of DNA already been learned. The signal comes from the regulatory proteins and is transmitted through the process of protein binding to DNA. Some models put forward to show symptoms (Hogan, 1979; Ptashne, 1986; Wang, 1988). We assume that the protein molecule induces conformational local distortion of the base pairs that cause respiratory soliton excitation. Protein regulator will increase the amplitude of respiratory soliton model PB (Sataric and Tuszyński, 2002).

In this study, we proposed a model Hamiltonian and the equations of motion of the interaction of DNA with proteins. The equation of motion obtained by lowering the Hamiltonian equation of the position where the result of a decrease in the equation obtained by the equations of motion. In the next section, to do the analysis and display system stability portraits phase of the system. While potentially used is composed of Cornell potential consists of Coulomb potential and linear potential. The general form Cornell potential equation can be seen in the article Hamzavi (2013) and Castro (2013).

2. Interaction Form, Hamiltonian Model, and Equation System of Movement

In this study, the researchers made the simplest model of interaction between DNA molecules with protein. The proteins or DNA molecules selection was adapted to the particular chemical structure of the hydrogen bonds between nucleotides of DNA and protein molecular bonds. The chains of DNA molecules was using adenine (A) and thymine (T), while for the protein molecules using glutamine (G). The bonds between adenine (A) with thymine (T), and adenine (A) with glutamine (G), occurred due to two hydrogen bonds. Interaction model that is used consists of two values of degrees of freedom, namely x_m , which represented the interaction between DNA molecules with protein molecules, and y_m , represented the interaction between the molecular chains of DNA. In this interaction model, the molecular chains of DNA were limited to merely obtain two DNA molecules. The model of interaction generally can be represented by a form of interaction that was appeared in Figure 1.

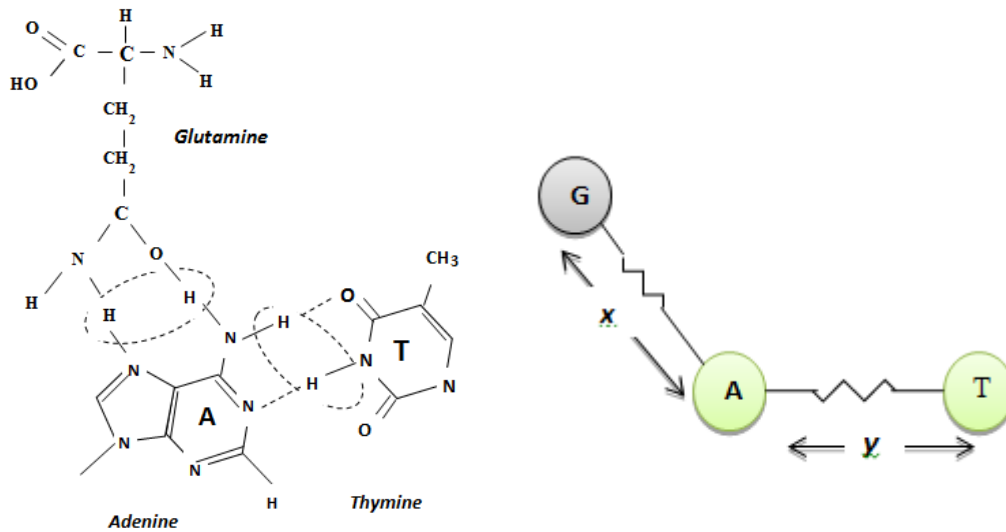


Figure 1. (left) chemical bonds of molecules of protein (glutamine) that interact with DNA (adenine thymine base pairs), and (right) models of interaction.

In this study, researchers used a Hamiltonian consisted of three parts, namely the Hamiltonian chain interaction of DNA, Hamiltonian protein interaction, and Hamiltonian interaction in general of both the bonds. While the review limits the dimensions used only in the direction of the x-axis and y-axis, or only on the two-dimensional planes. The Hamiltonian models were represented by the following equation:

$$H = H_{\text{DNA}} + H_{\text{Prot}} + H_{\text{int}} \quad (1)$$

With Hamiltonian DNA as followed:

$$H_{\text{DNA}} = \sum_n \frac{p_{y_n}^2}{2M_D} + \left[-\frac{a}{y_n} + by_n \right] + \frac{k}{2} (y_n - y_{n-1})^2 \quad (2)$$

The second term of Equation (2) was a common form of potential Cornell, while the index n was the nth DNA position. Mass MD and momentum Pym were considered homogeneous. k was a coupling parameter of the interaction between DNA molecules with each other's. Then, a and b were parameters of potential Cornell. Hamiltonian in the interaction between protein molecules of DNA was represented by the following equation:

$$H_{\text{Prot}} = \frac{p_{x_m}^2}{2M_P} + \left[-\frac{c}{x_m} + dx_m \right] \quad (3)$$

