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Numerical simulations for the protein mRNA coupled equation

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ABSTRACT*: Modelling the complex protein m RNA coupled equation that cause thecancer problem could be key to understanding and treating these abnormal cancer.* The promise of sequencing portable or desktop computers would help predict cancer.*We used the Peyrard-Bishop models using symmetric Morse potential.*It is imperative to analyze DNA with the influence of viscous medium and external forces with their corresponding sequencing in a portable way in the production of the type of proteins.

KEYWORDS*: Cancer, kinase inhibitors, Numerical simulations,*single nucleotide polimorphism, DNA inhomogeneous

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I. INTRODUCTION

Is imperative the numerical simulations in the Peyrard -Bishop model of DNA inhomogeneous [0-1] and DNA homogeneous [1-3]. There are problems related to the functions of the gene and the mechanisms of gene expression [4].

The development patterns are explained with the theoretical and experimental models of coupled oscillators (2).

The present study aims to describe in a computational simulation the dynamics of messenger of RNA and proteins. The stationary case is analyzed, which is equivalent to the experimental case, usually in the cell medium. In general, the solutions for a set of parameters are determined and they are observed as they behave as a station after a certain time.

II. METHODS

2.1 Peyrard Bishop model for DNA , RNA , Inosina in DNA with solvent and external potentials

The deoxyribonucleic acid DNA is a thread-like chain of nucleotides carrying the genetic information of all organisms. The coding sequences for genes and regulatory information are located in DNA and is marginally stable and undergoes a "melting phase transition". There are many experimental ways to study the fluctuations or breathing of DNA: Hydrogenexchange, formaldehyde probing, protein-nucleic acid interactions, DNA replication, DNA base analogue spectroscopy, single molecule DNA-protein interactions, two-dimensional fluorescence spectroscopy . The interaction between the viscous potential and external forces

prevent DNA to unzip perfectly but allows DNA to split at a certain distance from its original position . S.Flach gives the theory of the "discrete breathers" and applications.

The mobility and breathing of DNA depends of the harmonic bifurcation. The strong dependence on sequence, temperature and salt concentration for the breathing dynamics of DNA found here points at a good potential for applications and the effect of the viscous and external forces

First, the PB model is introduced. It is then followed by the dynamical and the thermodynamic formulations. We show that mobile breather can lead to the observed breathing, but the amplitude of the breather is determinant for the transient conformational fluctuations of DNA. The numerical simulations verify the existence of breather with the conditions describes by R.S. Mackay. The symmetric potential does not give a solution for the transition of the DNA. For that reason, it is necessary to investigate the effect of the solvent and external potentials. The calculation of hydrogen bond stretching using transfer integral operator and difference finite methods are presented.

We consider the Peyrard-bishop model with the symmetric Morse potential The biomechanics of DNA is represented by two degree of freedom X_n and Y_n which correspond to the displacement of the base pair from their equilibrium position along the direction of the hydrogen bonds connecting the two-base pair of nucleotides.

The studies of the Symmetric Peyrard-Bishop (S-PB) models that included the modified Morse potential was done by adding the absolute value:

$$V(u) = \frac{1}{2}\left[\exp(-|u|) - 1\right]^2 \quad (1)$$

Where V = symmetric Morse Potential.

The profile of symmetric Morse potential can be seen in Figure 1.

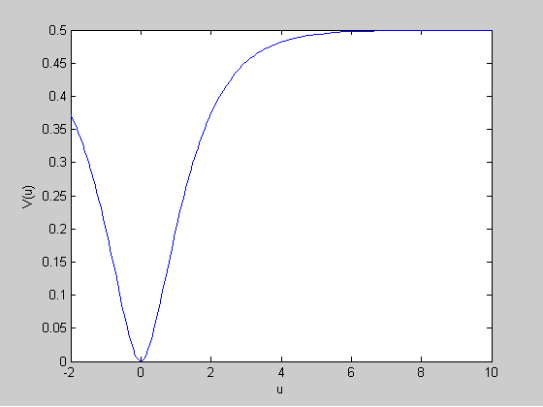

Figure 1. The symmetric Morse potential**.**

$$H = \sum_{n=1}^{N} \frac{m}{2} u_n^2 + \sum_{n=1}^{N} \frac{K}{2} (u_n - u_{n-1})^2 + \sum_{n=1}^{N} V_n(u_n) \quad (2)$$

Where N = number of the pairs of bases; K = coupling constant; $velocity = \dot{u}$; and u_n = stretching of the hydrogen bonds = $(X_n - Y_n)/\sqrt{2}$.

