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Review Article

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## Entropic Analysis of Protein Oscillations through Langevin Equations & Fokker-Planck Equations

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### Abstract

**Background:** Protein oscillations have been one of the major highlights in the field of biophysics and bio-molecules. These oscillations can give us insights into complex bio-molecules and reveal their nature at a very fundamental level. They can also show us the dynamics involved in the functioning of bio-molecules through the nature of these oscillations. **Method/Objective:** In this article, we have described the basics of protein oscillations, giving a very fundamental approach to the physics of oscillations. We have also described some bio-systems in which protein oscillations play a vital role. In this article, we have used the Langevin equations and Fokker-Planck equations to describe the oscillation dynamics of proteins. **Findings:** Finally, we have shown the trend of an increase in the entropy of the oscillations by involving a perturbation term in the regular nature of oscillations. The entropy of protein oscillations is very important in understanding protein dynamics.

**Keywords:** Langevin Equations; Fokker-Planck Equations; Entropy; Proteins; Oscillation.

### 1. Introduction

The cell division mechanism has been studied in great detail over the last couple of decades, and these studies have given us valuable insights into its functional dynamics [1]. Cell division and similar functions can be described by molecular dynamics. These molecular functions reveal that proteins convert chemical energy into mechanical energy [2-4]. Some complex biological systems that exhibit periodic and oscillatory motion are discussed.

One such example in which chemical energy is converted into mechanical energy is in eukaryotic cells. A eukaryotic cell contains a variety of organelles, wherein each organelle exhibits its own unique functionality [5]. The ability of each organelle in the eukaryotic cell is highly regulated based on what the eukaryotic cell needs from them. The eukaryotic cells contain separate sections that are bound by membranes [6]. A general example of a eukaryotic cell is shown in Figure 1.

Each of these sections has its own unique functions and is characterized by specific proteins. Each membrane has its own level of complexity, which contributes to the characteristics of each organelle. The functioning of a eukaryotic cell has its own complexity, and understanding the physics behind it is even more challenging.

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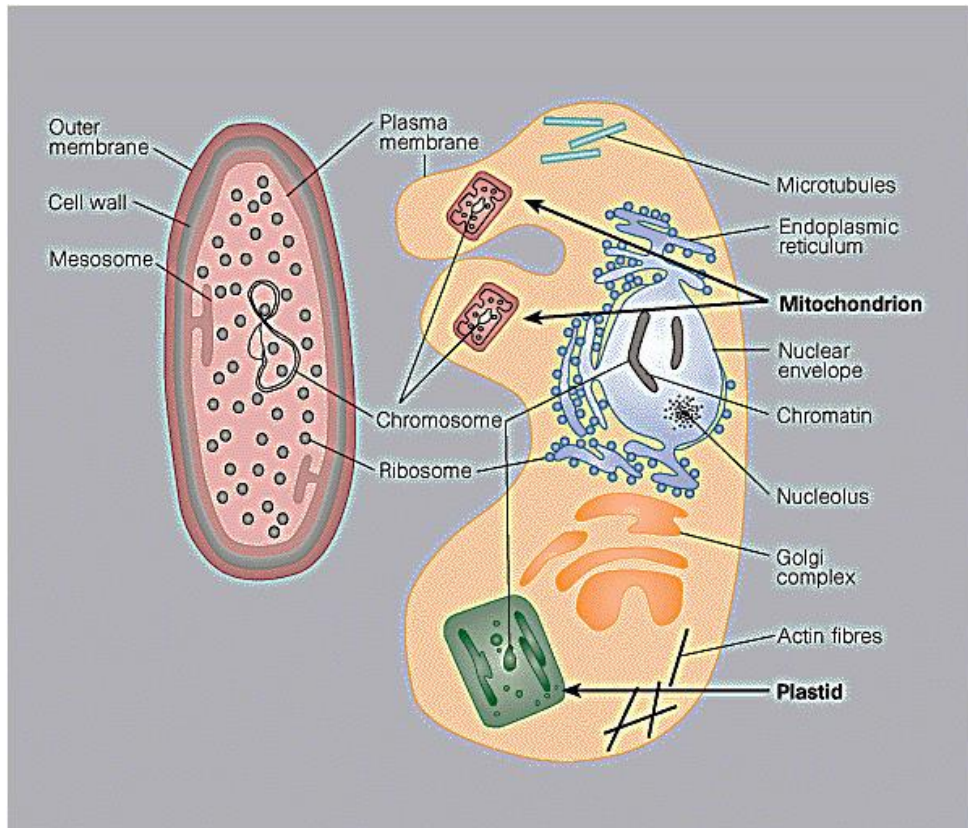


Figure 1. An example of a eukaryotic cell showing various organelles [7]

There are multiple light sensing organisms that feature circadian clocks [8]. Each of these generates a certain process known as endogenous molecular oscillations, which exhibit a specific periodicity and hence affect numerous physiological and behavioral events [9, 10]. The circadian clock is an inbuilt, rhythmic mechanism that naturally keeps time. This mechanism has evolved in organisms of all complexities, and this enables them to adapt and adjust to changes in the environment and their surroundings, such as light, motion, temperature, and their sensitivity to these properties [11]. An example of a circadian clock is shown in Figure 2.

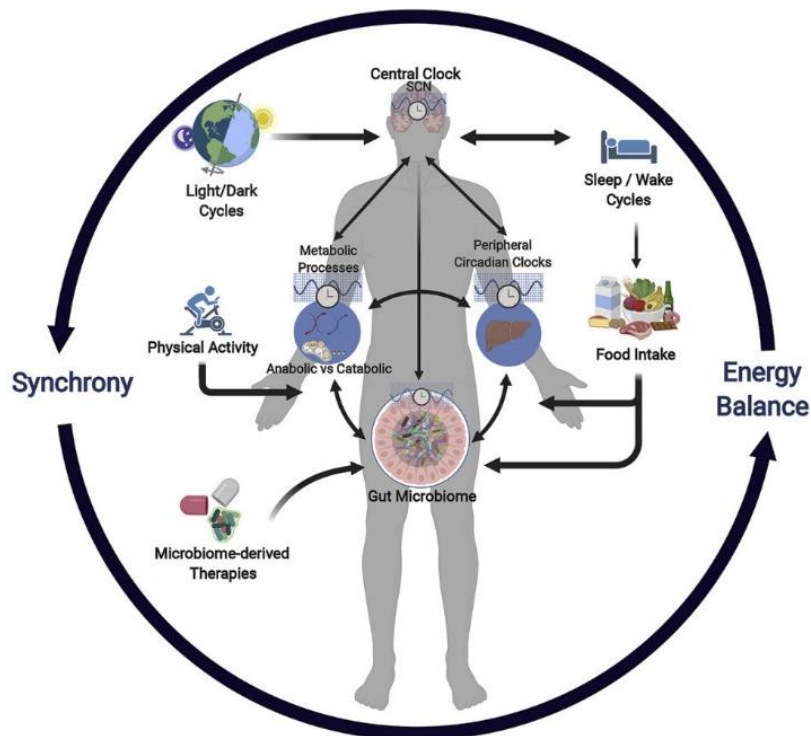


Figure 2. An example of circadian rhythm or clock [12]

