Artificial Intelligence Review (2023) 56:S2651–S2666
https://doi.org/10.1007/s10462-023-10586-1

Artificial glial cells in artificial neuronal networks: a systematic review

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Accepted: 25 August 2023 / Published online: 7 September 2023

Abstract

The concept of tripartite synapses has revolutionized the world of neuroscience and the way we understand how information is transmitted in the brain. Since its discovery, some research groups have incorporated into connectionist systems classically focused on the development of Artificial Neuron Networks (ANNs) as a single element, artificial astrocytes that try to optimize performance in problem solving.In this systematic review, we searched the ISI Web of Science for papers that focused on the development of such novel models and their comparison with classical ANNs. A total of 22 papers that satisfied the inclusion criteria were analyzed, showing three different ways of applying the neuromodulatory influence of artificial astrocytes on neural networks. Using Multilayer Perceptron Networks, Artificial Neuro-Glial Newtworks and Multilayer Perceptron with Self-Organizing Maps approaches, a detailed analysis of the incorporation of artificial astrocytic networks has been carried out, and the main differences between the different methods have been weighed up. Regardless of the type of inclusion performed, the greater the complexity of the problem to be solved, it has been observed that the influence of artificial astrocytes has improved the performance of classical ANNs, as occurs in the biological brain.

Keywords Conexionism · Tripartite synapse · Glial cells · Artificial astrocytes · Systematic review · Artificial neural networks

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Abbreviations

AAN	Artificial astrocyte networks
ANGN	Artificial neuro-glial networks
ANN	Artificial neuron networks
BMU	Best matching unit
BP	Back-propagation
CS	Connectionism system
ESN	Echo state networks
GA	Genetic algorithm
MCC	Matthews correlation coefficient
MSE	Mean squared error
MLP	Multi-layer perceptron
PGC	Pulse glial chain
PRISMA	Preferred reporting items systematic reviews meta-analyses
RMSE	Root mean squared error
RNN	Recurrent neural networks
SOM	Self-organizing map
SONG-NET	Self organizing neuro-glia network

1 Introduction

From a biological perspective, neuroscientists focus their research on the search for essential information about brain function, thus facilitating the creation of representative models of the brain. Neurons are considered the essential building blocks of the brain conducting electrical impulses, which result in the processing of information (Sajedinia 2015). Generally, neural network models have three components: neurons, synaptic plasticity and neural pathways (Lones et al. 2013).

From a computational perspective, a connectionist system (CS) is described as the modeling of brain functioning in an in silico manner, trying to simulate intelligent behaviors (Lippmann 1987). This is accomplished by artificial neural networks, which emerged as input information processing structures (Rumelhart et al. 1994). These are adaptive structures that process data quickly and simultaneously, learn and are able to find non-linear patterns between input and output information, and can be generalized and used with previously unseen data.

In ANNs, neurons are modeled primarily as activation functions that will range according to how we understand the behavior, from implementing a sigmoid to a derivative for biological neuron models in spiking (Lones et al. 2013). Synaptic plasticity refers to the ability of synapses to modulate the strength of signals traveling between neurons, and is considered the main mechanism for learning within the brain, thus, variations in connection weights are modeled. These are updated following: (i) either learning algorithms, such as backpropagation (BP) (Rumelhart et al. 1986), (ii) metaheuristics such as evolutionary algorithms (Yao and Liu 1998) or (iii) mechanisms motivated by learning in the brain, such as Hebbian learning, or (iv) mechanisms motivated by learning in the brain, such as Hebbian learning (Song et al. 2000).

Finally, neural pathways refer to the connectivity patterns that will determine the flow of signals through a neural network. There are several architectures used for this purpose, such as the multilayer perceptron (MLP) for feed-forward structures (Minsky and Papert

1969) or recurrent neuron networks (RNN) for interlayer feedback pathways (Mikolov et al. 2010). The classical conception of neuronal networks in their in silico design includes only neurons, however, in the human biological brain we can find another type of cells besides neurons, called glial cells, where in the field of artificial neuronal networks, studies that include them are scarce.

Neuroscience has shown that the release of neurotransmitters from the presynaptic neuron is modulated by glial cells, triggering an increase in calcium ions in neighboring glial cells (Perea et al. 2014). This process is known as tripartite synapse (Araque et al. 1999). Hence, glial cells will also release gliotransmitters that reach pre- and post-synaptic neurons and cause potentiation or depression beyond the release of neurotransmitters, conditioning information processing (Newman 2003). A remarkable aspect about astrocytes, a subtype of glial cell, is that it happens to be responsible for information processing in the human brain.