The associated equations for equation (4) are the system equations (n=1, 2... N)

$$\ddot{u}_n + sign(u_n)\left[e^{-2/u_n/} - e^{-/u_n/}\right] + K(2u_n - u_{n-1} - u_{n+1}) = 0 \quad , \qquad (3)$$

Using the approximation for the oscillator n and $T=2\pi/w_b$

$$u_n = z_n^0 + \sum_{k=1}^{k_m} 2z_n^k \cos(k\omega_b t). \qquad (4)$$

And substituting in (3) one has

$$k^2\omega_b^2 z^2{}_n + V_n'^k + K(2z^k{}_n - z^k{}_{n-1} - z^k{}_{n+1}) = 0 \qquad (5)$$

Which depend on the parameter K, and V'^k_n is the k^{th} Fourier coefficient for the periodic Function $V'(u_n(t))$.

The breather solution is obtained conditions (t=0) where all the oscillators are at rest, while the central one is shifted. The codification for one site breather is 0,0,…0,1,0,…,0,0.

In Fig. 2 the breather is depicted. This figure shows the numerical solution of the equations (5). The second derivative of the symmetric Morse potential is given by

$$V'' = \left[2e^{-2/u_n/} - e^{-/u_n/}\right].$$

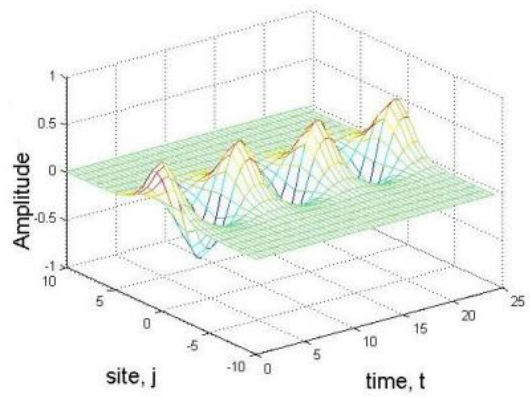

Figure 2. Spatial breather configuration of the symmetric Morse potential.

The dynamics of the DNA is a set of coupled oscillators, and the vibrational motion is equivalent to equations (3) which depend of the Symmetric Morse potential and constant *K* of coupling.

The amplitude of the breather is determinant for the transient conformational fluctuations of DNA. In our case the Figure 2 gives 0.6 angstrom of amplitude.

Harmonic bifurcation

We analyze the stability of the breather solution Let us introduce a function $\tilde{u}_n(t) = u_n(t) + \varepsilon_n(t)$, where $u_n(t)$ is the periodic breather solution shown in Figure 2. The term $\varepsilon_n(t)$ is a perturbation: $\tilde{u}_n(t)$ must satisfy the system (3) and expanding around $u_n(t)$ to first order (linearization), we obtain the following system of equations for $\varepsilon_n(t)$

$$\ddot{\varepsilon}_n + (V''(u_n(t)))\varepsilon_n + K(2\varepsilon_n - \varepsilon_{n-1} - \varepsilon_{n+1}) = 0. \quad (6)$$

We can associate a monodramamy matrix for this equation with Fouquet multipliers.

The solution is stable if the modules of Fouquet multipliers are one. The especial instability ("harmonic bifurcation") in our case happens when a pair of Fouquet multipliers merges at $\lambda = 1$ and splits off circle onto the positive real axis in Fig. 3.