This helps in the adaptive responses of organisms and their connection with the Earth's rotation period. Some situations where the circadian rhythm is observed are processes such as metabolism, hormone secretion, and cardiac function, just to name a few, and these exhibit regular oscillations. The circadian rhythm system also keeps in check the internal coordination of many oscillators within the organ systems. This is because it maintains to increase the fitness of the organism and provides an efficient response to the environment based on the conditions and situations involved.

Another complex system that exhibits oscillatory and periodic behavior are the cilia and flagella. Cilia and flagella are thin hair like structures that are part of many types of cells. In many cell systems, cilia are responsible for the motion that converts chemical energy into mechanical energy by exhibiting oscillatory periodic type motion [13].

Many cilia can also sense the oscillatory motion around them and can also give rise to oscillatory and periodic motion, connecting their motion to the surrounding motion based on the chemical and mechanical effects of the surroundings [13, 14–16]. An example of how cilia oscillations behave is shown in Figure 3.

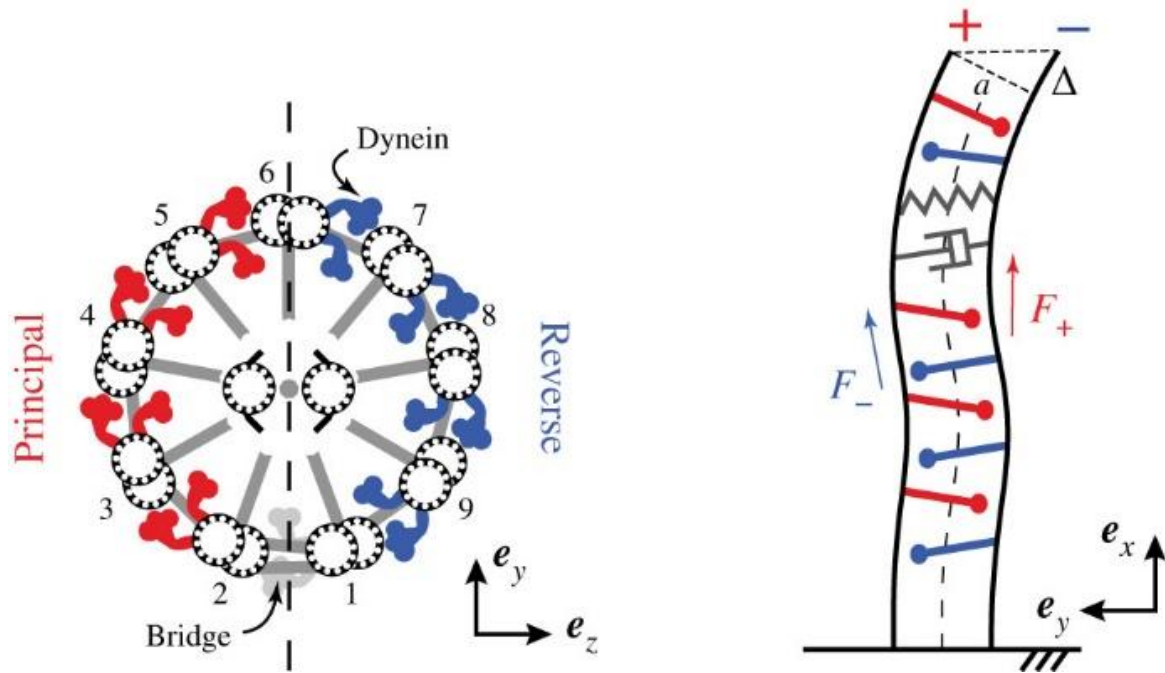


Figure 3. The cross section of a cilium.  $F_+$  and  $F_-$  are the sliding forces [17]

Flagella are structures which are used by unicellular organisms for locomotion purposes. There is no structural distinction between flagella and cilia. An example of oscillatory motion of flagella is shown in Figure 4.

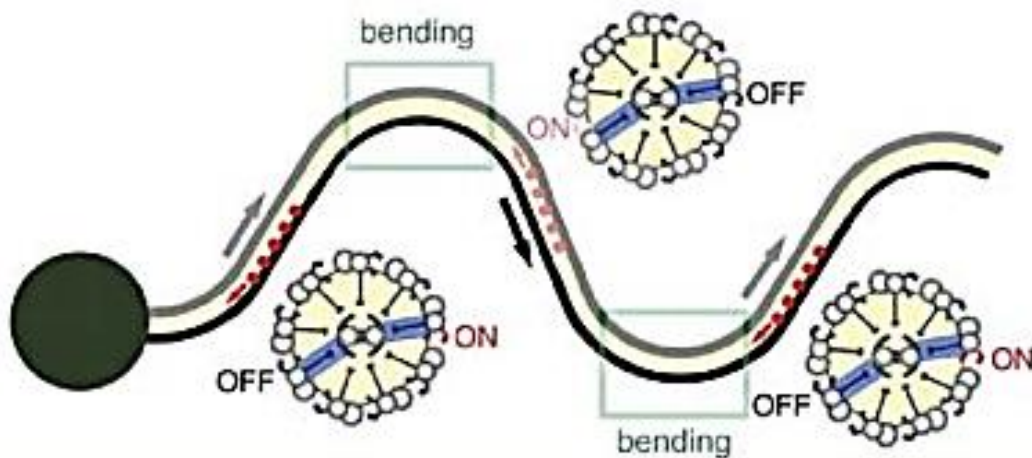
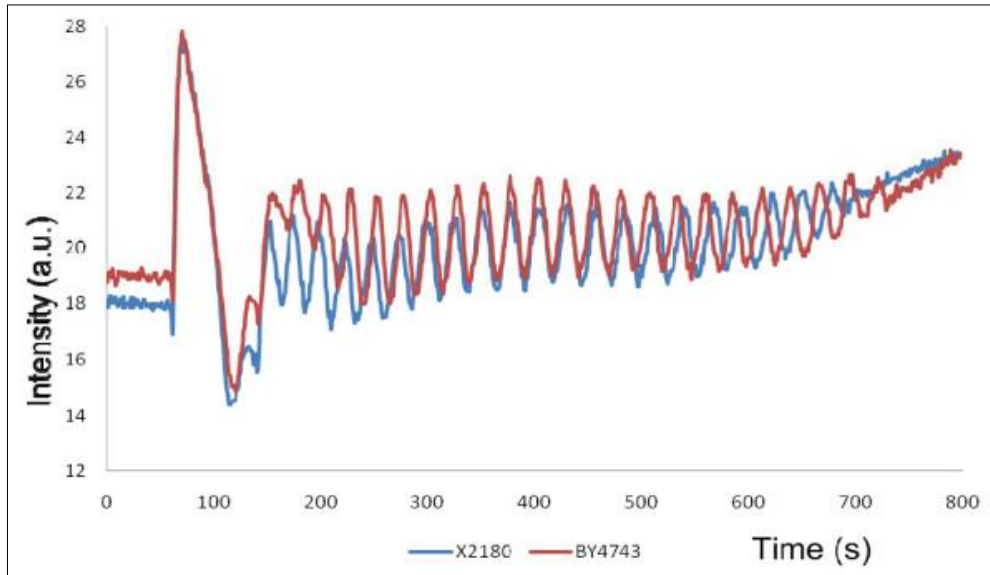