Inspired by this emerging concept, several groups of researchers have been developing new types of artificial neuron networks that, beyond the classical concept of representing only interconnected neurons, introduce new elements that seek to computationally simulate the modulatory effect produced by glial cells in the process of biological brain information transmission.

Currently, there are different approaches to integrate the tripartite synapse with neural networks. A growing number of studies have been proposed with different algorithms, architectures and ways of understanding the behavior of neurons. However, as far as we know, there is no review dedicated exclusively to the study of works in which a thorough analysis of all the existing connectionist models that try to simulate in silico the influence of astrocytes on an artificial neural network is made. There are only a few papers that briefly discuss the existing set of studies as the state of the art.

Although this is a new field and has limitations, the development of these models may be key to optimize and improve the ANN algorithms that are currently used and in high demand. To the best of our knowledge there is no systematic comparison of these studies, and this is a serious gap for the researchers that are undertaking this novel approach. The purpose of this review is to discuss the work carried out so far from different approaches, providing current and future researchers in the field with a point of reference that brings together the challenges achieved so far and the current state of the art.

The structure of the paper is as follows. In Sect. 2 we provide the results, first providing a summary of the existing bibliography in this emerging field, and then a classification and detailed description of the found techniques conducted to implement artificial glial cells in classical ANNs. In Sect. 3 we describe the methods and procedure for the selection of relevant papers for this paper. Section 4 is devoted to discussing the advantages and limitations of each approach, not only from a computational point of view, but also on the extent to which they represent a realistic mechanism from a biological point of view. Finally, we present some concluding remarks and future works in Sect. 5.

2 Results

2.1 Summary of results

Out of the 65 papers identified by the automated search in Scopus, while, manually, another 3 articles were included. Of these 68, 43 were excluded because their abstract did not match what was being searched for, while 3 were excluded after reading the full article. This process is shown in Fig. 1, also following the eligibility criteria stated in the figure and explained in the 3.2 section for the final selection of articles.

Table 1 shows the articles finally selected for this review. It includes a total of 22 studies comparing the performance of classical ANNs vs. those same ANNs including modulations of artificial astrocytes inspired by neuroscientific studies on biological synaptic transmission.

As mentioned above, Table 1 classifies these works according to different criteria, bringing them together in the first instance, according to the technique used for the design of the networks. Although it could be considered that all of them use the mathematical neuron model called multilayer perceptron, they are subdivided with different names regarding their architectures and the way of introducing the artificial astrocytes: Multilayer Perceptron (MLP), Artificial Neuro-Glial Networks (ANGN) and Self Organizing Neuro-Glial Networks (SONG-NET).

In the subdivision of the architecture, all of them are designed with artificial neurons that are represented as statistical models and organized in layers that maintain a unidirectional connection between them (feedforward networks), with the exception of the Echo State Networks described in the work of (Gergel and Farkaš 2019). The learning algorithm used in each of the models designed is also presented, along with a section that summarizes the different objectives of each of the works in the Table 1 footnote.

2.2 Implementation techniques for artificial astrocytes

Figure 2 illustrates a simplified representation of the subtypes of neuroastrocytic network types derived from the division of the papers presented in Table 1 based on the type of architecture they used.

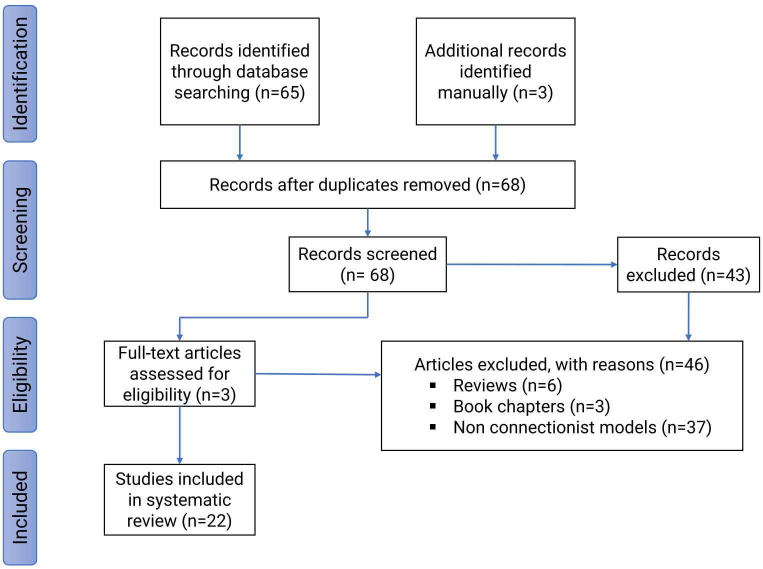

Fig. 1 PRISMA flow diagram of the study selection process

Table 1 Overview of key features of relevant software projects discussed in this paper

