A model of a nonlinear DNA-protein interaction system with general Hylleraas potential

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Abstract. All the functions of DNA depend on interactions with proteins. We proposed a model to describe the interaction between of them. For the simplest model, we took adenine and thymine molecule to represented each molecule. The interactions adapted from binding hydrogen atoms of the molecule. The General Hylleraas potential were used to describe both of the interactions. We proposed the Hamiltonian equation to describe the general model of interaction. The stability of the model from the DNA-protein interaction was investigated with Lyapunov function. We also have determined the equation of spectrum energy of the interaction model using WKB approximation method.

1. Introduction
DNA (deoxyribonucleic acid) is a repository of genetic information. In 1953, Frances Crick and James Watson discovered a molecular model of DNA as a double-stranded helical structure, or better known as the Watson-Crick double helix. DNA is a polynucleotide macromolecule polymer composed of nucleotides repeated, structured double, forming DNA double helix and twisting to the right [1, 2]. The specific structure was described in 1953 in his paper [2]. There have been many efforts to describe its complex dynamics. Some of them are both linear and nonlinear as described by Yakushevich [3]. The nonlinear effect might play an important role in DNA dynamic that was suggested in 1980 by Englander et al. [4].

The dynamic system of the DNA interactions can’t be separated from how the DNA’s molecule interacts with nearby molecules, either DNA molecule links directly or the others like protein molecule. Based on the chemical bond, there are three kinds of interaction that occurred among molecules, they are hydrogen, van der Waals, and electric bond. Hydrogen interaction among the three bonds interaction is the easiest one to observe.

In biological regulations, the interaction between DNA molecules and protein molecules provides a very important role in studying as making up the nucleosome, to control the gene expression, transcription factors, and cofactors [5]. Each process of transcription and replication will begin with the activity of a transcription factors (TFs) that triggers the signal [6]. Those proteins are often triggered in the cells by specific posttranslational modifications that allow TFs to bind to their specific sites of DNA. The activity status of these proteins also able to deducted by measuring such interaction of TFs. Such DNA-binding assay experiments sometimes able to combine with proteomics
experiments measuring specific phosphorylation events that can give a lot of information to the researchers about exact mechanisms of acting of this class of proteins [7]. While the process of DNA and protein binding, the regulatory proteins transmitted a high signal. This phenomenon become a trigger to make an assumption that the protein molecule induces conformational local distortion of the base pairs that cause respiratory soliton excitation. Some models put forward to show the symptoms [8-11]. The amplitude of respiratory soliton from model PB will be increase by protein regulator [12].

The specific model of interactions between DNA and protein were described in 2016 by Dwiputra et al and Syahroni E et al. [12,13]. Their model described the model of nonlinear interactions with different potential. Their research includes several stages of the model from the model description, stability system analysis, and spectrum energy protein binding to the DNA molecule [14]. The assumptions while the protein binding to the DNA molecule, the protein molecule treated as an object of an atom in mecanically stable state and well isolated from its surroundings. In this condition the protein molecule will behave like an electron bound to an atom's nucleus [15]. At last part of this research, we also describe the energy of interaction by assuming that the energy value of system was discrete. We used WKB (Wentzel, Kramer, and Brillouin) approximation method to determine the spectrum energy [16]. WKB approximation is often used to solve problems in quantum mechanics to determine either the wave function or energy [17]. Several studies using this approach have been proposed [18, 19]. In this research, Hylleraas potential [20] will be a potential to describe the interactions between protein molecule and DNA molecules. In molecular interaction between DNA and protein, while the DNA and protein make any interaction, the vibration of any molecular occur. The stabil proses while the vibration described by the harmonic osilator potential from the Hylleraas potential, the harmonic osilator potential represented with the expantions of eksonpentional form. By using Hyllerass potential, we propose a model of interaction DNA with protein that is inspired from the previous model and solutions of the Schrodinger equation.

2. Model Description
The model interaction between DNA and Protein can be observed with the focal point of Hydrogen's bond atom of the both elements. In this paper, we present the model of interaction between molecules of proteins bind to single of the DNA molecular. Our models only review the interaction of these two molecules on the x-axis and the y-axis. It means our model has two degrees of freedom such as on showed, describing the interaction of hydrogen atoms between molecules of proteins and DNA, and y_m, which describing the interaction of the hydrogen atom of the DNA chains. We use the glutamine molecule for example of the side chain of interaction.

