The Equation of Life

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Abstract:

This study will first define the “equation of life" via the principle of least action. Then the paper will show how this “equation of life" can be used to derive smaller equations, involving transcription and translation, for [computer] modeling and simulation of a cell. The conclusion will provide a terse description of its uses in the realm of Systems Biology.

1. *Introduction*

In the past, scientists have tried to derive models which attempt to adequately represent life. A couple of groups in academia, the JJ Tyson lab at Virginia Tech and the Molecular Networks Dynamics at Budapest University, or notable examples of scientists who have made efforts to simulate life [1,2]. Using the same underlying mechanisms [3], they have been able to produce workable eukaryotic cell models of cycling cells that are dependent upon certain variables like protein concentrations.

To aid in the endeavor of modeling cells, it might be appropriate to define the scientific laws which dictate processes like transcription and translation. When scientific laws are appropriately described and stated, they can be used to predict natural phenomena [4]. Ideally, mathematics is used to best summarize scientific laws for certain processes in particular fields, such as Physics, Chemistry, etc. There would be many possible uses for an “equation of life" when comes to modeling cell environments.

If an individual can derive an “equation of life," (s)he will be better able to predict the concentration of transcripts and proteins which dictate simulations or models of cell life. This paper will first describe the "equation of life" as a principle of least action. Then the following sections will show this equation can be used to derive known and unknown expressions of transcription and translation via functional differentiation. The conclusion of this study will focus on the possible usage of the equation in terms of modeling and simulations.

2. *Deriving the "equation of life"*

Lagrangian mechanics, which was established by Joseph-Louis Lagrange, is a formalism of classical mechanics, based upon stationary actions [5]. It considers the position of a set of masses for two given instances, times t_1 and t_2:

$$\mathcal{S}[q] = \int dt \mathcal{L}(q(t), \frac{\partial q(t)}{\partial t}, t), \tag{2.1}$$

where S is the principle of least action, L is the Lagrangian, and q is some quantity/item. For this paper, spatial dimensions will be considered in the principle of least action, thus:

$$\mathcal{S}[q] = \int dt dx^3 \mathcal{L}(q(t, \overrightarrow{x}), \frac{\partial q(t, \overrightarrow{x})}{\partial t}, t, \overrightarrow{x}). \tag{2.2}$$

Before proceeding, it is wise to discuss the types of transformation processes that will be utilized in this study. There are four different transformation processes described in this paper. *Covariant* index is the lower-case

index which represents a forward transform from one space to another space while the *contravariant* index is the upper-case index which represents a backward transform from one space to another space [6,7]. For example, the rate of synthesis for a transcript via gene and/or coupling constant ${s_j}^i$ has two transforms: the forward transform is *j*-index while the backward transform is the *i*-index. The first process involves the mapping from the gene space to the transcript space while the latter process represents the mapping from transcript space to back to the gene space. Also, transformations can either be *isomorphic* or *heteromorphic* [8,9,10]. The former process involves a one-to-one mapping while the latter process involves a differing number of mapping. Consider splice variants: one gene g_i may be responsible for the synthesis of multiple splice variants t_j.

To derive the "equation of life" in terms of principle actions, one must define the Lagrangian terms within the ultimate expression. The Lagrangian for the "equation of life" is defined as follows:

$$\mathcal{L} = \mathcal{L}_{\text{transcription}} + \mathcal{L}_{\text{translation}}, \tag{2.3}$$

where $\mathcal{L}_{\text{transcription}}$ and $\mathcal{L}_{\text{translation}}$ are the Lagrangian terms for transcription and translation, respectively. The Lagrangian of transcription can be expressed as:

$$\mathcal{L}_{\text{translation}} = \gamma_i \tau^j \sigma^i_j - \delta_j \tau_j \tau^j - \kappa_j \partial\tau_j \partial\tau^j, \tag{2.4}$$