Figure 4. A model for the oscillatory mechanism of flagella [18]

Flagella is structurally known to exert propulsion by driving the surrounding fluid in a continuous manner and in parallel to what is known as the flagellar axis. This differs from the motion of cilia because cilia push fluid orthogonally to their axis in a pulsating and periodic manner which can be connected to oscillatory motion [19, 20].

The motion of oscillation is also observed in glycolytic oscillations. Glycolytic oscillations were first observed in yeast cells and yeast cell extracts by Termonia and Ross [21]. Glycolytic oscillations are considered to be fluctuations in the products from metabolism. These oscillations are also time dependent and have a role to play in metabolism. There is also evidence of glycolytic oscillations in cancer cells and this was observed for the first time by Ibsen and Schiller [22]. There are multiple studies going on at the theoretically and experimentally to understand these oscillations at a more fundamental level and how they may play a role in the dynamics of complex bio-systems. An example of glycolytic oscillation is shown in Figure 5.



**Figure 5.** An example of glycolytic oscillations in wild-type yeast strains X2180 (blue trace) and BY4743 (red trace) [23]

Recently, there has been a great interest in applying quantum physics to complex biosystems and protein being one of the most important system has gained a large interest. Earlier, the application of quantum physics to such biosystems were purely theoretical because of the technology not being available then. Quantum aspects of biology has been of great interest since a long time. Quantum physics being one of the most successful theory every, is responsible for the dynamics of atoms, molecules and everything in this Universe. Systems in biology being made up of molecules will exhibit quantum properties [24-26].

We have discussed some complex biosystems which exhibit oscillatory behavior. In the following sections we will focus on protein oscillations, Langevin and Fokker-Planck equations. Then we will take a model independent example and calculate the entropy generation and entropy production of the oscillation.

## 2. Methodology

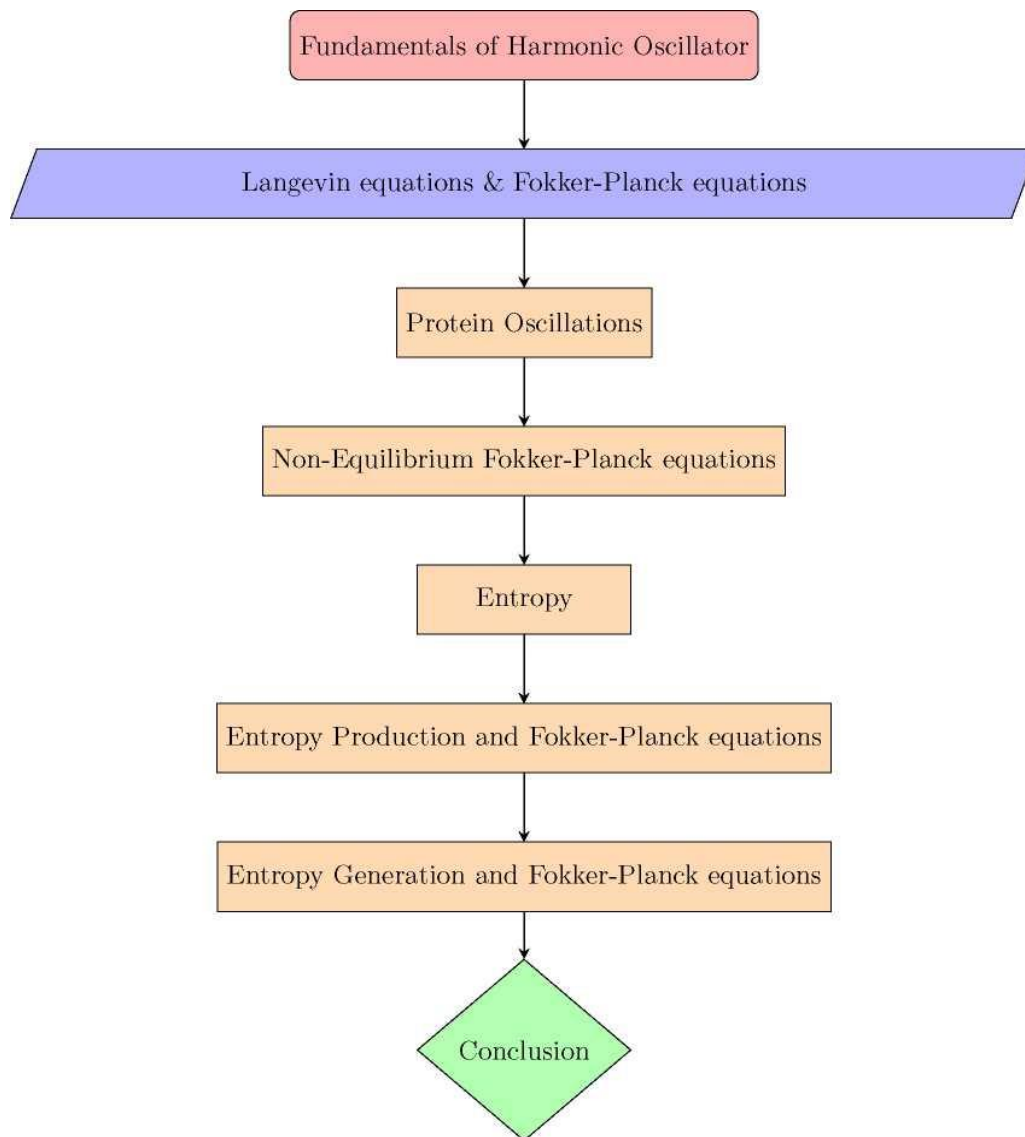
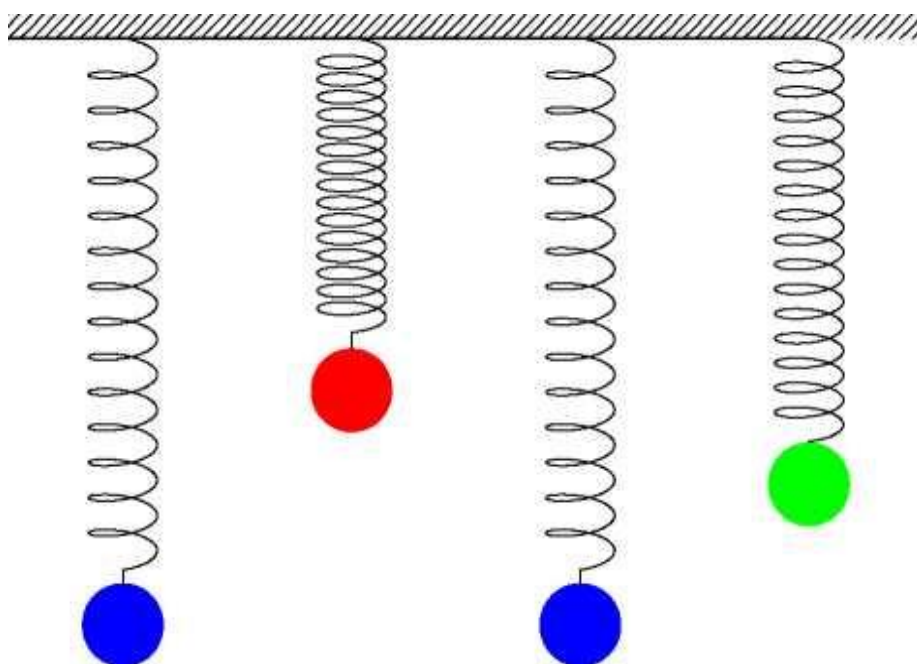
Flowchart of the research methodology shows in Figure 6.