Technique	Architecture	References	Learning algorithm	Objectives
MLP	Feed-forward multilayer	Ikuta et al. (2010)	Back Propagation (BP) algorithm	1
		Ikuta et al. (2011a, b, 2012c, a, b, 2014, 2016)	Back Propagation (BP) algorithm + pulse glial chain (PGC)	1, 2
		Gergel and Farkaŝ (2018)	Back Propagation (BP) algorithm	3
	Echo State Networks (ESN)	Gergel and Farkaš (2019)	Hebbian Learning algorithm	
SONG-NET	Feed-forward multilayer	Landolsi and Marzouki (2014); Marzouki (2015); Ben Chikha et al. (2015); Bertegi and Marzouki (2017)	Back Propagation (BP) algorithm + self-organizing map (SOM)	1
ANGN	Feed-forward multilayer	Porto et al. (2007); Porto-Pazos et al. (2011); Alvarellos-González et al. (2012); Pastur-Romay et al. (2017)	Hybrid: non-supervised (astrocyte modification) + GA	4
		Sajedinia (2014, 2015)	Hybrid: Back Propagation (BP) algorithm with updatings + algorithm that represents the astrocytes' connections	4
		Mesejo et al. (2015)	Hybrid: non-supervised (astrocyte modification) + GA	4, 5

Objectives: 1. To model the effect of astrocytes to develop a new type of artificial neural network operating on new mechanisms to improve the information processing; 2. To check if the pulse glial chain (PGC) accelerates the learning of the entire MLP network; 3. To explore the influence of astrocytes; 4. To check if these new CS were more efficient at solving problems currently solved by ANN; 5. To propose a novel learning approach for ANGNs with the aim of avoiding the manual tuning of its parameters

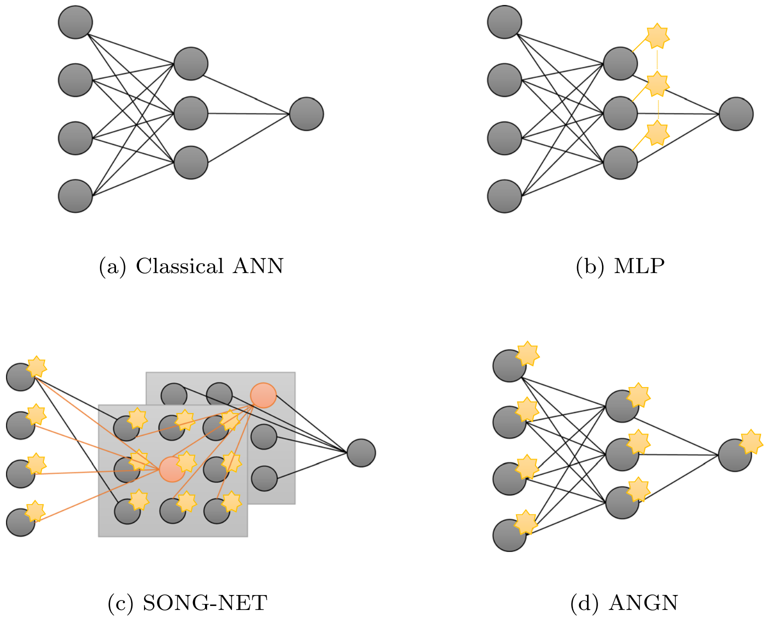

Fig. 2 Subdivision carried out on the basis of the papers selected according to the method in which the studies included the artificial astrocyte: **a** Classical feed-forward ANN, **b** MLPs with integrated astrocytes, **c** Multilayer Perceptron and Self-Organizing Maps or SONG-NETs and **d** Artificial Neuro-Glial Networks

This is a simplification of the biological inspiration behind the design of the different architectures. In 2a a classical feed-forward ANN is represented, in which only artificial neurons are introduced. In the 2b architecture we observe MLPs, architectures that have in their hidden layer artificial astrocytes associated with each of their neurons, depending on the paper, it is possible to find that this astrocytic network is independent or that the modulatory information is also transmitted in chain when any of the neurons associated with any of the artificial astrocytes is activated. On the other hand, in 2c we observed SONG-NETs, architectures that introduced independent astrocytes in the input layer and the first hidden layer that allowed them to find in the first part of the training, the best-fitting neuron for that problem and then move on to the second part of the training. Finally, 2d shows the ANGN, architectures that introduce independent neuromodulatory artificial astrocytes in all the neurons of the layers that conform the network.