where γ_i is the antisense DNA sequence of the *i*-th gene, $\sigma^i_j$is the rate of synthesis for *j*-th transcript via the *i*-th gene, τ_j is the *j*-th mRNA transcript, $\tau^j$is a small antisense RNA molecule (i.e., TSSaRNA, microRNA, etc.) of the *j*-th transcript, δ_j is the rate of degradation of the *j*-th mRNA transcript, and κ_j is the coefficient of [extracellular] diffusion of small screted RNA τ_j. Note: σ^i_j and δ_j also serve as coupling constants of various RNA species t^j with antisense DNA sequence of gene γ_i and transcript τ_j, respectively. On the other hand, the Lagrangian of translation can be expressed as:

$$\mathcal{L}_{\text{translation}} = \tau_j \rho^k \sigma^j_k - \delta_k \rho_k \rho^k - \kappa_k \partial\rho_k \partial\rho^k - \mathcal{L}_{\text{oligo}}, \tag{2.5}$$

where σ^j_k is the rate of synthesis for *k*-th protein via the *j*-th transcript, ρ_k is the *k*-th protein, ρ^k is the ribosomal protein complexes, disordered peptide sequences of the proteasome, etc. of the *k*-th protein, δ_k is the rate of degradation of the *k*-th transcript, and κ_k is the coefficient of [extracellular] diffusion of protein ρ_k. Note: σ^j_k and δ_k also serve as coupling constants of various protein ρ^k with transcript τ_j and protein ρ_k, respectively. $\mathcal{L}_{\text{oligo}}$ is the Lagrangian of hetero- and homo-oligomerization: it is dependent upon a set of protein r_k and utilizes principles of “mass conversation" among the proteins being studied. Assume a particular protein ρ_k exists also as a homo-oligomerization, then:

$$\begin{aligned}\mathcal{L}_{\text{oligo}} &= \textstyle\sum_{a=1}^{n-1} \left(r_{2a}\rho_{k^{a+1}} - r_{2a-1}\rho_k\rho_{k^a}\right)\left(\sum_{b=1}^{a}\rho^{k^b} - \rho^{k^{a+1}}\right) \\ &\quad + \sum_{a=1}^{n-1} \kappa_{k^{a+1}} \partial\rho_{k^{a+1}} \partial\rho^{k^{a+1}},\end{aligned} \tag{2.6}$$

where n is the number of homo-oligomerization, r_{odd} and r_{even} is a rate of association and/or dissociation. On the other hand, a particular protein ρ_k could exist as a hetero-oligomer, thus:

$$\begin{aligned}\mathcal{L}_{\text{oligo}} &= \left(r_2\rho_{\{1,\ldots,n\}} - r_1\left(\textstyle\prod_{a=1}^{n}\rho_a\right)\right)\left(\sum_{a=1}^{n}\rho^a - \rho^{\{1,\ldots,n\}}\right) \\ &\quad + \kappa_{\{1,\ldots,n\}} \partial\rho_{\{1,\ldots,n\}} \partial\rho^{\{1,\ldots,n\}},\end{aligned} \tag{2.7}$$

where $\rho_{\{1,\ldots,n\}}$represents the total hetero-oligomer, $\kappa_{\{1,\ldots,n\}}$is the coefficient of diffusion for that quaternary protein structure, and n is the total number tertiary protein structures in the hetero-oligomer.

The total principle of least action for a particular gene g_i and subsequent transcripts τ_j and proteins r_k becomes:

(2.8)

$$\mathcal{S}[\gamma_i, \tau_j, \rho_k] =$$

$$\int dtdx^3 \left(\gamma_i \tau^j \sigma^i_j + \tau_j \rho^k \sigma^j_k - \delta_j \tau_j \tau^j\right.$$

$$\left. -\delta_k \rho_k \rho^k - \kappa_j \partial \tau_j \partial \tau^j - \kappa_k \partial \rho_k \partial \rho^k - \mathcal{L}_{\text{oligo}}\right).$$

Ultimately, the "equation of life" is defined as the total principle of least action for all genes, transcripts, and proteins. In other words, an individual must consider the sum of all genes, transcripts, and proteins, or:

(2.9)

$$\mathcal{S}[\gamma_i, \tau_j, \rho_k] =$$

$$\int dtdx^3 \sum_i \sum_i \sum_k (\gamma_i \tau^j \sigma^i_j + \tau_j \rho^k \sigma^j_k - \delta_j \tau_j \tau^j$$

$$-\delta_k \rho_k \rho^k - \kappa_j \partial \tau_j \partial \tau^j - \kappa_k \partial \rho_k \partial \rho^k - \mathcal{L}_{oligo}).$$

Mathematica was used to solve the subsequent smaller equations to the basic “equation of life."