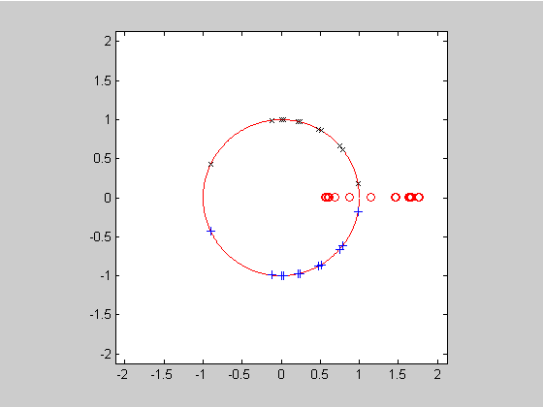

Figure 3. The instability "harmonic bifurcation" with the evolution of the Fouquet multipliers. Case SPB model with the parameters: *K*=0.004, wb=0.8 for the breather.

Mobile breather

For the coupling *K*=0.004 and *wb*=0.8 there is a harmonic bifurcation. In this case we can construct a dark breather mobile. Once the system of equations (3) is worked out by RungeKutta method for the Cauchy problem with the equations (3). We can use the Figure 2 for the initial conditions of the position and average speed of each position "*n*" respect to the harmonic oscillation corresponding to the DNA.

The center of energy of the breather mobile is given by[5]

$$X_E = \sum_{n=1}^{N} nH_n^d \ / H \qquad (7)$$

Where the density energy has the form

$$H_n^d = \frac{1}{2}u_n^2 + \frac{K}{4}(u_n - u_{n-1})^2 + \frac{K}{4}(u_{n+1} - u_n)^2 + V_n(\sqrt{2}u_n) \qquad (8)$$

It is very important the initial velocity of the BM for the displacement a long of sites of DNA and can be produced of DNA breathing.

This parameter initial velocity *v(0)* is transcendental for DNA breathing.

We can use the profiles of the stationary dark breather obtained of equations (3). The velocity is a vector which the components are given by

$$v_n(0) = (u_{n+1}(0) - u_{n-1}(0))/2 \qquad (9)$$

The components of this vector perturbation *V* are given by

$$V_n(0) = \lambda(v_n(0)/v) \tag{10}$$

Where v is the normal of the vector of the components $v_n(0)$.

The initial value problem is given by

$$\ddot{u}_n + V'(u_n) + K(2u_n - u_{n-1} - u_{n+1}) = 0 \tag{11}$$

Initial conditions: $u_n(0)$ = profiles of the solutions of the Figure 2. The velocities are given by the expression (10) with λ=0.1. We can obtain the solutions of the equations using initial condition with the software Fortran (for a review, see ref. 3).

The evaluation of the partition of equation (2) using the transfer integral operator method in the thermodynamic limit reduces to solving the pseudo-Schrodinger equation (12):

$$\{-1/(2\beta^2 K)d^2/du_n^{\,2} + U(u_n,\beta)\}\psi(u_n) = \varepsilon\psi\ (u_n) \tag{12}$$

$$U\ (u_n,\beta) = V(\sqrt{2}u_n) + (1/2\beta)\ln(\beta K/2\pi) \tag{13}$$

$$\beta = 1/(K_B T) \tag{14}$$

We use the symmetric Morse potential. The fluctuations or breathing of DNA can be performed numerically using the finite difference methods. Firstly, we obtain the ground state wave function of equation (12). For estimate the mean value of the fluctuations we use the formula

$$< u >= \int_{-\infty}^{+\infty} \psi^2{}_0 u du \tag{15}$$

The ground state wave function for the symmetric Morse potential is symmetric in consequence the mean value of the fluctuations is approximately zero (for a review, see ref. 3).

In Figure 4 is depicted the example of the ground state wave function for the symmetric Morse potential.

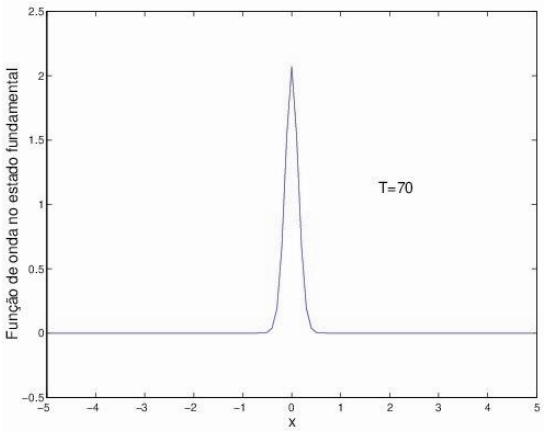

Figure 4. Ground state wave function for the symmetric Morse potential with the control parameter Temperature=70 °K**.**