The three architectures presented here (MLP, SONG-NET and ANGN) are mostly designed as a feed-forward multilayer architecture, except in one of the studies where echo state networks are applied in a novel way in the hidden layer (Gergel and Farkaš 2019), in Fig. 2 simplified to make a more visual generalization. This is because in attempting to simulate biological networks, the transmission of information has a targeted place of arrival, so the networks must have a structure that allows them to finish the path going from the first layer forward. In this sense, any circular feedback approach would not meet the minimum requirements, because recurrent networks return to the same layer, making closed loops (Fausett 2006). The only study that differs from these feed-forward networks, does not try to make a biological simulation of brain functioning, but only seeks to see the involvement of astrocytes in this type of architecture (Gergel and Farkaš 2019).

Furthermore, they are all networks composed of complex networks (with one or more hidden layers), because they are capable of solving more complex problems than the simple ones. However, it must be taken into account that, although they also have the ability to store important information in the connection of weights of the hidden layers, their training will be more complicated than that of simple networks (Fausett 2006).

2.2.1 Multilayer perceptron with integrated astrocytes

On one side, the first of the approaches observed would be the Multilayer Perceptron (MLP) incorporating artificial astrocytes. In their design, the connection of neurons consists of a system of simple interconnected nodes. These are connected through weights and vary accordingly to their activation. Likewise, the models designed with these MLPs learn by training through supervised learning. In these works, the study of the relationship within the glia takes precedence, considering that a glial network can provide positional relationships to neurons. A significant difference compared to models following the ANGN architecture (section 2.2.3) is that the artificial astrocyte layer here is only connected to the hidden layers of MLP networks. In all papers a classical hidden layer of a feedforward network is used, however, in Gergel's latest paper (Gergel and Farkaš 2019), he proposes to change that hidden layer influenced by astrocytes, by a reservoir layer used in echo state networks, a type of RNN.

With respect to MLP studies there is a generic rule regarding the learning algorithm employed, in which most researchers usually employ the BP learning algorithm. Specifically, (Ikuta et al. 2010; Gergel and Farkaŝ 2018) rely solely on this learning algorithm, while (Ikuta et al. 2011a, b, 2012c, a, b; Landolsi and Marzouki 2014; Ikuta et al. 2016) combine the BP technique by combining it with the inclusion of a glial pulse chain (PGC). These studies proposes a new neural network model called MLP with PGC, which introduces an individual period of inactivity for each glia to break the periodic pulse generation. By varying the length of the inactivity period, the network learning obtains diversity and the pulse generation pattern becomes more diverse. The last of the studies using this type of network is (Gergel and Farkaš 2019), which proposes training them by means of Hebbian learning. Hebbian learning is a type of unsupervised learning used in artificial neural networks. It is based on the Hebbian principle (Hebb 2005), which states that neurons that fire together, wire together. In other words, when two neurons are activated simultaneously, the strength of the connection between them is increased. Hebbian learning is used to modify the weights between neurons in an artificial neural network based on the correlation of their activation patterns.

Research dedicated to the creation of MLPs has as a common objective, although with certain nuances, to be able to propose a glial network that is able to improve the efficiency and enhance the performance of traditional ANNs (Ikuta et al. 2010, 2014, 2016). Some of the experiments that implemented with MLP focused their objective more than on a biological orientation or on the improvement of classical neuron networks, to explore what their role would be and if they would help to improve results in different artificial neuron architectures (Gergel and Farkaŝ 2018; Gergel and Farkaš 2019).

2.2.2 Multilayer perceptron and self-organizing maps

After reviewing related works published on the subject, Marzouki's group, between 2014 and 2017 propose a new algorithm based on the MLP architecture with BP, including a novel astrocytic modification (Landolsi and Marzouki 2014; Marzouki 2015; Ben Chikha et al. 2015; Bertegi and Marzouki 2017). The learning algorithm proposed in the study models neural modulation, specifically calcium waves and the determination of preferential circuits, using Self Organizing Map (SOM) and Multi-Layer Perceptron (MLP). The preferred circuit is defined using the concept of Best Matching Unit (BMU) from SOM and the Best BMU (BBMU) represents the preferred path in the artificial network through the hidden layers. In the learning step, a new rule is introduced by combining SOM and MLP learning rules, where the unit's weight update is influenced by a Gaussian function centered on the BBMU. The proposed approach uses MLP structure with each hidden layer as a SOM map and the BMU is found using Euclidean distance. The Best BMU is then determined as the most selected unit as BMU at the end of each test step. Thus, developing a combined MLP + SOM network, which they called Self Organizing Neuro-Glia Network (SONG-Net)

This approximation appeared as an extension of the works of the 2.2.1 section. Being a sequel to previous studies, the main objective of these models is still along the lines of trying to improve the classical ANN models through the application of artificial astrocytes.