3. *Deriving the transcript and protein equations for non-dividing cells*

Non-dividing cells are simply known as cells which either are arrested or leave some form of cell division (i.e., mitosis, meiosis) [11,12]. An example of cells that are arrested in cell division, or quiescent, are stem cells while mature/adult cells exemplify cells that leave (a series) of cell division[s] [13,14]. Both quiescent and mature/adult cell types leave the cell cycle [indefinitely] and enter the G_0 phase (figure 1). The environment inside these entities is relatively stable, thus one should not see the periodic appearance of proteins, such as cyclins, that are critical for dividing cells. It is expected that the expression of genes in non-dividing cells is indefinite for quiescent states and permanent for mature adult conditions.

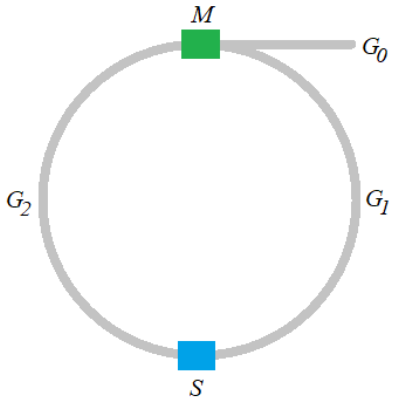


Figure 1: The different phases of the cell cycle. The diagram above shows the different phases of the cell cycle. Initially, cells prep early for division, or enter G_1 phase, by doubling their DNA/chromosome content that will occur in the S phase. Then cells prep late for division, or enter G_2 phase, by segregating their DNA/chromosome content that will occur in the M phase. If a cell wants to arrest or leave the cell cycle, it must enter the G_0 phase.

To ascertain transcription in quiescent or mature cells, one must generate the equation for transcript τ_j in a non-dividing cell. It is assumed that non-dividing cell possesses a first order transcript propagator within its Hamiltonian, or:

$$\mathcal{H}\left(\gamma_i, \tau_j, \rho_k\right) = \Pi_\tau \tau^j - \mathcal{L}\left(\gamma_i, \tau_j, \rho_k\right), \tag{3.1}$$

where:

$$\Pi_\tau = \tfrac{\partial \tau_j}{\partial t}. \tag{3.2}$$

The above suggests the new principle of least action, in terms of the Hamiltonian $\mathcal{H}$, becomes:

(3.3)

$$\mathcal{S}[\gamma_i, \tau_j, \rho_k] =$$

$$\int dt dx^3 \sum_i \sum_j \sum_k (\frac{\partial \tau_j}{\partial t}\tau^j - \gamma_i \tau^j \sigma^i_j - \tau_j \rho^k \sigma^j_k + \delta_j \tau_j \tau^j$$

$$+\delta_k \rho_k \rho^k + \kappa_j \partial \tau_j \partial \tau^j + \kappa_k \partial \rho_k \partial \rho^k + \mathcal{L}_{\text{oligo}}).$$

The functional differentiation of this equation with respect to the contravariant transcript τ^j, specifically, produces:

$$\textstyle\sum_i \sum_j \left(\frac{\partial \tau_j}{\partial t} - \kappa_j \Delta \tau_j - \gamma_i \sigma^i_j + \delta_j \tau_j\right) = 0 \tag{3.4}$$

and

$$\kappa_j = 0, \tag{3.5}$$

Reducing the above equation to a particular transcript τ_j produces the following 1st order ordinary differential equation:

$$\tfrac{\partial \tau_j}{\partial t} - \gamma_i \sigma_j + \delta_j \tau_j = 0. \tag{3.6}$$

