ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 4, Issue 3, pp: (90-95), Month: July - September 2016, Available at: www.researchpublish.com

Fuzzy logic as a Tool for Mathematical Modeling in Life Sciences

[1]Jose Arturo Molina Mora

[1]School of Mathematics, University of Costa Rica, San Pedro de Montes de Oca, San José, Costa Rica

Abstract: **The aim of modeling is to represent, manipulate and communicate real-world objects of daily life and that somehow allows the simulation of complex processes, generate hypotheses and suggest experiments. Many of the systems areas in biology, health, medicine, humanities and engineering are unwieldy with traditional analytical and mathematical methods, so in early 1990 it started to propose the concept of soft-computing or computational intelligence to refer to computational techniques and algorithms that exploit the tolerance for imprecision, uncertainty and partial truth. One such case is represented by fuzzy logic, a powerful tool for managing complex problems in a position where you have incomplete or not very accurate information. A review of the potential of fuzzy logic as a tool for mathematical modeling in life sciences is presented.**

Keywords: **Fuzzy logic, mathematical modelling, Life sciences, biological systems.**

I. INTRODUCTION

Mathematical Modeling

Modeling has the aim of represent, manipulate and communicate real-world objects of daily life and that somehow allows the simulation of complex processes, generate hypotheses and suggest experiments. In short, a good model should reflect the causal structure of the system under study, and be able to predict the outcome efficiently with new experiments [1] . However, there are many ways of observing an object or, equivalently, there are many different observers for the same object, so that the choice of the model (which is not unique) directly affects the interpretation and design; plus model selection are supported directly with the system under investigation, in which knowledge and information gained expert, structure, model assumptions, conceptual model and the required mathematical formalism, quality and type of experimental data is included (quantitative or qualitative), and the state of prior knowledge [2], [3].

Although one of the ultimate goals of classical mathematical modeling is to obtain expressions that allow quantitatively understand all the details and principles of biological systems, it is often difficult to perform [4]. Many of the systems areas in biology, medicine, humanities and engineering are unwieldy with traditional analytical and mathematical methods, so in early 1990, it proposed the concept of soft-computing or computational intelligence to refer to techniques and computational algorithms that exploit the tolerance for imprecision, partial truth and uncertainty for a specific problem, unlike hard-computing in which the accuracy and the whole truth is sought [5]. The methods of soft-computing can be considered derivatives of Machine Learning, which is as known to the branch of artificial intelligence that aims to develop techniques that allow a computer to generalize behavior from examples [6].

Mathematical modeling based on conventional mathematical tools, such as those based solely on differential equations, is not very useful understood systems by the inability to calculate the required parameters or complexity to do, plus they do not allow the incorporation of information additional, qualitative or imprecise [7].

In response, several *in silico* models have been proposed and describing the dynamic behavior of biological systems with soft-computing [4]. The revolutions in biotechnology, post-genomic technology and information technology have produced huge amounts of data and are accelerating the process of discovering knowledge in biological systems [3]. Chai et al (2009) suggest that computer intelligence can be divided into 3 categories, nature-based: algorithms inspired by biological processes, algorithms inspired by physical-non-biological processes and algorithms inspired by industrial processes or social-human invention [8]. In each category you can detach sud-divisions, which combine wing can create new hybrid algorithms, according to the needs of the system (see Figure 1).

Many of the techniques of soft-computing often inspired by biology and includes models such as neural networks, fuzzy systems, Petri nets, Bayesian networks, evolutionary algorithms, optimization ant colony, swarm intelligence, immune algorithms, among others [1], [5]. Algorithms have been developed that attempt to mimic or reproduce human learning and information processing expressed by everyday language. This requires to design architectures and radical models that are conceptually different from traditional models, as well as the extraction of relevant information by data mining techniques [9].

