COMPUTATIONAL MODELING OF ALZHEIMER'S DISEASE SYMPTOMS USING VENN'S NETWORK

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Abstract – Alzheimer's disease is a degenerative disorder of the brain that is still without cure and affects millions of people around the world. Understanding the disease mechanisms is important for therapeutics. A first step would be to use an explanatory model of the disease's symptoms. For that one would need an adaptive computational approach that resembles the biological system, upon which the Alzheimer's lesions like are to be simulated. Artificial Neural Networks may function as the needed test bed; Venn network is an artificial neural network (ANN) that has capability of simulating the behavior of a functioning brain under physiological and pathological scenarios. Hopfield network is another ANN that can recover previously stored patterns. This paper aims at presenting a computational approach that combines Venn and Hopfield networks in order to model of Alzheimer's disease. During the modeling phase, we have developed an artificial neural network structure based on Venn networks and the training algorithm of standard Hopfield model. The neural network was trained to recognize certain patterns of training, in this case, binary images. On top of that the Alzheimer's disease was modeled computationally taking into consideration some of its neuropathological aspects. Throughout various simulations, we have found that the Alzheimer's disease model disturbed the performance of a regular trained neural network, thus mimicking the pathological effects in the human brain.

Keywords – Alzheimer's Disease, Venn's Network.

1. Introduction

Computational neuroscience is an intrinsically interdisciplinary science, which extends itself from areas like psychology to physics and pure mathematics. One of the highlights of computational neuroscience is its ability to model anatomical and physiological aspects (i.e. shape and behavior, respectively) of the brain and other components of the neural system. Through mathematical and computational models, it is now possible to understand some of the emerging functions and complex mechanisms of this cumbersome system. This paper main objective is to produce a computational model of the Alzheimer`s Disease (AD), focusing on some of its known symptoms. AD is still cureless and generally affects people at the age of 50 and above. In general it deteriorates some regions of the brain, producing changes on physical and mental behavior, speech and other cognitive functions [1]. The impact of Alzheimer's neurological dysfunction on the functioning of a natural healthy brain has many peculiar features, mainly depending on areas affected.

The functioning of the brain may be considered, at various granularities ranging from sub-cellular processes (i.e. micro-scale) up to network or interregional processes (i.e. macro-scale). All of them can be viewed as computational processes, hence modeled, like any other. Before any high cognitive function or even small reactive behavior arises, each stimulus is processed by simple processing units - the neurons and its functional groups the cortical microcolumns. They work just like a computational system, i.e., the output signal is generated by applying a function in an input source. A reason for building computational

models, such as the one produced here is that cause-effect relation (i.e. input-output mapping) is still little known. The same as the neuropathology of the Alzheimer disease, which some of the disruptive effects and symptoms are to be captured by our model. The hypothesis is that the relations between physiological structures' activities of the brain and their neuroanatomical features, be influenced by lesions and neuropathological changes caused by also modeled [2]. During modeling using Venn Networks, all deemed information about the dysfunction will be applied in order that some inferences about the prognosis can be put forward in a plausible manner.

2. Background

2.1. Alzheimer's Disease

The Alzheimer Disease is essentially a neurodegenerative disorder that progressively disabilitates the central nervous system. It was first described by Alois Alzheimer in 1907, on a 51 year old woman who presented a fast dementia progress [3]. The effects of the disease are many and varied. Depending on the patient and how the disease acts in the brain, the AD can cause loss of intellectual functions such as memory, speech, eye sight, capacity of solving problems, etc. Most likely AD induces abnormal behavior, and disturbance of the executive and motor functions.

The dysfunction also causes the loss of sociability of patients and, at some stages of the disease, they become incapable of satisfactorily communicate with the outside world. The Alzheimer Disease turns out to be irremediably very painful for the patient and his family.

The neuropathology of AD is of various consequences, mainly, progressive atrophy and death of among neural population [1]. Some changes are also observed on the cytoskeleton; neurithical plaque formation is present, which is result of abnormal deposit of amyloid composits in the brain. The disease's progression can also slow down the signal propagation and may lead to connection loss between neurons. In short, the principal disabling mechanisms of AD are: neuron loss, neural atrophy and synaptic loss.