With the MP was a mass of the protein, c and d were parameters at the Cornell potential interactions with proteins. In addition to the second Hamiltonian, interaction was the interaction between the protein molecules with a system of DNA molecules. In the last part, the interaction Hamiltonian could represent the condition. Here was the general form of the Hamiltonian interaction.

$$H_{\text{int}} = \sum_n \chi x_m^i y_n^j \quad (4)$$

Coupling parameter χ projected the sensitivity and the strength of the interactions occurred. While the value of the rank i and j would determine the most within their model of interaction with the condition of interaction expected. To determine the dynamics of DNA-protein interactions, we need to review the form of the Hamiltonian interaction equation. The steps you need to do is setting the value of the rank i and j . Doni (2016), in his article explaining the value of each parameter adapted to the special conditions depended on the biological requirements were affected by the oscillators initial conditions. In our proposed model we expected of a protein molecule to come and interact with the DNA chain would trigger pulses on DNA binding. This meant that it obtained the initial shift x_m to trigger a shift y_n , or changed the condition.

However, the initial shift DNA, y_n , it should not change the state of a protein that was currently in a state of rest (i.e when $x_m = 0$), as at the time if there was no protein so that the protein would not steadily bind. This could be understood by considering the equations of motion derived from the Hamiltonian. It aimed to determine the value of the rank i and j where to obtain $\frac{dH}{ds}$ as equation of motion. The equation shown as followed:

$$m \ddot{y}_m = -\frac{a}{y_m^2} - b + k(2y_m - y_{m+1} - y_{m-1}) - j\chi x_m^i y_m^{j-1} \quad (5)$$

$$m \ddot{x}_m = -\left[\frac{c}{x_m^2} + c \right] + i\chi x_m^{i-1} y_m^j \quad (6)$$

In equation (5), part of the third was expected not to contain variable y . So the expected conditions were accomplished in which those conditions, the presence of the protein molecules would affect the dynamics of change in the motion of the DNA and was not influenced by the adjacent DNA. In this case the value of each parameter i and j are fulfilling that $b = 1$ and $a > 1$. Thus, to form the simplest interaction equation researchers used the equation $H_{int} = \frac{1}{2} x_m^2 y_n$.

3. The Analysis of The Interaction Stability

This section discussed the stability of a system. Stability of a nonlinear system is required to define the system in accordance with the desired conditions. Lyapunov function is one of the most frequently used functions in the process of analyzing the stability of the system (Tuwakotta, 2002). By approaching the Hamiltonian equation, supposed that Hamiltonian equation behaves as a Lyapunov function, we could determine the stability of the nonlinear system. If we approach the equation of harmonic $\frac{k}{2}(y_n - y_{n-1})^2$ by assuming that y_{n-1} comparable to $u y_n$, with u is parameter, the equation can be written in the simpler form, the tribes of the Hamiltonian equation could be written as

$$U(x, y) = \left[-\frac{a}{y} + by + \frac{k}{2}(1-u)^2 y^2 \right] + \left[-\frac{c}{x} + dx \right] + \frac{1}{2} \chi x^2 y \quad (8)$$

The local minima can be determined with $\nabla U(x_0, y_0) = 0$, we obtain

$$\left\{ \frac{a}{y^2} + k(1-u)^2 y + b \right\} + \frac{1}{2} \chi x^2 = 0$$

$$\left\{ \frac{c}{x^2} + d \right\} + \chi xy = 0. \tag{9}$$

The equilibrium point and stability system could be determined after we determined the value of each parameter. Meanwhile, to determine the stability of the models interaction could be done by determining the determinant of the Hamiltonian $\det(H)_{(x_0, y_0)}$. Determinants of Hamiltonian DNA could be obtained by using Hessian matrix.

$$\text{Det H} = \left[k(1-u)^2 - 2\frac{a}{y^3} \right] \left[-2\frac{c}{x^3} + \chi y \right] - [\chi x]^2 \tag{10}$$

For the value $x = 0$ and $y = 0$, the value of the determinant of Hamiltonian was undefined. By using the approach (when the value of x and y equal to zero, and the value $\frac{1}{y^n}$ and $\frac{1}{x^n}$ were equal to the current value of x and y near to zero) it would obtain the determinant of Hamiltonian $\det(H)_{(x_0, y_0)}$ was defined in any values of x and y . If the determinant value $\det(H)_{(x_0, y_0)} > 0$, then the system is stable. However, if $\det(H)_{(x_0, y_0)} < 0$, then the system is unstable.

