I. J. Mathematical Sciences and Computing, **2022, 4, 41-48**
Published Online on October 8, 2022 by MECS Press (http://www.mecs-press.org/)
DOI: 10.5815/ijmsc.2022.04.04

Slow Invariant Manifold Analysis in a Mitotic Model of Frog Eggs via Flow Curvature Method

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Received: 10 March 2022; Revised: 14 April 2022; Accepted: 21 May 2022; Published: 08 October 2022

Abstract: A slow-fast dynamical systems can be investigated qualitatively and quantitatively in the study of nonlinear chaotic dynamical systems. Slow-fast autonomous dynamical systems exhibit a dichotomy of motion, which is alternately slow and quick, according to experiments. Some investigations show that slow-fast dynamical systems have slow manifolds, which is supported by theory. The goal of the proposed study is to show how differential geometry may be used to examine the slow manifold of the dynamical system known as the mitotic model of frog eggs. The algebraic equation of the flow curvature manifold is obtained using the flow curvature technique applied to the dynamical mitosis model. Using the Darboux invariance theorem, we then argue that this slow manifold equation is invariant with regard to the flow.

Index Terms: Mitotic Model, Darboux Theorem, Slow-Fast System, Differential Geometry, Flow Curvature Manifold.

1. Introduction

Biology is one of the fundamental subjects including anatomy, microbiology, botany, biotechnology, agriculture, medicine, physiology, and others. To develop and improve the technological growth of any nation, the subject of biology education is very important. Recently, the development of biological sciences, analysis of the genome, post-genomic and cell signal transduction has great attention. The cell division process is very essential for the growing cells. In the biological analysis, the extraction of frog eggs through mitotic control with the harmless fetus is important. This cell cycle controlling process can be described by ordinary differential equations. This set of differential equations can express slow-fast dynamical behavior by considering a control parameter of the model. On the other side, the determination of a slow-fast dynamical model’s slows invariant manifold aids model reduction. By removing the fast mode from the slow-fast system, this slow manifold may be created, potentially reducing the model's calculation cost. Many researchers have studied various slow-fast dynamical models that contribute to the science and engineering field [1, 2, 3]. Our work aims to provide a study regarding the natural slow-fast dynamical biological system and its geometrical analysis. In many dynamical systems, slow invariant manifolds can provide substantial rules. Many dynamical systems have a slow-fast structure, in which the system's dynamics are sluggish yet, when it approaches the slow invariant manifold, the system's trajectory from any initial point dramatically relaxes. In both singularly and non-singularly perturbed systems [4, 5, 6], slow invariant manifolds may exist. The conventional Geometric Singular Perturbation (GSP) approach [7, 8, 9, 10] is one of several asymptotic expansion-based methods for determining the slow manifold's equation. Only a single perturbed dynamical system is suitable for this method. The Flow Curvature Approach (FCM) [11, 12, 13, 14, 15] is another innovative method for determining the equation of slow manifold, and it may be used for any system. Ginoux [16] used the FCM to get the equation for the L-K model's slow manifold. In [17], FCM was used to obtain the slow invariant manifold equation of the heartbeat model.

The theoretical and numerical analysis of the dynamical mitotic model of frog eggs was investigated by LU et. al. [18]. Modeling the cell division and the numerical analysis was performed of a M-phase control model in Xenopus in [19, 20]. Feng and Zeng performed a qualitative analysis in a dynamical mitotic model in [21]. Recently, a review article was published on the bi-stability, traveling waves, and oscillations of a model related to the frog eggs extract in [22].

The determination of the slow invariant manifold equation in the dynamical mitotic model of frog eggs is the primary goal of this study. Since FCM is the best technique as it does not need the use of the asymptotic expansion methodology and hence, we employ this method to the dynamical mitotic model. We look at a two-dimensional dynamical mitotic model of frog eggs in this paper. The slow manifold equation is obtained directly from the flow curvature manifold by applying the FCM to the dynamical mitotic model of frog eggs. The Darboux invariance theorem is then used to verify the slow manifold's invariance with regard to the flow.

