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Submitted by

MANCHI SRI SAI KIRAN (AP21110010698)
ROUTHU JAYA ROHITH (AP21110011323)
AKURATI BALA VENKATA SRI SAI (AP21110010591)
KODURU YOGANANDA SAI (AP21110010646)

Under the Guidance of

Dr. Supravat Dey

SRM University–AP

Neeru Konda, Mangala Giri, Guntur

Andhra Pradesh – 522 240

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Certificate

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This is to certify that the work present in this Project entitled "**SYNCHRONIZATION OF BIOCHEMICAL OSCILLATIONS**" has been carried out by **SAI KIRAN, JAYA ROHITH, SRI SAI, YOGANANDA SAI** under my/our supervision. The work is genuine, original, and suitable for submission to the SRM University – AP for the award of Bachelor of Technology/Master of Technology in **School of Engineering and Sciences**.

Supervisor

(Signature)

Dr. **Supravat Dey**

Designation,

Affiliation.

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Abstract

This study explores the synchronization dynamics of biochemical oscillators through numerical simulations of differential equations. The investigation involves a detailed analysis of the onset of oscillations in a single oscillator and the synchronization behaviour of two interconnected oscillators.

The model incorporates critical parameters such as decay rate and time delay, exploring their influence on the emergence and coordination of oscillatory behaviour. The results showcase the impact of parameter variations on the oscillators' dynamics, providing insights into the conditions for sustained oscillations and synchronization.

This research contributes to a deeper understanding of the regulatory mechanisms in biological systems and sets the stage for further exploration of complex oscillatory phenomena.

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List of Equations

The key equations used in the simulation of a single biochemical oscillator without using code.

Hill Function:

The Hill function is a mathematical model commonly employed to describe cooperative interactions in biological systems. It is expressed as:

H(x,h)=1/(1+x^h) in Single Oscillator

- H(x,h):Hill function output.
- x: Input variable
- h: Hill coefficient, determining the steepness of the curve.

$H(x_1,x_2,h_1,h_2)=1/(1+x_1\hat{}h_1+x_2\hat{}h_2)$

The Hill function introduces non-linearity to the model, representing phenomena such as cooperative binding or inhibition.

Differential Equation for a Single Oscillator:

The differential equation governing the behaviour of a single biochemical oscillator is given by:

dx/dt = K . H(delayed term, h) – r . x

- dx/dt: Rate of change of the oscillator's state (x) with respect to time (t).
- K: Brith Rate, influencing the overall amplitude of the oscillations.
- H(delayed term, h): The Hill function applied to a delayed term, capturing the non-linear response.
- r: Decay rate, determining the rate at which the oscillations decrease.
- Delayed term: Represents the influence from the past state of the oscillator, incorporating a time delay.

This differential equation describes how the state of the oscillator changes over time, considering the impact of coupling, non-linearity and decay.

Time Delay:

The time delay (τ) is a critical parameter in the model, representing the time it takes for the system to respond to changes. It influences the period and dynamics of the oscillator. In the context of the code, the time delay is incorporated through the delayed term in the hill function and the differential equation.

Coupling Strength and Decay Rate:

- The coupling strength (K) determines the strength of interaction between components in the system.
- The decay rate (r) influences how quickly the oscillations diminish over time. A smaller decay rate can result in sustained oscillations, while a larger rate leads to quicker damping.

These equations collectively define the dynamics of a single biochemical oscillator, capturing essential features such as non-linear responses, time delays, coupling, and decay. Numerical simulations based on these equations provide insights into the onset and behaviour of oscillations in biochemical systems.

Introduction:

Biological systems often exhibit intricate patterns and dynamic behaviours driven by the underlying oscillatory processes. Biochemical oscillators, integral to the regulation of biological functions, play a pivotal role in governing phenomena ranging from cellular cycles to circadian rhythms. Understanding the dynamics of these oscillators and their synchronization mechanisms is crucial for unravelling the complexities of life processes.

