

Glia-Augmented Artificial Neural Networks: Foundations and Applications

by

© *Zahra Sajedinia*

A thesis submitted to the
School of Graduate Studies
in partial fulfilment of the
requirements for the degree of
Master of *Computer Science*

Department of *Computer Science*
Memorial University of Newfoundland

May 2015

St. John's

Newfoundland

Abstract

Information processing in the human brain has always been considered as a source of inspiration in Artificial Intelligence; in particular, it has led researchers to develop different tools such as artificial neural networks. Recent findings in Neurophysiology provide evidence that not only neurons but also isolated and networks of astrocytes are responsible for processing information in the human brain. Artificial neural networks (ANNs) model neuron-neuron communications. Artificial neuron-glia networks (ANGN), in addition to neuron-neuron communications, model neuron-astrocyte connections. In continuation of the research on ANGNs, first we propose, and evaluate a model of adaptive neuro fuzzy inference systems augmented with artificial astrocytes. Then, we propose a model of ANGNs that captures the communications of astrocytes in the brain; in this model, a network of artificial astrocytes are implemented on top of a typical neural network. The results of the implementation of both networks show that on certain combinations of parameter values specifying astrocytes and their connections, the new networks outperform typical neural networks. This research opens a range of possibilities for future work on designing more powerful architectures of artificial neural networks that are based on more realistic models of the human brain.

Acknowledgements

Foremost, I would like to express my sincere gratitude to my supervisor Dr. Todd Wareham for the continuous support of my masters study research and also providing me with many curricular and extracurricular opportunities, and also for his patience, motivation, and enthusiasm. I have learned so many things from him and I am truly blessed to have him as my supervisor. This thesis definitely would not have been possible without his encouragement and guidance. In one sentence I can say that I could not have imagined having a better supervisor. Also, I would like to thank Dr. Iris van Rooij, for her guidance, patience and encouragement; Her guidance helped me in all the time of my study.

Also, I would like to thank Dr. Antonina Kolokolova for her support and thoughtful comments specifically during departmental cognitive and neuroscience talks, her encouragement and insightful comments always motivated me in continuing my research. Also, I'd like to thank her for her helpful suggestions on the relation between noise and astrocytes. Also, my gratitude extended to Dr. Siwei Lu, for introducing me to artificial neural networks and providing me with the opportunity to start working on artificial glia networks. Furthermore I would also like to acknowledge with much appreciation Ms Darlene Oliver, Brenda Hillier, and Sharon Deir at the Computer Science general office.

Last but not the least, I would like to thank my family and friends, specifically my parents Mohamad Sajedinia and Nahid Pahlavan for their endless love and support, though no words can begin to express my heartfelt thanks for their kindness and thoughtfulness.

Contents

Abstract	ii
Acknowledgements	iii
List of Tables	vi
List of Figures	vii
1 Introduction	1
2 Background	6
2.1 Biological Neurons and Neural Networks	6
2.2 Biological Glia Cells	10
2.3 Artificial Neural Networks	13
2.3.1 Architecture	15
2.3.2 Activation function	16
2.3.3 Training Algorithm	16
2.4 Adaptive Neuro-Fuzzy Inference Systems	20
2.4.1 Fuzzy sets, if-then rules, and inference systems	20

2.4.2	ANFIS architecture and algorithms	22
2.5	Artificial Neuron-Glia Networks	28
3	Adaptive Neuro-glia Fuzzy Inference System (ANGFIS)	33
3.1	Architecture and Learning Algorithm	34
3.1.1	Architecture	34
3.1.2	Learning Algorithm	34
3.2	Performance	36
3.3	Discussion	40
4	Artificial Astrocytes Networks (AANs)	42
4.1	Architecture and Learning Algorithm	43
4.1.1	Architecture	43
4.1.2	Learning Algorithm	45
4.2	Performance	46
4.3	Discussion	50
5	Summary and Future Work	54
5.1	Summary	54
5.2	Future Work	55
	Bibliography	58

List of Tables

3.1	Astrocyte parameters used for implementing ANGFIS	39
3.2	The RMSE error for ANGFIS and ANFIS	40
4.1	Parameters used in implementing ANGN and AAN	50
4.2	The accuracy of classification on test data for ANN, ANGN and AAN	50

List of Figures

1.1	Biological neuron, artificial neuron, biological synapse and ANN synapses	2
1.2	A representation of a tripartite synapse	4
2.1	A biological neuron	7
2.2	A biological synapse	8
2.3	Transmission of a signal through a synapse	10
2.4	Neurons and astrocytes in the brain	11
2.5	Tripartite synapse	12
2.6	Connections between astrocytes in the brain	13
2.7	An example of an artificial neural network	14
2.8	Components of a Fuzzy Inference System	23
2.9	ANFIS Architecture	24
2.10	An example of an Artificial Neuron-glia Network	29
2.11	An artificial neuron and its associated astrocyte	32
3.1	Architecture of an ANGFIS	35
4.1	ANGN and AAN	44
4.2	A flowchart of the AAN algorithm	47

Chapter 1

Introduction

The human brain has always been considered as a source of inspiration in developing tools and algorithms in computer science. The human brain seems to have an advantage in solving problems where no explicit rules are given [5]. To benefit from this characteristic of the brain, researchers developed computational tools that mimic the way the human brain works. Artificial neural networks (ANNs) are one of these computational tools which for representing biological neural systems. They are capable of learning from experience [12]. Currently, ANNs are used in different fields of science from business to medicine and robotics [11].

In 1943 McCulloch and Pitts introduced the first artificial neural networks [27, 33]. Many different models of ANNs have been proposed, which generally consist of two elements: neurons and weights. Neurons are the individual computational elements representing a simplified model of biological neurons, and weights represent the connections called synapses between biological neurons. Figure 1.1 presents a biological neuron, synapse and corresponding elements in artificial neural networks.

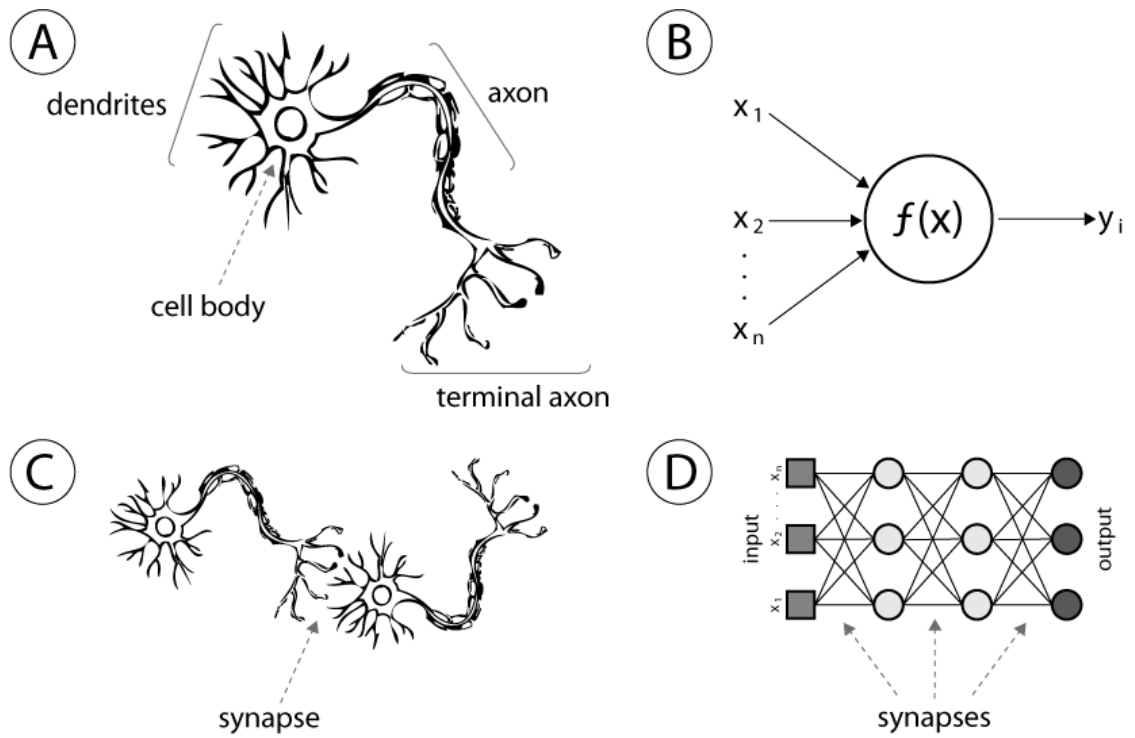


Figure 1.1: (A) Human neuron; (B) artificial neuron or hidden unity; (C) biological synapse; (D) ANN synapses (This figure is reprinted from [31], with permission from InTech Publisher.)

Although the human brain consists of neurons and glia cells, ANNs generally represent only neurons. It is estimated that there are 10 to 50 times more glia cells than there are neurons in the brain [16]. Recent discoveries in neuroscience show that glia cells, in addition to doing passive functions such as providing nutrition for neurons and collecting wastes from neurons, modulate synapses and process information [64, 49]. In more detail, the process by which glia cells modulate synapses begins with the release of neurotransmitters from a pre-synaptic neuron; this release then evokes an increase in calcium ions in neighbouring glia cells. Glia cell in response release transmitters. These transmitters will reach pre-synaptic and post-synaptic neurons and enhance or depress further release of neurotransmitters. Therefore, glia cells regulate synaptic transmissions and as a result they affect information processing [39].

Presently, the concept of tripartite synapse is well known in neurophysiology, which states that each synapse consists of three parts: presynaptic elements, post-synaptic elements, and surrounding astrocytes (see Figure 1.2).

Neurons and astrocytes internally transfer information in different ways. Neurons mainly transfer electrical signals; and astrocytes propagate information by chemical waves. [42, 4, 3, 44, 45, 48, 46, 47, 6, 55, 17].

Inspired by the way in which glia astrocytes modulate synapses, researchers have developed a novel type of neural network called an *artificial neuron-glia network (ANGN)* [52, 1]. In ANGNs, each neuron is connected to one astrocyte cell, and activation (inactivation) of the neuron for a specific period of time will make the connected astrocyte active; as a result, the connected weights will be increased (or decreased) by a pre-defined factor [1]. Chapter 2 provides greater details on the

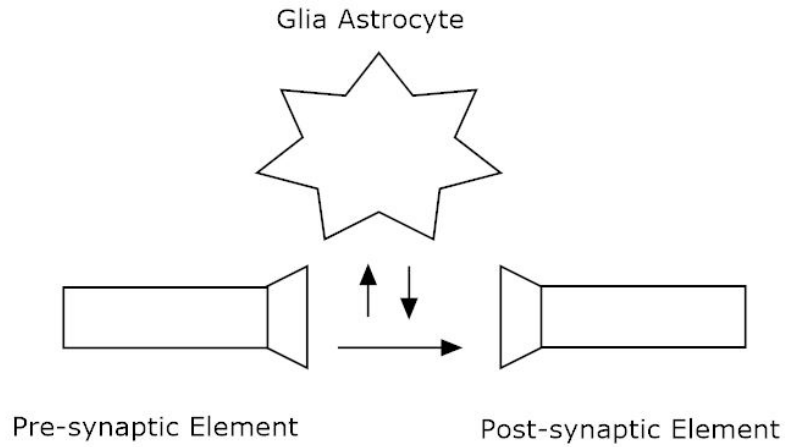


Figure 1.2: A representation of a tripartite synapse. The astrocyte (star-shaped cell) is able to modulate the synapse by releasing neuro transmitters (This figure is drawn based on the definition of a tripartite synapse in [68].)

architecture and algorithms of ANGNs.

From a physiological perspective, isolated astrocytes do not capture the whole story. Some recent studies have shown that similar to neurons, astrocytes are connected to each other, and exchange information through gap junctions [14, 49, 41, 50, 26]. Some scientists even believe that conscious processing is the result of the propagation of information in astrocyte networks. In particular, they believe that astrocyte networks act as a “Master Hubs” that integrate information patterns from different parts of the brain to produce conscious states [49, 53].

In continuation of published research on neuron-glia networks, we have done two separate implementations. Firstly, we combine ANGNs with adaptive neuro fuzzy inference systems (ANFIS). We investigate the performance of ANFIS on two sample problems with and without astrocytes. The results show a decrease of the overall error in the systems that contain astrocytes. Secondly, we design a new type of ANGNs in which artificial astrocyte networks (AANs) are connected to neurons rather than single isolated astrocytes. The networks of astrocytes are implemented on top of a multi-layer back propagation ANN, and the resulting network is tested for classifying two data sets. The results show that having an attached network of astrocytes on top of a typical neural network improves the performance.

This thesis is organized as follows. Chapter 2 provides some background information on physiological and artificial neurons, glia cells, neural and glia networks, and fuzzy inference systems. Chapter 3 introduces and evaluates the proposed system of adaptive neuro-glia fuzzy inference system (ANGFIS). Chapter 4 presents the new concept of artificial astrocyte networks (AANs), and evaluates the performance of this network in comparison to other types of artificial neural networks. Note that the material in Chapters 3 and 4 is partially published as [57], and [56]. Finally, Chapter 5 presents a summary of the research presented in this thesis and discusses some possible directions for future work.