2.2.3 Artificial neuro-glial networks

Inspired by the tripartite synapse, in which glial astrocytes exhibit chemical communication to propagate information and affect neuronal behavior (as opposed to electrical transmission of neurons), the researchers adopted a novel term for neural networks called "artificial neuron-glia network" (ANGN) (Porto 2004). These networks consist of each neuron being connected to an astrocyte in each of the layers, and the activation (inactivation) of the neuron for a specific period of time will cause the linked astrocyte to become activated, the result of which will cause the connected weights to increase (or decrease) according to a predefined factor. A strong point regarding the representation of the biological synapsis transmission of these approximation is that the artificial astrocytes were designed to resemble the signaling properties of biological astrocytes, which respond to neurotransmitters released under high synaptic activity and regulate neurotransmission in a larger temporal scale. However, at the moment these studies do not consider biological circuits as they are actually connected.

Within the ANGN techniques we can find mainly two different learning algorithms. On the one hand, in the works of Porto's group (Pastur-Romay et al. 2017; Mesejo et al. 2015; Alvarellos-González et al. 2012; Porto-Pazos et al. 2011; Porto et al. 2007) they postulate a hybrid algorithm, based on a first part of unsupervised learning in which it is going to be modulated through different glial algorithms adjusting the weights, in order to be later trained in a supervised way through a GA, comparing it with ANN that only counted with this supervised training; Moreover, in one of their works, (Mesejo et al. 2015) proposed that instead of using the evolutionary algorithm they were using until then, the second part should be carried out with a cooperative coevolutionary technique in a novel way, evolving the weights of the glial network and those of the ANN evenly as they were modulating. On the other hand, Sajedinia from a connectionist perspective (Sajedinia 2014, 2015), designed a couple of different architectures inspired by previous studies and carried out a learning algorithm also hybrid, where in a first phase he carried out one similar to backpropagation with a modification of updating the parameters and then an algorithm for independent astrocyte learning. Sajedinia also carried out a parallel study in 2015 (Sajedinia 2015), where she developed an ANGN using Porto's hybrid learning (Porto-Pazos et al.

2011) along with an additional algorithm representing connections between astrocytes inspired by the work of Pereira and Furlan (Pereira Jr and Furlan 2010).

Most of the works of this architecture have as a clear objective to create neural networks taking into account the biological model of the tripartite synapse and check if these not only work well and solve the problems, but the fact of having the astrocytic network helps to give a significant increase in performance (Pastur-Romay et al. 2017; Alvarellos-González et al. 2012; Porto-Pazos et al. 2011; Porto et al. 2007; Sajedinia 2014, 2015), in (Mesejo et al. 2015) a new learning technique is also proposed in which it is possible to suppress and automate the fact of needing manual tuning the parameters, because the networks of connectionist systems are going to be problem-dependent and that takes a lot of work until finding out what would be the ideal structure.

2.3 Performance of ANN vs ANN with astrocytes

To test the efficacy of ANNs with astrocytic modulation versus classical ANNs, different architectures were tested in all the papers and the performances obtained in different classification problems were compared. In order to be able to benchmark the results, both neuroglial networks and an ANN with the same parameters, without modulation, were run for the same problems. The problems that were tested range from classification simulations, to standardized datasets widely used for ANNs, to one of the studies in which they test datasets of their own creation. The conclusions obtained from the use of the new models inspired by the tripartite synapse against ANNs will be described below, according to the implementation technique of the artificial astrocytes.

Different studies have explored the application of MLP networks with integrated astrocytes in a simulation problem called ‘Two Spirals’. These studies, including (Ikuta et al. 2010, 2011b, 2012c, b; Gergel and Farkaŝ 2018), aimed to achieve better performance and tried different forms of applying this approach. Despite being a similar MLP approximation, they found that the more learning points the MLP network had to classify, the more it struggled to reach a certain level of complexity. The inclusion of astrocytes in the network allowed for the avoidance of local minima through oscillations, resulting in improved performance in some cases with a p-value less than 0.001. In addition, studies by (Ikuta et al. 2011a, 2012a) also explored the beforementioned networkds in other simulated problems such as chaotic time series. The results showed that the conventional method was the worst in terms of average error, and that both MLP with glial networks (impulse glial network and glial network) outperformed the conventional MLP and MLP with random noise. To verify that this was not noise introduced into the MLPs, a total of six modulated ANN models were developed in another study, in two cases applying glial behavior (Ikuta et al. 2016). Now applied such modulations on more complex classification datasets, they observed that with a p-value less than 0.05, it was always achieved if you compared the rest of the simple models or with chaotic noise versus the MLP with PGC. In the last of the presented work of this type of networks (Gergel and Farkaš 2019), to test how ANNs with astrocytes trained with Hebbian learning worked, different architectures were tested with UCR database (Bagnall et al. 2017). By using the Matthews Correlation Coefficient (MCC) as a metric for unbalanced data, they found that while astrocytes with fixed values did not always give significant results, Hebbian learning favored a significant performance gap compared to the other methodologies.