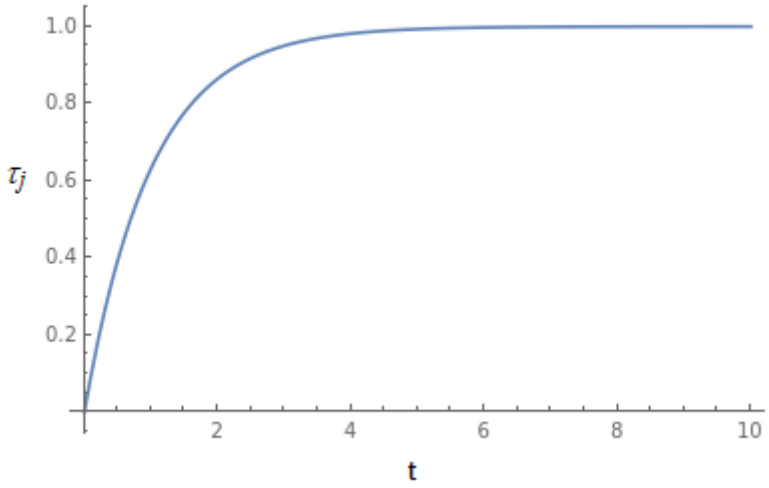
One of the solutions of the prior equation for a particular transcript τ_j using the generating function technique, or GFT, [15] is:

$$\tau_j(t) = \tfrac{a_{10} e^{-i\delta_j}}{A} + \tfrac{\gamma_i \sigma^i_j}{\delta_j}. \tag{3.7}$$

If one lets A equal -1 and a_{10} equal $\frac{\gamma_i \sigma^i_j}{\delta_j}$, then the solution becomes:

(3.8) $$\tau_j(t) = \frac{\gamma_i \sigma^i_j}{\delta_j} - \frac{\gamma_i e^{-t\delta_j} \sigma^i_j}{\delta_j}.$$

Assuming the initial concentration of transcript τ_j is *0.0*, then the plot of the above solution is simply:



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With respect to the starting time point *0.0*, there is an appreciable lag in the concentration of transcript t_j hitting its steady-state level.

Unlike products of transcription, proteins may be secreted from cells. The process of cellular secretion generally requires special organelles called porosomes located at the cellular membrane [16]. Contents within secretory vesicles are released into the environment upon fusing of the vesicles with porosomes. In terms of the "equation of life," the rate of diffusivity for a particular protein ρ_k, or κ_k, is dependent on secretory vesicle-porosome fusion events. If the protein remains in the cell, then κ_k is approximately *0.0*.

Next, an individual must derive the equation for protein monomer and oligomer inside a cell. The protein propagator for both dividing and non-dividing cells is as follows:

(3.9) $$\mathcal{H}(\gamma_i, \tau_j, \rho_k) = \Pi_\rho \rho^k - \mathcal{L}\left(\gamma_i, \tau_j, \rho_k\right),$$

where

(3.10) $$\Pi_p = \frac{\partial \rho_k}{\partial t}.$$

Therefore, the principle of least action, in terms of the Hamiltonian, for protein ρ_k becomes:

(3.11)

$$S[\gamma_i, \tau_j, \rho_k] =$$

$$\int dt dx^3 \sum_i \sum_j \sum_k (\frac{\partial \rho_k}{\partial t}\rho^k - \gamma_i \tau^j \sigma^i_j - \tau_j \rho^k \sigma^j_k + \delta_j \tau_j \tau^j$$

$$+\delta_k \rho_k \rho^k + \kappa_j \partial \tau_j \partial \tau^j + \kappa_k \partial \rho_k \partial \rho^k + \mathcal{L}_{\text{oligo}}).$$

By performing the functional differentiation of this action with respect to contravariant protein ρ^k, specifically, (s)he will generate the following expression:

(3.12) $$\sum_j \sum_k \left(\frac{\partial \rho_k}{\partial t} - \tau_j \sigma_k^j + \delta_k \rho_k - \Delta \rho_k \kappa_k + \frac{\delta \mathcal{L}_{\text{oligo}}}{\delta \rho^k} \right) = 0.$$