## 3. Fundamentals of a Harmonic Oscillator

### 3.1. Regular Oscillator

The harmonic oscillator is one of the most useful concepts in theoretical and experimental physics equally. The applications of a harmonic oscillator have been widely used in all fields such as physics, engineering, chemistry, biology and even in fields such as biomechanics [27, 28]. The interdisciplinary uses have been numerous. Even though we understand the physics behind the harmonic oscillator pretty well, there is still so much more to understand and apply this system. Some examples where the understanding of a harmonic oscillator is being applied other than physics are as a thermostat trying to adjust a temperature, interactions involved and driving chemical reactions, growth of bacterial colonies and how they survive and evolve, and even as diverse as foxes eating rabbits and rabbits eating plants [29]. The list is endless, but all of this can be explained on the basis of the simplest system which represents a regular harmonic oscillator, that is, a mass on a spring which is shown in Figure 7 where the red color shows compression, blue color shows elongation and green shows any intermediate position between maximum and minimum stretch. This system as shown here is not under the effect of any external forces.



**Figure 6. Research methodology****Figure 7. Harmonic oscillator diagram**

Taking the simple case of a linear spring so that the force pulling the string back when it is stretched, is proportional to the amount of stretch. The force equation is written as:

$$m \frac{d^2x}{dt^2} = -kx \quad (1)$$

where  $m$  is the mass and  $k$  is the spring constant. The initial conditions of such a system are  $x(t = 0) = x_0$ , and  $\frac{dx}{dt}(t = 0) = v_0$ . The general solution of Equation 1 can be written as:

$$x = x_0 \cos(\omega t) + \frac{v_0}{\omega} \sin(\omega t) \quad (2)$$

where  $\omega = \sqrt{k/m}$ .

### 3.2. Forced Oscillator

In this case we will discuss about an oscillator under the effect of an external force. So there is an external force making changes in the way the oscillations happen. The equation for a forced oscillator can be written as:

$$m \frac{d^2x}{dt^2} = -kx + F(t) \quad (3)$$

where  $F(t)$  is the force which is causing the change and deviation from the regular motion of an oscillator. In this situation,  $m$  oscillates at the frequency that the force makes it to and also upon the frequency of the regular motion of the oscillator. There have been numerous studies on the types of forced oscillations and the applications of it in interdisciplinary fields are numerous [30-33]. However, the scope of this article is not to go into the details of forced vibrations.

## 4. Langevin Equations & Fokker-Planck Equations

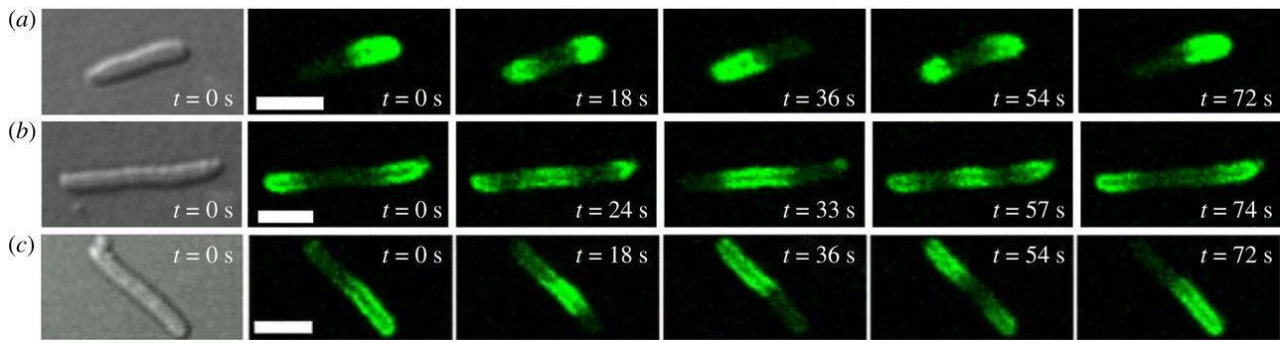
Langevin equations and Fokker-Planck equations are generally used to explain Brownian motion. These equations have been under study for a long time. There are numerous studies that have even successfully expressed and explained the Langevin and Fokker-Planck equations for systems which deviate from the regular Brownian motion. Fokker-Planck equations were generally used to describe the statistical physics of a system in equilibrium. Recent calculations have also shown a way to describe systems following non-equilibrium statistical physics. Some of these studies have found applications in a variety of fields ranging from physics to even network analysis. Some such application and studies are mentioned below:

- Fokker-Planck equation is applied to study discrete chemical reactions in for example diffusion in a potential function with a barrier. This is also used to derive the rate formula. The application of Fokker-Planck equation describes very well, the physical concepts of chemical reactions in condensed phase [34].
- Fokker-Planck equations have found immense use in systems biology too. They accurately describe the structure of stochastic population dynamics. Some systems are the number of molecules in biochemical reactions, number of cells in an organism, or even the number of individual in an ecology [34].
- Various studies in the physics and chemistry start with a Fokker-Planck equation based on the system and its phenomenology which calculates the free energy diffusivity. These studies have yielded experimental results with a high degree of accuracy [35].
- This equation along with the Langevin equation has been used to describe the weights of deep networks when we update them using stochastic gradient [36].
- Fokker-Planck equation has found great application in the finance industry too. These are distribution of asset returns depending on time. Using Fokker-Planck equations to describe the analogy between hydrodynamical turbulent cascades information cascades in stock markets [37, 38].

These are some applications where Langevin equations and Fokker-Planck equations are used. In the next sections of this article we will apply these equations to a model independent system of protein oscillations. From this we will calculate the entropy generated and entropy produced and finally understanding the trend of the entropy change.

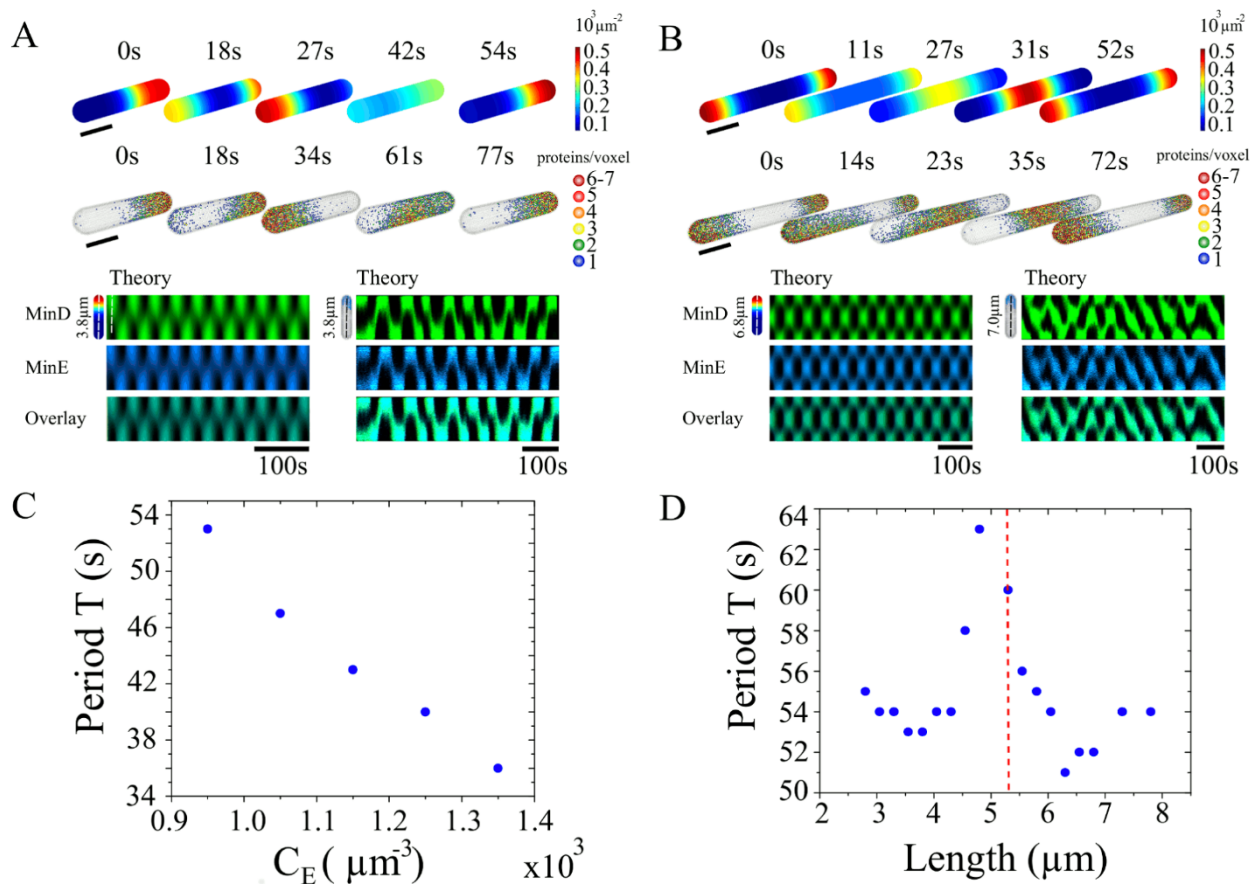
## 5. Protein Oscillations

The applications of physics in other fields has been always a matter of interest and revolutionary results [28, 39, 40]. An application of prime interest is of the principles of a harmonic oscillator in complex bio-systems [41, 42]. One such system is oscillations in proteins. This further can be divided in to various systems and sub-systems as we will discuss here. Figure 8 shows oscillations in Min-proteins.



**Figure 8. Min-protein oscillations. Snapshots of MinD-GFP in live *E. coli*. Adapted from [43, 44]**

Figure 9 shows the pole to pole oscillations and the waves between nodes. It also describes the period as a function of the length of the system.