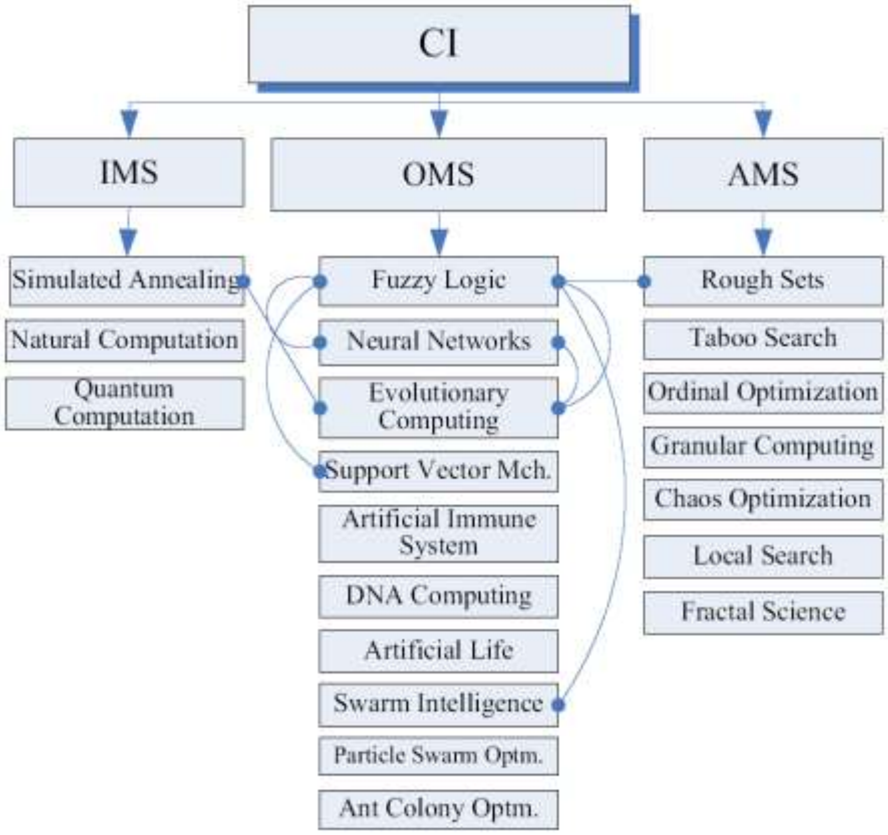

Figure 1. Classification of computational intelligence algorithms (taken from [8]).

II. FUZZY LOGIC IN LIFE SCIENCES

A. Fuzzy logic

The concept of fuzzy logic or fuzzy sets was introduced in 1960 by Zadeh as a generalization of the theory of conventional sets [10]. Fuzzy logic is a type of logic with a series of values specified as a degree of truth instead of the true or false binary values [11]. Therefore, it is considered that the most important application of the fuzzy logic is in the managing of uncertainty [12].

Fuzzy logic is a powerful and suitable tool for handling complex problems in a position where there is incomplete or not very accurate information [13]. In addition, the way that non-probabilistic uncertainties have been addressed with fuzzy logic have made the rise of the models with this paradigm has become popular in many areas of knowledge, to the point of establishing related areas, occasionally identified as graphics diffuse, fuzzy interpolation fuzzy topology, fuzzy reasoning, fuzzy systems and fuzzy inference modelling [9].

According to Zadeh, the essence of fuzzy logic is that the exact reasoning is seen as a limiting case of approximate reasoning; also it proposes that everything is a matter of degree and that any system of logic can undergo the theory of fuzzy logic [10], [11]. This latter contributes to justify the features of fuzzy logic [14]:

- It is conceptually easy to understand. Fuzzy logic is a more intuitive without the complexity of other far-reaching mathematical modeling method.
- It is flexible in accepting degrees and not only binary systems.
- It is tolerant of imprecise data.
- It is possible to model nonlinear functions of arbitrary complexity.
- It can build based on the experience of experts.
- It is based on the natural language of human communication.

Fuzzy sets can be considered as a generalization of the classical sets. Basically, a fuzzy set can have elements with a partial degree of membership and the membership degree is characterized by membership functions, which give flexibility fuzzy sets to model linguistic expressions employed daily. Operations are not based on the frequency of the phenomenon, but are rather based in terms of possibility that are qualitative and refer to capacities and potentialities. According to classical logic, an element can only be in one of the sets (exclusive), while according to the fuzzy logic, an element has different membership of the two sets lesser or greater extent (see Figure 2).

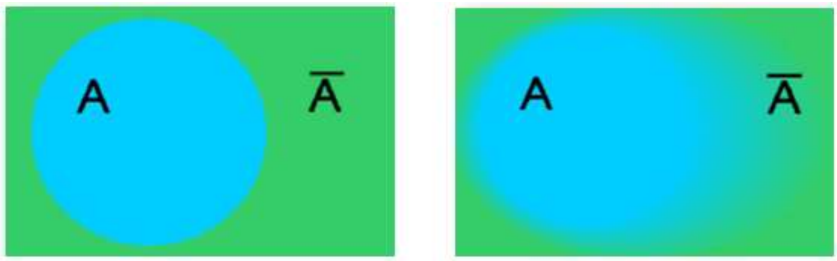

Figure 2. Sets in classical logic (left) and fuzzy logic (right).