4. Result and discussion

In this section, we discuss several result obtained in the previous section. By substituting eq. (2), eq. (3), and eq. (4) to eq. (1) than comparing with eq. (8) we obtained the general equation of Hamiltonian as followed by:

$$H(x, y) = \frac{p^2}{2M_d} - \frac{a}{y} + by + \frac{k}{2}(1-u)^2 y^2 + \frac{p^2}{2M_p} - \frac{c}{x} + dx + \frac{1}{2} \chi x^2 y \tag{11}$$

We need to set the value of all parameter to illustrate the field phase (phase portrait) of the model. In this section the value of each parameter is determined by the specified value as $k = 2$, $a = 0:02$, $b = 0.2$, $c = 0:01$, $d = 0.1$, $u = 0.3$ $\chi = 1$. After we substituting those parameter into the general eq. (11), by using Mat lab 2013, we plotting the phase portrait and shown by Figure 2.

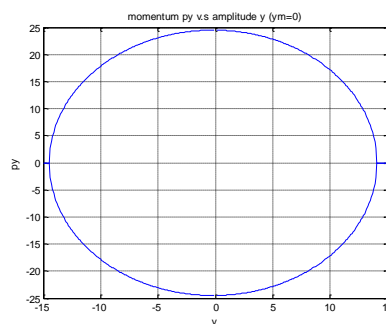


Figure 2. Phase portraits of the systems with no initial amplitude $y_m=0$

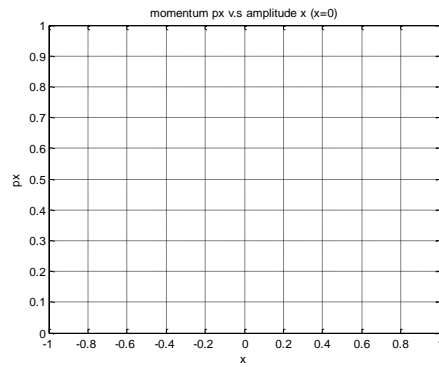


Figure 3. Phase portraits of the systems with no initial amplitude $x_m=0$

By inspecting Figure 2 it can be inferred that the form of the trajectory of p_{yn} with y_n with no initial amplitude in x_m , it is the simple trajectory for DNA dynamic. At Figure 3 shown there is no trajectory at p_{xn} with x_n because the interaction of DNA and protein has not happened yet.

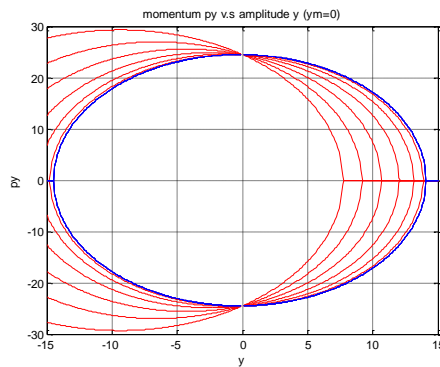


Figure 4. Phase portraits of the systems changes in phase space trajectory due to the presence of protein

Figure 4 shows trajectory changes as a result of the relationship between momentums p_y with y because of the existing protein on x axis. The value of x not only affected the value of amplitude range in y axis but also caused shift of center-line as well as affected the value of momentum. In addition, the changes also happened at shift of the maximum and minimum value momentum.

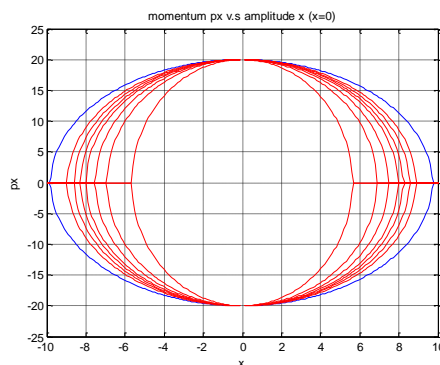


Figure 5. the shape of the trajectory on the interaction of DNA with proteins to change by the interaction of the DNA chain

Figure 5 shows trajectory changes as a result of the relationship between momentums p_x with x because of the existing DNA change on y axis. However, the value only affected the value of amplitude range without shifting the center-line and affecting the momentum. It's corresponding with condition at eq. (5) and (6). By substituting the value of each parameters to eq. (9) we obtained the equilibrium point at (0,0) and (0.39,-0.40). We substitute the value of equilibrium point into eq. (10) to identify the stability. The result gives the condition with equilibrium point at (0,0) stable and (0.39,-0.40) not stable.

5. Conclusion

A Model of nonlinear interactions systems of DNA-protein can be obtained using the Cornell Potential. This model is only an early step towards how to understand the interaction. The existences of molecule protein causing a shift to DNA chain, however the interaction among the molecules of DNA will not give the effect to Protein interaction significantly. In our model, the system can reached the stability with Determinant of Hamiltonian $\det(H)_{(x_0,y_0)} < 0$. This condition can be obtained by treating the Hamiltonian into Lyapunov function.

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