This report delves into the exploration of biochemical oscillators and their synchronization, employing numerical simulations based on differential equations. The investigation aims to shed light on the conditions that lead to the onset of oscillations in a single oscillator and further extends to the study of synchronization between two interconnected oscillators.

In the realm of biological systems, the interplay between components often involves intricate feedback mechanisms, time delays, and non-linear interactions. The mathematical modelling of biochemical oscillators captures these complexities, providing a computational framework to simulate and analyse their behaviour. By examining the synchronization of oscillators, we seek to elucidate the emergent collective dynamics that contribute to the orchestration of biological processes.

The report navigates through the fundamental equations governing the oscillators' behaviour, explores the impact of key parameters such as decay rate and time delay, and visually represents the simulation results. Through this study, we aim to contribute to the understanding of synchronization phenomena in biochemical systems, fostering insights that can inform future research and deepen our comprehension of the regulatory principles in biological processes.

Objective:

1. **Investigate Single Oscillator Dynamics:**
    - Explore the behaviour of a single biochemical oscillator through numerical simulations.
    - Analyse the impact of key parameters, including decay rate and time delay, on the onset and characteristics of oscillations.

2. **Study Two-Oscillator Synchronization:**
    - Extend the analysis to a system of two interconnected oscillators.
    - Investigate the synchronization dynamics between the two oscillators under varying conditions of decay rate and time delay.

3. **Examine the Role of Time Delay:**
    - Assess the influence of time delay on the synchronization behavior of interconnected oscillators.
    - Explore scenarios where synchronization is enhanced or disrupted based on specific values of time delay.

4. **Visualize Oscillator Behaviour:**
    - Generate visual representations, such as graphs, to illustrate the temporal evolution of oscillator states.
    - Provide graphical insights into the emergence of oscillations and synchronization phenomena.

5. **Identify Critical Parameter Values:**
    - Determine the critical values of decay rate and time delay that led to the onset of sustained oscillations.
    - Investigate conditions under which synchronization occurs and explore the sensitivity of the system to parameter variations.

6. **Contribute to Understanding Biological Dynamics:**
    - Provide insights into the regulatory mechanisms of biochemical systems through the study of oscillator behaviour.
    - Enhance our understanding of the conditions conducive to synchronization, offering implications for broader biological processes.

Methodology:

Methodology for Single Oscillator Code:

1. **Model Formulation:**
    - **Objective:** Develop a mathematical model for a single biochemical oscillator.
    - Formulate a differential equation incorporating the Hill function to represent the non-linear interactions within the oscillator.
    - Introduce key parameters such as initial state(x_0), coupling strength(K), decay rate(r), Hill coefficient(h), and time delay(τ).

2. **Numerical Simulation:**
    - **Objective:** Simulate the behaviour of a single oscillator over time.
    - Implement a numerical integration method (Euler's method) to solve the differential equation numerically.
    - Iterate over time steps to update the state of the oscillator based on the differential equation.

3. **Parameter Variation:**
    - **Objective:** Explore the impact of key parameters on the oscillator's behaviour
    - Systematically vary parameters such as decay rate(r) and time delay(τ).
    - Observe and analyse the changes in oscillatory behaviour under different parameter condition.

4. **Data Visualization:**
    - **Objective:** Create visual representation of the oscillator's behaviour.
    - Plot the simulation results over time.
    - Visualize how the state of the state of the oscillator evolves, providing insights into the onset and characteristics of oscillations.

Methodology for Two oscillators:

1. **Model Formulation:**
    - **Objective:** Extend the model to represent two interconnected biochemical oscillators.
    - Formulate a system of coupled differential equations describing the interaction between two oscillators.
    - Introduce delayed terms to account for the communication delay between oscillators.

2. **Numerical Simulation:**
    - **Objective:** Simulate the behaviour of two interconnected oscillators.
    - Extend the numerical integration method to solve the system of coupled differential equations.
    - Update the states of both oscillators based on the interdependence captured in the model.