The main feature of models that added SOM to MLPs is that they will achieve results in a very significantly shorter time. In fact, in the study by (Landolsi and Marzouki 2014), 4 classification problems were tested with the aim of checking how long it took a classical MLP to reach a Root Mean Squared Error (RMSE) of 0.001 versus a SONG-NET, with the SONG-NET being 10 times faster in the simplest architectures. In later studies they also measured the Mean Squared Error (MSE) of one versus the other in addition to the execution time (Ben Chikha et al. 2015). Here it is shown how not only the SONG-NET networks are 5 to 6 times faster, but the MSE obtained was 0.19 for the SONG-NET versus 0.37 obtained by the MLP. It is with this type of networks that in (Bertegi and Marzouki 2017) tests SONG-NETs not only with data from public repositories, but also with own databases. They report that SONG-NET is up to 11 times faster than MLP, and that the performance is better by a few tenths.

As for the models defined as ANGN, their main characteristic is that in all cases they are very significant with respect to the ANNs against which they are compared, however, when trained in different ways with GA, the ANGNs are much slower than the ANNs. They also begin their first approaches (Porto et al. 2007; Porto-Pazos et al. 2011; Alvarellos-González et al. 2012) with classification problems created by simulations, in this case the MUX problem, and several more complex problems from the UCI repository (Dua and Graff 2017). In all cases they found that the higher the complexity in the number of hidden layers and neurons per layer, the better the performance for the same problems in the case of ANGNs. They also designed different variants of ANGNs and in virtually all cases showed significant difference in performance from ANGNs to ANNs trained with GA alone. As a novelty and continuing in this line, (Sajedinia 2014) presents a specialization of ANGNs called Artificial Astrocyte Networks (AAN), in which the best path of astrocyte connections is chosen, achieving superior performance. In (Mesejo et al. 2015), 5 more problems from the UCI repository were tested to study ANGN versus ANN, and using the Wilcoxon test statistic it was observed that the coevolution algorithm designed for this work improved 18 out of 20 times significantly the performance of ANGN, especially in validation, endowing it with a higher generalization capability.

It is interesting to note that, for the most part, the classification datasets used by all the papers are repeated on many occasions. The works with MLP use in many of the cases the simulation problem 'Two Spirals' with different difficulties (Ikuta et al. 2010, 2014, 2016), and in one of the occasions the 'N-parity' problem, although in this one they do not achieve significant results (Gergel and Farkaŝ 2018). In addition, classification problems found in different databases are also used, such as the Proben1 (Prechelt et al. 1994), from here they prove the problems of: 'Cancer', 'Card' and 'Glass' for the MLP with PGC Ikuta et al. (2016). In (Gergel and Farkaš 2019) uses the UCR time series database, testing problems of different complexities such as: 'FaceFour', 'MoteStrain', 'OSULeaf', 'SwedishLeaf' and 'ToeSegmentation1'. In the case of the SONG-NET and ANGN techniques, the problems used are mostly the same, so that an extrapolation of the performance of some techniques versus more realistic ones could be made. The UCI repository is where most of the classification problems used come from, such as: 'Iris', 'Ionosphere', 'Breast Cancer', 'Lung Cancer', 'PIMA', 'Sonar' and 'Heart Disease'. In addition to these, the simulation problems XOR (Landolsi and Marzouki 2014) and MUX (Porto et al. 2007) are used in first approximations of the SONG-NET and ANGN papers, respectively. Finally highlight that the only work of a model tested with real-world data was (Gergel and Farkaš 2019).

In general, after reviewing the different models presented here, it can be concluded that in all approaches the algorithms that included glia significantly improved the performance of classical ANNs. Depending on the case, we can observe that the astrocytic influence was reflected in performance, minimizing error or execution time. Furthermore, they conclude in almost all cases that making the structure of the networks more complex or using it on more complex problems shows a greater difference between ANNs and ANNs with any type of glial modulation. Such behavior shows similarities with neuroscience studies, in which they propose that tripartite synapse is more common in brain areas that process more complex problems, and astrocytes tend to exist in greater proportion to neurons in more complex animals (Herculano-Houzel 2014).