More in detail, a classic set A can be expressed by the following membership function:

$$\mu_A(x) = \begin{cases} 1 & si\ x \in A \\ 0 & si\ x \notin A \end{cases}$$

In this case, the values to belong, μ_A(x) are only 0 and 1, depending on whether the variable x belongs or not to set A given. Meanwhile, a fuzzy set A in a universe of discourse X is defined by a membership function or membership $\mu_A(x)$ taking values in the interval [0,1], and can be represented as a set of ordered pairs:

$$A = \{(x, \mu_A(x))/x \in X\}\ A\colon X \to [0,1]$$

The membership values of $\mu_A(x)$ range from 0 (does not belong) and 1 (total membership) and where $\mu_A(x)$ is the function of belonging or membership.

B. Fuzzy mathematical models in life sciences

The fuzzy logic based systems have been used for models involving mining or oil exploration, communication systems, automation, fault diagnosis in nuclear electrical and power systems, engineering design, planning and transport, economy and finance, robotics, study and weather forecasting, aircraft design, flight simulators, search oilfields, study and prediction of tornadoes, assigning codes in mobile stations, bioinformatic problems, among many others [5], [15], [16].

In the medical-biological area there are many systems in which qualitative data are included and have therefore been favored with the application of fuzzy logic models. Thus, the fuzzy logic method is suitable for biomedical applications because of the uncertain nature of medical and biological and relationships between these concepts; due to the complexity of the practice of medicine and biology, traditional approaches to quantitative analysis are not appropriate in many cases [14], [17]. Some applications of fuzzy logic in the biomedical area include:

- Analysis of risk, diagnosis, prognosis, treatment and other medical decisions regarding cancer and other diseases.
- Analysis of medical images (magnetic resonance, smears, mammograms, X-rays) or biological (environmental samples, deforestation, rivers and oceans, species distribution, habitat studies and niches).
- Classification (separating benign from malignant lesions, animal sounds, anthropology).
- Show quantitative estimates of substances (drug use, distribution of oil in water, heavy metal contamination).
- Data analysis gene expression microarray.
- Modeling biological networks.

Moreover, the creation of hybrid mathematical models, inspired by different paradigms, is one of the tasks of data analysis has shown great response capacity. So, combine several methods of computational intelligence with other types of development of analysis is often given to give attention to the different levels and perspectives in solving problems, they can achieve very good results [8]. For example, about 70% of all studies covering problems of medical prediction uses neural networks, but produce a "black box" for the interpretation of the models [18]. This can be solved using other tools and applications, being the combined with fuzzy logic one of the most popular. Because of this, it has increased the potential and interest of these hybrid models to explain real-life problems [9].

The use of fuzzy logic in biochemical models requires some numerical parameters in order to operate as initial values and coefficients of change, but the exact values of these numbers are not generally critical. Since the dynamic rules are defined in terms of fuzzy numbers, fuzzy logic models allow the calculation of the consequences of the dynamics of complex systems with imprecise variables. At the same time, fuzzy logic models are capable of representing complex systems to extremely high degree of accuracy when data are required [8].

Sokhansanj et al in 2004 showed a study in which they used fuzzy logic to analyze microarray data, identifying common patterns between different models evaluated and achieving a better understanding of the system and its evolution. For these conclusions, they used an exhaustive search of cell cycle genes in yeast and assessed regulation at the transcriptional level, making the model was able to predict the behavior of the system, even after adjusting the model with a data set different [19]. Another pioneering work on the use of fuzzy logic in the study of biological systems it is a model that analyzes the kinase pathway in TNF/EGF-induced insulin signaling in an article by Aldridge et al in 2009. The objective using fuzzy logic responds to the fact that it can encode probabilistic transitions and dynamics between network conditions in order to create simple representations and quite realistic of cellular signaling networks, which allowed a comprehensive analysis of the data obtained experimentally. The construction of the fuzzy model was done by hand, because the authors wanted to test whether the fuzzy model could be adapted to test a priori knowledge and hypotheses with data to refine the understanding of the network and generate testable hypotheses [20].

Also in 2009, a study fuzzy modeling was performed by analyzing pathways of signal transduction of IL-6 and TNF, which initially were established key variables for the transduction pathway, and then establish a set of rules diffuse that they described how the inputs and the values of these behaved in the system, to finally determine the parameters of the membership functions from data, with the consequent prediction and assessment model [15]. Khashei and colleagues (2012) presented a study with a hybrid model that combines artificial intelligence with fuzzy logic for the analysis of gene expression. Empirical results of the classification of gene expression indicated that the proposed model presented a classification accuracy improved compared to the efficiency with traditional neural networks, which recommended to be applied with an appropriate alternative approach to solving model problems with limited data [13].