Let:

(3.13) $$\kappa_k = 0,$$

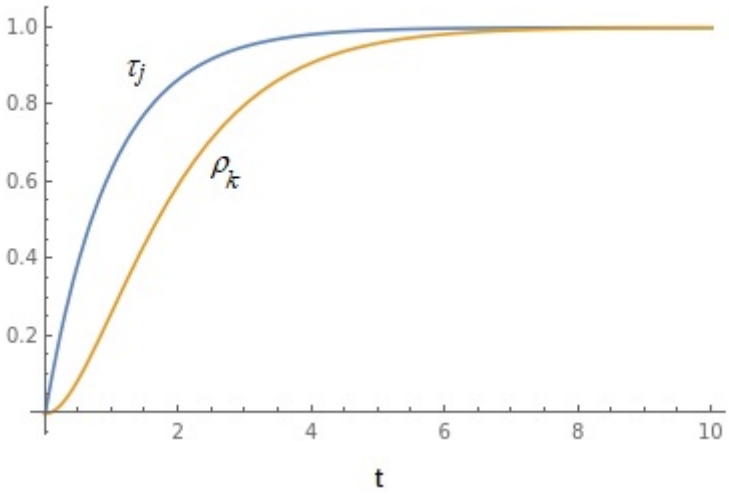
and

(3.14) $$\mathcal{L}_{\text{oligo}} = 0$$

thus, the ordinary differential equation for a particular protein ρ_k in the form of a monomer is also a 1st order expression:

(3.15) $$\frac{\partial \rho_k}{\partial t} - \tau_j \sigma_k^j + \delta_k \rho_k = 0.$$

Using the Runge-Kutta [iterative] method to solve for protein ρ_k, one would obtain the following plot:



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Note: there is an even larger lag in protein ρ_k hitting its steady-state levels with regards to the starting time point.

Next, one must determine the Lagrangian density for the homodimer of a particular protein r_k. By working with the expression (2.6) and setting $n = 2$, one obtains the following Lagrangian:

(3.16) $$\mathcal{L}_{oligo} = \left(r_2 \rho_{k^2} - r_1 \rho_k^2 \right) \left(\rho^k - \rho^{k^2} \right) + \kappa_{k^2} \partial \rho_{k^2} \partial \rho^{k^2}.$$

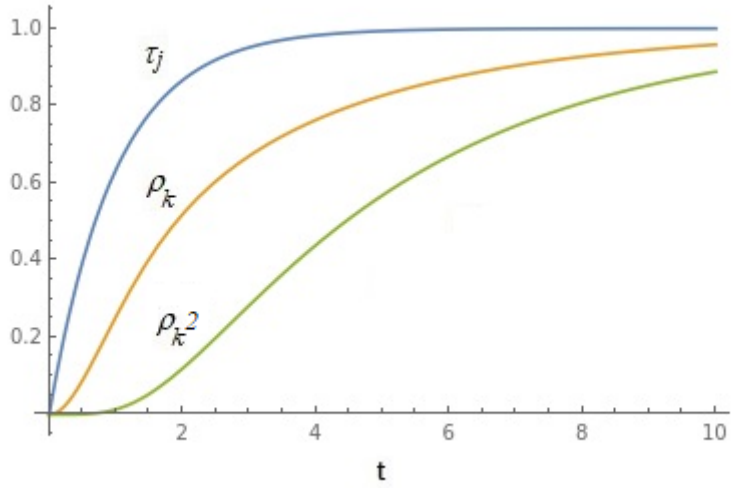
If one plug (3.16) into (3.12), sets κ_{k^2} equal to *0.0*, and allows ρ_{k^2} to be the homodimer of protein r_k, then (s)he will generate two 1st order nonlinear differential equations after performing functional differentiation with respect to both contravariants ρ_k and ρ_{k^2}:

(3.15) $$\frac{\partial \rho_k}{\partial t} - \tau_j \sigma_k^j - r_2 \rho_{k^2} + \delta_k \rho_k + r_1 \rho_k^2 = 0,$$

and

$$\frac{\partial \rho_{k^2}}{\partial t} + r_2 \rho_{k^2} - r_1 \rho_k^2 = 0. \tag{3.16}$$

It is important to state that one must also apply a unique protein propagator, hence establish a separate Hamiltonian and principle of least action for the homodimer ρ_{k^2}. The individual generates the following plot if (s)he uses the Runge-Kutta method to solve for both the monomer and homodimer for a particular protein ρ_k:



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Note the appreciable lags in transcript τ_j, monomeric protein ρ_k, and homodimeric protein ρ_{k^2} when approaching their relative steady-state levels.

4. *Deriving the transcript and protein equations for dividing cells*

The hallmark feature of dividing is the oscillatory behavior of intracellular concentration of a transcript and the extracellular concentration of a secreted protein. To produce an oscillating solution, one must use a second-order transcript propagator; thus, the Hamiltonian of for transcript τ_j is defined as:

$$\mathcal{H}\left(\gamma_i, \tau_j, \rho_k\right) = \Pi_\tau^2 - \mathcal{L}\left(\gamma_i, \tau_j, \rho_k\right), \tag{4.1}$$

where:

$$\Pi_\tau = \frac{\partial \tau_j}{\partial t}. \tag{4.2}$$

The principle of least action regarding the Hamiltonian of transcript τ_j is as follows:

(4.3)

$$\mathcal{S}[\gamma_i, \tau_j, \rho_k] =$$

$$\int dt dx^3 \sum_i \sum_j \sum_k \left(\frac{\partial \tau_j}{\partial t}\frac{\partial \tau^j}{\partial t} - \gamma_i \tau^j \sigma^i_j - \tau_j \rho^k \sigma^j_k + \delta_j \tau_j \tau^j\right.$$

$$+\delta_k \rho_k \rho^k + \kappa_j \partial\tau_j \partial\tau^j + \kappa_k \partial\rho_k \partial\rho^k + \mathcal{L}_{\text{oligo}}\,).$$

After setting κ_j equal to null, the functional differentiation of the principle of least action apropos the contravariant transcript τ^j, specifically, produces:

$$\sum_i \sum_j \left(\frac{\partial^2 \tau_j}{\partial t^2} - \gamma_i \sigma^i_{\ j} + \delta_j \tau_j \right) = 0. \tag{4.4}$$

If one is trying to derive the solution for a particular transcript τ_j, (s)he must use the next equation:

$$\frac{\partial^2 \tau_j}{\partial t^2} - \gamma_i \sigma^i_{\ j} + \delta_j \tau_j = 0. \tag{4.5}$$

The general solution to a particular transcript τ_j using GFT is:

$$\tau_j(t) = \tfrac{1}{2} \left((a_{10} - a_{20}) A e^{it\sqrt{\delta_j}} + \tfrac{(a_{10}+a_{20}) e^{-it\sqrt{\delta_j}}}{A} + \tfrac{2\gamma_i \sigma^i_{\ j}}{\delta_j} \right). \tag{4.6}$$

Assuming A is equal to negative unity or *-1.0*, a_{20} is equal to *0.0*, and a_{10} is equal to $\frac{\gamma_i \sigma^i_{\ j}}{\delta_j}$, then the solution becomes:

$$\tau_j(t) = -\tfrac{\gamma_i \sigma^i_{\ j} \left(\cos\left(t\sqrt{\delta_j} \right) - 1 \right)}{\delta_j}. \tag{4.7}$$