Reviews are based on the Valence Shell Electron Pair Repulsion (VSEPR), molecular geometry of the bond between DNA molecules with protein molecules shows that the Nitrogen atom has a number of three electron pairs, which are bonded with two atoms of hydrogen and one atom of another of the constituent molecules of adenine. While on the bond, no free electrons obtained. Based on this, analisii geometry on these molecules form a triangle planar or flat triangle [21], with the value of each angle formed from the three shared electrons are 120°.

In our research, the potential of the hydrogen bonds is estimated by the general Hylleraas potential. To distinguish the interaction between the chains of DNA and DNA-protein binding we propose a general Hamiltonian equation represented by the following equation.

\[ H = H_{DNA} + H_{prot} + H_{int} \]  

where the first part is DNA chain interactions containing the kinetic energy, general Hylleraas potential and coupling interaction with the following equation.

\[ H_{DNA} = \sum p_n^2 \frac{1}{2m} + \left( V_1 \left[ \frac{a + e^{\alpha_n}}{b + e^{\alpha_n}} \right] - V_2 \left[ \frac{d + e^{\alpha_n}}{b + e^{\alpha_n}} \right] + \frac{k}{2} \left( y_n - y_{n-1} \right)^2 \right) \]
We assume that the mass \( m \) of nucleotide bases and momentum \( p_i \) is homogenous. The second term of the Eq. (2) is the general equation of Hylleraas potential. The general form is given by equation [22-24]:

\[
V = V_1 \left[ \frac{a + e^{\alpha x}}{b + e^{\beta x}} \right] - V_2 \left[ \frac{d + e^{\gamma x}}{b + e^{\delta x}} \right] - \sum_{n=1}^{\infty} \frac{P_{1n}^2 y_n - P_{2n}^2 y_{n-1}}{1 + Pe^{\epsilon x}} \tag{3}
\]

The parameters for Hylleraas potential consist of \( a, b, d, \) and \( \alpha, \beta, \delta \), with \( a \neq b \) and \( d \neq b \). The third term is the harmonic coupling between two neighboring base pair and parameter \( k \) is coupling parameter. If we change any parameters as \( A = \frac{aV_1}{b}, P_1 = \frac{V_1}{b}, D = \frac{dV_2}{b}, P_2 = \frac{V_2}{b}, \) and \( P = \frac{1}{b} \), then substituting into Eq. (2), we have

\[
H_{DNA} = \sum_{n} \frac{P_{1n}^2}{2m} + \left[ \frac{(A - D) + (P_1 - P_2) e^{\alpha x}}{1 + Pe^{\epsilon x}} \right] + \frac{k}{2} (y_n - y_{n-1})^2 \tag{4}
\]

Whereas for Hamiltonian equation of protein is represented by

\[
H_{prot} = \frac{P_{2n}^2}{2M} + \left[ \frac{F - I + (Q_1 - Q_2) e^{\beta x}}{1 + Q e^{\rho x}} \right] \tag{5}
\]

With the same case, if we change any parameters as \( F = \frac{fV_1}{g}, Q_1 = \frac{V_1}{g}, I = \frac{iV_1}{g}, Q_2 = \frac{V_2}{g} \) and \( Q = \frac{1}{g} \) and substituting into Eq. (4), we have

\[
H_{prot} = \frac{P_{2n}^2}{2M} + \left[ \frac{(F - I) + (Q_1 - Q_2) e^{\beta x}}{1 + Q e^{\rho x}} \right] \tag{6}
\]

The indices \( m \) and \( n \) is the notation of the position of the chain molecules as DNA and protein. The coupling constant \( \chi \) determines the sensitive and strong interaction. The value is not specified yet, but it could be set to obtain a good value for the interaction. The last part of Hamiltonian interaction about those two bonds is represented with general form

\[
H_{int} = \sum_{n} \chi x_m^n y_n^l \tag{7}
\]

We will set and retract the value of \( s \) and \( t \) in Eq. (7). It aims to determine the simplest model from the dynamic interactions system. The value of the parameter depends on biological requirement influenced by oscillator’s initial conditions [12]. If we substituting Eq. (4), Eq. (6), and Eq. (7) into Eq. (1), we obtained the Hamiltonian equation as:

\[
H = \frac{p_m^2}{2m} + \left[ \frac{(A - D) + (P_1 - P_2) e^{\alpha x}}{1 + Pe^{\epsilon x}} \right] + \frac{k}{2} (y_n - y_{n-1})^2 + \frac{p_{1n}^2}{2m} + \left[ \frac{(F - I) + (Q_1 - Q_2) e^{\beta x}}{1 + Q e^{\rho x}} \right] + \chi x_m^n y_n^l \tag{8}
\]