Chapter 2

Background

This chapter is divided into five sections. Each section provides an introductory overview of a topic addressed in this thesis. The first section presents biological neurons and neural networks; the second section introduces biological glia cells; The third section provides artificial neural network, and the forth and fifth sections introduce adaptive neuro fuzzy inference systems and artificial neuron-glia networks respectively.

2.1 Biological Neurons and Neural Networks

The human brain is considered as one of the most complex systems in the universe [59]. Despite tremendous efforts to understand the mechanisms that underlie the brain's architecture and processes, many aspects are still poorly understood [43]. However, some fundamental information about the brain, such as the structure and functions of neurons and synapses have been discovered by neuroscientists in the last two centuries. This information has helped researchers to make simplified models of

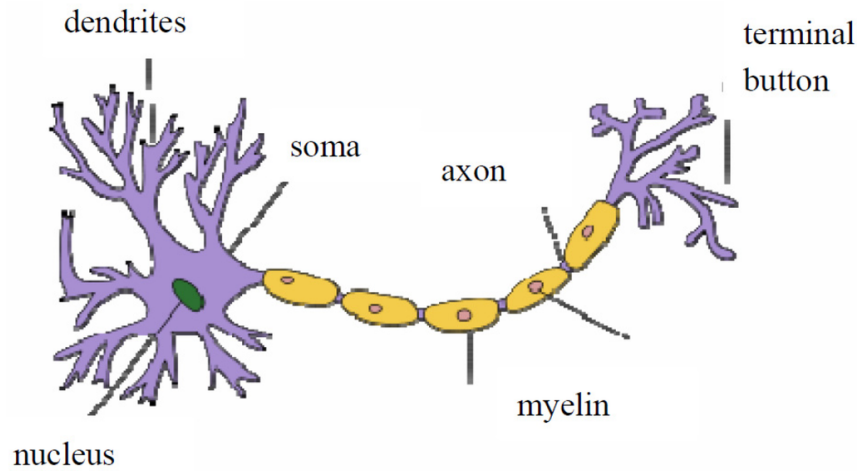


Figure 2.1: A biological neuron. The three main parts of the neuron (dendrites, soma, and axon), nucleus of the neuron, myelin sheath (yellow) that speeds up the electrical signals, and the axon’s terminal buttons can be seen in the figure (This figure is released under the GNU Free Documentation License.)

the brain [40].

Neurons or nerve cells are the basic building blocks of the brain. Neurons conduct electrical impulses, which result in processing information. As shown in Figure 2.1, a biological neuron consists of three main parts: dendrites, soma, and axon:

- Dendrites are considered as the inputs of a neuron¹ They receive electrical signals from other neurons and send them to the soma [43, 11, 5].
- Soma or cell body receives signals from dendrites. If the electrical charge pro-

¹In modern Neuroscience, dendrites are shown to be more than an input channel [8]. However, in this thesis, we only consider the ‘input’ characteristic of dendrites to remain consistent with the definition of artificial neural networks [11].

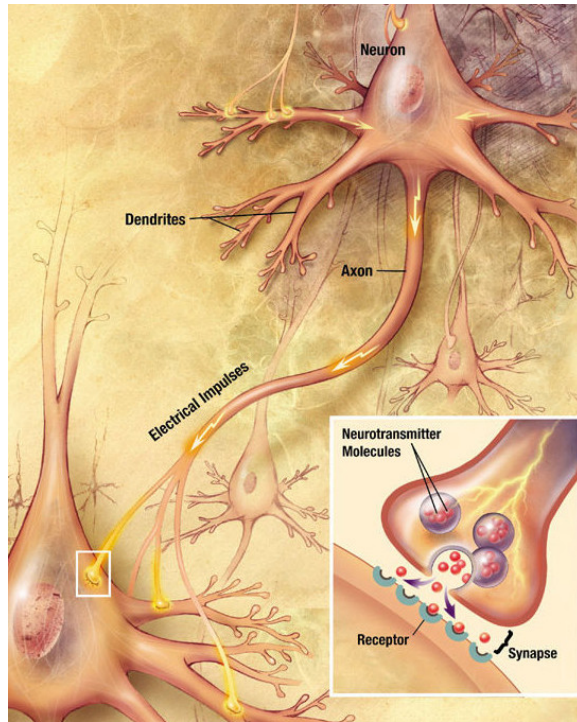


Figure 2.2: A biological synapse. A synapse is a junction between two neurons, consisting of a gap across which impulses pass by diffusion of neurotransmitters (This figure is reprinted from NIH, with permission from the publisher.)

duced by the received signals is sufficient, then the neuron fires; this means that the neuron sends a signal through its axon to all of the connected neurons. Most often, it is supposed that in any instant of time, a neuron either fires or not. This characteristic makes it possible to look at the output of a neuron as a binary function (fired or not fired.) However, in reality, the frequency of firing is different and can be seen as a signal of either greater or lesser magnitude. This corresponds to looking at discrete time steps and accumulating all of the activity (signal received or signals sent) at a particular point in time [11].

- Axons are the output units². They transfer the firing signal from the soma to neurons connected to axon terminals. Unlike dendrites, which are many short branches connected to a neuron's soma, neurons have only one axon that connects soma to other neurons. It should be mentioned that an axon may branch hundreds of times before it terminates. The transmission of a signal is completed by an action potential resulting from differential concentrations of ions, such as potassium, sodium and chloride on either side of an axon [43, 11].

A single neuron may be connected to many other neurons. The connections are made through synapses. Figure 2.2 shows a synapse. Communication between neurons is the result of the release of chemicals called neurotransmitters. The pre-synaptic neuron release neurotransmitters and the post-synaptic neuron subsequently absorbs these neurotransmitters [11, 43]. The process begins by the movement of an action potential through the axon from the pre-synaptic soma to its membrane, which is

²Similar to dendrites, axons can serve more as output channels; signals can reach the soma from the neuron's axon [65]. However, in order to be consistent with the assumptions in artificial neural networks [11], in this thesis, we consider axons only as output units.

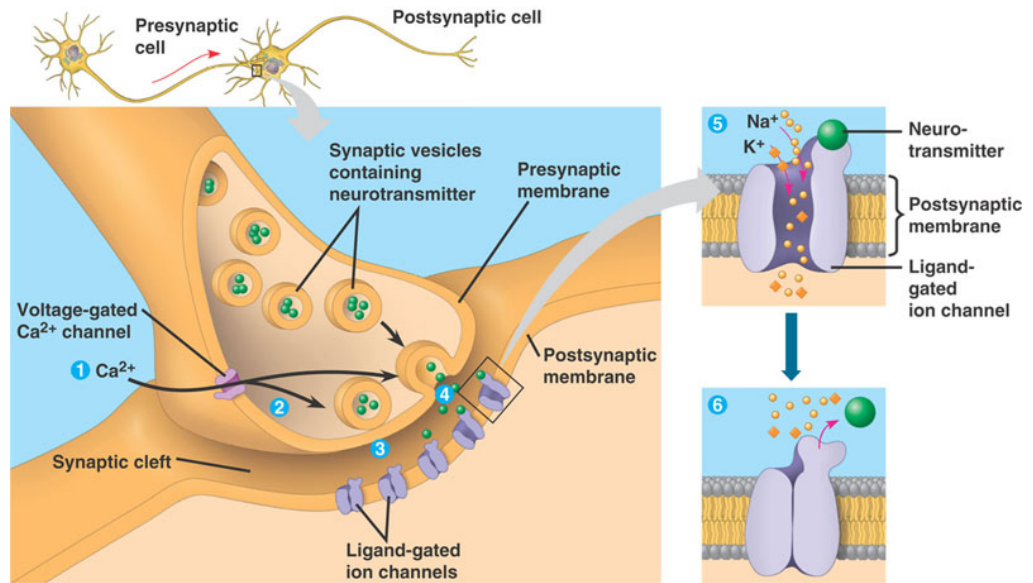


Figure 2.3: Transmission of a signal through a synapse (This figure is reprinted from [66], with permission from the publisher.)

located at the axon's terminal buttons. When the action potential arrives at the pre-synaptic membrane, it changes the permeability of the membrane and causes an influx of calcium ions. These calcium ions cause the vesicles containing neurotransmitters to fuse with the pre-synaptic membrane, resulting in the release of neurotransmitters into the synaptic cleft. If the receptors of the post-synaptic neuron receive enough neurotransmitters, an electrical signal will be sent through the dendrites of the post-synaptic neuron [43]. This process is illustrated in Figure 2.3.

2.2 Biological Glia Cells

The human brain consists of two main types of cells, neurons and glia cells. It is estimated that there are 10 to 50 times more glia cells than there are neurons in the brain [16]. Figure 2.4 shows a portion of the brain in which both neurons and glia

cells can be seen. Until two decades ago, it was widely believed that glia cells only performed passive functions and did not interfere with processing information [49].

New evidence supports the conception that a specific type of glia cells named astrocytes³ affect learning by modulating synapses. This has led to a new concept in neurophysiology, the tripartite synapse, which consists of three parts: pre-synaptic elements, post-synaptic elements, and surrounding astrocytes (Figure 2.5.) While neurons communicate by electrical signals, astrocytes use chemicals for propagating information; therefore, astrocytes are slower than neurons in processing information [42, 4, 3, 44, 45, 48, 46, 47, 6, 55, 17].

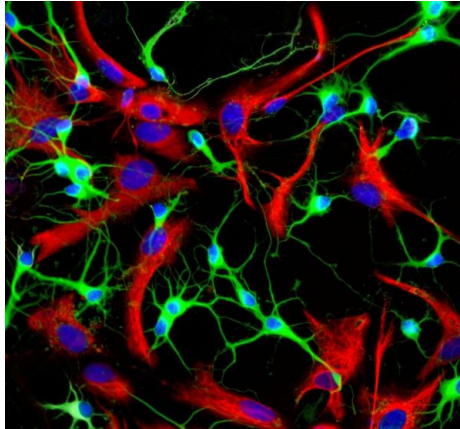


Figure 2.4: Neurons (green) and glia cells (red) in the brain (This figure is reprinted from Image: IN Cell Image Competition (© GE Healthcare - All rights reserved.), with permission from the publisher.)

Recent studies suggest that not only neurons, but also astrocytes are connected into networks. While neurons exchange information through synapses, gap junctions

³Astrocytes are also known as glia astrocytes. In this thesis we refer to this type of cells as astrocytes.

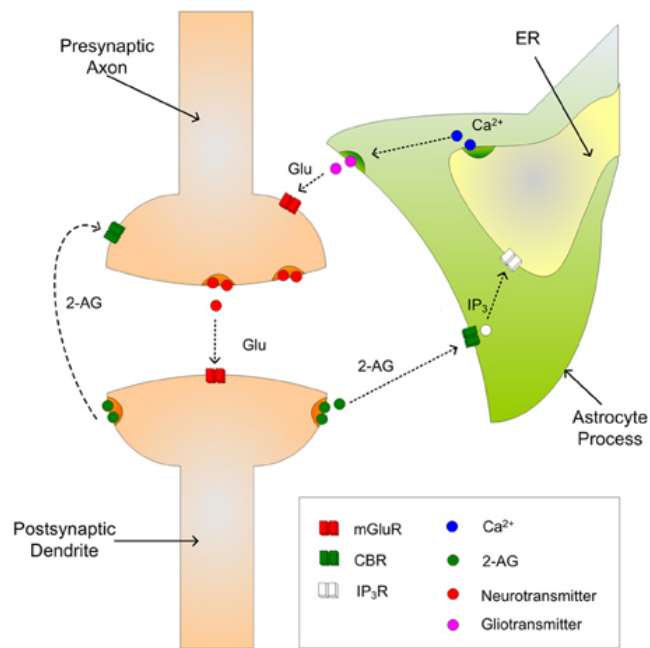


Figure 2.5: Tripartite synapse. The astrocyte is able to modulate the synapse by releasing transmitters (This figure is reprinted from [68], with permission from the publisher.)

are the path of communication for astrocytes [14, 49, 41, 50, 26]; however, the exact connections between astrocytes is not completely elucidated. Some other studies have taken a further step and assigned integration of data from different parts of the brain (which is in turn hypothesized to underlie conscious processing) to astrocyte networks [49, 53]. Pereira, Jr. and Furlan in their 2010 paper stated that

“the division of work in the brain is such that the astrocyte network conveys the feeling, while neural networks carry information about what happens.”

They believe consciousness is the result of integration of data by means of wavelike computing in the astrocytic networks [49]. Figure 2.6 illustrates connections between glia astrocyte in the human brain.