The loss of neurons is one of the most present effects in Alzheimer's disease. However, this characteristic is difficult to study. This is because the decrease in the number of neurons is a natural phenomenon in older individuals. However, not all types of cell are affected, and this effect is more common in pyramidal neurons of layers III and V of the cerebral cortex. Depending on the age, the loss varies between 38% and 67% [4], [5]. This feature is also present in efferent and afferent regions of the hippocampus. The loss of neurons also strongly reflects the loss of long and short-term memory[6].

Similarly to the loss of neurons, neuronal atrophy is closely linked with the severity of dementia. In AD patients, it is possible to observe a progressive decrease in the size of the cell nucleus [6] and the amount of ribonucleic acids in the cytoplasm [6], [7]. The neuronal atrophy is mainly caused by decreased ability of the brain affected by the DA to synthesize proteins [2]. Therefore, it is also possible to observe a certain dendritic loss.

Synaptic losses are caused by neurofibrillary tangles and neuritics plaques. Neurofibrillary tangles may also be present in other neurological disorders [8]. Unlike the loss of neurons and neuronal atrophy may be related to the increase of dementia in affected individuals. His presence is not common in all types of neurons. The formation of neurofibrillary tangles is related to the deposit of tau protein in the cytoplasm of cells [9]. Thus, because the tau is concentrated in the axon of the neuron, there are significant changes in this component. Moreover, neuritic plaques are spherical substances with a diameter of around 200 microns that has considerable importance in synaptic degeneration.

Neurofibrillary tangles and neuritic plaques cause synaptic disorders. However, as a vicious circle, synaptic changes may cause the formation of these substances.

2.2. Venn's Network

Despite of the complex brain constitution and diversity [10], the majority of the connectionist systems do not include, therefore do not explore this known facts. In most cases, the artificial neural systems possess only one type of neuron for all the processing tasks. This is even worse when ignoring the importance played by the brain's structure on the emerging computation. To take all that in consideration, Buarque [11] proposed in his doctoral thesis, the Venn networks.

Venn Network is an artificial neural network architecture that allows the definition of many kinds of processing units, further on it allows these units to group in regions, each one with its own properties. The denomination "Venn" is originated from the resemblance between the two dimension maps having many regions which are used in the network's processing and the Venn diagrams.

Figure 1 presents an schematic view of a basic Venn network.