3. **Parameter Variation:**
    - **Objective:** Investigate the synchronization dynamics by varying key parameters.
    - Systematically vary parameters such as decay rate(r), time delays(τ_1 and τ_2) and coupling strength(K).
    - Explore conditions that lead to synchronization or desynchronization between the two oscillators.

4. **Data Visualization:**
    - **Objective:** Create visual representations of the synchronized behavior of two oscillators.
    - Plot the simulation results for both oscillators over time.
    - Visualize how the states of the oscillators converge or diverge, providing insights into synchronization phenomena.

Discussion:

Single Oscillator Observations:

The provided tables outline the critical values of decay rate (r), time delay(τ), that lead to the onset of oscillations in single oscillator. The observation offers valuable insights into the behaviour of the biochemical oscillator under different conditions.

r (Decay rate)	τ (Time delay)
0.1	13.5
0.12	11.6
0.2	7.32
0.21	7.15
0.25	6.15
0.3	5.3
0.35	4.7
0.5	3.6

Table-1

1. **Effect of Decay Rate(r):**
    - The table illustrates that as the decay rate (r) increases, the critical time delay(τ) for oscillation onset decreases.
    - Higher r values lead to faster decay of oscillation, requiring shorter time delays to sustain the oscillatory behaviour.
2. **Periodic Peaks:**
    - At r = 0.1, the graph exhibits a characteristic where the first peak is significantly higher than subsequent peaks.
    - The periodicity of oscillations is maintained, but the amplitude decreases with each successive peak.

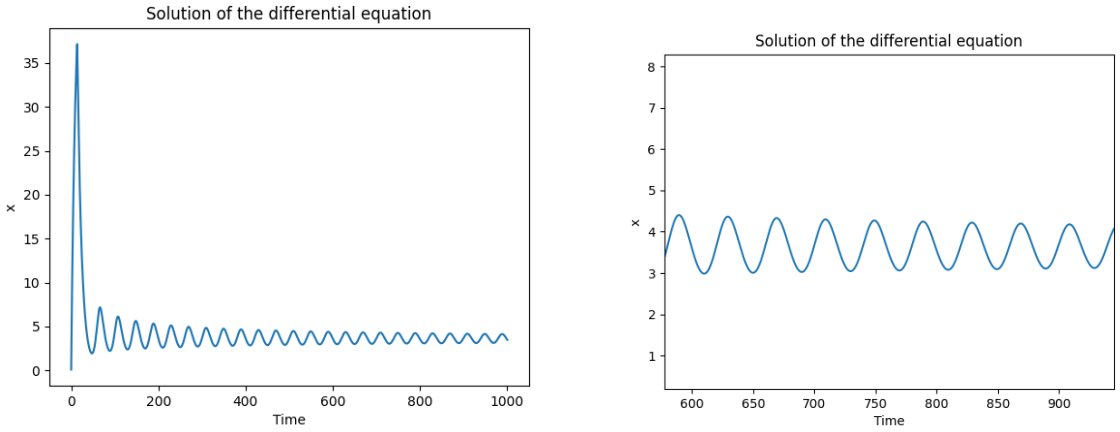

Figure-1

Two Oscillators Observations:

The provided tables outline the critical values of decay rate (r), and dual time delays (τ_1) and (τ_2) that lead to the onset of oscillations in two interconnected oscillators scenarios. The observations offer valuable insights into the behaviour of the biochemical oscillators under different conditions.

r(decay rate)	τ_1	τ_2
0.1	13.5	7.4
0.12	11.6	5.8
0.2	7.32	3.36
0.21	7.15	3.14
0.3	5.3	2.16
0.35	4.7	2.1
0.5	3.6	1.65
0.7	2.9	1.3

Table-2

1. **Impact of Dual Time Delays (τ_1 and τ_2):**
    - Similar to the single oscillator case, there is an inverse relationship between decay rate(r) and the critical dual time delays (τ_1 and τ_2).
    - As r increases, the required time delays for synchronization decrease.
2. **Symmetry in Peaks:**
    - When $\tau_2 = 2\ \tau_1$ or vice versa, the two graphs exhibit symmetry I their peaks.
    - The synchronization of peaks between the two oscillators is influenced by the ratio of τ_1 and τ_2.