Vineetha and colleagues showed a study in which they propose a regulatory network of genes microarray data of patients with colon cancer. The model used was based on fuzzy logic in combination with a neural network for extracting the rules relationship between genes and thus reconstruct the gene regulatory network. The results show a regulatory ratio of 27 differentially expressed genes in the dataset of microarrays, and to compare the method used, also they developed a modified genetic algorithm and a recurrent neural network, obtaining the three methods are essentially equivalent [21]. In India, the same authors presented a study on the analysis of microRNAs with a fuzzy model to explain the regulation of gene expression during various fundamental cellular processes such as differentiation, proliferation and apoptosis, particularly in cases of colorectal cancer. a type of neural network recurrent diffuse to infer and analyze profiles of miRNA and mRNA in patients with colo-rectal cancer was used in the study, and for a good performance was obtained between the model and experimentally verified associations of data microRNA and mRNA. 17 validated microRNA identified and who are directly involved in the process of colo-rectal cancer, information that can be useful to prevent recurrence of the disease and also to control the growth of advanced metastatic tumors [22].

In other hand, studies have combined fuzzy logic with differential equations in a hybrid model are scarce. More in detail, some of these studies have generated hybrid models to study biological processes and mainly at the level of metabolism. One of the first hybrid approaches of differential and logic equations diffuse was presented by Lee et al in 1999, which established a strategy to incorporate qualitative or semi-quantitative information on the kinetic equation of an enzymatic process, in which factors based on logic diffuse managed to change the algebraic speed laws, and expressing them as partial kinetic parameters which were introduced by the fuzzy factors. In the study, they included the effect of ATP in *Escherichia coli*, founding that phosphoenolpyruvate carboxykinase (PCK) was biphasic: accelerates the reaction at low concentrations of ATP, but is inhibited at high concentrations [23].

Meanwhile, another study conducted in 2005 showed a modeling system that required time series of concentrations of metabolites as input data using qualitative differential equations system for modeling ten reactions involved in glycolysis. For the development of the platform, they used various computational algorithms for extracting patterns in the data series intelligence, allowing a detailed description of the reactions involved with fuzzy sets [1]. Bosl et al (2007) presented a model with qualitative differential equations to model the biochemical dynamics in cells, primarily for metabolic pathways, for which the parameters were adjusted membership functions of fuzzy logic. Thus, the fuzzy modeling was given two main tasks: First, the simulation of a biochemical system configured with computational intelligence algorithms, and second, the discovery of the system from the time series data. The result showed that the curves adjustment model had far better than other algorithms evaluated experimental data and did not include fuzzy logic [17].

As shown in the examples presented, the development of research into hybrid systems seeks to improve how to implement and build more powerful mechanisms to solve some problems that are very difficult to cope using a unique method of reasoning. The disadvantage of increasing the applicability of hybrid models is that predictions are not necessarily deterministic, and therefore a number of possible solutions needs to judged by experts [1].

III. CONCLUSION

Because knowledge of the various problems of study may limit the use of ODE models for mathematical approach, the use of modeling techniques softcomputing, such as fuzzy logic, provides an opportunity to extract enough information to understand the system and make decisions despite not having accurate knowledge of the system. Particularly in biomedical sciences, the use of mathematical modeling with fuzzy sets provides the advantage that they are able to handle data in a non-discrete and manage uncertainty in the various stages of study.

REFERENCES

[1] R. D. King, S. M. Garrett, and G. M. Coghill, “On the use of qualitative reasoning to simulate and identify metabolic pathways.,” Bioinformatics, vol. 21, no. 9, pp. 2017–26, May 2005.

[2] N. Friedman, “Inferring cellular networks using probabilistic graphical models.,” *Science (80-.).*, vol. 303, no. 5659, pp. 799–805, Feb. 2004.

[3] S. Motta and F. Pappalardo, “Mathematical modeling of biological systems.,” *Brief. Bioinform.*, vol. 14, no. 4, pp. 411–22, Jul. 2012.

[4] K.-Y. Tsai and F.-S. Wang, “Evolutionary optimization with data collocation for reverse engineering of biological networks.,” *Bioinformatics*, vol. 21, no. 7, pp. 1180–8, Apr. 2005.

[5] O. Cordón, F. Gomide, F. Herrera, F. Hoffmann, and L. Magdalena, “Ten years of genetic fuzzy systems: current framework and new trends,” *Fuzzy Sets Syst.*, vol. 141, no. 1, pp. 5–31, Jan. 2004.