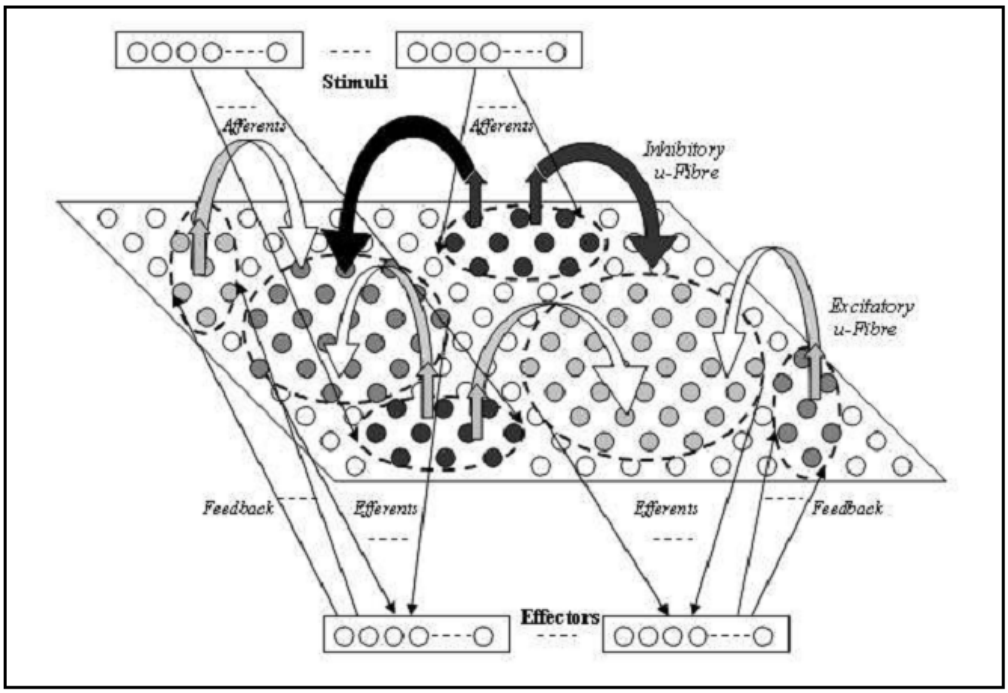

Figure 1 – Schematic view of Venn network. Arrows are connections of various types and small circles are processing elements comprising distinct regions.

2.3. Modeling of Alzheimer's Disease

The computational model presented in this paper uses Artificial Neural Networks to evoke its overall processing. More specifically, it was conceived as a computational system which its structure is based on Venn Networks [11] and the training routines is executed with the Hopfield algorithm [12].

The motivation for the use of Venn networks is the fact that this architecture is based on the same modular manner as the brain. This feature will be very relevant to simulate the neurological dysfunction. In the proposed model, the main concepts used were the idea of several processing regions and the heterogeneity of their processing units. These features are deemed to simulate the behavior of Alzheimer's disease as the disease does not affect the nervous system as a whole, targeting specific regions of the brain or even, specific types of neurons.

Regarding functionality, the Hopfield algorithm presents a feature that is closely related to the performance of Alzheimer's disease. That is, Hopfield networks can act as a associative memory. As it is known that in certain stages of AD, the patient shows clear signs of memory loss [13], this could be considered as a decay in the healthy associative-memory system. Thus, the representation of the brain taking into account the topology of Venn networks together with the ability to associate memories to specific regions makes this combination a strong candidate for a suitable Alzheimer computational model. Specially because damages caused by Alzheimer Disease could be interpreted as variations on the performance of the memory association.

To simulate the Alzheimer's disease, three neurological aspects were considered within the proposed modified Venn model with Hopfield training algorithm. They are: loss of neurons, neuronal atrophy and synaptic loss. Figure 2 shows a schematic view of the computational modeling of Alzheimer's developed in this article.

In the literature, there are several computational models of Alzheimer's disease [2][14], even including Artificial Neural Networks [15][16]. One of the main contributions of this paper is that the

modeling of AD was developed using the Venn Network, never before used to simulate this neurological dysfunction. Another point that deserves emphasis is the modification of the Venn Network training algorithm, substituted by Hopfield`s. Also notice that this article also employs Venn network in a totally different pathological scenario form the originally considered.

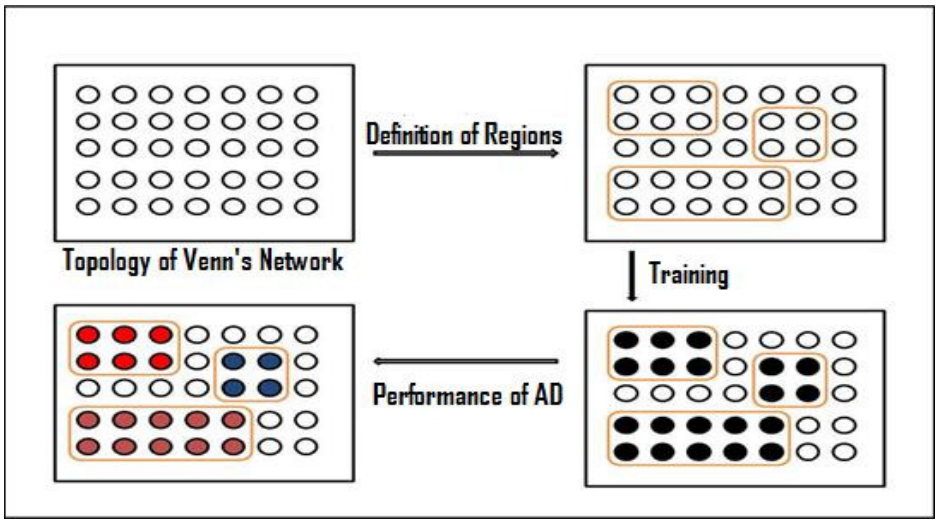

Figure 2 – Schematic view of the computational modeling of Alzheimer disease using the Venn Network topology.