Thermodynamics in the PB modelwith solvent and external potentials

We can consider the new potential for the equation (13):

$$U\ (u_n) = V(\sqrt{2}u_n) + Vsolvent(u_n) + V_0 \exp(-0.1u_n^2) + (1/2\beta)\ln(\beta K/2\pi) \quad (16)$$

The solvent potential is given by: $V_{solvent} = 0.04*\nu*\text{than}\ (u_n/5 - 1)$. In Figure 5 is depicted the example of the solvent potential.

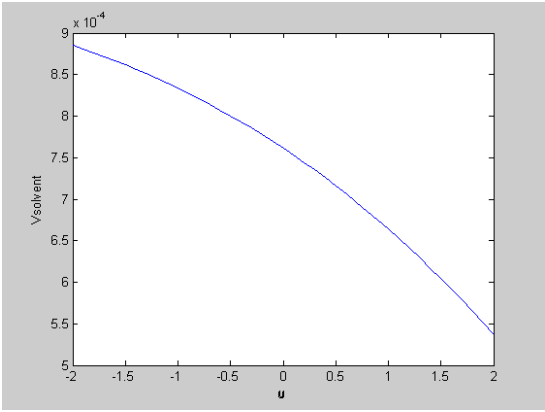

Figure 5. The solvent potential with the control parameter ν=0.025.

For the symmetric Morse potential in the S-PB Model we can get many values of the melting temperatures. For example, for T =270 K and the control parameter $\nu = 0.001$, $V_0 = 0.005$ the mean value of the fluctuations $\langle u \rangle$ = 1.9586 Å. The hydrogen bond stretching as a function of temperature gives a melting temperature depicted in Figure 6.

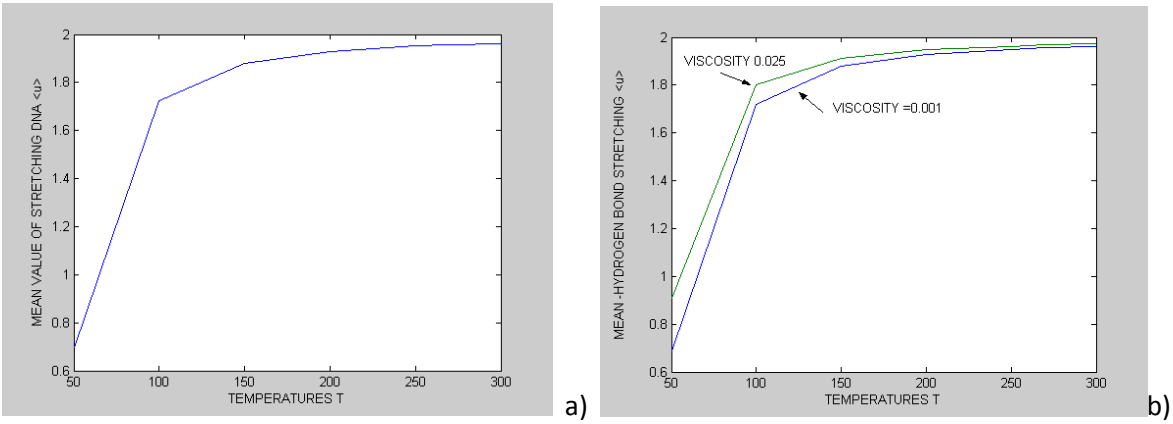

Figure 6. The hydrogen bond stretching as a function of temperature for external

Potential $V = V_0 \, exp\,(-0.1\, u^2)$, V_0 =0.005 and solvent potential with the viscosity control parameter *v: a*) v=0.001 and b) v=0.025.

The solutions of the dynamical equations (5) give the dark breather mobile. We have the mobile breather using the center of energy for the initial velocity of 0.1. This method is based on the literature

We have obtained harmonic bifurcation using the symmetric Morse potential with the parameter K=0.004.