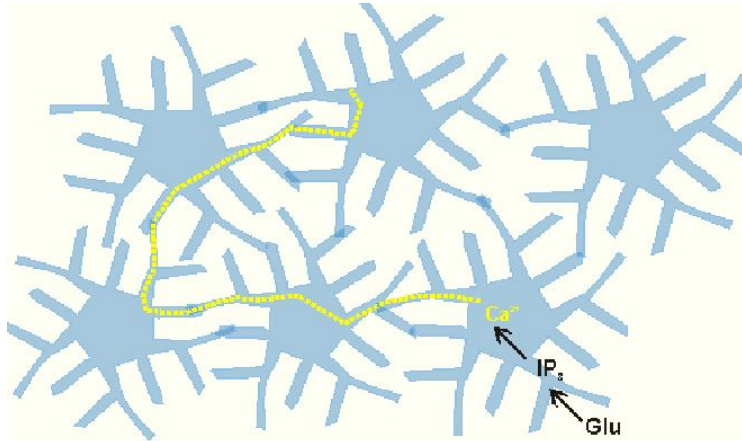


Figure 2.6: Connections between astrocytes in the brain (This figure is reprinted from Synapse Web, Kristen M. Harris, PI, <http://synapses.clm.utexas.edu/>, with permission from the publisher.)

2.3 Artificial Neural Networks

Artificial neural networks or AANs are information processing systems that are inspired by biological neural networks [11]. From 1943 when McCulloch and Pitts introduced the first simple ANNs until the present time, many different types of ANNs have been proposed. They are applied in solving problems in different fields, such as risk assessment, optimization, and pattern recognition [43]. Most AANs are designed based on the following assumptions [11]:

- Simple elements called neurons are responsible for processing information.
- The connections between neurons provide the possibility of transferring signals from one neuron to another.
- Each connection has an associated weight, which strengthens or weakens the transferred signal.

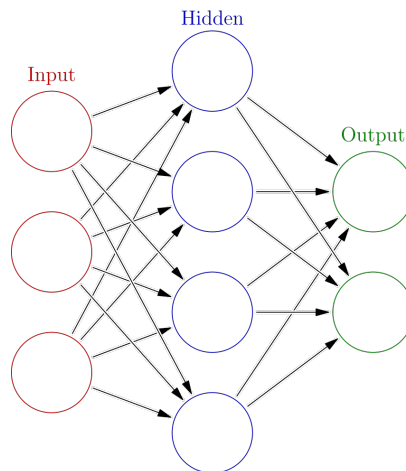


Figure 2.7: An example of an artificial neural network. Input (red), hidden (blue), and output (green) layers are shown in the network. In this network, the layers are fully connected to each other; it means, each neuron, if fires, will send a signal to all of the neurons of the next layer (This figure is reprinted from Glosser.ca, with permission from the publisher.)

- A neurons determines its output signal by calculating the output of its activation function on its net input (summation of weighted input signals.)

An artificial neural network is specified as a collection of neurons which serve as parallel processors connected together in the form of a directed graph. Figure 2.7 shows a typical ANN. The number of neurons and connections between them are determined based on the problem that the network solves [12].

More precisely, we can define an artificial neural network by the following components [11]:

1. Architecture: the pattern of connections between neurons.

2. Activation function: the function that determines the output of a neuron based on its net input.
3. Learning or training algorithm: a method that determines how to change the weights on the connections.

Each of these components is described in more details below:

2.3.1 Architecture

For designing an ANN's architecture, it is more convenient to arrange neurons into layers. Most neural networks have an input layer. Each neuron in the input layer receives an external input signal, and send it to the connected neurons. If we have only two layers, input and output, then the network is called a single-layer net [12, 11]. Usually, single-layer nets can solve relatively less complicated problems in comparison to multi-layer networks. Multi-layer networks have one or more layers between input and output layer, named hidden layers. These networks have the ability to save important information in the weights connected to hidden layers, and use them in solving more complicated problems; however training is more difficult in multi-layer networks rather than the single-layer nets [11]. The connections between neurons can be feed-forward or recurrent. In feed-forward nets the signal flows from the first layer to the last layer in a forward direction. However, in recurrent nets, the signals from a neuron can come back to itself or to the neurons in the same or earlier layers, allowing the connections in the network to make closed loops [11].

2.3.2 Activation function

As stated earlier, an artificial neuron is responsible for collecting its weighted input signals and producing an output. An activation function is used for calculating the output based on the received signals. Typically, all of the neurons in the network use the same activation function. The following are commonly used as activation functions (In the following equations, x is the overall input to a neuron):

- Identity function:

$$f(x) = x, \text{ for all } x. \quad (2.1)$$

- Binary step function:

$$f(x) = \begin{cases} 1, & \text{if } x \geq \theta. \\ 0, & \text{if } x < \theta. \end{cases} \quad (2.2)$$

- Binary sigmoid:

$$f(x) = \frac{1}{1 + \exp(-\sigma x)} \quad (2.3)$$

- Bipolar sigmoid:

$$f(x) = \frac{2}{1 + \exp(-\sigma x)} - 1 \quad (2.4)$$

2.3.3 Training Algorithm

Given an architecture and its activation functions, we need to define the training algorithm of a network. Training algorithms are typically divided into supervised and

unsupervised algorithms⁴. In supervised training, a sequence of training vectors, or patterns with an associated target vectors is presented to the ANN [11]. Presenting a training vector will produce an output vector, and based on the difference between these output and the associated target vector, an error will be calculated and the weights will be modified in a way to reduce the error. Backpropagation is a well-known supervised algorithm [43, 11, 5]. In unsupervised training, we do not need a training session prior to using the network because in some cases we do not know of the response we should expect from the neural network. The neural network reorganizes itself to decides what output is best for a given input. There are two main types of unsupervised learning, reinforcement and competitive learning. In reinforcement learning, the network tries to modify the weights in order to produce the maximum reproduction of the output. Hebbian learning is one of the well-know reinforcement algorithms, which is explained in more detail at the following paragraph. In competitive learning, the neurons compete with each other by increasing and decreasing their weights until finally one node wins and this node will represent the answer [11, 54].

Hebb's rule (see Algorithm 1) is a physiology-based theory proposed by Donald Hebb in 1949. It describes how learning happens in neural networks, and provides an algorithm to update weight of neuronal connections within a neural network. It states that the weights connections between neurons is a function of neuronal activity [28]. This means that if a pre-synaptic neuron repeatedly sends a signal to a post-synaptic neuron, then the synapse between these neurons will become stronger and increase the strength of the signal in future transmissions. Mathematically, this is shown in

⁴There are training algorithms which are neither supervised nor unsupervised [11], but in this thesis, these types of algorithms are not considered.

Equation 2.5 in Algorithm 1 [43, 11, 5].

In backpropagation algorithm (see Algorithm 2), the term “backpropagation” is an abbreviation for “backward propagation of errors.” Backpropagation consists of two phases, forward and backward propagation. In the forward propagation phase, the training input propagates through the network and generates an output. In the backward propagation phase, the difference (delta) between the current output and the desired output is determined. Then, for each weight, the gradient of the weights, which is the multiplication of the delta and input activation, is calculated. Finally, a ratio of the gradient will be subtracted from the current weights. This ratio, which is called the learning rate, determines the speed and accuracy of training. Usually, the learning rate is a number between 0 and 1 [43, 11, 5].

Algorithm 1 Hebb Training Algorithm

INPUT

- x_j : the output of the pre-synaptic neuron.
- x_i : the output of the post-synaptic neuron.
- α : The learning rate, which adjusts the speed of learning.

WEIGHT MODIFICATION AFTER EACH ITERATION

$$\Delta W_{ij}(t) = \alpha x_j x_i \tag{2.5}$$

where $\Delta W_{ij}(t)$ is the change in the weight of the synapse between neurons i and j at iteration t .

Algorithm 2 Backpropagation learning algorithm.

The activation function is assumed to be a sigmoid function.

Initialize all weights to small random numbers.

Until the error is less than a threshold, **Do**

for each training example **do**

FORWARD PASS

Input the training example to the network and compute the network output.

BACKWARD PASS: CALCULATE THE ERROR OF OUTPUT UNITS

For each output unit k :

$$\delta_k = o_k(1 - o_k)(t_k - o_k) \quad (2.6)$$

where o_k is the output, and t_k is the desired output for neuron k

BACKWARD PASS: CALCULATE THE ERROR OF HIDDEN UNITS

For each hidden unit h :

$$\delta_h = o_h(1 - o_h)\left(\sum_k w_{hk}\delta_k\right) \quad (2.7)$$

where o_h is the output of neuron h

BACKWARD PASS: UPDATE EACH WEIGHT w_{ij} :

For each neuron:

$$\Delta W_{ij} = \alpha \delta_j x_i \quad (2.8)$$

where W_{ij} represents the weight between neuron i and j , and α

is the learning rate, and x_i is the input of the neuron i .

end for

2.4 Adaptive Neuro-Fuzzy Inference Systems

Conventional mathematical tools such as differential equations are not always beneficial in modeling uncertain or ill-defined problems. For this reason, tools like fuzzy inference systems have been designed to implement qualitative knowledge rather than precise quantitative analyses. Adaptive Neuro-fuzzy Inference Systems (ANFIS) are a specific type of fuzzy inference systems that are able to adjust their own parameters in order to generate the stipulated input-output pairs [21]. In the remainder of this section, first we introduce fuzzy sets, fuzzy if-then rules and fuzzy inference systems, and then we present the architecture and algorithms of ANFIS.

2.4.1 Fuzzy sets, if-then rules, and inference systems

In the classical set theory, the membership is defined precisely, an object is either belongs or does not belong to a set; However, in reality the classes of object might or might not precisely define criteria of membership; for example, we can clearly define the class of real numbers which are greater than 1 but we cannot precisely define the class of tall people. The human thinking process uses imprecise definitions of classes to recognize patterns, communicate and do abstraction [72, 73]. Introduced by Zadeh in 1965, fuzzy sets were to model these imprecise definitions. The objects in a fuzzy set are described by a continuum of grades of membership. These grades of membership are numbers between 0 and 1, and they are assigned by the membership function of the fuzzy set [72].

A more formal definition of fuzzy sets, which is presented by Zadeh in [72, p. 339]:

“Let X be a space of objects, with a generic element of X denoted

by x . Thus, $X = \{x\}$. A fuzzy set (class) A in X is characterized by a membership function $f_A(x)$, which associates with each object in X a real number in the interval $[0, 1]$, with the value of $f_A(x)$ at x representing the grade of membership of x in A . Thus the nearer the value of $f_A(x)$ to unity, the higher the grade of membership of x in A . When A is a set in the ordinary sense of the term, its membership function can take on only two values 0 and 1, with $f_A(x) = 1$ or $f_A(x) = 0$, according as x does or does not belong to A .”

For example, a fuzzy set can be described as

$$X = \{1, 2, 5\}, f_A(1) = 0.1, f_A(2) = 0.35, f_A(5) = 1.$$

As stated earlier, for modeling the fuzziness of human thinking and behavior, we need approaches that avoid precise mathematical formalisms. We need some degree of tolerance to imprecision and partial truth. The approach of interest in this thesis is systems that benefit from fuzzy if-then rules. Regular if-then rule consist of a premise (IF) and a conclusion (THEN):

$$\text{IF } m \text{ is } A \text{ THEN } n \text{ is } B.$$

Fuzzy if-then rules are the same except that variables m and n can be linguistic terms that are represented by fuzzy variables (objects) [73]. An example of a fuzzy if-then rule is [22]:

$$\text{IF pressure is high and temperature is low THEN volume is small.}$$

In this example, “high”, “low” and “small” are linguistic terms that can be presented by fuzzy variables, and characterized by appropriate membership functions. A fuzzy

if-then rule that only allows the premise to involve fuzzy sets is called *Takagi and Sugeno fuzzy if-then rule* [62, 21].

A system that applies fuzzy if-then rules is known as a *fuzzy inference system*. A fuzzy inference system is composed of five functional units [21]:

1. Rule base unit, which consists of fuzzy if-then rules;
2. Database unit, which defines the membership function;
3. Decision-making unit, which applies the inference operations on the rules;
4. Fuzzification unit, which transforms the crisp inputs into linguistic terms (fuzzy variables); and
5. Defuzzification unit, which transforms the fuzzy results into crisp output.

Figure 2.8 illustrates the components of a fuzzy inference system.

A fuzzy inference system starts with fuzzifying the crisp inputs into membership degrees. The next unit, decision maker, evaluates the fuzzified inputs to determine the strength of the rule's "If" parts, and infers the consequences of the rules. The final part, the defuzzification unit, transform the fuzzy results into crisp data.