3. Results

In this section the results of all simulations of Alzheimer disease using the proposed model are presented. The computational experiments performed illustrate the behavior of a network of Venn using the Hopfield model as a training algorithm. The network is composed of one hundred neurons, arranged in a 10x10 grid. The rationale is that the neural network is trained to recognize pictorial representation of numbers input as image matrices. In every matrix, values "+1" represent a black pixel and values "-1" represent a white pixel. Figure 3 shows the images, represented by 10x10 matrices, which were used as standards of training.

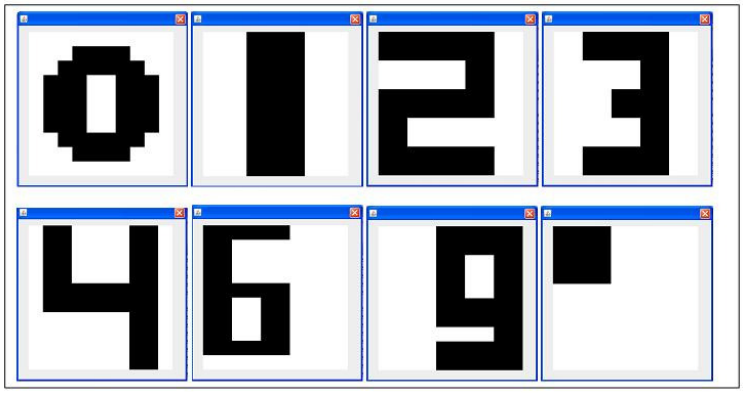

Figure 3 – Training patterns without noise used in the simulations.

We hypothesized that the AD could harm the successful memory association performed by the network.

Assuming a noise of 20%, i.e. a probability of 20% for each pixel to change its value, the neural network (without any damage AD like) still produces good results. Table 1 shows the average number of iterations necessary to recover well the patterns presented to the trained network.

Table 1 – Behavior of neural network trained to recovery patterns.

Standard	Noise (%)	Average number of iterations needed to retrieve a standard
0	20	445
1	20	288
2	20	343
3	20	364
4	20	350
6	10	382
9	10	353
“ ”	5	290

Next, some experiments were performed this time considering the type of damage generate by Alzheimer's disease. Different sets of simulations were carried out for each distinct neuropathological feature related to AD. Following that we merged all features and assessed the produced results. In all networks trained we defined number of regions and neurons accordingly to the feature investigated. Features od AD investigated were: (i) loss of neurons, (ii) neuronal atrophy and (iii) synaptic loss.

In all simulations, the functionality of processing units was varied as different activation function and threshold for excitation were tested. For all experiments, training patterns presented noise varying from 20 to 30%.

3.1. Loss of Neurons

In this case, memory recall decay produced by neuronal loss was simulated. Table 2 shows the parameters used in the simulations carried out. Figure 4 shows the result obtained for one single pattern.

Table 2 – Parameters for simulation of Loss of Neurons (at 20% noise).

Region	Number of Neurons	Activation Function	Threshold	Performance of AD	Probability (%)
Region 1	30	Logistic	0.1	Loss of Neurons	75
Region 2	35	Hyperbolic Tangent	0.2	-	-
Region 3	35	Logistic	0.25	-	-

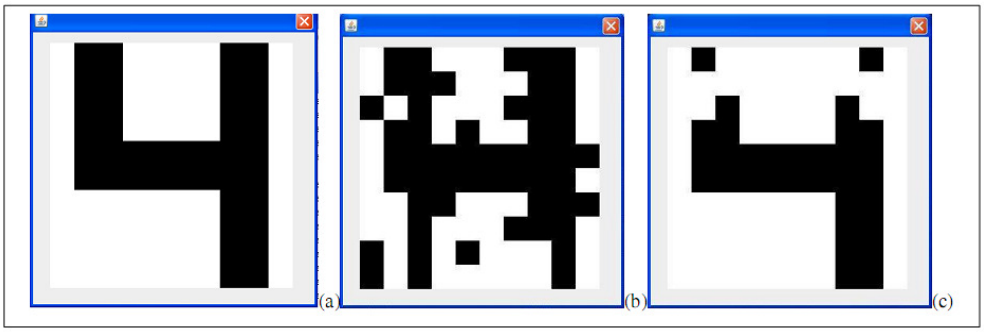

Figure 4 – Simulation on neural loss: (a) Regular pattern of training; (b) same pattern with 20% noise; and, (c) the network response.