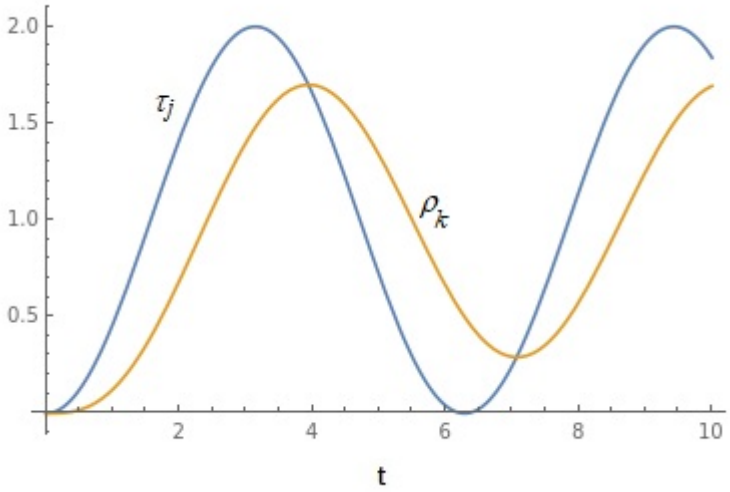
Next, one must solve for the concentration of the secreted monomeric protein ρ_k. Using the same Hamiltonian (3.7), (s)he will be left with the principle of least action (3.10). Since an individual is dealing with a monomer protein, expression (3.13) is true, and the following equation is left after performing functional differentiation with respect to the contravariant protein ρ^k, specifically:

$$\sum_j \sum_k \left(\frac{\partial \rho_k}{\partial t} - \tau_j \sigma^j_{\ k} + \delta_k \rho_k - \Delta \rho_k \kappa_k \right) = 0. \tag{4.8}$$

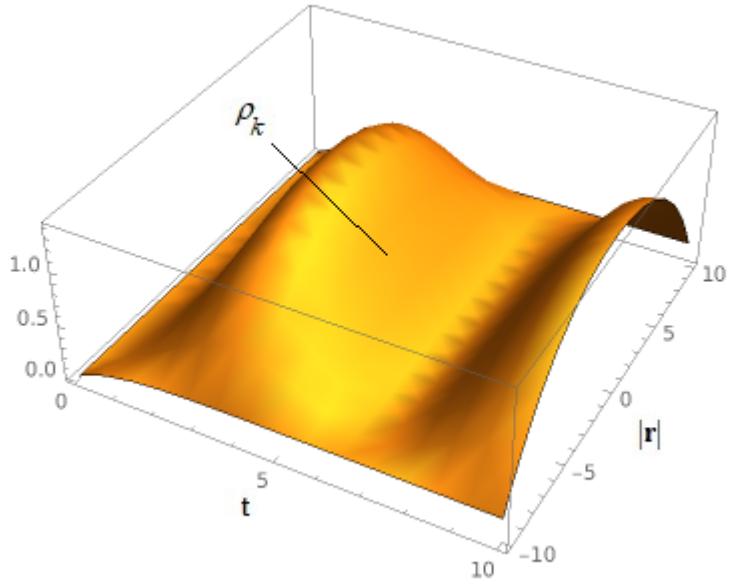
Note: the delta symbol is a Laplacian operator, thus the protein r_k is dependent upon three spatial dimensions $\{x,y,z\}$ or radius r besides time t. By limiting the above expression to a particular protein ρ_k, one must solve the following 2nd order partial differential equation:

$$\frac{\partial \rho_k}{\partial t} - \tau_j \sigma^j_{\ k} + \delta_k \rho_k - \Delta \rho_k k_k = 0. \tag{4.9}$$

Implementing the Runge-Kutta method to solve (4.9) produces the following plot assuming the initial [derivative] values for transcript τ_j and protein



ρ_k:



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Note: $|\mathbf{r}|$ from the cell is set at *0.0* for the top plot. Both the transcript τ_j and secreted monomeric protein ρ_k oscillate from the starting time point *0.0*. Also, the peaks and troughs of secreted monomeric protein ρ_k lag just behind the peaks and troughs of transcript τ_j.

5. *Conclusion*

By using some concepts in cell biology and classical mechanics, one can generate the "equation of life." The equation can be utilized in various ways to help model important elements inside and outside the cell. For instance, an individual can stimulate transcription for dividing and non-dividing cells. Also, (s)he can model intracellular and secreted protein concentrations in the same set of cells. Ultimately, one should be able to simulate more sophisticated environments, such as transduction and transfection.

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