By the similar expectation with the previous research, a pulses will be triggered by a protein molecule. That mean a shift in \( y_n \) requires an initial shift from \( x_m \). It mean that this requires an initial shift in \( x_m \) to trigger a shift in \( y_n \), or to alter the state. However, an initial shift in DNA, \( y_n \), should not alter the state of a rest protein (i.e. \( x_m = 0 \)), as if there is no protein. Otherwise, the protein would not steadily bind. These specific requirements trigger the result of special condition for integers: \( t = 1 \) and \( s > 1 \). This can be understood by considering the equation of motion derived from Hamiltonian,

\[
m \ddot{y}_m = \left[ \frac{(P_1 - P_2 - PA + PD) e^{\alpha x}}{(1 + Pe^{\epsilon x})^2} + k(2y_m - y_{m-1} - y_{m+1}) + t \chi x_m^n y_n^l \right]
\]
\[
m_x = \frac{(Q_1 - Q_2 - Q_F + Q_I) \beta e^\beta y}{(1 + Q e^\beta)^2} + s \chi x^2 y_i
\]  

(9)

We use the Hamiltonian interaction with the simplest form \( H_{\text{int}} = \frac{1}{2} x^2 y \) to get good phase portraits.

In Eq. (9), 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 \( s \) and \( t \) are fulfilling that \( b = 1 \) and \( a > 1 \). Thus, to form the simplest interaction equation researchers used the equation \( H_{\text{int}} = \frac{1}{2} x^2 y \).

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 frequently used functions in the process of analyzing the stability of the system [25, 26]. The stability analysis is calculated within the protein and the nearest base pair. Based on [12, 25], we only need to consider the Hylleraas potentials and the interaction term. Here the harmonic coupling is neglected because it is just longitudinally transferring an amplitude. Consider the potential function

\[
U(x, y) = \frac{(A - D) + (P_1 - P_2)e^{\gamma y}}{1 + Pe^{\gamma y}} + \frac{(F - I) + (Q_1 - Q_2)e^{\beta y}}{1 + Qe^{\beta y}} + \frac{1}{2} \chi x^2 y
\]  

(10)

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

\[
\frac{(P_1 - P_2 - PA + PD)\alpha e^{\gamma y}}{(1 + Pe^{\gamma y})^2} + \frac{1}{2} \chi x^2 = 0,
\]  

(11)

The equilibrium and stability can be determined after we set the value of each parameter. Now we will determine the system in stable or unstable. It can be done by determining the determination of Hamiltonian (det \( H \)) using hessian matrix.

\[
\text{det}(H)_{x(\alpha, \gamma), y(\alpha, \beta)} > 0 \text{ indicates the system is stable and the } \text{det}(H)_{x(\alpha, \gamma), y(\alpha, \beta)} < 0 \text{ indicates the system is unstable.}
\]

In this stage, we can determine the system stability in general form, but we cannot claim that the system is already fully stable. To determine the stability, we pick \( a, b, d, f, g, h, V_1, V_2, V_3, V_4, x, \beta, \), and \( \chi \) as an example when the hydrogen bonds between the base pair are stronger than those between the DNA-protein.

4. WKB approach method

In this research, Hylleraas potential \( V(x) \) is potential that represented the interaction between DNA and protein, while the energy of protein represented by \( E \). We used the WKB approximation to determine the spectrum energy from the interaction as equation [16]:

\[
\int_a^b k(x)dx = (n + \frac{1}{2})\pi
\]  

(13)

with \( n=0,1,2,3, \ldots \), \( k(x) = \frac{1}{B} \sqrt{2m(E - V(x))} \), \( a \) and \( b \) are the classical turning point, the value of \( a \) and \( b \) can be obtained with condition \( E - V(x) = 0 \) (\( a \) and \( b \) are the root’s value of \( x \)). If we substitute Hylleraas potential to eq. (1) we have the equation to determine the spectrum energy as:
The classical turning point $a=0$ and $b = \frac{1}{\beta} \ln \left( \frac{E-F+I}{Q_1-Q_2-EQ} \right)$. By substituting $a$ and $b$ into Eq. (14), we obtained the general equation of Energy as:

$$E_n = \frac{\left(3\pi\hbar\beta \frac{(Q-FQ+Q_1+Q_2)}{2\sqrt{m(1+Q)}} \left(n + \frac{1}{2}\right) \right)^2}{(1+Q)} - I + F - Q_2 + Q_1$$

Eq. (15) was the solution to obtained the energy interaction between DNA and protein. WKB approach can only be used for one-dimensional systems or a system that has been reduced to one dimension, and the calculation is simply using algebra.