3.2. Neural Atrophy

By raising the threshold of excitation of the affected processing units one my simulate the behavior of neuronal atrophy. Tables 3 and 4 show the parameters of the experiments at 20 and 30% noise levels. Figures 5 and 6 show the respective results for the two simulations.

Table 3 – Parameters for simulation of Neural Atrophy (at 20% noise).

Region	Number of Neurons	Activation Function	Threshold	Performance of AD	Probability (%)
Region 1	30	Logistic	0.1	-	-
Region 2	35	Hyperbolic Tangent	0.2	Neural Atrophy	75
Region 3	35	Logistic	0.25	-	-

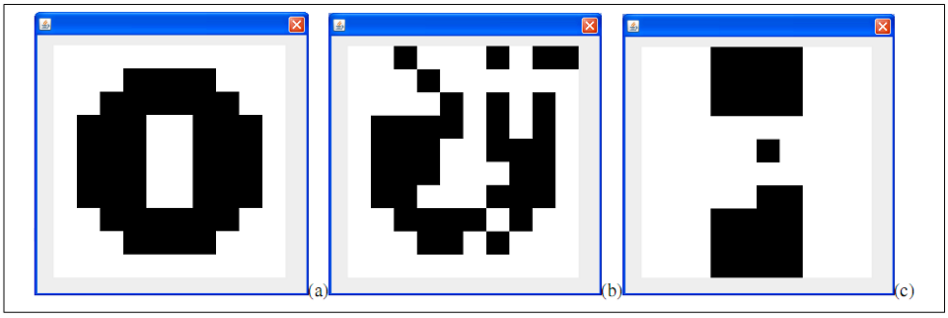

Figure 5 – Simulation on neural atrophy: (a) Regular pattern of training; (b) same pattern with 20% noise; and, (c) the network response.

Table 4 – Parameters for simulation of Neural Atrophy (at 30% noise).

Region	Number of Neurons	Activation Function	Threshold	Performance of AD	Probability (%)
Region 1	20	Logistic	0.1	-	-
Region 2	30	Hyperbolic Tangent	0.2	Neural Atrophy	75
Region 3	20	Logistic	0.25	-	-
Region 4	30	Hyperbolic Tangent	0.1	Neural Atrophy	75

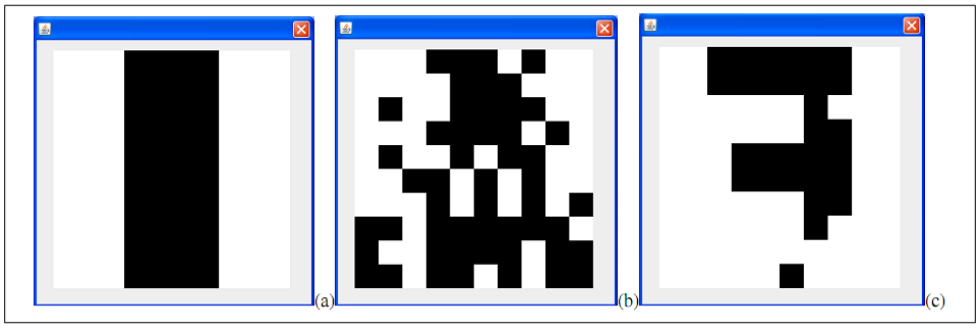

Figure 6 – Simulation on neural atrophy: (a) Regular pattern of training; (b) same pattern with 30% noise; and, (c) the network response.

3.3. Synaptic Loss

The experiments in this section simulate the behavior of synaptic loss, or the cancellation of some connections between neurons. Table 5 shows the parameters for this experiment, while the Figure 7 shows the results of the simulation.