The following is how the rest of the article is arranged. Section 2 describes the dynamical mitotic model. In part 3, we look at a flow curvature approach based on differential geometry. The study of the flow curvature manifold in the dynamical mitotic model of frog eggs is discussed in section 4. In section 5, we offer some final observations and comments about this work.

2. Dynamical Mitotic Model of Frog Eggs

Borisuk and Tyson [23] concerned with the meiotic and mitotic cell divisions of frog eggs. Fig.1 Shows the development of frog eggs through cell divisions. Frog eggs expand to about 1 mm in diameter and stop with replicated DNA before the first meiotic division. Immature oocytes are what they're called while they're in this condition. When immature oocytes are exposed to hormone (progesterone), they undergo two meiotic divisions, resulting in mature eggs that are stalled in metaphase of meiosis II. The egg nucleus completes meiosis II after fertilization and unites with the sperm nucleus to form a zygote. To produce a hollow ball of 3985 cells, the zygote goes through 12 fast, synchronous mitotic cycles. Cell division in the embryo slows and becomes asynchronous at this time (known as the midblastula transition), and large changes in mRNA expression occur. This cell division mechanism can be converted into the following set of non-linear ordinary differential equations introduced by Novak and Tyson [19].

$$\begin{aligned} \frac{dx}{dt} &= p(x - x^3 - y), \\ \frac{dy}{dt} &= (x-a)(b-y) - c, \end{aligned} \tag{1}$$

where $a, b, c,$ and p are all parameters.

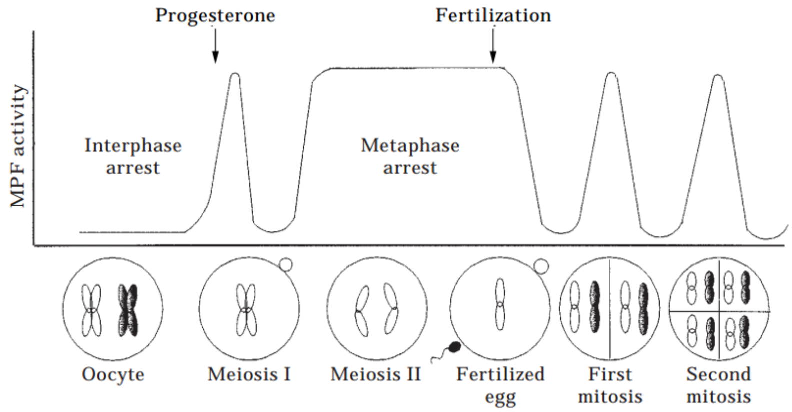


Fig.1. Meiotic and mitotic cycles of frog eggs [24]

3. The Flow Curvature Technique

We will go through the applications of differential geometry to the dynamical model in this section. This technique uses the characteristics of the curvatures of the trajectory curve. By calculating the curvatures, the flow curvature manifold can be obtained easily. Any n-dimensional dynamical model can have a $(n-1)$ dimensional flow curvature manifold, which means the information about the flow with the maximum curvature is stored in the flow curvature manifold.

The invariant manifold plays a crucial role in explaining a system's stability as well as dynamical behavior, of a slow-fast system. On the other side, the geometric perturbation methodology is a classical technique for determining the equation of a slow manifold, it differs from the flow curvature method in that it does not involve asymptotic expansions or eigenvectors. Another distinction is that this approach may be used to any dynamical system that is singularly perturbed or not.

Lemma 3.1 The set of locations where the curvature of the flow of the dynamical model disappears is represented by the flow curvature manifold equation of the dynamical system.

$$\phi(\vec{X}) = \det\left(\dot{\vec{X}}, \ddot{\vec{X}}, \dddot{\vec{X}}, \cdots, \vec{X}^{(n)}\right) = 0$$

Proof See [12, 15]

Lemma 3.2 The slow manifold's implicit analytical equation is directly obtained from the flow curvature manifold.