2.4.2 ANFIS architecture and algorithms

An ANFIS which can stand for *Adaptive Network-Based Fuzzy Inference System* [21] or *Adaptive Neuro-Fuzzy Inference System* [15], is a fuzzy inference system that applies ANNs to data samples to determine properties of these samples [15, 21, 22]. In

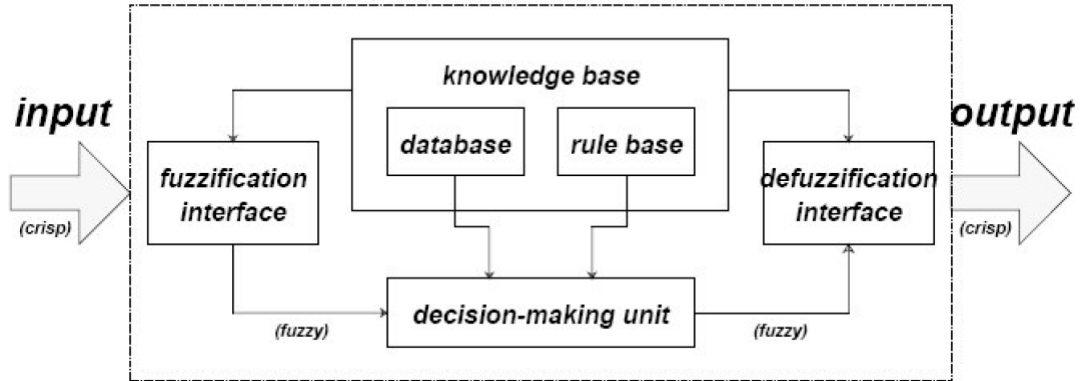


Figure 2.8: Components of a Fuzzy Inference System (©1993 IEEE. This figure is reprinted from [21], with permission from the publisher.)

other words, an ANFIS learns features in a data set and adjusts membership parameters according to a given error criterion. ANFISs essentially use the verbal power⁵ of fuzzy systems in addition to the numeric power of neural networks [10]. Different types of ANFIS have been introduced and have been successfully used in modeling nonlinear functions [36, 63, 23, 21, 15, 20]. The ANFIS we have studied in this thesis is based on the Takagi-Sugeno model [21].

The architecture of ANFISs are consistent with fuzzy inference systems. Moreover, this architecture is a multilayer feed-forward network, in that each node in an ANFIS has its own activation function and related parameters. Unlike typical neural networks, no weights are associated with the links between nodes; however, there are

⁵By verbal power, we mean the ability to convert verbal descriptions into well-defined mathematical formulas [32].

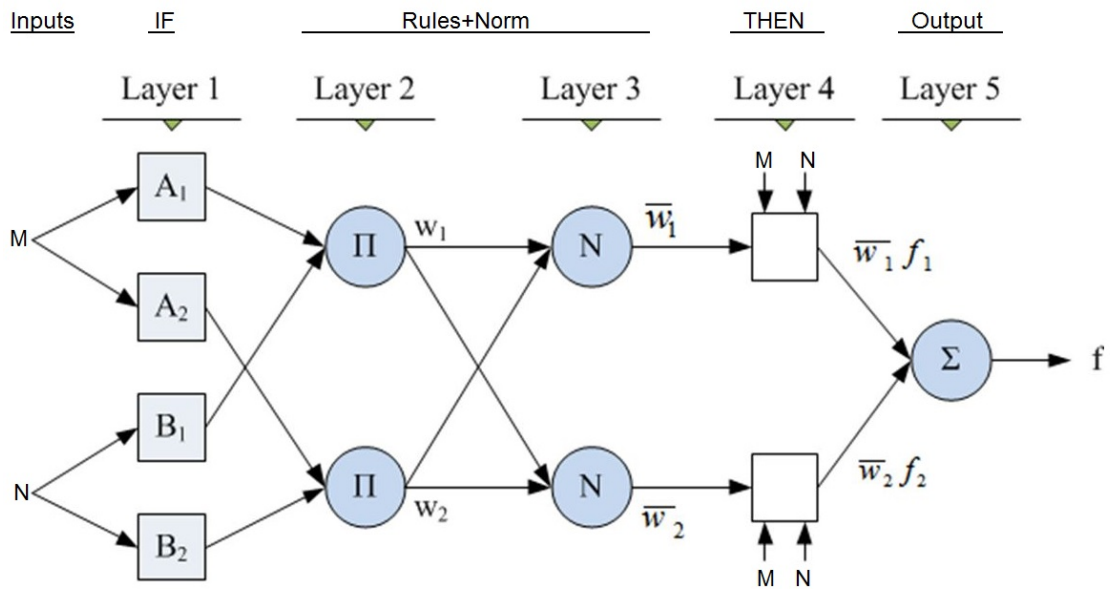


Figure 2.9: ANFIS Architecture (This figure is adapted from [13], with permission from InTech publisher.)

parameters associated with some nodes in an ANFIS that have a similar role to the weights of typical neural networks. These parameters are modified during training to reduce the total error.

Figure 2.9 illustrates the architecture of an ANFIS. Layers 1 and 5 perform fuzzification and defuzzification respectively, and rest of the layers implement fuzzy if-then rules.

The steps of fuzzy reasoning performed by an ANFIS can be stated in four steps

[21, 22]:

1. Compare the input variables with the membership function on the premise part to obtain the membership values (or compatibility measures) of each linguistic label (this step is often called fuzzification;)
2. Combine (through a specific T-norm operator, usually multiplication or minimum.) the membership values on the premise part to get firing strength (weights) of each rule;
3. Generate the qualified consequent (either fuzzy or crisp) of each rule depending on the firing strength; and
4. Aggregate the qualified consequent to produce a crisp output (this step is called defuzzification)

The following example provides a more detailed explanation on how the architecture and algorithm of ANFIS works: assume we have one output f and two inputs m and n ; also, we have two Takagi and Sugeno fuzzy if-then rules:

- Rule 1: If (m is A_1 and n is B_1) then $f_1 = p_1m + q_1n + r_1$
- Rule 2: If (m is A_2 and n is B_2) then $f_2 = p_2m + q_2n + r_2$

where the parameters p_1, p_2, q_1, q_2, r_1 and r_2 are linear, and A_1, A_2, B_1 and B_2 are nonlinear [30, 21].

To design an ANFIS corresponding to these parameters and rules, we need the architecture shown in Figure 2.9. Similar to other ANFIS architectures, there are 5 layers.

- Layer 1 considers the “if” parts of the given if-then rules: “If m is A_1 or A_2 ” and “If n is B_1 and B_2 .” This layer receives m and n as input, and determines to what degree m belongs to A_1 and A_2 and n belongs to B_1 and B_2 . The activation function of this layer can be expressed as:

$$O_{1i} = \mu_{A_i}(m) \text{ for } i \in 1, 2 \quad (2.9)$$

$$O_{1j} = \mu_{B_j}(n) \text{ for } j \in 1, 2 \quad (2.10)$$

where O_{1i} is the output function for node A_i , O_{1j} is the output function for node B_j in layer 1, and μ_{A_i} and μ_{B_j} denote the membership functions [30, 21].

- Informally, Layer 2 determines the strength of the “If” part by multiplying the outputs of Layer 1. The number of nodes in Layer 2 and the links between Layer 1 and Layer 2 are determined by the rules. For example, Rule 1 presents “If (m is A_1 and n is B_1)”; to implement this rule, we make links from A_1 and B_1 to the first node in Layer 2 (note that each node in Layer 2 represent a specific rule, where the first node represents the first rule, and so on). To implement “If (m is A_2 and n is B_2)” in Rule 2, we link A_2 and B_2 to the second node in Layer 2. The activation function of the nodes in Layer 2 is as follows:

$$O_{2i} = w_i = \mu_{A_i}(m) * \mu_{B_i}(n) \text{ for } i \in 1, 2 \quad (2.11)$$

where, O_{2i} denotes the output of Layer 2, node i [30, 21].

- The third layer normalizes the outputs from Layer 2. The activation function of this layer is

$$O_{3i} = \bar{w}_i = \frac{w_i}{w_1 + w_2} \text{ for } i \in 1, 2 \quad (2.12)$$

where, O_{3i} denotes the output of node i in Layer 3 [30, 21].

- The fourth layer performs the “Then” part of the rules. The nodes in this layer in addition to the outputs of Layer 3, receive the original inputs (m and n), and then by applying the activation function on these parameters, produce their results. The activation function in this layer uses three parameters, p_i , q_i , and r_i , and calculate the output as

$$O_{4,i} = \bar{w}_i f_i = \bar{w}_i (p_i m + q_i n + r_i) \text{ for } i \in 1, 2 \quad (2.13)$$

where, $O_{4,i}$ denotes the output of node i in Layer 4 [30, 21].

- Layer 5 is the output layer. It integrates the outputs from Layer 4. The activation function of this node is

$$O_5 = \frac{\sum_i \bar{w}_i f_i}{\sum_i \bar{w}_i} \quad (2.14)$$

where O_5 denotes the output of the node in layer 5 [30, 21].

The learning algorithm of ANFISs is similar to the backpropagation algorithm (see Section 2.3.3), in that there is a feed-forward flow of data followed by an update of the parameters. For updating the parameters the followings formulas will be used. Assume we have a training data set that has P elements. The overall error is

calculated as

$$E = \sum_{p=1}^P E_p, \quad (2.15)$$

where, E_p is the error for the p th ($1 \leq p \leq P$) element in the data set is calculated as

$$E_p = \sum_{m=1}^{|L|} (T_{m,p} - O_{m,p}^L)^2, \quad (2.16)$$

where, $T_{m,p}$ is the m th component of the p th desired output vector and $O_{m,p}^L$ is the m th component of actual output vector produced by presenting the p th input vector.

Given the above, each parameter in the network will be updated as

$$\Delta(param) = -\alpha \frac{\delta E}{\delta(param)}, \quad (2.17)$$

where $param$ presents the parameter studied and α is the learning rate [30, 21].

2.5 Artificial Neuron-Glia Networks

Inspired by the concept of tri-partite synapse, Porto in 2004 developed a novel type of neural networks called an *Artificial Neuron-Glia Network (ANGN)* [51]. It was successfully implemented in different ANN architectures [56, 25, 1, 18], and successfully tested on real world problems [25, 52]. These tests showed that adding artificial astrocytes to typical ANNs improves performance of the network, but the degree of success is highly dependent on the complexity of the problem [52]. The architecture of an ANGN can be described as an extension of a typical ANN. ANGNs include a novel type of processing element, the artificial astrocyte, and each neuron is associated with one astrocyte. Figure 2.10 shows the architecture of an ANGN.

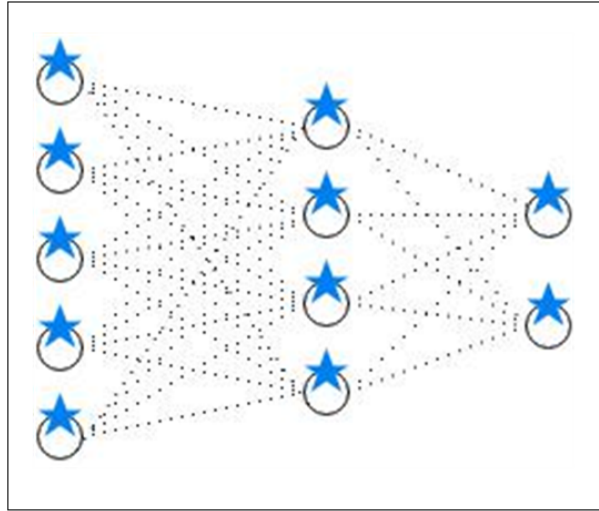


Figure 2.10: An example of an Artificial Neuron-glia Network. Each neuron (circles) are associated with one glia astrocyte (blue stars) (This figure is adapted from [1], with permission from the publisher.)

The exact biological interactions between neurons and astrocytes have not been completely elucidated; therefore, different algorithms for describing the behavior of artificial astrocytes have been proposed. However, the key concept underlying all of these algorithms is the same: the lower processing speed in glia astrocytes in comparison to neurons leads to the decay of astrocyte activation [52, 1, 19, 18]. One of the models proposed by Porto [1] for modeling astrocytes is described in the following paragraphs.

An astrocyte is defined as a set of parameters and a set of functions. The pa-

parameters are $k \in \mathbb{N} \setminus 0$, $\theta \in 1, \dots, k$, $a, b \in [0, 1]$ and $ft \in \mathbb{R}$. The activity of the corresponding astrocyte to each neuron will be represented by the following functions:

- $U : \mathbb{R} \rightarrow \mathbb{Z}$, determines whether the corresponded neuron to the astrocyte is fired or not, and is defined as follows:

$$U(x) = \begin{cases} -1, & \text{if } x \leq ft. \\ 1, & \text{if } x > ft. \end{cases} \quad (2.18)$$

where x is the output of the corresponding neuron, ft is the threshold of firing, and the output of U indicates whether the neuron has fired ($U(x) = 1$) or not ($U(x) = -1$).

- $r : \mathbb{N} \rightarrow [-\theta, +\theta]$, where r represents how many times the neuron was fired in the k consecutive cycles. The output of $-\theta$ or $+\theta$ results in the activation of the astrocyte. $-\theta$ means that in the the k preceding cycles, the corresponded neuron did not fire for θ times, and $+\theta$ represents the firing of the neuron for θ times.