**Figure 9. A) Pole-to-pole oscillations, B) Standing wave with two nodes, C) Deterministic oscillation period as function of the total MinE concentration, D) Deterministic period as function of the system length Adapted from [43]**

There are various bio-molecules which exhibit protein oscillations in their functioning. The scope of this article is not to go into detail of the dynamics of these bio-molecules but understand a general idea of the oscillation in proteins through entropy. Some examples of such bio-molecules are mentioned here which shows how protein oscillations are important in their dynamics.

- A very interesting example where we observe oscillations is of *Escherichia coli*. In *E. coli*, the Min system is based on the dynamic behavior of the MinC, D, and E proteins [45]. Here the Min protein acts in a way that it helps in determining the center of the cell [44]. This pattern was observed to emerge spontaneously from Min-protein interactions in filamentous bacteria. There was also evidence of self-organization of Min proteins in *E. coli* [46]. Geometry has played a vital role in understanding the dynamics of *E. coli*. It has been observed that proteins move by rotation or oscillation [47].
- Another bio-molecule where protein oscillation plays a vital role is PAR proteins. PAR proteins are made up of a highly conserved network of scaffolds, adaptors and enzymes. This network controls the polarity of a cell through

development and physiology [48, 49]. In PAR proteins the network of its members are asymmetric in polarized cells. PAR proteins were observed in mutations that affect cell division in the *C. elegans*. It is seen that the cell contracts after the network assembles and relaxes again when the network disassembles. After each cycle is completed, we see that the original state has been reached [50].

In his article we will be talking about the entropy of a model independent protein and in future research we aim to focus on a certain type of protein and the entropy associated with it.

### 5.1. Non-Equilibrium Fokker-Planck Equations

Let us consider  $n$  interacting particles. The dynamics of the particles can be defined in a way that they evolve with time given by the Langevin equations given by:

$$\frac{dx_i}{dt} = f_i(x) + r_i(t) \quad (4)$$

where  $x_i$  is the position of the  $i$ th particle,  $x = \{x_i\}$ ,  $f_i(x)$  is the force acting on the  $i$ th particle,  $r_i$  is the noise that is considered to be a stochastic variable in such a way that:

$$\langle r_i(t) \rangle = 0 \quad (5)$$

$$\langle r_i(t)r_j(t') \rangle = 2D_i\delta_{ij}\delta(t-t') \quad (6)$$

with  $D_i \geq 0$ , different constants for each particle. The associated Fokker-Planck equations describe how the probability distribution,  $P(x, t)$  evolves as a function of time [51]. This can be written as:

$$\frac{\partial P(x, t)}{\partial t} = -\sum \frac{\partial}{\partial x_i} [f_i(x)P(x, t)] + \sum D_i \frac{\partial^2}{\partial x_i^2} P(x, t) \quad (7)$$

The Fokker-Planck equation can be written as a continuity equation given by:

$$\frac{\partial P(x, t)}{\partial t} = -\sum \frac{\partial}{\partial x_i} J_i(x, t) \quad (8)$$

$$J_i(x, t) = [f_i(x) - D_i \frac{\partial}{\partial x_i}] P(x, t) \quad (9)$$

where  $J_i$  is the  $i$ th component of the current of probability. The condition of irreversibility can be expressed as:

$$D_i \neq D_j, i \neq j$$

or

$$D_i = D_j = D, i \neq j$$

but

$$\frac{\partial f_j}{\partial x_i} \neq \frac{\partial f_i}{\partial x_j} \quad (10)$$

The Fokker-Planck equation has to be solved inside a given region of the space spanned by the set of variables  $x_i$  subject to a prescribed boundary condition which governs the behavior of  $P(x, t)$  and  $J_i(x, t)$ . When the system is in thermodynamic equilibrium, the Langevin equation and the associated Fokker-Planck equations are given as:

$$\frac{\partial f_j}{\partial x_i} = \frac{\partial f_i}{\partial x_j}$$

for any pair  $i$  and  $j$  and

$$D_i = D_j \quad (11)$$

## 6. Entropy

Entropy is generally defined as the measure of disorder in a system. There are many other definitions of entropy in physics, chemistry and engineering and also depending on the type of system. The more disorder we observe in a system, higher is the entropy of that system. Thermodynamically, entropy can be connected to the heat involved and the temperature. In this article we will work with entropy as being derived from Fokker-Planck equations which in turn are



connected to the Langevin equations. We will take a simple model of protein oscillation and calculate the entropy generated and entropy produced.

### 6.1. Entropy Production and Fokker-Planck Equations

The entropy production of an active system is generally thought to be defined in terms of the Fokker-Planck equations. The rate of change of the entropy  $S$  of any system can be written as [52]:

$$\frac{dS}{dt} = \zeta - \Omega \quad (12)$$

where  $\zeta$  is the entropy production due to the irreversible processes in the system and  $\Omega$  is the entropy flux which flows from the system to the environment. If the system is considered to be in equilibrium, then the entropy is a well defined quantity but in non-equilibrium systems the entropy is not well defined. Since a non-equilibrium system is defined by the Fokker-Planck equations, hence we have attempted to calculate the production of entropy in such systems. The Gibbs entropy of a system at any time  $t$  is given by [53, 54]:

$$S(t) = - \int P(x, t) \ln[P(x, t)] dx \quad (13)$$

where  $dx = dx_1 dx_2 \dots dx_n$ . Using Equations 8 and 9 we can express the derivative of the entropy as:

$$\frac{d}{dt} S(t) = - \int [\ln P(x, t) + 1] \sum \frac{\partial}{\partial x_i} J_i(x, t) dx \quad (14)$$

Integrating we get

$$\frac{d}{dt} S(t) = - \int \sum J_i(x, t) \frac{\partial}{\partial x_i} \ln P(x, t) dx \quad (15)$$

using Equation 9 we can write

$$\frac{d}{dt} S(t) = - \int \sum \frac{1}{D_i} J_i(x, t) f_i(x) dx + \int \sum \frac{[J_i(x, t)]^2}{D_i P(x, t)} dx \quad (16)$$

Comparing this with Equation 12 we see that

$$\Omega = \int \sum \frac{1}{D_i} J_i(x, t) f_i(x) dx \quad (17)$$

And:

$$\zeta = \int \sum \frac{[J_i(x, t)]^2}{D_i P(x, t)} dx \quad (18)$$

Using Equation 9 we can write Equation 17 as:

$$\Omega = \int \sum \left\{ \frac{1}{D_i} [f_i(x)]^2 + f_{ii}(x) \right\} P(x, t) dx \quad (19)$$

where  $f_{ii}(x) = \frac{\partial f_i(x)}{\partial x_i}$ . This can be expressed as an average over the probability distribution.

$$\Omega = \langle \sum \left\{ \frac{1}{D_i} [f_i(x)]^2 + f_{ii}(x) \right\} \rangle \quad (20)$$

There is another study which shows total entropy production of a process. They authors clearly mentioned that the total entropy production ( $EP$ ), that is,  $\dot{S}_{tot}$  is the sum of two constitutive parts, namely so called adiabatic  $\dot{S}_A$  and nonadiabatic  $\dot{S}_{nA}$  contribution.