Table 5 – Parameters for simulation of Synaptic Loss (at 20% noise).

Region	Number of Neurons	Activation Function	Threshold	Performance of AD	Probability (%)
Region 1	30	Logistic	0.1	-	-
Region 2	35	Hyperbolic Tangent	0.2	Sinaptic Loss	75
Region 3	35	Logistic	0.25	-	-

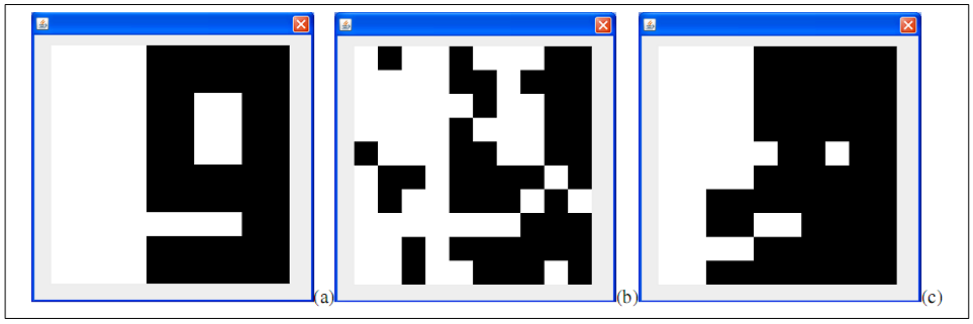

Figure 7 – Simulation on synaptic loss: (a) Regular pattern of training; (b) same pattern with 20% noise; and, (c) the network response.

4. Conclusion

This article put forward a computational model of Alzheimer's disease based on Venn networks and Hopfield training algorithm. AD is a devastating neurological disorder responsible for deaths and low quality of life in thousands people around the world. A series of simulations were carried out focusing at three different features of AD, namely, loss of neurons, neuronal atrophy and synaptic loss.

As anticipated in the initial hypothesis, all investigated features of Alzheimer`s Disease using our proposed computational model impaired the normal operation of the neural network when compared to "disease free" networks. Furthermore, the type of impairments observed resemble very much the effects in real AD patients, whom systematically present memory recall problems.

Although the actual impact of each parameter is not established well, as noticed throughout the simulations, changes in the various parameters of the simulation model cause impact in the satisfactory recall of the network for different patterns. This has occurred both in the independent simulations, i.e., considering the features of Alzheimer's disease separately, as well as in simulations where combined AD features were investigated.

It should be noted that, for each one of the models, the tendency is that the performance of the neural network is worse as a result of raise in unfavorable conditions. These conditions occur, for example, with presence of more noise and with more regions affected by the disease.

An interesting feature, noticed in the simulations, is shown in figures 5 and 6. When the neural atrophy aspect was applied to the network, the system apparently tries to recall “memories" which are distinct to the cue. One could interpret this as a sort of "mental confusion". Notice that this result was not programmed it is an emergent property of the proposed model.

In general, the results produced here were indications that it is possible to mimic the most one important characteristic of Alzheimer´s disease, i.e. memory loss, with a simple computational model presented. Finally, another highlight is the possibility afforded by the model, which is its ability to simulate various pathological scenarios in an easy manner. This is possible because the inference capability of Venn networks operating in various problem domains.

5. Future works

The present paper pointed out various research possibilities. However, other new developments may target better qualitative results (system calibration) as well as quantitative scenarios (scaling up the number of regions and neurons) to better generalize practical results. Hereafter, some of the suggested work, complement the development of computational modeling of Alzheimer´s Disease.

- The computational model could be extrapolated to cover others features of Venn´s network, for example, fibers differentiation;
- Consideration of clinical studies about the neuropathological aspects of Alzheimer´s Disease. So that others features of this dysfunction could be modeled and simulated;
- The simulations were made using artificial data. The model could be directed to cover the use of real data of disease, extracted from others works or even experimentally;

- The computational modeling of Alzheimer´s disease could inspire the modeling of others neuropathological dysfunction. A likely good candidate could be modeling the Parkinson disease, for example.

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