

# Chapter 24

## Mathematical Modeling of the $\lambda$ Switch: A Fuzzy Logic Approach

**Dmitriy Laschov**  
*Tel Aviv University, Israel*

**Michael Margaliot**  
*Tel Aviv University, Israel*

### ABSTRACT

*Gene regulation plays a central role in the development and functioning of living organisms. Developing a deeper qualitative and quantitative understanding of gene regulation is an important scientific challenge. The  $\lambda$  switch is commonly used as a paradigm of gene regulation. Verbal descriptions of the structure and functioning of the  $\lambda$  switch have appeared in biological textbooks. We apply fuzzy modeling to transform one such verbal description into a well-defined mathematical model. The resulting model is a piecewise-quadratic, second-order differential equation. It demonstrates functional fidelity with known results while being simple enough to allow a rather detailed analysis. Properties such as the number, location, and domain of attraction of equilibrium points can be studied analytically. Furthermore, the model provides a rigorous explanation for the so-called stability puzzle of the  $\lambda$  switch.*

### 1. INTRODUCTION

Gene regulation plays a fundamental role in the development and evolution of organisms. Understanding gene regulation within living cells is a major scientific challenge in the post-genome era. Indeed, the analysis of gene regulating networks may have important implications in many fields of science, including biology and gene therapy. It may also lead to methods of synthesizing artificial networks with applications in biotechnology and biocomputing (Gardner, Cantor, & Collins, 2000).

The  $\lambda$  switch (Ptashne, 2004) is a relatively simple gene regulating network that controls two alternative patterns of gene expression in the bacterial virus  $\lambda$ . This epigenetic switch ensures an efficient change from one pattern to the other in response to suitable environmental cues. Bistable switches are

DOI: 10.4018/978-1-60566-685-3.ch024

common motifs in gene regulation networks, and the  $\lambda$  switch provides a convenient test case, as the virus is one of nature's simplest organisms. In a recent survey paper, (Zhu et al., 2007) point out that the  $\lambda$  switch "has indeed established itself as one of the fundamental elements in biological processes and as a paradigm for both experimental and theoretical studies in biology."

Developing suitable mathematical models for gene regulating networks is a non-trivial task. Several researchers have tried to gain a deeper understanding of the  $\lambda$  switch by deriving mathematical models for its dynamic behavior (see the review in Section 2.4 below). Most of the models are quite complex and, consequently, can be studied primarily using simulations and numerical analysis.

In this chapter, we apply *fuzzy modeling* (FM) to derive a new mathematical model for the  $\lambda$  switch. FM plays an important role in the fields of artificial intelligence and computational intelligence (Zadeh, 1994; Klir & Yuan, 1995). It is routinely used to transform the knowledge of a human expert, stated in *natural language*, into an *artificial expert system* (AES) that imitates the human expert's functioning (Siler & Buckley, 2004; Kandel, 1992). Indeed, the real power of fuzzy logic lies in its ability to handle and manipulate linguistic information based on perceptions (Dubois, Nguyen, Prade, & Sugeno, 1998; Margaliot & Langholz, 1999, 2000; Zadeh, 1996; Novak, 2005). FM provides a simple yet highly efficient approach for transforming *verbal* descriptions into well-defined mathematical models or algorithms.

Recently, FM has been used to derive mathematical models for *biological phenomena*. Biologists often provide verbal descriptions and explanations of the phenomena they study. FM provides a convenient tool for transforming these verbal descriptions into well-defined mathematical models. Note that this application of FM is somewhat different than the typical approach applied in the construction of AESs. The motivation is not to replace the human expert with an automatic algorithm, but rather to assist a human expert in transforming his/her knowledge concerning a biological phenomenon, stated in words, into a well-defined mathematical model. The usefulness of this approach was demonstrated by developing mathematical models for animal behavior (Tron & Margaliot, 2004, 2005; Bajec, Zimic, & Mraz, 2005; Rashkovsky & Margaliot, 2007; Rozin & Margaliot, 2007; Margaliot, 2007).