The associated weights of an active astrocytes⁶ will be modified as follows:

$$w(t + \Delta t) = w(t) + \Delta w(t) \quad (2.19)$$

where $\Delta w(t)$ is defined as

$$\Delta w(t) = |w(t)|z(t) \quad (2.20)$$

⁶The associated weights of an astrocyte are the weights connecting the astrocyte's associated neuron and the neurons in the next layer.

and function $z : \mathbb{N} \setminus 0 \rightarrow \mathbb{R}$ indicates the percentage of the change of the weights based on the astrocyte activation⁷. Figure 2.11 shows how an astrocyte can modify the weights of a neuron.

⁷In this thesis, the output of the z function will be a if the astrocyte is positively activated and b if it is negatively activated. In other words if output of the r function is greater than θ then the output of z will be a , and if the output of the r function is less than θ then the output of z will be b .

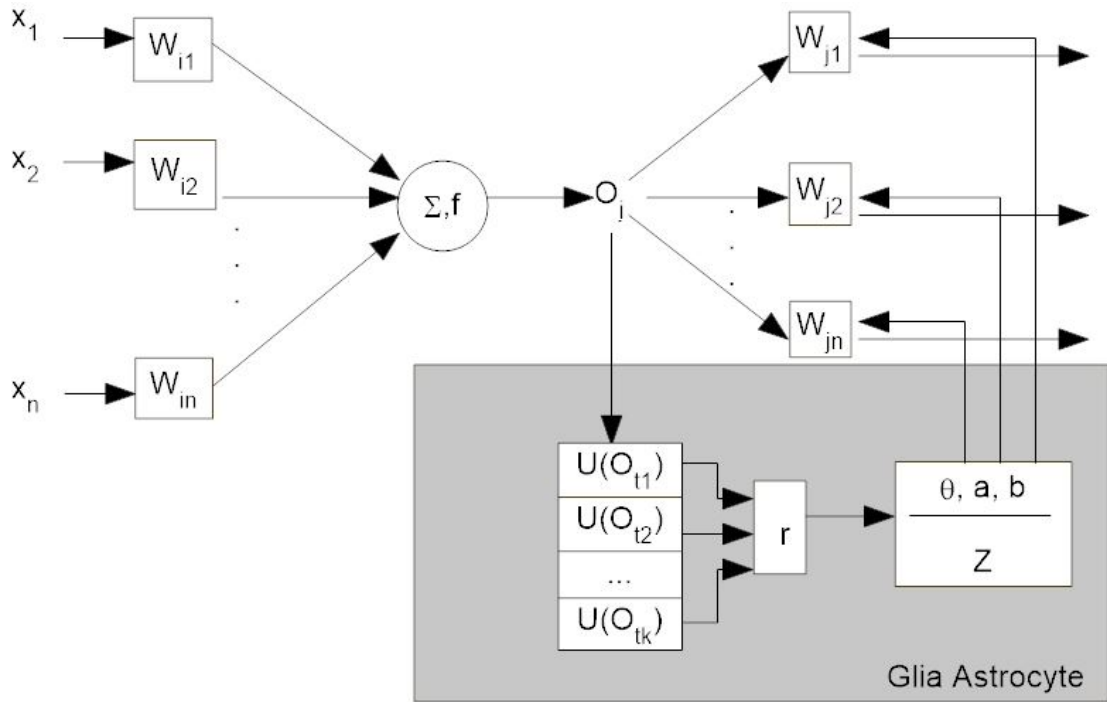


Figure 2.11: An artificial neuron and its associated astrocyte (grey box). The output of the neuron j , O_j is the input of its augmented glia astrocyte. The U function determines the strength of O_j (neuron has fired or not), and the r function counts how many times the neuron has fired or has not fired in every k iterations. The Z function then compares the output of r with θ ; if this output was more than θ , then the weights associated with the current neuron and the neurons in the next layer will be increased by the percentage a , and if this output is r is less than $-\theta$ then the weights will be decreased by the percentage b (This figure is adapted from [1], with permission from the publisher.)

Chapter 3

Adaptive Neuro-glia Fuzzy Inference System (ANGFIS)

Adaptive neuro fuzzy inference systems (ANFIS) are frameworks that integrates and benefits from both fuzzy principles and artificial neural networks (see Section 2.4.2). The underlying neural networks in an ANFIS help this system to learn and adjust the parameters of its fuzzy if-then rules, and give ANFIS the ability to approximate nonlinear functions [21]. In this chapter, we propose a specific type of ANFIS, which benefits from isolated artificial astrocyte elements alongside using fuzzy concepts and artificial neural networks.

This chapter is organized into three sections. Section 3.1.1 introduces the proposed model of adaptive neuro-glia fuzzy inference systems (ANGFIS). Section 3.2 evaluates ANGFIS, and provides a comparison between the performance of ANGFIS and ANFIS on two sample problems. Finally, Section 3.3 presents a discussion on the ANGFIS performance.

3.1 Architecture and Learning Algorithm

This section introduces the architecture and the learning algorithm of ANGFIS, which are presented in Sections 3.1.1, and 3.1.2 respectively.

3.1.1 Architecture

ANGFIS can be considered as a specific type of Artificial Neuron-glia Networks (ANGNs). Similar to the architecture of all ANGNs, ANGFIS benefits from astrocytes, which are associated with its critical nodes. In more detail, we can describe the architecture of ANGFIS as an ANFIS¹ augmented with astrocytes in its *4th* layer. Figure 3.1 illustrates the architecture of an ANGFIS. The reason for choosing the *4th* layer for augmenting astrocytes is the role of this layer in modifying parameters as explained in Equation 2.13. The nodes in other layers do not apply one or more parameters in their activation functions; therefore, astrocytes are not helpful in those layers.

3.1.2 Learning Algorithm

An ANGFIS applies the same activation functions as those used by an ANFIS. Detailed information on these activation functions is available in Section 2.4.2. Similar to ANGNs, the learning algorithm of ANGFISs is divided into two phases:

1. The first phase applies the learning algorithm for ANFIS as presented in Section

¹More details about the architecture of and learning algorithm for ANFIS are given in Section 2.4.2.

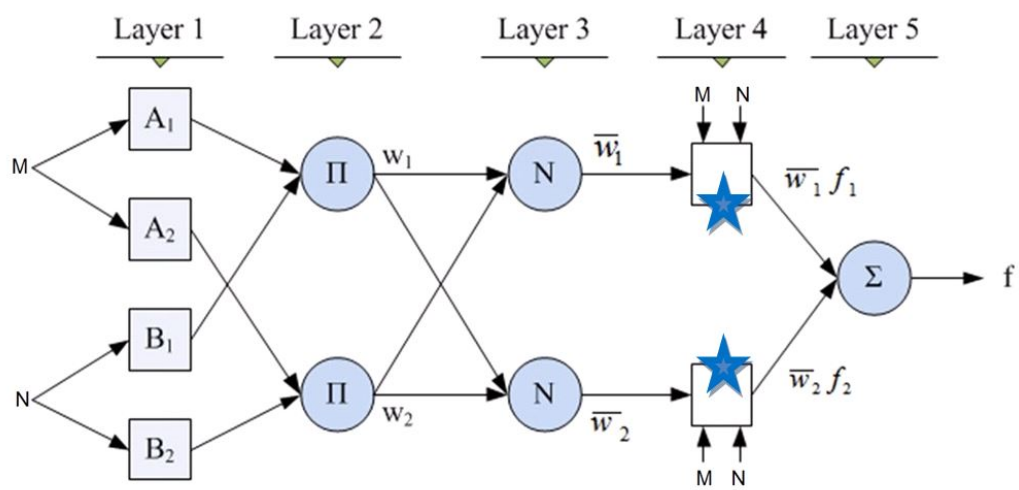


Figure 3.1: Architecture of an ANGFIS. An ANGFIS is a specific type of ANGNs, which is designed based on the architecture of ANFIS. As can be seen, the 4th layer is augmented with astrocytes (stars) (This figure is adapted from [13], with permission from the publisher.)

2.4.2, and updates the parameters at the end of each cycle².

2. The second phase is the algorithm for astrocytes' learning, and is independent from the first phase. Astrocytes receive outputs of their corresponding nodes, and based on the activity of the nodes, independently increase or decrease the parameters by some pre-defined percentages. Section 2.5 provides a detailed explanation of the algorithm of each astrocyte.

3.2 Performance

In this section, we investigate the performance of ANGFIS on two problems; and study how isolated astrocytes in ANGFIS can reduce overall output errors. More precisely, for testing the performance of ANGFIS, we answer the following question:

Are there parameter values for astrocytes of ANGFIS that increase the performance of ANGFIS in comparison to ANFIS?

The implementation described here³ aimed to test the performance of the proposed ANGFIS and to compare it with ANFIS⁴. ANFIS use a back propagation algorithm for training as explained in Section 2.4.2. The architecture features, such as number of

²A cycle is defined as presenting all training data set to the system.

³The implemented codes are available at the supplementary materials of this thesis.

⁴The performance of ANFIS was already evaluated by Jang in 1993 [21]; we will use the same programming codes to do our implementations.

rules, should be decided by an expert; however, in this thesis, we have used the same number of rules, empirically⁵ determined by Jang for studying the same problems⁶ [21]. The training and testing of ANGFIS were implemented on a system with a 3 GHz processor and 3 GB of RAM using the Ubuntu operating system, C language source code and the GNU compiler; ANGFIS were implemented by modifying the previous available codes of ANFIS used in [21].

The performance is measured by using Root Mean Square Error (RMSE.) The use of RMSE is very common and it is an excellent metric for measuring numerical errors [9]. RMSE is shown in the following formula:

$$RMSE = \sqrt{\frac{1}{n} \sum_{t=1}^n (o_r(t) - o_d(t))^2}, \quad (3.1)$$

where, n is the total number of data, $o_r(t)$ represents the real output of the system for the data instance t , and $o_d(t)$ is the desired output of the system for the data instance t .

We implement ANGFIS to solve these two sample problems below:

1. The first problem is modeling a three-input nonlinear function. The following equation provides the training data [21]:

$$output = (1 + x^{0.5} + y^{-1} + z^{-1.5})^2 \quad (3.2)$$

This problem has been used by researchers such as Jang [21], Takagi et al. [61], and Sugeno et al. [60] to verify their proposed approaches.

⁵In this thesis an empirical method is equivalent to a trial and error method.

⁶Similar to the problem of choosing number of nodes in the hidden layer of ANNs, there is no specific rule for choosing number of rules in an ANFIS [21].

2. The second problem aims to identify nonlinear components in a control system. The nonlinear $F(\cdot)$ function in the following equations is implemented by ANGFIS where parameters are updated in each time index [21].

$$y(k+1) = 0.3y(k) + 0.6y(k-1) + F(u(k)), \quad (3.3)$$

where k represents the time index in the control system, $y(k)$ is output, $u(k)$ is input. This problem has been used by different researchers, such as Jang [21], and Narendra et al. [37] to verify their proposed approaches.

The ANGFIS designed for the first problem has the general five-layer architecture of ANFIS (see Figure 3.1). The first (input) layer of ANGFIS has three nodes, each of which receives one input of the problem instance. The second (membership) layer has 6 membership functions; the number of nodes in this layer has been empirically determined by Jang [21] for solving a similar problem by ANFIS. Both of Layers 3 and 4 contain 8 nodes, where each node represents a rule; similarly, the number of rules has been adapted from [21]. Finally, the fifth layer integrates the output into one number, and provide us with the final output. For training and testing ANGFIS, we have used 216 training samples uniformly selected from the input range $[1, 6] \times [1, 6] \times [1, 6]$ and 125 testing data in the range of $[1.5, 5.5] \times [1.5, 5.5]$. These data also were used by Jang for investigating the performance of ANFIS [21]. Each node in the 4th layer is associated with one astrocyte and the astrocyte parameters were determined empirically (see Table 3.1.) Detailed information about the astrocyte parameters is available in Section 2.5.

Parameters	k	θ	a	b	ft
Problem 1	200	175	1.01	0.99	4
Problem 2	15	12	1.01	0.95	0

Table 3.1: Astrocyte parameters used for implementing ANGFIS. These parameters are determined empirically (See Footnote 5.)

The ANGFIS designed for the second problem also has the general five-layer architecture of ANFIS. The first (input) layer of this ANGFIS has one node, which receives the input of the problem instances. The second (membership) layer has seven membership functions; once again, the number of nodes in this layer has been empirically determined by Jang [21] for solving a similar problem by ANFIS. Both of Layers 3 and 4 contain 7 nodes, where each node presents a rule; similarly, the number of rules has been adapted from [21]. Finally, the fifth layer integrates the output into one number, and provide us with the final output. For training and testing this ANGFIS, 75 training samples were selected from the input range $[0.1, 0.6]$ and 25 testing data in the range of $[0.1, 0.6]$ were used. Each node in Layer 4 is associated with one astrocyte and the astrocyte parameters were determined empirically (see Table 3.1.)

Table 3.2 provides the final results of our implementation of ANFIS and ANGFIS for Problems 1 and Problem 2. We have applied RMSE to measure the error. As can be seen, the produced error by ANGFIS is less than the error observed for ANFIS.