5. Result and discussion
In this section, we discuss several findings in the previous section. By setting the value of each parameter. To obtain the phase portraits of the system we used Eq (8), and the stability analysis with Eq. (10), Eq. (11), and Eq. (12). Whereas and the spectrum energy with Eq. (15).

5.1. Phase portraits of the system and stability analysis
We set the value of each parameters and substituting its into Eq. (8), we obtain the phase portraits of the system as illustrated in Figure 1. The values of parameter on the hydrogen bond of the DNA chain and DNA with protein are $a=0.4$, $b=0.8$, $d=0.2$, $f=0.3$, $g=0.6$, $i=0.1$, $V1=4eV$, $V2=2eV$, $V3=2eV$, $V4=1eV$, $\alpha=2$, $\beta=2$ and $\chi=1eV.m^{-3}$. After we insert the parameter, we obtain the phase portraits of the system as illustrated in Figure 1 and 3,

![Figure 1a](image1.png)  ![Figure 1b](image2.png)

**Figure 1a.** Phase portraits of the systems with no initial amplitude $y_m=0$  **Figure 1b.** Phase portraits of the systems with no initial amplitude $x_m=0$

By inspecting Fig 1a, we can be concluded that the form of the trajectory of $p_{yn}$ in wich $y_n$ has no initial amplitude in $x_m$, this can be said that is a simple trajectory for DNA dynamic. The Fig 1b shows the trajectory of amplitude of $x_m$, where the interaction of DNA with protein was not occurred yet. The momentum $p_{xn}$ of protein can be approach as a stable state.
Figure 2a. Phase portraits of DNA chain system change due to the molecule existence of a protein molecule.

Figure 2b. Phase portraits of DNA binding with protein system changes due to the molecule existence of a protein molecule.

Figure 2a shows the change of trajectory as result of momentums $p_y$, which is connection of $y$ that was caused by the shifting of protein on the $x$ direction. The change of $y$ was affected by the shift of amplitude range in the $x$ and also caused to the shift of center-line as well as affected the value of momentum. It’s shown that the vibration on DNA chains will shift toward the negative $y$-axis.

Figure 2b shows trajectory changes as a result of the relationship between momentums $p_x$, which is connection of $x$ that was caused by the existence of DNA on the $y$-axis. However, the change of $y$ is only affected to the maximum and minimum of amplitude, but it is not affected by the center-line shifting.

In accordance as the expected condition that initial shift in $x_m$ will trigger a shift in $y_n$, or to alter the state. However, an initial shift in DNA, $y_n$, should not alter the state of a resisting protein (i.e. $x_m=0$) as if there is no protein.

From Eq. (10) we obtain the equilibrium points: $\approx (0,0)$ with required condition and $\approx (-0.3427,0.0033)$. After we insert the value of the equilibrium point into Eq. (11), we obtain the stability with $\approx (0,0)$ equilibrium has the determinants value (0.0012) and indicated the system at stable condition and $\approx (-0.3427,0.0033)$ has the determinants value (-8.8286) and indicated the system at unstable condition. An unstable condition can be associated with the process of the separation of DNA molecules in strands of his bases pairs, and the separation processes of the protein molecules from DNA-protein peptide groups [27].

5.2. Spectrum energy

In this section, we discuss several findings in the previous section of spectrum energy. We obtained some energy value with a variety of any parameters shown in the table below.

| Table 1. The values of energy corresponding to several state $n$ of molecule with the variation of $V_3$ and $V_4$, $V_3$ and $V_4$ are in eV. |

| Energy (eV)          | $V_3=1$ eV | $V_3=2$ eV | $V_3=2$ eV |
|----------------------|------------|------------|------------|
| $V_4= 5$ eV          | $V_4= 5$ eV | $V_4= 6$ eV |
| 0                    | -1.2088    | -0.3168    | -0.8628    |
| 1                    | 0.6583     | 1.6361     | 1.3104     |
| 2                    | 2.1171     | 3.1621     | 3.0086     |
| 3                    | 3.3882     | 4.4916     | 4.4881     |
| 4                    | 4.5420     | 5.6984     | 5.8311     |
| 5                    | 5.6126     | 6.8183     | 7.0773     |
| 6                    | 6.6199     | 7.8719     | 8.2497     |
| 7                    | 7.5766     | 8.8726     | 9.3633     |
Table 2. The values of energy corresponding to several state $n$ of molecule DNA under the influence of Hylleraas potential with variation of $\beta$.