Proof See [12, 15]

4. Dynamical Mitotic Model Analysis Using the Flow Curvature Method

This approach, according to the FCM, may be used on any system, whether it is a singly perturbed or not. The dynamical mitotic model (1) is regarded as a slow-fast system.

The flow model (1) represents the following velocity vector:

$$\vec{V} = \{p(x - x^3 - y), -c + (-a + x)(b - y)\}$$

The Jacobian matrix for the model (1) at the fixed point is shown below

$$\begin{pmatrix} p - 3px^2 & -p \\ b - y & a - x \end{pmatrix}$$

Table 1. Parameter values of the model (1) taken from [20]

Parameters	a	b	c	p
Values	0.0001	5	0.1	2

For the numerical simulations, we employ the specific parameter values for (1) shown in Table 1 as well as the following state variable ranges.

$$[x_{min}, x_{max}] = [-3, 3];$$
$$[y_{min}, y_{max}] = [-5, 10];$$

We get the system's unique fixed point as follows:

$$x_1 = 0.02,\ y_1 = 0.02$$

The Jacobian matrix for the model (1) at the fixed point is shown below

$$\begin{pmatrix} 2 - 6x^2 & -2 \\ 5 - y & 0.0001 - x \end{pmatrix}$$

At the fixed point, the eigenvalues of the aforementioned Jacobian matrix corresponding to model (1) may be expressed as

$$\{0.98885 - 2.99039\ i,\ 0.98885 + 2.99039\ i\}$$

To solve the flow model (1), we use the fourth order Runge-Kutta technique, with $(x_0, y_0) = (1.12, 0)$ as the beginning point. The phase plot in Fig.2 (a) displays a two-dimensional graphical characteristic, with time t ranging from 0 to 100. We construct a two-dimensional parametric plot of x, y numerically, with t ranging from 0 to 1000. The positive fixed point of the model (1) is indicated by the purple point in Fig.2 (a).