	Problem 1	Problem 2
ANFIS (Training Data set)	0.605402	0.168400
ANGFIS (Training Data set)	0.605370	0.057043
ANFIS (Testing Data set)	0.831868	0.258672
ANGFIS (Testing Data set)	0.823220	0.128272

Table 3.2: The RMSE error for ANGFIS and ANFIS.

3.3 Discussion

As is shown in Tables 3.2 and 3.1, by choosing appropriate parameters, the performance of ANGFIS can be higher than the performance of ANFIS. The architecture, activation functions, training algorithm, and also the problems and training and testing data-sets are similar in both implemented ANFIS and ANGFIS; the only difference is the inclusion of astrocytes in ANGFIS. It means, this difference solely is the result of inclusion of astrocytes and it can be interpreted as the contribution to performance made by astrocytes.

Porto in 2011 showed that the inclusion of astrocytes in a feed-forward neural network (ANGNs) can improve the performance of the network [52] (see Section 2.5). Here we show that the inclusion of astrocytes in a different architecture of neural networks, ANFIS, can also reduce the error and enhance the performance. The higher performance achieved by the inclusion of astrocytes can be explained in two ways. Firstly, inclusion of astrocytes and modeling tripartite synapses provides us with a more accurate model of the human brain, which is known to be a powerful information processing system. Secondly, previous research shown that in general,

noise and chaotic behavior can help algorithms to escape local minima [58, 67], and in particular in neural networks it is known that injecting noise during training can increase the overall performance of the network [35, 2, 75, 29]; here, astrocytes can be considered as a source of noise in the ANNs that improves performance ⁷.

For the purpose of further improving the performance of ANGFIS, different modifications in the architecture and algorithms of astrocytes can be applied. Some preliminary implementations' results not reported here suggest that if we modify the astrocyte's algorithm in a way that increases the output of neurons rather than modifying the parameters, the overall RMSE error will also be decreased. Hence, having astrocytes in all layers rather than only the fourth may increase the performance of the network. More detailed information on these modifications is given in Chapter 5.

⁷Researchers such as An [2] and Brown et al.[7] have shown that in their studied networks adding noise into an artificial neural network will increase the performance. Glia astrocytes by increasing and decreasing the weights outside the training algorithm of ANNs might be considered as a source of noise propagation.

Chapter 4

Artificial Astrocytes Networks (AANs)

Artificial Neural Networks (ANNs) (see Section 2.3) are defined as brain-inspired systems that have the ability to process information and complete tasks in different areas such as classification, prediction and evaluation. A more recent model of ANNs called Artificial Neuron-glia Networks (ANGNs) (see Section 2.5) benefit from biologically-inspired elements, artificial astrocytes. ANGNs model astrocytes as single isolated elements; however, recent physiological findings summarized in Section 2.2 claim that activation of one astrocyte propagates to other astrocytes through gap junctions. Inspired by this new finding, we designed a novel neural network architecture that benefits from a network of artificial astrocytes on top of a neuron-glia network, rather than using isolated astrocytes. The remainder of this chapter introduces and evaluates artificial astrocyte networks (AANs). First, in Section 4.1, the architecture of and the learning algorithm for AANs are introduced; then in Section 4.2, we describe

an implementation of an AAN and discuss the results obtained by testing this implementation on two classification problems. Finally, Section 4.3 presents a discussion on the AAN performance.

4.1 Architecture and Learning Algorithm

In this section, we present the proposed model of AANs. The first subsection introduces the architecture of AANs, and the second subsection describes the learning algorithm for AANs.

4.1.1 Architecture

The structure of the artificial astrocyte networks is founded on artificial neuron-glia networks; each neuron is associated with one astrocyte and the appropriate activity of the corresponding neuron turns the astrocyte on or off. This structure as presented in Section 2.2 mimics the release of neurotransmitters by astrocytes in the brain's tripartite synapses [50, 4, 52]. In this chapter, in addition to the components of artificial neuron-glia networks, there are connections between astrocytes that comprise the astrocyte networks. An active astrocyte results in the activation of all other astrocytes in the same network. This behavior is inspired by the propagation of calcium wave through astrocyte's gap junctions in the brain [49] as presented in Section 2.2.

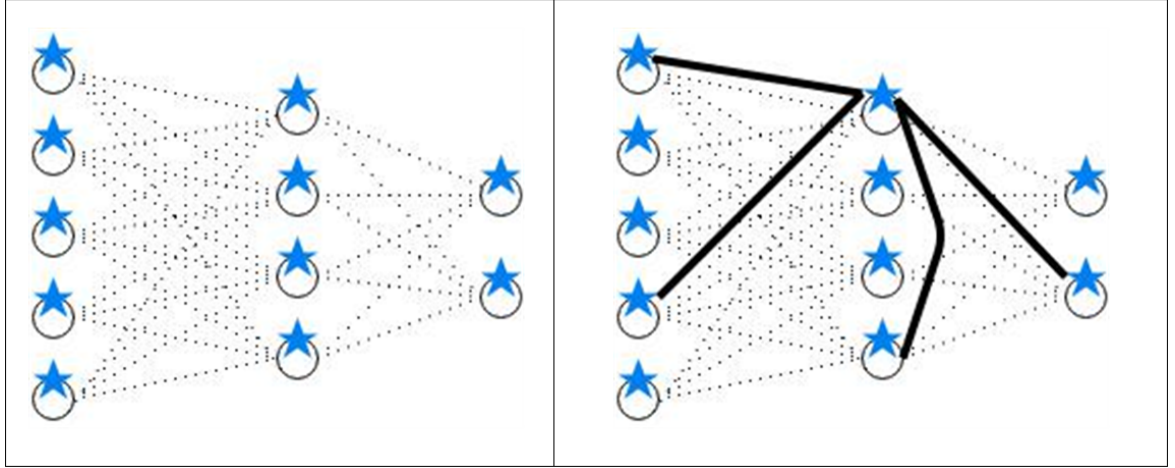


Figure 4.1: ANGN and AAN. The left image depicts a neuron-glia network (astrocytes are shown with stars), and the image on the right is a neuron-glia network with an artificial astrocyte network. The solid lines in the latter image shows one possible astrocyte network (These figures are adapted from Figure 3 in [52], with permission from the publisher).

As explained in Section 2.2, the exact nature of the connections between biological astrocytes is not yet clear. The model we suggest for astrocyte networks is based on connecting random astrocytes. A set which is composed of n randomly chosen astrocytes will be determined. Then, each pair of astrocytes in the set will be connected by an edge. The result will be a complete astrocyte network (i.e., there is an edge between each pair of nodes). Having a complete network is inspired by the work of Pereira and Furlan [49]. Each astrocyte network may contain two to n astrocytes¹,

¹In each portion of the brain, generally more than one astrocyte network is connected to neurons,

where the maximum value for n is the total number of neurons in all layers. The efficient number of astrocytes participating in an AAN can be determined empirically (i.e. by trial and error method). Figure 4.1 presents an ANGN and a possible structure for its corresponding AAN; note that in this figure, the astrocyte network is not a complete network.

4.1.2 Learning Algorithm

Artificial astrocyte networks use ANGN algorithms (see Section 2.5) plus an extra algorithm that represents the connections between astrocytes. This extra algorithm, which implements the signal receiving and sending processes is described in the following paragraphs. Each astrocyte in an AAN runs the same algorithm. This algorithm can be divided into two phases: the first phase determines the state of the astrocyte (active or inactive), and in the second phase, the weights are updated and signals are sent to connected astrocytes. The following paragraphs provide more information on these two phases.

In the first phase, we initially check the input signals to an astrocyte. If the astrocyte receives an activation signal from a connected astrocyte, then immediately it will become active and act exactly similar to an active isolated astrocyte² (a positive signal will activate the astrocyte positively³ and a negative signal will activate an astrocyte negatively). If no activation signal is received, then the astrocyte will run

but for simplicity of the artificial networks, in this thesis, we assume that only one astrocyte network can be implemented on top of an ANN.

²This signal receiving process is part of the previously mentioned “extra algorithm”.

³From the Physiological perspective, positive and negative activation corresponds to increase and decrease of synaptic strength respectively.

an isolated astrocyte’s algorithm, and check the activity of its corresponding neuron. All functions and parameters used here are the same as those used in the ANGN algorithms described in Section 2.5. Lastly, if the activation conditions of an astrocyte are satisfied (either by receiving an activation signal or by the result of running the algorithm of isolated astrocyte), the astrocyte will become activated and the second phase will be started.

The second phase initially updates the weights of active astrocytes by some pre-defined percentages (the details of this updating process are available in Section 2.5). Furthermore, in AANs, the active astrocytes send an activation signal to all the connected astrocytes⁴(a positive signal if it is positively activated and a negative signal if it is negatively activated). Figure 4.2 depicts a flowchart of the AAN algorithm for positively active astrocytes.

4.2 Performance

In this section, we investigate the performance of artificial astrocyte networks on two classification problems, and study how isolated and networks of artificial astrocytes can affect the accuracy of classification. For testing the performance of AAN, we answer the following question:

Are there possible patterns of connections between astrocytes of a neuron-glia network that produce more accurate classification results?

⁴This signal sending process is part of the previously mentioned “extra algorithm”.

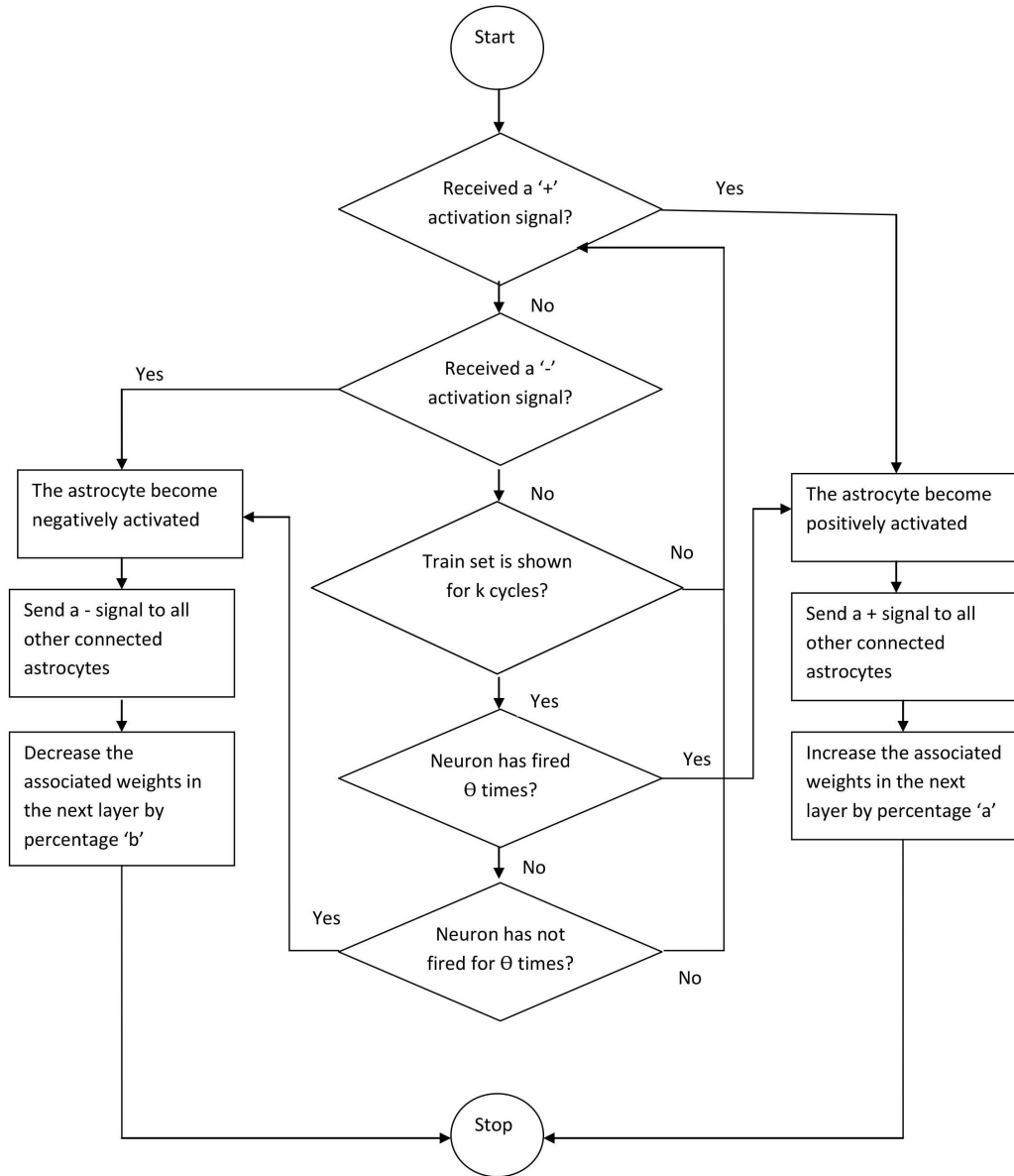


Figure 4.2: A flowchart of the AAN algorithm. This algorithm is executed by every single astrocyte. For simplicity, computations involving $-\theta$, which represents the negatively active astrocytes, are omitted from the algorithm above.