### 6.2. Entropy Generation and Fokker-Planck Equations

It has been discussed by Jaynes that Gibbs' formalism for statistical physics of systems under equilibrium can be understood as a generalized form in a statistical inference theory for non-equilibrium systems [55]. Jaynes developed non-equilibrium statistical physics for the stationary state constraint on the basis of maximum entropy, and his approach consisted of maximizing the path. The Shannon information entropy for the path can be written as:

$$S = - \sum_{\gamma} p_{\gamma} \ln(p_{\gamma}) \quad (21)$$

With respect to  $p_{\gamma}$  of the path  $\gamma$ . According to Shannon, the information entropy can be written as the logarithm of the number of outcomes  $i$  with non negligible probability  $p_i$ , while in non-equilibrium statistical physics it is the given as

the logarithm of the number of microscopic phase-space paths  $\gamma$  having non negligible probability  $p_\gamma$  [55, 56] Following this approach, we know that the information entropy for open systems is related to their entropy generation by [57-59]:

$$S_g = \kappa_B S = -\kappa_B \int P_\gamma(x, t) \ln[P_\gamma(x, t)] dx \quad (22)$$

with  $p_\gamma = P_\gamma(x, t)$ . This relation is the statistical definition of entropy generation. This can also be explained as the missing information which is necessary for predicting which path a system of the ensemble takes during the transition from one state to another. The Guoy-Stodola theorem [56] gives:

$$\bar{W} = T_0 S_g \quad (23)$$

where  $\bar{W}$  is work lost due to internal irreversibility in a system. By definition, the entropy generation can be related to the power lost,  $P$  due to irreversibility,

$$S_g = \frac{1}{T_0} \int_0^\tau P dt \quad (24)$$

where  $T_0$  is the environmental temperature, considered constant and  $\tau$  is the time duration of a physical process. The power lost by definition is given as:

$$P = \langle \sum f_i(x) \frac{dx_i}{dt} \rangle \quad (25)$$

Using the Langevin equation we can write this as:

$$P = \langle \sum f_i(x) [f_i(x) + r_i(t)] \rangle \quad (26)$$

and so  $S_g$  can be written as:

$$S_g = \frac{\tau}{T_0} \langle \sum ([f_i(x)]^2 + D_i f_{ii}(x)) \rangle \quad (27)$$

where  $f_{ii} = \frac{\partial f_i}{\partial x_i}$  Considering the mean value, we can finally write this as:

$$S_g = \frac{\tau}{T_0} \int \sum ([f_i(x)]^2 + D_i f_{ii}(x)) P_\gamma(x, t) dx \quad (28)$$

and hence

$$S_g = \frac{\tau}{T_0} \int \sum f_i(x) J_i(x, t) dx \quad (29)$$

where the last term is related with the Fokker-Planck equation.

## 7. A Generalized Model-Independent Example for Protein Oscillation

Protein oscillations have been a very integral part of bio-molecules and a very active research topic in biophysics and there have been numerous studies aiming to understand how these oscillations might enable us to observe and understand these bio-molecules at a more fundamental level. Oscillations in general have a very clear formulation as we have seen in the case of a harmonic oscillator in section 2. We will take the example of a simple harmonic oscillator and an extra term which might affect the change in the oscillation also known as the deviation/perturbation in the regular term.

Taking the example of a regular oscillator, we know that the oscillating term is written as:

$$m \frac{d^2 x}{dt^2} = -kx \quad (30)$$

writing the force term as:

$$f_i(r) = \alpha \quad (31)$$

where  $\alpha = -k/m$ .

For the entropy production approach, using the force term we can write Equation 20 as

$$\Omega = \langle \left\{ \frac{1}{D} (\alpha x)^2 + \alpha \right\} \rangle \quad (32)$$

also, Equation 9 can be written as:

$$J(r, t) = [\alpha x - D \frac{\partial}{\partial r}]P(r, t) \quad (33)$$

and we can write Equation 18 as:

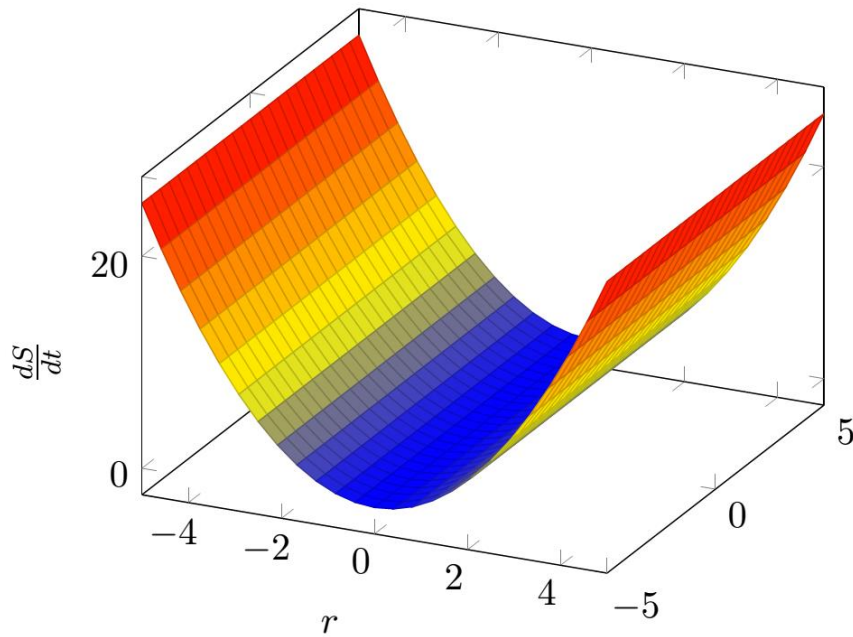
$$\zeta = \frac{1}{D} \int \frac{[[\alpha x - D \frac{\partial}{\partial r}]P(r, t)]^2}{P(r, t)} dr \quad (34)$$

and finally we can express Equation 12 as:

$$\frac{dS}{dt} = \frac{1}{D} \int \frac{[[\alpha x - D \frac{\partial}{\partial r}]P(r, t)]^2}{P(r, t)} dr - \left\{ \frac{1}{D} (\alpha x)^2 + \alpha \right\} \quad (35)$$

Similarly, for the entropy generation approach we can express Equation 29 as:

$$S_g = \frac{\tau}{T_0} \int \{(\alpha x)^2 + \alpha\} P(r, t) dr \quad (36)$$



**Figure 10. The graph shows the increase of the entropy change with respect to time**

Here we see that the trend in entropy increase is given in the plot. This is a trend as to how the entropy will increase in a model independent protein oscillation with a pure harmonic oscillator type dynamics.