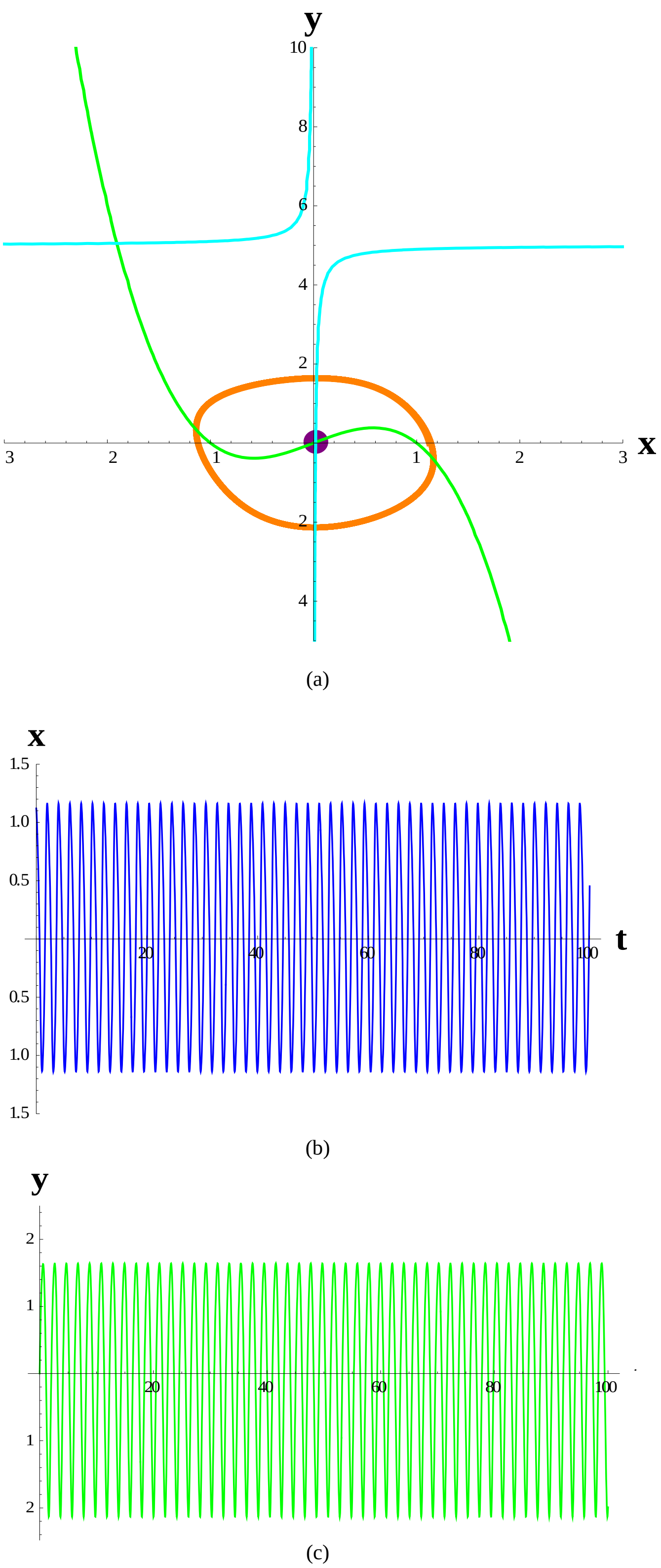


Fig.2. (a) The positive fixed point along with the Phase plane result, (b) Time series solution of x, (c) Time series solution of y.

Using the numerical simulation of model (1), we exhibit two-dimensional parameter graphs with t ranging from 0 to 100. Fig.2b depicts the graph of x and t, which represents the periodic solution, and Fig.2c depicts the graph of y and t, which reflects the periodic solution as well.

Now, according to the FCM, we should calculate the velocity and acceleration vectors first.

The velocity vector of the mitotic model (1) is as follows

$$\overrightarrow{V_1}=\{2(x-x^3-y),-0.1+(-0.0001+x)(5-y)\}$$

The acceleration vector may be written as follows using the $\overrightarrow{V}_2 = J\overrightarrow{V_1}$ formula.

$$\overrightarrow{V_2}=\{-2(-0.1+(-0.0001+x)(5-y))+2(2-6x^2)(x-x^3-y),(0.0001-x)(-0.1+(-0.0001+x)(5-y))+2(5-y)(x-x^3-y)\}$$

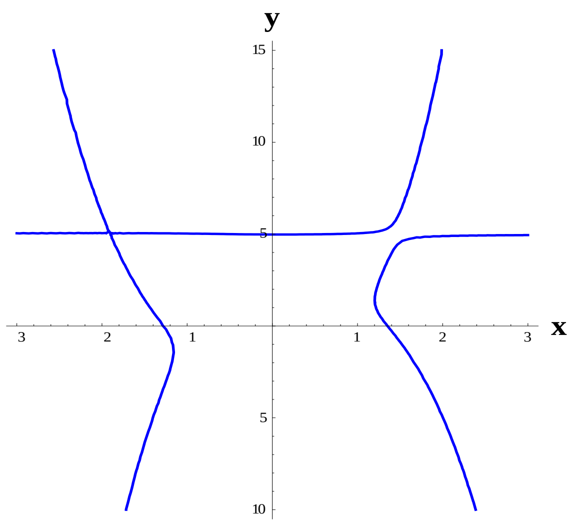
$$\phi(\mathrm{x},\mathrm{y}) = 8.(0.00252506-0.201003x+6.27525x^2-1.451x^3+4.97475x^4+1.40075x^5-5.x^6-0.0502525y-2.4748xy-1.0993x^2y-2.2498x^3y-0.99995x^4y-0.25015x^5y+x^6y+2.50005y^2+0.5xy^2-0.00015x^2y^2+0.5x^3y^2-0.5y^3)$$

The slow manifold function may be expressed as follows:

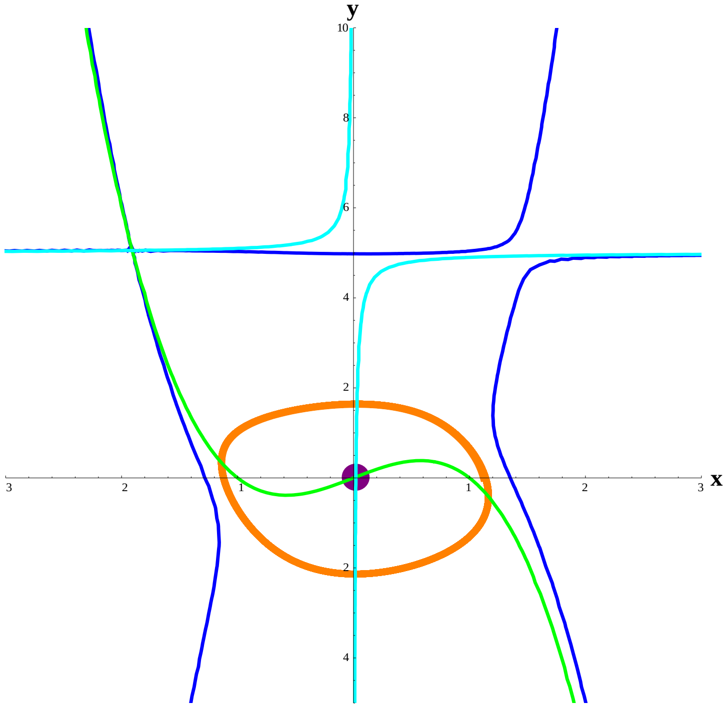
The slow manifold's equation is now dictated by the flow curvature manifold of model (1).

$$\phi(x,y)=0 \tag{2}$$

Fig.3(a) depicts a graphical representation of the model (1)'s slow manifold. Fig.3(b) shows a graphical representation of the phase diagram with the slow manifold.



(a)



(b)

Fig.3. (a) The flow curvature manifold of the model (1), (b) the phase diagram along with the flow curvature manifold

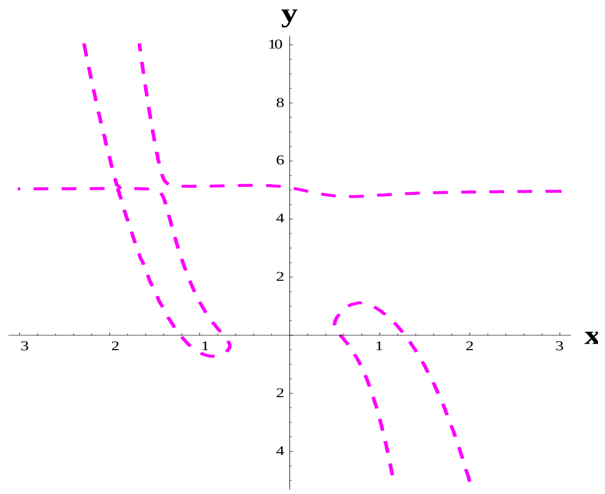
On the flow curvature manifold, we first find the normal vector. The Darboux theory may then be used to derive the Lie derivative using this normal vector.

$$\vec{\nabla}\phi = 8.(-0.201003+12.5505x-4.35299x^2+19.899x^3+7.00375x^4-30.x^5-2.4748y-2.1986xy-6.7494x^2y-3.9998x^3y-1.25075x^4y+6.x^5y+0.5y^2-0.0003xy^2+1.5x^2y^2),8.(-0.0502525-2.4748x-1.0993x^2-2.2498x^3-0.99995x^4-0.25015x^5+1.x^6+5.0001y+1.xy-0.0003x^2y+1.x^3y-1.5y^2)$$