We implement AAN to solve two classification problems⁵. The first problem is classifying breast cancer cells into healthy and unhealthy cells⁶ and the second one is a classification of ionosphere data into good and bad⁷; both problems are binary classification tasks, which means there are two possibilities for the output and the input will be categorized either into group one or group two. The breast cancer and the ionosphere data sets used in this work were part of the UCI data sets [34], which are based on real world data and repeatedly have been used in the machine learning literature [71, 69, 70, 74, 24]. As stated earlier, the breast cancer data set categorized instances into either “healthy” and “unhealthy”. The instances are described by nine attributes, some of which are linear and others are nominal. The available 286 breast cancer instances in the data set were organized into 143 training and 143 testing instances. The ionosphere data set consisted of 351 instances, with each instance having 34 attribute classified as either “good” or “bad”. The 351 instances of ionosphere data set were divided into 175 training and 176 testing instances. The

⁵The implemented codes are available at the supplementary materials of this thesis.

⁶Originally, this breast cancer domain was obtained from the University Medical Centre, Institute of Oncology, Ljubljana, Yugoslavia. Thanks go to M. Zwitter and M. Soklic for providing the data.

⁷Based on the information provided in [34] “This data was collected by a system in Goose Bay, Labrador. This system consists of a phased array of 16 high-frequency antennas with a total transmitted power on the order of 6.4 kilowatts ... The targets were free electrons in the ionosphere. “Good” radar returns are those showing evidence of some type of structure in the ionosphere. “Bad” returns are those that do not; their signals pass through the ionosphere. Received signals were processed using an auto-correlation function whose arguments are the time of a pulse and the pulse number. There were 17 pulse numbers for the Goose Bay system. Instances in this database are described by 2 attributes per pulse number, corresponding to the complex values returned by the function resulting from the complex electromagnetic signal.”

training and testing of the networks were implemented on a system with a 1.30 GHz processor and 2 GB of RAM using the Windows 8 operating system, Java language source code and the Eclipse compiler.

These experiments aimed to test the performance of the proposed artificial astrocyte networks and to compare them with a typical ANN and ANGN. The typical ANN is designed as a multi-layer back propagation network which is composed of three layers. For the breast cancer problem, the input layer consists of nine neurons, each of which receives one feature of the cells recognized as the input. The output layer consists of two neurons, which represents healthy and unhealthy cells. The hidden layer consists of eight neurons. The number of neurons in the hidden layer was determined empirically by adjusting the number of neurons in the hidden layer from 1 to 14. For the ionosphere problem, the input layer consisted of 34 neurons, such that each input neuron corresponds to one input attribute and the output layer had two neurons, representing “good” and “bad”. The number of neurons in the hidden layer was also empirically determined to be 18.

The neuron-glia network was implemented on top of the ANN, as explained in Section 4.1.1 , by including the following astrocyte parameters: k, θ, a, b and $ft \in \mathbb{R}$. The values of these parameters were experimentally determined. Table 4.1 gives the final parameter values chosen for the training and testing of the networks.

The network of interest in this research, the artificial astrocyte network, was implemented by employing the same parameters of the ANGN (see Table 4.1). The astrocyte networks were defined based on the random selection of the astrocytes as explained in Section 4.1. The astrocyte network for breast cancer data set was tested by involving three random astrocytes, and for ionosphere data with 5 astrocytes; the

Parameters	Neurons in first Layer	Neurons in 2nd Layer	Neurons in 3rd Layer	α	k	θ	a	b	ft
Breast cancer	9	8	2	0.1	100	40	1.25	0.75	0.75
Ionosphere	34	18	2	0.1	90	27	1.25	0.75	0.6

Table 4.1: Parameters used in implementing ANGN and AAN . The first four columns define the ANNs. The rest present the parameters related to astrocytes.

Network	Test Accuracy (Breast Cancer)	Test Accuracy (Ionosphere)
ANN	0.87	0.80
ANGN	0.91	0.86
AAN	0.93	0.88

Table 4.2: The accuracy of classification on test data for ANN, ANGN and AAN.

accuracy of classification in these experiments on testing data is reported in Table 4.2.

4.3 Discussion

Table 4.2 shows a comparison between typical neural networks, neuron-glia networks and artificial astrocyte networks. It can be seen that the inclusion of the single as-

trocytes (ANGNs) improves the performance of the typical neural network (as also discussed in [52]) and the performance of ANGNs can further be enhanced by connecting astrocytes and forming astrocyte networks. It should be noted that the common parameters have the same value in all models. Therefore, the variations of the accuracy between ANN and ANGN is solely for the inclusion of single astrocyte elements and between ANGN and AANs is for the connections established between some astrocytes.

In an Artificial Astrocyte Network, providing a complete analysis of the sensitivity of the error of the network relative to each of the parameters and combination of parameters requires intensive research in the field of parameter sensitivity. The complexity of these analysis is due to the relation between the five parameters of astrocytes to each other, and also the relation of these parameters to the connections between astrocytes. The possibility of using real values for three of the astrocyte parameters also increases the complexity of this problem.

A preliminary analysis has shown that there is no linear relation between these parameters and the error of the network. In the Breast Cancer problem, we set the value of all parameters except one to a constant values and then varied the value of the selected parameter. When we did this for parameter a we observed that decreasing the value of a does not significantly affect the results; however, increasing the value of a decreases the performance and reduce the accuracy from 0.96 to around 0.5. On the other hand, the parameter b does not follow the same behavior: increasing b first increases the accuracy, then decrease it and finally again increase it. For the parameters k and ft , the same behavior is observed. But for the parameter θ the behavior is different again: from the value zero to a specific point, there is no significant change

in the performance, and after that specific point the performance increases in a non linear manner. This demonstrates that astrocyte parameters have complex individual behaviors and are thus likely to have even more complex behaviours when they are co-varied. In Future research we will investigate in much greater depth the relation of these parameters and their effects on the error of the network.

The higher computing power achieved by the inclusion of the artificial astrocyte networks can be explained in two ways. Firstly, there is some similarity between AANs and liquid state machines [38], and recurrent neural networks [11], which results in the reception of time-varying inputs from external astrocyte sources, as well as neurons. In the AAN algorithm, astrocytes are randomly connected to each other. The recurrent nature of the connections turns the time varying input into a spatio-temporal pattern of activation in the network nodes that enables the network to compute a large variety of non-linear functions on the input. In other words, the astrocytes serve as a memory that records information about the past k cycles and allow the use of this information to shape the network in a way that reduces error. Secondly, from a physiological point of view, astrocyte networks give a simple interpretation of data integration in the brain [49]. Therefore, having an AAN on top of typical neural networks add the benefit of data integration; this gives us a more realistic model of the human brain that is able to provide a more detailed analysis and yields a more powerful artificial neural network.

To further improve the performance of AANs, we can apply different modification to AANs and determine if any of these modifications will improve the results. Two possible modifications are

- First, we can modify the algorithm of single isolated astrocytes by assigning each astrocytes an activation function, or we can directly increase or decrease the output of the associated neurons rather than modifying the associated weights.
- Second, we can modify the network of astrocytes by having some separate structurally-different astrocyte networks on top of an ANN, or corresponding more than one astrocyte (neuron) to a neuron (astrocyte).

Chapter 5

Summary and Future Work

In this chapter, we first provide a summary of the research done in this thesis and then discuss the possible directions for future work.

5.1 Summary

The learning procedures in the human brain inspired researchers to develop tools such as artificial neural networks that have the ability to learn. Artificial neural networks (ANN) attempt to imitate the structure of biological neural networks. In Chapter 2 first, we provided some information on recent research in biology that indicates astrocytes in addition to neurons are responsible for processing information in the human brain. Then in Section 2.5, we explained how this concept is found its way into artificial intelligence and is modeled in feed-forward multi-layer artificial neural networks called Artificial Neuron-glia Networks (ANGN). In Chapters 3 and 4, in continuation of this research, we proposed two models of artificial neuron-glia networks. In Chapter 3, we added artificial astrocytes into a different architecture

of neural networks, adaptive neuro fuzzy inference systems (ANFIS), and evaluated the performance of such systems with and without the inclusion of astrocytes. Our results show that including astrocytes with some specific parameter values will result in some improvements in the performance of the system. In Chapter 4, we proposed the concept of artificial astrocyte networks, and showed that connecting astrocytes to each other and making a network of astrocytes on top of a feed-forward multi-layer neural network can result in more accurate classification results and thus enhance the performance of such networks.

Taken together, our set of results suggested that for some specific parameter values representing networks and astrocytes, we can achieve more accurate results rather than typical neural networks. This provides us with some insight on how an artificial astrocyte might be an appropriate element for increasing the performance of ANNs; however our specific results for specific problems do not yet answer the question of whether our proposed models will be successful in general or not. The next section sketches some directions for future work that will help us to answer this question.

5.2 Future Work

The research on ANGFIS presented in this thesis can be continued in five ways.

1. We can implement ANGFIS for solving a greater variety of real-world problems than those examined in this thesis, such as EEG signal processing, and investigate how each single and combination of astrocyte parameters affect the results of each problem. This can then be used to find general rules for choosing astrocytes parameter values.

2. We can have a comparison between noise, chaotic behavior and astrocytes to study if astrocytes obey the current models on noise propagation and chaotic behaviors in neural networks and thus answer the question if we can use current models of noise injection in the networks to describe the behavior of astrocytes in artificial and biological neural networks.
3. We can analyze the training of astrocyte-enhanced fuzzy networks from the classical and parameterized computational complexity perspective; these analyses will hopefully help us to design more efficient models of astrocytes.
4. We can implement astrocytes on other ANN architectures, such as learning vector quantization [11, 12], bidirectional associative memory [11, 12], and adaptive resonance theory [11, 12] to study how the inclusion of astrocytes will affect the results.
5. We can include astrocytes in other layers of ANFIS rather than the fourth layer, and design more neurally realistic parameters and functions for modeling astrocytes, and study the resulting changes in the performance of networks.

Possible future work on AANs can be divided into four main directions.

1. We can focus on designing more accurate models for describing artificial astrocytes and astrocyte networks. Since 2004, when artificial astrocytes were introduced until now, new physiological studies revealed other aspects of the functionality and structure of astrocytes and their networks [14, 17, 49]; a simplified version of these aspects, specifically astrocyte networks with the ability to learn can be added to current astrocyte models. We can also provide more

realistic models of astrocytes in their distribution in the network such as connecting one astrocyte to several nodes, or having random number of astrocytes on random nodes in the network,

2. We can address theoretical issues regarding the computational complexity of training astrocyte-enhanced networks. Analyzing these networks from the computational complexity perspective in general and parametrized complexity in particular, will help us to recognize the aspects of these networks that allow restricted networks that operate more quickly.
3. We can implement AANs on different neural network architectures and evaluate their performance with and without the added astrocyte networks.
4. We can evaluate other types of astrocyte networks. In this work, we only test the performance of one random astrocyte network. It may be of use to evaluate the performance by considering all types of astrocyte networks, which are represented in the form of trees, bi-partite graphs or other types of graphs. Delays in transmitting data on astrocyte connections could also be considered in these networks.

Bibliography

- [1] A. Alvarellos-González, A. Pazos, and A. B. Porto-Pazos. Computational models of neuron-astrocyte interactions lead to improved efficacy in the performance of neural networks. *Computational and Mathematical Methods in Medicine*, 2012, 2012.
- [2] G. An. The effects of adding noise during backpropagation training on a generalization performance. *Neural Computation*, 8(3):643–674, 1996.
- [3] A. Araque, G. Carmignoto, and P. G. Haydon. Dynamic signaling between astrocytes and neurons. *Annual Review of Physiology*, 63(1):795–813, 2001.
- [4] A. Araque, V. Parpura, R. P. Sanzgiri, and P. G. Haydon. Tripartite synapses: glia, the unacknowledged partner. *Trends in Neurosciences*, 22(5):208–215, 1999.
- [5] R. Bharath and J. Drosen. *Neural Network Computing*. Windcrest/McGraw-Hill, 1994.
- [6] C. Bonansco, A. Couve, G. Perea, C. Á. Ferradas, M. Roncagliolo, and M. Fuenzalida. Glutamate released spontaneously from astrocytes sets the threshold for synaptic plasticity. *European Journal of Neuroscience*, 33(8):1483–1492, 2011.