3 Methods

3.1 Protocol used to sample the papers

The selection of the articles presented in this review were chosen according to the standards of *Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol* (PRISMA) (Moher et al. 2009). Additionally, all of them are studies written in English, selected on the basis of the results obtained without establishing time limits.

As part of the systematic review process, a Git repository (Alvarez-Gonzalez 2023) was created to perform a fully reproducible search on Scopus. The search included 7 different keyword filtering combinations, using the boolean operator 'AND', in an attempt to include all possible combinations of denominations of projects with a similar aim in a very specific field. This approach ensured full transparency and reproducibility of the search strategy, enabling a more rigorous and reliable search process. The last search was carried out on May 11, 2023. The combinations of keywords and operators were:

1. "TITLE-ABS-KEY(artificial astrocytes neural networks) AND TITLE-ABS-KEY(glia).
2. "TITLE-ABS-KEY(connectionist system) AND TITLE-ABS-KEY(astrocyte)".
3. "TITLE-ABS-KEY(glial networks) AND TITLE-ABS-KEY(perceptron)"
4. "TITLE-ABS-KEY(neuro-glial) AND TITLE-ABS-KEY(artificial network)".
5. "TITLE-ABS-KEY(neuroglial) AND TITLE-ABS-KEY(artificial network)".
6. "TITLE-ABS-KEY(neuron-glia) AND TITLE-ABS-KEY(artificial network)".
7. "TITLE-ABS-KEY(neuron-astrocyte) AND TITLE-ABS-KEY(artificial network)".

Supplementary 1 provides an Excel file generated from the reproducible search, detailing different aspects such as: type of publication, title and journal to which they belong, among others.

3.2 Eligibility criteria

Despite the fact that there is not a large number of articles that corresponded to the filtering performed, several of the articles did not correspond to the objective of this review. The following are the minimum criteria they had to meet to be selected:

- In silico models that attempt to simulate the behavior of information transmission at the biological level must do so by means of connectionist models. Excluded those works of realistic, neuromorphic or hardware models, among others.
- Reviews and book chapters will not be included.

Which of initial 65 papers in the Scopus search matched the criteria are detailed in Supplementary 2. Due to the small number of papers selected from the database search, a manual search was performed looking for other papers by the selected authors that worked along the same lines and had also designed artificial astrocytes to improve classical ANNs. In this search, a total of 3 new articles were added, which are shown in Supplementary 3 in the same format as shown in Supplementary 2.

4 Discussion

This research has focused on identifying scientific papers that investigate the effects of artificial astrocytic modulation on classical neural networks. A total of 22 papers in this field have been analyzed, and the models developed have been subtyped based on the architecture used in three types: ANGN, MLP, and SONG-NET.

The concept of tripartite synapses, which involves communication between neurons and astrocytes, is still relatively new in the field of neuroscience. However, researchers in the field of artificial intelligence are already developing different connectionist models that draw inspiration from this process.

One of the key premises of this review is that introducing astrocytic cells into neural networks can enhance their processing performance. Therefore, the studies presented here aim to demonstrate that including artificial astrocytes in these models can also improve problem solving in various domains such as object recognition in images, classification, and regression. To do this, the researchers have created various types of architectures and observed a significant improvement in problem-solving performance when artificial astrocytes are introduced to optimize the chosen ANN model. This effect was particularly evident as the complexity of the task increased, which is a characteristic shared by the biological brain.

The main feature that makes the difference between the models developed has been what kind of influence the artificial astrocytes exerted on the functioning of the base artificial neuronal network. On the one hand, MLP models focused on the astrocytic effect from a more mathematical perspective, modeling neuronal regulation, such that glial regulation occurred as information received information and trained the (Gergel and Farkaš 2019) network. On the other, ANGN models focused on the regulation of astrocyte-induced synaptic plasticity (Porto et al. 2007; Alvarellos-González et al. 2012). This perspective is presented by including astrocyte regulation modulating neuronal activity on a higher time scale (seconds vs milliseconds, respectively). Thus, astrocytes were activated after intense neuronal transmission and consequently regulated synapse weights on a slower time course. Each neuron was linked to a single astrocyte, and hyperparameter tuning required specialized hypertuning, approached by automatically searching for parameters based on the cooperative coevolution of astrocytes and neurons throughout training (Mesejo et al. 2015).