[6] V. Soler, “Lógica difusa aplicada a conjuntos imbalanceados : aplicación a la detección del Síndrome de Down,” Tesis para optar por el grado de Doctor en Informática. Departamento de Microelectrónica en sistemas electrónicos. Universidad Autónoma de Barcelona, España, 2007.

[7] M. Irízar, “La inteligencia computacional en la identificación de sistemas,” *Ing. Electrónica, Automática y Comun.*,

ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 4, Issue 3, pp: (90-95), Month: July - September 2016, Available at: www.researchpublish.com

vol. 26, no. 1, pp. 35–41, 2005.

[8] Y. Chai, L. Jia, and Z. Zhang, "Mamdani model based adaptive neural fuzzy inference system and its application," *Int. J. Inf. Math. Sci.*, pp. 22–29, 2009.

[9] Y. Bravo and D. García, "Estudio y aplicación de los modelos ANFIS de MATLAB.," Tesis para la obtención del grado de Licenciatura en Ingeniería electrónica y control. Escuela Politécnica Nacional. Quito, Ecuador., 2002.

[10] L. A. Zadeh, "Fuzzy logic, neural networks, and soft computing," *Commun. ACM*, vol. 37, no. 3, pp. 77–84, Mar. 1994.

[11] S. Zhang, R. Wang, X. Zhang, and L. Chen, "Fuzzy System Methods in Modeling Gene Expression and Analyzing Protein Networks," *Fuzzy Syst. Methods Model. Gene Expr.*, vol. 9, pp. 165–189, 2009.

[12] M. Neshat and A. Adeli, "A Comparative Study on ANFIS and Fuzzy Expert System Models for Concrete Mix Design," *Int. J. Comput. Sci.*, vol. 8, no. 3, pp. 196–210, 2011.

[13] M. Khashei, A. Zeinal Hamadani, and M. Bijari, "A fuzzy intelligent approach to the classification problem in gene expression data analysis," *Knowledge-Based Syst.*, vol. 27, pp. 465–474, Mar. 2012.

[14] A. Yilmaz and K. AYAN, "Cancer risk analysis by fuzzy logic approach and performance status of the model," *Turkish J. Electr. Eng. …*, pp. 1–27, 2013.

[15] Z. Huang and J. Hahn, "Fuzzy modeling of signal transduction networks," *Chem. Eng. Sci.*, vol. 64, no. 9, pp. 2044–2056, May 2009.

[16] J. Muñoz Perez, "Inteligencia computacional inspirada en la vida," *Serv. Publicaciones la Univ. Málaga*, vol. 1, pp. 1–10, 2010.

[17] W. J. Bosl, "Systems biology by the rules: hybrid intelligent systems for pathway modeling and discovery.," *BMC Syst. Biol.*, vol. 1, p. 13, Jan. 2007.

[18] E. Bonilla, B. Duval, and J.-K. Hao, "Fuzzy logic for elimination of redundant information of microarray data.," *Genomics. Proteomics Bioinformatics*, vol. 6, no. 2, pp. 61–73, Jun. 2008.

[19] B. Sokhansanj, J. P. Fitch, J. N. Quong, and A. a Quong, "Linear fuzzy gene network models obtained from microarray data by exhaustive search.," *BMC Bioinformatics*, vol. 5, p. 108, Aug. 2004.

[20] B. B. Aldridge, J. Saez-Rodriguez, J. L. Muhlich, P. K. Sorger, and D. a Lauffenburger, "Fuzzy logic analysis of kinase pathway crosstalk in TNF/EGF/insulin-induced signaling.," *PLoS Comput. Biol.*, vol. 5, no. 4, p. e1000340, Apr. 2009.

[21] S. Vineetha, C. Chandra Shekara Bhat, and S. M. Idicula, "Gene regulatory network from microarray data of colon cancer patients using TSK-type recurrent neural fuzzy network.," *Gene*, vol. 506, no. 2, pp. 408–16, Sep. 2012.

[22] S. Vineetha, C. Chandra Shekara Bhat, and S. M. Idicula, "MicroRNA-mRNA interaction network using TSK-type recurrent neural fuzzy network.," *Gene*, vol. 515, no. 2, pp. 385–90, Feb. 2013.

[23] B. Lee, J. Yen, L. Yang, and J. Liao, "Incorporating qualitative knowledge in enzyme kinetic models using fuzzy logic," *Biotechnol. Bioeng.*, vol. 62, no. 6, pp. 722–729, 1999.