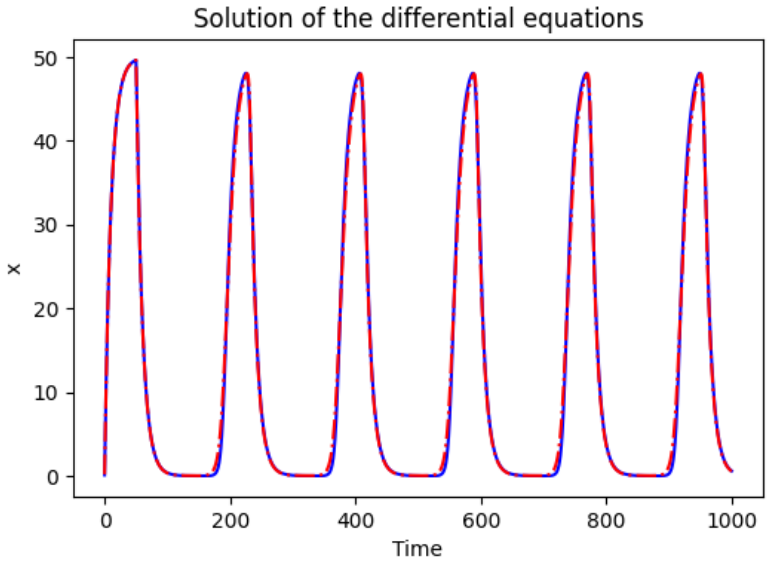

Figure-2

3. **Transition to Square-like Format:**
    - As r increases, both graphs tend to take on a square-like format, indicating a more synchronized and periodic behaviour.

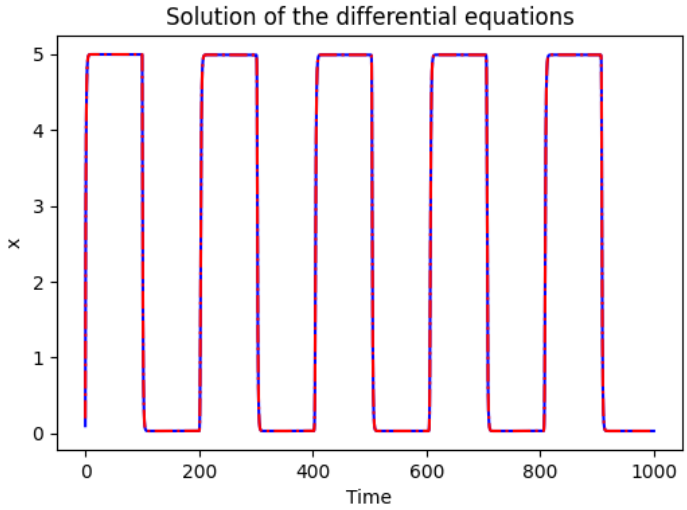

Figure-3

4. **Synchronization at Equal τ_1 and τ_2:**
    - A critical Observation is that synchronization occurs when τ_1 becomes equal to τ_2.
    - This points to the importance of the equality of time delays in achieving synchronization between the two oscillators.

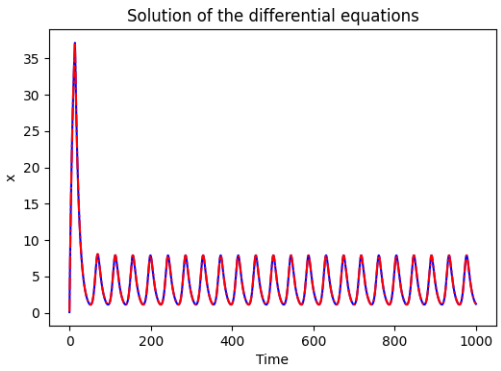

Figure-4

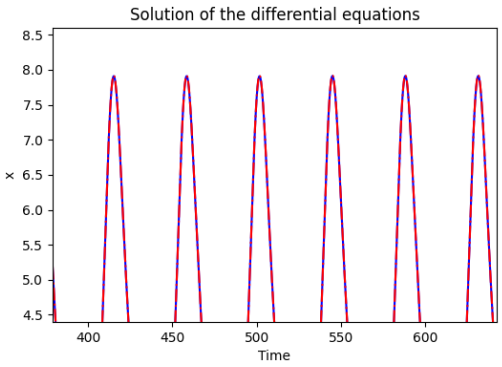

Figure-5

Overall Trends:

1. **Decay Rate and Synchronization:**
    - The increase in decay rate(r) tends to stabilize and synchronize the oscillations in both single and dual oscillator scenarios.
2. **Critical Time Delays:**
    - The critical time delays (τ and τ_1, τ_2) determine the onset of oscillations and synchronization, with shorter time delays supporting sustained oscillations.
3. **Symmetry and Synchronization:**
    - Symmetry in the dual oscillator scenario contributes to synchronization emphasizing the importance of balanced time delays.
4. **Transition to Square-like Format:**
    - A higher decay rate leads to a transition to a square-like format, indicating a more regular and synchronized oscillatory pattern.

Concluding Remarks:

The exploration into the synchronization dynamics of biochemical oscillators has provided valuable insights into the intricate behaviour of these systems. Through numerical simulations and analysis of single and two interconnected oscillators, several key observations and trends have emerged, shedding light on the interplay of critical parameters.

Here are the concluding remarks:

1. **Decay rate and Synchronization:**
    - The influence of the decay rate(r) on the oscillatory behaviour cannot be understated. Higher r values tend to stabilize and synchronize the oscillations, while lower values lead to sustained periodic behaviour.
2. **Critical Time Delays:**
    - Time delays (τ and τ_1,τ_2) are pivotal in determining the onset of oscillations and synchronization. Shorter time delays favour sustained oscillations, and synchronization is achieved when the dual time delays are balanced.
3. **Symmetry and Synchronization:**
    - Symmetry in the peaks of two interconnected oscillators contributed to synchronization. Achieving a balanced ratio τ_1 and τ_2 is crucial for this symmetry and synchronous behaviour.
4. **Transition to Regular Oscillation:**
    - As the decay rate(r) increase, both single and dual oscillators tend to transition to a more regular and square-like oscillatory format. This indicated a higher level of synchronization and periodicity.
5. **Interdisciplinary Significance:**
    - The study of biochemical oscillators and their synchronization has interdisciplinary significance, bridging mathematics, biology, and physics. The models and observations contribute to a broader understanding of regulatory mechanisms in biological system.

Future Work and Optimizations:

- Investigate the impact of external stimuli or perturbations on the synchronization dynamics of biochemical oscillators. Understanding how external factors influence the system can provide insights into the robustness of synchronization in real-world scenarios.
- Extend the study to explore synchronization in systems with more than two interconnected oscillators. Investigate the emergence of collective behaviours and synchronization patterns in larger networks of biochemical oscillators.
- Introduce additional nonlinearities and feedback loops into the mathematical models. Biological systems often exhibit intricate regulatory mechanisms, and considering these complexities can lead to more realistic and nuanced simulations.
- Explore strategies for controlling and manipulating the synchronization of biochemical oscillators. This could have implications for the design of interventions in biological systems, with potential applications in therapeutic interventions or bioengineering.

By delving into these future research directions, scientists and researchers can advance our understanding of biochemical oscillators, their synchronization mechanisms, and their broader implications in the dynamic regulation of biological processes.

References

1. Winfree, A. T. (1967). Biological rhythms and the behaviour of populations of coupled oscillators. Journal of Theoretical Biology, 16(1), 15-42.

2. Kuramoto, Y. (1984). Chemical Oscillations, Waves, and Turbulence. Springer Series in Synergetics.

3. Strogatz, S. H. (2000). From Kuramoto to Crawford: exploring the onset of synchronization in populations of coupled oscillators. Physica D: Nonlinear Phenomena, 143(1-4), 1-20.