As briefly discussed earlier, despite using biological models of information transmission as inspiration, there are models that try to be more accurate to what has been demonstrated in neuroscientific studies than others. Those more similar to what occurs in the brain would be the ANGN models, due to the fact that the action of artificial astrocytes is in each of the artificial neurons, versus the MLP models that choose only the hidden layers to be regulated by these artificial glial cells. Moreover, the learning algorithm employed in the latter is BP, a mathematical model, as opposed to the former, which used GA training, a bio-inspired algorithm based on the theory of biological evolution.

Artificial astrocytes, in their biological version, form a network in themselves, not distributed independently in our brain. Most works focus the artificial astrocytic action independently in one or all the neurons that form the architectures (Porto et al. 2007; Mesejo et al. 2015; Ikuta et al. 2010), however, the biological astrocytic networks have the characteristic that if they receive stimuli from the neurons they regulate, they will emit calcium waves that will also regulate the nearby astrocytes, causing them to modulate in a certain way the neurons they also have nearby. With this in mind, there are approaches in these models that try to create glial pulse networks (Ikuta et al. 2011a, b, 2012c, a, b, 2014, 2016), simulate these calcium waves (Sajedinia 2015; Ben Chikha et al. 2015) to try to see if co-regulation further enhances the neuronal network.

Regarding the regulation of astrocytes on the neurons of the architecture, it has been observed that a higher optimization in terms of model performance was achieved when using astrocyte regulation methods that were dependent on the problem and the neuron they influenced, as opposed to when fixed weights of influence were established for all the artificial astrocytes as a whole.

The main limitation found in these works, probably due to the fact that they are in an emerging phase in the field of study, is that the application of the different models that include elements that consider artificial astrocytes, even those that try to simulate their action in a more realistic way, have problems to justify that the improvement in performance is due to the action of an element that behaves as an astrocyte, or that it is only due to the addition of more elements that enhance the base architecture of the ANN with which they compare the results.

As possible future avenues, it is interesting to find that in one of the last papers presented, (Pastur-Romay et al. 2017) suggest that, due to the fact that all the papers point out that the complexity of the problem enhances the effect of the artificial astrocyte, it would be interesting to study the effect of the same on ANNs that work with higher dimensionality data, as occurs in ANNs that work with Deep Learning algorithms.

5 Conclusions

Based on the findings of this review, it can be concluded that introducing artificial glial cells in the process of information transmission through tripartite synapses can help in creating a more biologically realistic model. This review is the first of its kind and aims to provide researchers interested in this field with a guide sheet of the work that has already been done. The importance of these findings is highlighted for both neuroscience and artificial intelligence, as the development of a new kind of ANN based on these studies could have significant benefits in various sectors. Therefore, this research presents a promising avenue for future work in this field.

For this purpose, 22 scientific papers that investigated the effects of artificial astrocytic modulation on classical neural networks were analyzed and subtyped based on the architecture used. The studies presented here aimed to demonstrate that including artificial astrocytes in these models can significantly improve problem-solving performance in various domains. The main feature that made the difference between the models developed was the kind of influence the artificial astrocytes exerted on the functioning of the base artificial neuronal network. The ANGN models focused on the regulation of astrocyte-induced synaptic plasticity, while the MLP models focused on the astrocytic effect from a more mathematical perspective. Despite using biological models of information transmission as inspiration, some models try to be more accurate to what has been demonstrated in neuroscientific studies than others.

It is interesting to note that artificial astrocytes, in their biological version, form a network in themselves, and most works focus the artificial astrocytic action independently in one or all the neurons that form the architectures. The main limitation found in these works is that the improvement in performance is not always solely due to the action of an element that behaves as an astrocyte but could also be due to the addition of more elements that enhance the base architecture of the ANN. As a future avenue, it would be interesting to study the effect of the same on ANNs that work with higher dimensionality data, as occurs in ANNs that work with Deep Learning algorithms. Overall, this research suggests that introducing artificial astrocytes into neural networks can enhance their processing performance, and further studies in this field may contribute to the development of more efficient artificial intelligence models.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10462-023-10586-1.

Acknowledgements We are particularly grateful to CESGA (Galician Supercomputing Centre) for providing access to their infrastructure. We wish to acknowledge the support received from the Centro de Investigación de Galicia "CITIC", funded by Xunta de Galicia and the European Union (European Regional Development Fund-Galicia 2014–2020 Program), by grant ED431G 2019/01. Aid to support the pre-doctoral stage in the universities of the SUG, in the public research bodies of Galicia and in other entities of the Galician R+D+i System, partially co-financed by the FSE Galicia 2014–2020 Operational Program.

Funding Open Access funding provided thanks to the CRUE-CSIC agreement with Springer Nature.

Code availability The public Git repository with the search methodology followed to retrieve the publications found in Supplementary 1 can be found at: https://github.com/saraalgo/Glial_ANN_review.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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