Fuzzy modeling of biological systems offers several advantages (Margaliot, 2008). The resulting model represents the real system in a form that corresponds closely to the way humans perceive it. Thus, the model is understandable, even by non-professionals, and each parameter has a readily perceivable meaning. The model can be easily altered to incorporate new phenomena, and if its behavior is different than expected, it is usually possible to determine which rule/term should be modified and how.

In this chapter, we apply FM to systematically transform (part of) the *verbal* description given in (Santillan & Mackey, 2004) into a mathematical model of the  $\lambda$  switch. The state-variables are the amounts of two regulatory proteins (*CI* and *Cro*), and the resulting model is a piecewise-quadratic second-order differential equation.

Simulations indicate that the model demonstrates adequate functional fidelity to the biological behavior. Furthermore, the piecewise-quadratic nature of the model makes it amenable to rigorous analysis. Various properties that were previously shown in simulations can now be studied analytically. These include the location and stability of the equilibrium points, and the analysis of bifurcations that may explain the *stability puzzle* in the  $\lambda$  switch (Santillan & Mackey, 2004).

The remainder of this chapter is organized as follows. Section 2 briefly reviews the genetic switch. Section 3 applies FM to derive a mathematical model for the  $\lambda$  switch. Simulations and a rigorous analysis of the mathematical model are presented in Sections 4 and 5. The final section concludes.

29 more pages are available in the full version of this document, which may be purchased using the "Add to Cart" button on the publisher's webpage:

[www.igi-global.com/chapter/mathematical-modeling-switch/38252](http://www.igi-global.com/chapter/mathematical-modeling-switch/38252)

## Related Content

---

### Simulation of Multiple Cell Population Dynamics Using a 3-D Cellular Automata Model for Tissue Growth

Belgacem Ben Youssef and Lenny Tang (2012). *Nature-Inspired Computing Design, Development, and Applications* (pp. 201-220).

[www.irma-international.org/chapter/simulation-multiple-cell-population-dynamics/66778](http://www.irma-international.org/chapter/simulation-multiple-cell-population-dynamics/66778)

### Ultra High Frequency Polynomial and Trigonometric Higher Order Neural Networks for Control Signal Generator

Ming Zhang (2017). *Nature-Inspired Computing: Concepts, Methodologies, Tools, and Applications* (pp. 648-681).

[www.irma-international.org/chapter/ultra-high-frequency-polynomial-and-trigonometric-higher-order-neural-networks-for-control-signal-generator/161047](http://www.irma-international.org/chapter/ultra-high-frequency-polynomial-and-trigonometric-higher-order-neural-networks-for-control-signal-generator/161047)

### Swarm-Based Clustering for Gene Expression Data

P. K. Nizar Banu and S. Andrews Samraj (2017). *Bio-Inspired Computing for Information Retrieval Applications* (pp. 123-149).

[www.irma-international.org/chapter/swarm-based-clustering-for-gene-expression-data/177985](http://www.irma-international.org/chapter/swarm-based-clustering-for-gene-expression-data/177985)

### Decoding Algorithm by Cooperation Between Hartmann Rudolph Algorithm and a Decoder Based on Syndrome and Hash

My Seddiq El Kasmi Alaoui and Said Nouh (2021). *International Journal of Natural Computing Research* (pp. 15-27).

[www.irma-international.org/article/decoding-algorithm-by-cooperation-between-hartmann-rudolph-algorithm-and-a-decoder-based-on-syndrome-and-hash/274935](http://www.irma-international.org/article/decoding-algorithm-by-cooperation-between-hartmann-rudolph-algorithm-and-a-decoder-based-on-syndrome-and-hash/274935)

### Solving Uncapacitated Facility Location Problem Using Heuristic Algorithms

Soumen Atta, Priya Ranjan Sinha Mahapatra and Anirban Mukhopadhyay (2019). *International Journal of Natural Computing Research* (pp. 18-50).

[www.irma-international.org/article/solving-uncapacitated-facility-location-problem-using-heuristic-algorithms/225822](http://www.irma-international.org/article/solving-uncapacitated-facility-location-problem-using-heuristic-algorithms/225822)