We have obtained the Eigen functions of the pseudo-Schrodinger equation (12) for demonstrate that the mean value breathing of DNA is zero. The analysis is based on the reference[12].

For the symmetric Morse potential in the S-PB Model, we can get the melting temperature for

T = 270 K, control viscosity parameter v = 0.001 and the constant of the external potential V_0 = 0.005. For these values the mean value of the fluctuations $\langle u \rangle$ is 1.9586 Å. In this case, we can get the DNA breathing with the variations of temperatures (Figure 6(a)).

Figure 6(b) indicates that mean value of stretching $\langle u \rangle$ is direct proportional to the coefficient of viscosity. The increase of the viscosity will increase the hydrogen bond stretching. The viscous and external potential effect is direct proportional to hydrogen bond stretching. For V_0 = 0.5 the mean value of hydrogen bond is $\langle u \rangle$= 3.82 with the temperature T = 270 K and viscosity v = 0.025.

The figure 6 shows that for T > 150 K the viscous force is not important for the DNA breathing. This result is similar to that obtained in the literature.

The stability of thebreather have been obtained with the Fouquet's theory. It is very important to emphasize that dark breathers at low coupling are shown to be stable in the PB model with k<0.004. For k=0.004 we have harmonic bifurcation and the mobile dark breather. In this case and using numerical simulations we can demonstrate that the mean value of the hydrogen bond stretching is zero.

For the symmetric potentials we have significant fluctuations in the analysis of the breathing DNA with solvent and external potentials. The external potential is more important than the viscous force for the estimated melting temperature and the mean value of the hydrogen bond stretching.

4.2 Concentrations are asymptotic to stationary solution

m: Messenger concentration.
p :Proteins

A system of differential equations was used to analyze the dynamics of mRNA concentration (m), and protein concentration (p).

$$\dot{p} = Lm - Up \quad (1)$$

$$\dot{m} = f(p) - Vm$$

The constant L is the translation coefficient and U is the protein degradation coefficient.
U is the degradation coefficient of mRNA. The function f (p) is the transcription function. The classical method of solving systems of differential equations is with Runge -Kutta fourth order method and is computationally processed with the ODE tool 45 of the MATLAB program.
To determine the stationary solution, we have considered the set of parameters: L = U = V = 1 and the function f (p) given by:

- $f(p)=10/(1+ p^2 /25)$

The stationary solution was found by solving the system:

$$0 = Lm - Up \quad (2)$$

$$0 = f(p) - Vm$$

.

A concentration of m = p = 5 will be horizontal asymptote for dynamic solutions.
The system of coupled equations generates two solutions as indicated in figure 7. Figure 7 shows its final vibration equal to 5.

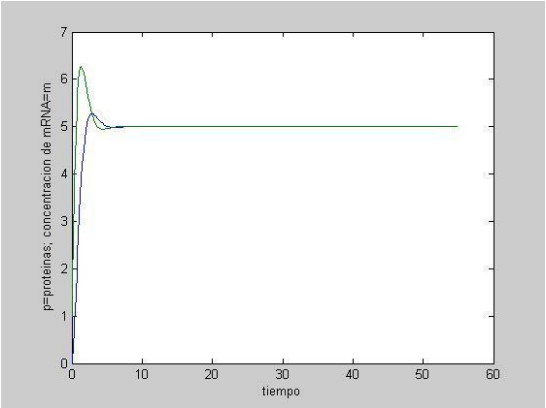

Fig.7. coupled solutions

The system (1) can be controlled in a computational manner depending on the set of parameters. These results can be optimized by manipulating the constants L, U, V and the function f (p). There are a complexity problem with the folding protein .Numerical methods with MATLAB are found in Di Stefano's reference [4].
It can be analyzed with an optimal control theory and better control of proteins. Biologically it is based on microRNAS controllers.

4.3 **Kinase-targeted cancer therapies: G-protein coupled receptors**
Recent advances have elucidated a crucial role for kinases in the carcinogenesis and metastases of cancer [5].

III. CONCLUSION

For the protein – mRNA coupled equation the concentrations are asymptotic to stationary solution.
It is imperative to analyze DNAwith the influence of viscous medium and external forces with their corresponding sequencing in a portable way in the production of the type of proteins

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