- [7] W. M. Brown, T. D. Gedeon, and D. I. Groves. Use of noise to augment training data: a neural network method of mineral–potential mapping in regions of limited known deposit examples. *Natural Resources Research*, 12(2):141–152, 2003.
- [8] E. P. Cook, J. A. Guest, Y. Liang, N. Y. Masse, and C. M. Colbert. Dendrite-to-soma input/output function of continuous time-varying signals in hippocampal ca1 pyramidal neurons. *Journal of Neurophysiology*, 98(5):2943–2955, 2007.
- [9] P. E. Dennison, K. Q. Halligan, and D. A. Roberts. A comparison of error metrics and constraints for multiple endmember spectral mixture analysis and spectral angle mapper. *Remote Sensing of Environment*, 93(3):359–367, 2004.
- [10] M. O. Efe and O. Kaynak. A comparative study of neural network structures in identification of nonlinear systems. *Mechatronics*, 9(3):287–300, 1999.
- [11] L. V. Fausett. *Fundamentals of Neural Networks*. Prentice-Hall, 1994.
- [12] J. A. Freeman and D. M. Skapura. *Neural Networks: Algorithms, Applications, and Programming Techniques*. Addison-Wesley Publishing Company, 1991.
- [13] T. M. Geronimo, C. E. Cruz, E. C. Bianchi, F. de Souza Campos, and P. R. Aguiar. *MLP and ANFIS Applied to the Prediction of Hole Diameters in the Drilling Process*. INTECH Open Access Publisher, 2013.
- [14] C. Giaume, A. Koulakoff, L. Roux, D. Holcman, and N. Rouach. Astroglial networks: a step further in neuroglial and gliovascular interactions. *Nature Reviews Neuroscience*, 11(2):87–99, 2010.

- [15] I. Güler and E. D. Übeyli. Adaptive neuro-fuzzy inference system for classification of EEG signals using wavelet coefficients. *Journal of Neuroscience Methods*, 148(2):113–121, 2005.
- [16] G. I. Hatton and V. Parpura. *Glial neuronal signaling*, volume 1. Springer, 2004.
- [17] P. G. Haydon. Glia: listening and talking to the synapse. *Nature Reviews Neuroscience*, 2(3):185–193, 2001.
- [18] C. Ikuta, Y. Uwate, and Y. Nishio. Chaos glial network connected to multi-layer perceptron for solving two-spiral problem. In *Proceedings of 2010 IEEE International Symposium on Circuits and Systems (ISCAS)*,, pages 1360–1363. IEEE, 2010.
- [19] C. Ikuta, Y. Uwate, and Y. Nishio. Performance and features of multi-layer perceptron with impulse glial network. In *Proceeding of The 2011 International Joint Conference on Neural Networks (IJCNN)*, pages 2536–2541. IEEE, 2011.
- [20] J.-S. Jang. Self-learning fuzzy controllers based on temporal backpropagation. *IEEE Transactions on Neural Networks*, 3(5):714–723, 1992.
- [21] J.-S. Jang. ANFIS: adaptive-network-based fuzzy inference system. *IEEE Transactions on Systems Man and Cybernetics*, 23(3):665–685, 1993.
- [22] J.-S. R. Jang et al. Fuzzy modeling using generalized neural networks and kalman filter algorithm. In *Proceedings of the Ninth National Conference on Artificial Intelligence*, volume 91, pages 762–767, 1991.

- [23] J.-S. R. Jang, C.-T. Sun, and E. Mizutani. Neuro-fuzzy and soft computing—a computational approach to learning and machine intelligence [book review]. *IEEE Transactions on Automatic Control*, 42(10):1482–1484, 1997.
- [24] H. Kim and H. Park. Data reduction in support vector machines by a kernelized ionic interaction model. In *SDM*, pages 507–511. SIAM, 2004.
- [25] E. KONISHI. Modeling quantum mechanical observers via neural-glia networks. *International Journal of Modern Physics B*, 26(09):1250060, 2012.
- [26] J. Lallouette and H. Berry. Topology drives calcium wave propagation in 3d astrocyte networks. In *Proceedings of the European Conference on Complex Systems 2012*, pages 453–463. Springer, 2013.
- [27] H. Landahl, W. S. McCulloch, and W. Pitts. A statistical consequence of the logical calculus of nervous nets. *Bulletin of Mathematical Biology*, 5(4):135–137, 1943.
- [28] C.-C. J. Lee. *Investigation of synaptic plasticity as memory formation mechanism and pathological amyloid fibrillation caused by amyloids aggregation: Modeling work combined with experiments*. PhD thesis, Massachusetts Institute of Technology, 2008.
- [29] S. Z. Li. Improving convergence and solution quality of Hopfield-type neural networks with augmented lagrange multipliers. *IEEE Transactions on Neural Networks*, 7(6):1507–1516, 1996.
- [30] S.-P. Lo. The application of an ANFIS and grey system method in turning

- tool-failure detection. *The International Journal of Advanced Manufacturing Technology*, 19(8):564–572, 2002.
- [31] V. G. Maltarollo, A. B. F. da Silva, and K. M. Honório. *Applications of Artificial Neural Networks in Chemical Problems*. INTECH Open Access Publisher, 2013.
- [32] M. Margaliot. Biomimicry and fuzzy modeling: A match made in heaven. *Computational Intelligence Magazine, IEEE*, 3(3):38–48, 2008.
- [33] W. S. McCulloch and W. Pitts. A logical calculus of the ideas immanent in nervous activity. *Bulletin of Mathematical Biophysics*, 5(4):115–133, 1943.
- [34] P. Murphy and D. Aha. UCI repository of machine learning databases, University of California, Department of Information and Computer Science, Irvine, CA, 1994.
- [35] A. F. Murray and P. J. Edwards. Enhanced MLP performance and fault tolerance resulting from synaptic weight noise during training. *IEEE Transactions on Neural Networks*, 5(5):792–802, 1994.
- [36] L. Naderloo, R. Alimardani, M. Omid, F. Sarmadian, P. Javadikia, M. Y. Torabi, and F. Alimardani. Application of ANFIS to predict crop yield based on different energy inputs. *Measurement*, 45(6):1406–1413, 2012.
- [37] K. S. Narendra and K. Parthasarathy. Identification and control of dynamical systems using neural networks. *IEEE Transactions on Neural Networks*, 1(1):4–27, 1990.

- [38] T. Natschläger, W. Maass, and H. Markram. The” liquid computer”: A novel strategy for real-time computing on time series. *Special Issue on Foundations of Information Processing of TELEMATIK*, 8:39–43, 2002.
- [39] E. A. Newman. New roles for astrocytes: regulation of synaptic transmission. *Trends in neurosciences*, 26(10):536–542, 2003.
- [40] C. R. Noback, N. L. Strominger, R. J. Demarest, and D. A. Ruggiero. *The human Nervous System: Structure and Function*. Springer, 2005.
- [41] U. Pannasch, L. Vargová, J. Reingruber, P. Ezan, D. Holcman, C. Giaume, E. Syková, and N. Rouach. Astroglial networks scale synaptic activity and plasticity. *Proceedings of the National Academy of Sciences*, 108(20):8467–8472, 2011.
- [42] L. Pasti, A. Volterra, T. Pozzan, and G. Carmignoto. Intracellular calcium oscillations in astrocytes: a highly plastic, bidirectional form of communication between neurons and astrocytes in situ. *The Journal of Neuroscience*, 17(20):7817–7830, 1997.
- [43] D. W. Patterson. *Artificial Neural Networks: Theory and Applications*. Prentice Hall PTR, 1998.
- [44] G. Perea and A. Araque. Communication between astrocytes and neurons: a complex language. *Journal of Physiology-Paris*, 96(3):199–207, 2002.
- [45] G. Perea and A. Araque. Properties of synaptically evoked astrocyte calcium signal reveal synaptic information processing by astrocytes. *The Journal of Neuroscience*, 25(9):2192–2203, 2005.

- [46] G. Perea and A. Araque. Astrocytes potentiate transmitter release at single hippocampal synapses. *Science*, 317(5841):1083–1086, 2007.
- [47] G. Perea and A. Araque. Glia modulates synaptic transmission. *Brain Research Reviews*, 63(1):93–102, 2010.
- [48] G. Perea, M. Navarrete, and A. Araque. Tripartite synapses: astrocytes process and control synaptic information. *Trends in Neurosciences*, 32(8):421–431, 2009.
- [49] A. Pereira Jr and F. A. Furlan. Astrocytes and human cognition: modeling information integration and modulation of neuronal activity. *Progress in Neurobiology*, 92(3):405–420, 2010.
- [50] T. M. Pirttimaki and H. R. Parri. Astrocyte plasticity implications for synaptic and neuronal activity. *The Neuroscientist*, 19(6):604–615, 2013.
- [51] A. Porto. *Computational models for optimizing the learning and the information processing in adaptive systems*. PhD thesis, Faculty of Computer Science, University of A Coruña, 2004.
- [52] A. B. Porto-Pazos, N. Veiguela, P. Mesejo, M. Navarrete, A. Alvarellos, O. Ibáñez, A. Pazos, and A. Araque. Artificial astrocytes improve neural network performance. *PloS One*, 6(4), 2011.
- [53] J. M. Robertson. The astrocentric hypothesis: proposed role of astrocytes in consciousness and memory formation. *Journal of Physiology-Paris*, 96(3):251–255, 2002.

- [54] R. Rojas. *Neural networks: a systematic introduction*. Springer Science & Business Media, 1996.
- [55] D. A. Rusakov, K. Zheng, and C. Henneberger. Astrocytes as regulators of synaptic function a quest for the ca^{2+} master key. *the Neuroscientist*, 17(5):513–523, 2011.
- [56] Z. Sajedinia. Artificial glia astrocytes; a new element in adaptive neuro fuzzy systems. *Proceedings of the 22th Annual Newfoundland Electrical and Computer Engineering Conference (NECEC 2013)*, 2013.
- [57] Z. Sajedinia. Artificial astrocyte networks, as components in artificial neural networks. In *Unconventional Computation and Natural Computation*, pages 316–326. Springer, 2014.
- [58] B. Selman, H. A. Kautz, and B. Cohen. Noise strategies for improving local search. In *AAAI*, volume 94, pages 337–343, 1994.
- [59] L. R. Squire. *Fundamental Neuroscience*. Academic Press, 2013.
- [60] M. Sugeno and G. Kang. Structure identification of fuzzy model. *Fuzzy Sets and Systems*, 28(1):15–33, 1988.
- [61] H. Takagi and I. Hayashi. Nn-driven fuzzy reasoning. *International Journal of Approximate Reasoning*, 5(3):191–212, 1991.
- [62] T. Takagi and M. Sugeno. Fuzzy identification of systems and its applications to modeling and control. *IEEE Transactions on Systems, Man and Cybernetics*, (1):116–132, 1985.

- [63] Z. Tan, C. Quek, and P. Y. Cheng. Stock trading with cycles: A financial application of ANFIS and reinforcement learning. *Expert Systems with Applications*, 38(5):4741–4755, 2011.
- [64] M. K. Temburni and M. H. Jacob. New functions for glia in the brain. *Proceedings of the National Academy of Sciences*, 98(7):3631–3632, 2001.
- [65] C. Thome, T. Kelly, A. Yanez, C. Schultz, M. Engelhardt, S. B. Cambridge, M. Both, A. Draguhn, H. Beck, and A. V. Egorov. Axon-carrying dendrites convey privileged synaptic input in hippocampal neurons. *Neuron*, 83(6):1418–1430, 2014.
- [66] G. Trevor. *Online resources: Gallant’s Biology Stuff*. <http://kvhs.nbed.nh.ca/gallant/biology/biology.html>, 2015.
- [67] M. van Turnhout and F. Bociort. Chaotic behavior in an algorithm to escape from poor local minima in lens design. *Optics Express*, 17(8):6436–6450, 2009.
- [68] J. Wade, L. McDaid, J. Harkin, V. Crunelli, and S. Kelso. Self-repair in a bidirectionally coupled astrocyte-neuron (an) system based on retrograde signaling. *Frontiers in Computational Neuroscience*.
- [69] W. H. Wolberg, W. N. Street, D. M. Heisey, and O. L. Mangasarian. Computerized breast cancer diagnosis and prognosis from fine-needle aspirates. *Archives of Surgery*, 130(5):511, 1995.
- [70] W. H. Wolberg, W. N. Street, and O. Mangasarian. Machine learning techniques

- to diagnose breast cancer from image-processed nuclear features of fine needle aspirates. *Cancer Letters*, 77(2):163–171, 1994.
- [71] W. H. Wolberg, W. N. Street, and O. L. Mangasarian. Image analysis and machine learning applied to breast cancer diagnosis and prognosis. *Analytical and Quantitative Cytology and Histology*, 17(2):77–87, 1995.
- [72] L. A. Zadeh. Fuzzy sets. *Information and Control*, 8(3):338–353, 1965.
- [73] L. A. Zadeh. Outline of a new approach to the analysis of complex systems and decision processes. *IEEE Transactions on Systems, Man and Cybernetics*, (1):28–44, 1973.
- [74] Z.-H. Zhou and Y. Jiang. Neural ensemble based c4. *IEEE Transactions on Knowledge and Data Engineering*, 16:770–773, 2004.
- [75] R. M. Zur, Y. Jiang, L. L. Pesce, and K. Drukker. Noise injection for training artificial neural networks: A comparison with weight decay and early stopping. *Medical Physics*, 36(10):4810–4818, 2009.