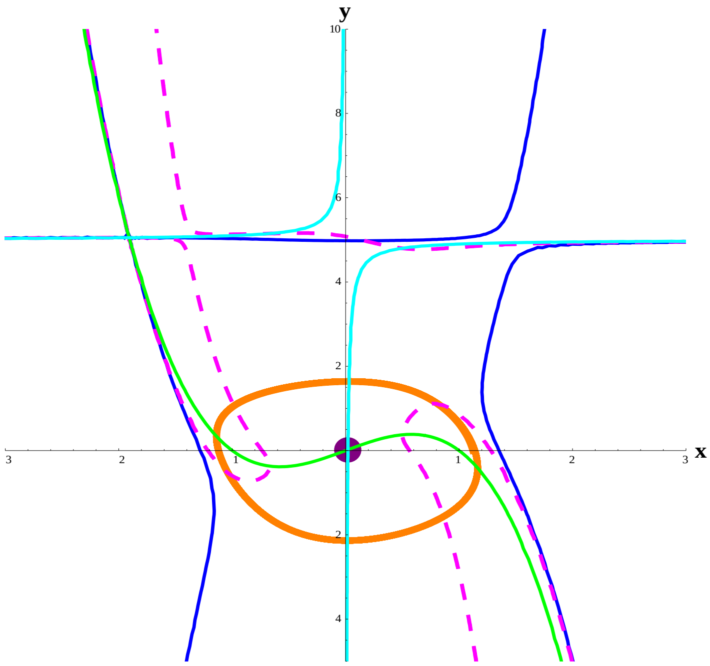
The slow manifold's Lie derivative may now be represented as

$$\mathcal{L}_{\vec{V}}\phi = \text{-}96\begin{pmatrix} -0.000420865+0.0337125x-1.06979x^2+1.1312x^3-0.295708x^4-1.47824x^5+8.4291x^6+ \\ 0.750625x^7-5.x^8+0.00837584y+0.42505xy-0.981959x^2y+3.94584x^3y+0.86335x^4y- \\ 5.99977x^5y-1.68749x^6y-0.125125x^7y+1.x^8y-0.425071y^2+0.5919xy^2-1.04152x^2y^2- \\ 0.833333x^3y^2-0.125175x^4y^2+1.25x^5y^2+0.0833458y^3-0.12505xy^3+0.25x^2y^3 \end{pmatrix}$$

The equation $\mathcal{L}_{\vec{V}}\phi = 0$, which signifies the rate of change of the flow curvature manifold $\phi(x, y)$ is zero, is depicted graphically in Fig.4(a). Fig.4(b) shows a graphical representation of the phase diagram as well as the slow manifold's invariance equation.



(a)



(b)

Fig.4. (a) The slow manifold's invariance equation, (b) the slow manifold's phase diagram as well as the invariance equation

5. Conclusion

In the computational study, it is important to reduce the computation cost of a model. The cell cycle control mechanism through the mitotic process in the frog eggs model can give us a system of ordinary differential equations that indicates the rate of change of each component of the model with respect to each time. The determination of a slow attractive manifold from this system can reduce the dimension of the model. Various approximating methods exist to determine this slow manifold. We analyzed a slow-fast two-dimensional dynamical system, called a mitotic model of frog eggs through differential geometry-based method called FCM. The main goal of this paper is to figure out where a slow invariant manifold of the dynamical mitotic model of frog eggs, is located. An implicit equation of the flow curvature manifold was found by applying the FCM to the dynamical mitotic model of frog eggs. The Darboux invariance theorem was then utilized to verify the slow manifold's invariance with regard to the flow. Using the flow curvature manifold, we also constructed the osculating plane equation.

Acknowledgement

This research work is supported by the Centennial Research Grant, University of Dhaka, Bangladesh.

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How to cite this paper: A. K. M. Nazimuddin, Md. Showkat Ali," Slow Invariant Manifold Analysis in a Mitotic Model of Frog Eggs via Flow Curvature Method", International Journal of Mathematical Sciences and Computing(IJMSC), Vol.8, No.4, pp. 41-48, 2022. DOI: 10.5815/ijmsc.2022.04.04