Considering the deviation/perturbation in the force term we use the force term as:

$$f_i(r) = \frac{\exp(-ar)}{(\beta r^6 + \delta)} \quad (37)$$

where  $\alpha$ ,  $\beta$  and  $\delta$  are constants related to the strength of the force. There are many types of forces or potential functions which are active in a protein oscillations such as Van-der-Waals forces, covalent forces and electrostatic forces. We will consider the London type forces being active in the bio-molecular interactions in this section.

For the entropy production approach, using the force term we can write Equation 20 as:

$$\Omega = \left\langle \frac{1}{D} \frac{\exp(-2ar)}{(\beta r^6 + \delta)^2} - \frac{\exp(-ar)}{(\beta r^6 + \delta)} \left[ \alpha + \frac{6br^5}{(\beta r^6 + \delta)} \right] \right\rangle \quad (38)$$

also, Equation 9-can be written as:

$$J(r, t) = \left[ \frac{\exp(-ar)}{(\beta r^6 + \delta)} - D \frac{\partial}{\partial r} \right] P(r, t) \quad (39)$$

and we can write Equation 18 as:

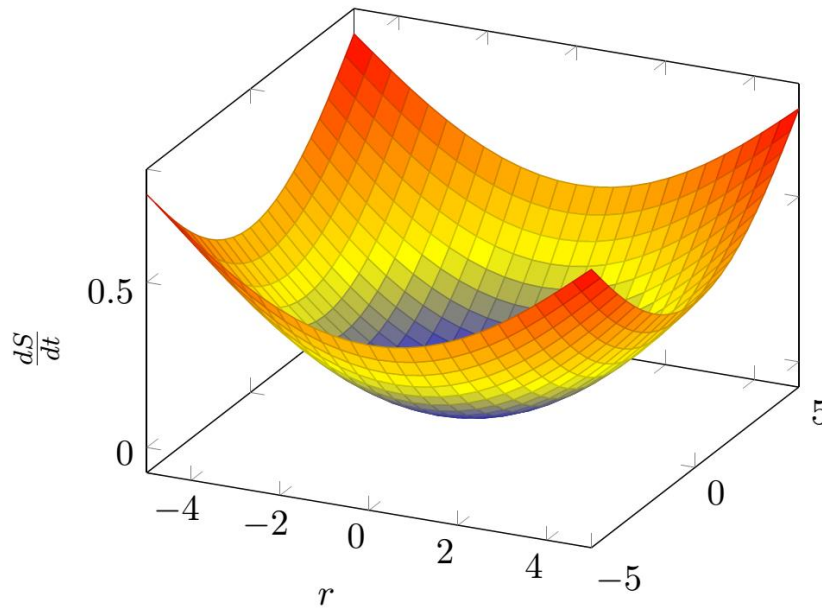
$$\zeta = \frac{1}{D} \int \frac{[\frac{\exp(-\alpha r)}{(\beta r^6 + \delta)} - D \frac{\partial}{\partial r}] P(r, t)]^2}{P(r, t)} dr \quad (40)$$

and finally we can express Equation 12 as:

$$\frac{dS}{dt} = \frac{1}{D} \int \frac{[\frac{\exp(-\alpha r)}{(\beta r^6 + \delta)} - D \frac{\partial}{\partial r}] P(r, t)]^2}{P(r, t)} dr - \left\langle \left\{ \frac{1}{D} \frac{\exp(-2\alpha r)}{(\beta r^6 + \delta)^2} - \frac{\exp(-\alpha r)}{(\beta r^6 + \delta)} \left[ \alpha + \frac{6\beta r^5}{(\beta r^6 + \delta)} \right] \right\} \right\rangle \quad (41)$$

Similarly, for the entropy generation approach we can express Equation 29 as:

$$S_g = \frac{\tau}{T_0} \int \left\{ \frac{\exp(-2\alpha r)}{(\beta r^6 + \delta)^2} - D \frac{\exp(-\alpha r)}{(\beta r^6 + \delta)} \left[ \alpha + \frac{6\beta r^5}{(\beta r^6 + \delta)} \right] \right\} P(r, t) dr \quad (42)$$



**Figure 11.** This graph shows the increase in entropy change when we use the perturbation term only

We see that the trend in the entropy is increasing because of the perturbation term alone. In both cases, we see how the entropy increases. As the interactions or perturbations increase, there will be a rapid increase in entropy.

## 8. Conclusion

In this article, we have described oscillation from a physics point of view. We have shown, using Langevin equations and Fokker-Planck equations, how to calculate entropy generation and entropy production. Finally, we have shown the trend of the increase of entropy in a model independent protein oscillation of the regular oscillation and a deviation term. In both cases, we see that entropy increases. In the regular oscillation term, the entropy increase is at a faster rate than the perturbation term. Entropy is a very fundamental concept in nature, and expressing a process through entropy gives us a deep understanding of the process. The future work will focus on applying this to a certain type of protein and understanding how entropy can be used to understand oscillations in that particular protein, further explaining the dynamics of the protein.

## 9. Declarations

### 9.1. Author Contributions

Conceptualization, P.S. and G.B.; methodology, P.S. and G.B.; investigation, P.S.; writing—original draft preparation, P.S. and G.B.; writing—review and editing, P.S. and G.B.; project administration, P.S. and G.B.; funding acquisition, G.B. All authors have read and agreed to the published version of the manuscript.

### 9.2. Data Availability Statement

Data sharing is not applicable to this article.

### 9.3. Funding

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#### 9.5. Declaration of Competing Interest

The authors declare that there is no conflict of interests regarding the publication of this manuscript. In addition, the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancies have been completely observed by the authors.

#### 9.6. Ethical Approval

Not applicable.

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