| N  | $\beta = 1$       | $\beta = 2$       | $\beta = 3$       |
|----|-------------------|-------------------|-------------------|
| 0  | -1.2088           | -0.1934           | 0.6583            |
| 1  | 0.6583            | 2.7704            | 4.5420            |
| 2  | 2.1171            | 5.0862            | 4.5420            |
| 3  | 3.3882            | 7.1039            | 10.2205           |
| 4  | 4.5420            | 8.9354            | 12.6205           |
| 5  | 5.6126            | 10.6350           | 14.8475           |
| 6  | 6.6199            | 12.2339           | 16.9427           |
| 7  | 7.5766            | 13.7526           | 18.9327           |

Table 3. Energy values corresponding to several state $n$ of molecule DNA under the influence of Hylleraas potential with the variation of mass. Mass is in atomic mass unit (AMU).

| N  | $m=6$         | $m=12$        | $m=24$        |
|----|--------------|--------------|--------------|
| 0  | -1.2471      | -1.7506      | -2.1502      |
| 1  | 1.3887       | 0.3415       | -0.4897      |
| 2  | 3.4482       | 1.9761       | 0.8077       |
| 3  | 5.2425       | 3.4003       | 1.9381       |
| 4  | 6.8713       | 4.6931       | 2.9642       |
| 5  | 8.3828       | 5.8927       | 3.9163       |
| 6  | 9.8047       | 7.0213       | 4.8121       |
| 7  | 11.1553      | 8.0932       | 5.6629       |

Based on Table 1, it is shown the value of energy corresponding to the condition of a particle-bound, as electrons bound to the nucleus. The energy turned toward positive corresponding with quantum state $n$. The change of potential $V_3$ comparable with the change of energy. If we increase the value of $V_3$, it will raise the value of energy. Meanwhile, by increasing the value of potential $V_4$ will decrease the value of energy. The similar condition was shown in Table 2, by increasing the value of the parameter $\beta$ will increase energy. We take three different value of $\beta$ to prove that condition. In table 3 shown the value of energy correlation with several variations of mass. The value of bounding energy decreased. It means the bounding energy by DNA to protein was increased.

By inspecting the result of Energy bellow, all of the results have determined the condition of interaction corresponding to the condition of a particle-bound, as electrons level energy bound to the nucleus.

Based on the results of obtained the specktturm energy, some energy has a negative value. In quantum theory, these values indicate the condition of the protein molecule is still bound to the DNA molecule. The more negative the value of the energy obtained, the greater the energy needed protein for could be separated from the DNA molecule, while the energy is positive showing protein molecule
is not bound to the DNA molecule. Condition dependent DNA molecules can be associated with the condition at the time of reducing protein DNA molecule so that it can carry out its activities both replication and transcription, even doing both simultaneously [28].

6. Conclusion
By using Hyleras potential we have obtained a model of nonlinear interactions systems of DNA and protein. Based on Eq. (9), this potential can be use to show that DNA chains shift due to the presence of protein molecule, however, for the case of the DNA interation shows that the side chain of the DNA molecule will not give a significan effect to the interactios of protein. From the result, the stability of system can be obtained after we get the equations of Determinant of Hamiltonian. The Hamiltonian was treated as Lyapunov function. The stability was shown by substituting the value of each parameter into Eq. (13), phase space on Figure 1a., Figure 1b., Figure 2a., and Figure 2b. From the figure 1 and 2, we find the different change of form both trajectory before and after the interactions. Both trajectories are shifting, but a noticeable shift is apparent in changes in the trajectory of DNA occurring as a result of protein molecules.

We also determined the spectrum energy from the DNA-protein interaction. Its can be done by using the WKB approximation. The results obtained are adapted to the conditions of a molecule bound by the nucleus or condition of a particle-bound, as electrons bound to the nucleus. From the calculation of mathematically obtained the value of energy turned toward positive and its corresponding with quantum state condition.

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8
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