

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

ANDERSON TENÓRIO SERGIO*, DIEGO DE SIQUEIRA BRAGA*, FERNANDO BUARQUE DE L. NETO*

**Department of Computing and Systems - Pernambuco State University (UPE) - Recife - PE - Brazil*

Emails: ats@dsc.upe.br, dsb@dsc.upe.br, fbln@dsc.upe.br

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, especially 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. Through simulations, the proposed model is able to perform inferences about the prognosis of the pathology's symptoms thought time. This initial effort may, in the future, reduce uncertainties of doctors and patients on that devastating disease.

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

Resumo— A doença de Alzheimer é uma disfunção degenerativa do cérebro ainda sem cura, que atinge milhões de pessoas ao redor do mundo. Compreender os mecanismos da doença é importante para os terapeutas. Um primeiro passo seria utilizar um modelo explicativo dos sintomas da patologia. Para isso seria necessária uma modelagem computacional adaptativa que se assemelhasse ao sistema biológico, Redes Neurais Artificiais é uma abordagem com características de funcionamento que atendem esse requisito. Redes de Venn é uma arquitetura de Redes Neurais Artificiais (RNA) que tem a capacidade de simular o comportamento do funcionamento do cérebro em cenários fisiológicos e patológicos. Redes de Hopfield é outra RNA que pode recuperar padrões previamente armazenados. Este trabalho tem como objetivo apresentar uma modelagem computacional que combina redes de Venn e de Hopfield a fim de modelar a doença de Alzheimer. Através de alguma simulações, o modelo proposto é capaz de realizar inferências iniciais acerca da prognose dos sintomas da doença ao longo do tempo. Esse esforço inicial pode, no futuro, reduzir as incertezas de médicos e pacientes sobre essa devastadora doença.

Palavras-chave— Doença de Alzheimer, Redes de Venn.

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 (Bergeron, 1990). 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 emotion or even the the mind arises, each stimulus is processed by minimal processing units - the neurons and its functional groups the cortical micro-columns. They work just like a computational system, i.e., one (or more) input source is processed for that one (or more) output is produced, generally many.

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 (Duch, n.d.). 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 disabilitate 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 (Alzheimer, 1907). 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 induce 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 are several, mainly a progressive atrophy and the death of some neural population. Some changes are also observed on the cytoskeleton; neurithical plaque formation is present, which is result of abnormal deposit of amyloid composites 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.

2.2 Venn's Network

Despite of the complex brain constitution and diversity (Kandel, 1982), 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 (Buarque de Lima Neto, 2002) 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.

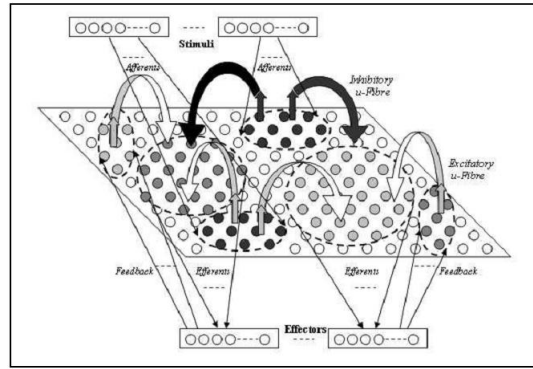


Figure 1: Schematic view of Venn network. Arrows are connections of various types and small circles are processing elements comprising distinct regions.

3 Computational Modeling of Alzheimer's Disease

3.1 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 Network (Buarque de Lima Neto, 2002)s and the training routines is executed with the Hopfield algorithm (Hopfield, 1982).

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 (Friedlander, 2006), 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 (Duch, n.d.)(Howard, 1996), even including Artificial Neural Networks (Horn, 1993) (Ruppin, 1995). 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 from the originally considered.

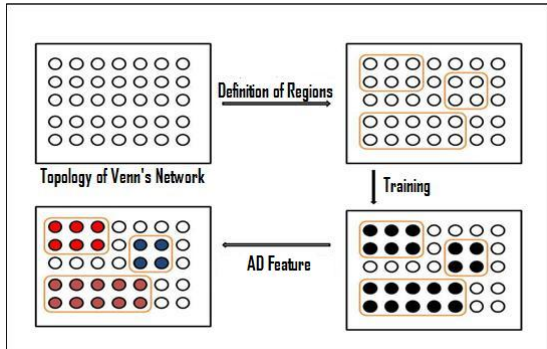


Figure 2: Schematic view of the computational modeling of Alzheimer disease using the Venn Network topology.

4 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.

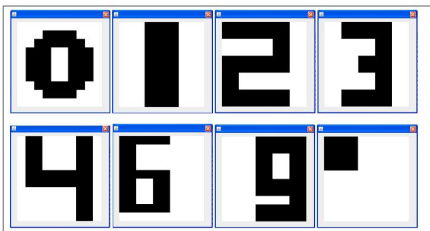


Figure 3: Training patterns without noise used in the simulations.

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 (without AD damage) to recovery patterns.

Pattern	Noise (%)	Iterations ¹
0	20	445
1	20	288
2	20	343
3	20	364
4	20	350
6	10	382
9	10	353
Square	5	290

¹Average number of iterations needed to retrieve a standard

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 of AD investigated were: (i) loss of neurons, (ii) neuronal atrophy and (iii) synaptic loss.

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

4.1 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.

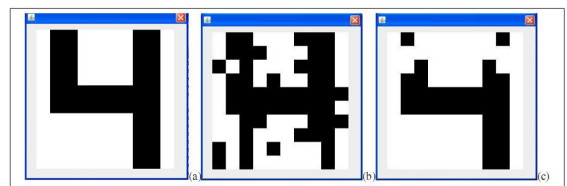


Figure 4: Simulation on neural loss: (a) Regular pattern of training; (b) same pattern with 20% noise; and, (c) the network response.

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

R. ¹	Num ²	Act. Funct. ³	Thres. ⁴	AD Feat. ⁵	Prob. (%)
1	30	Logistic	0.1	Loss	75
2	35	H Tangent	0.2	-	-
3	35	Logistic	0.25	-	-

¹Region

²Number of Neurons

³Activation Function

⁴Threshold

⁵AD Feature

4.2 Neural Atrophy

By raising the threshold of excitation of the affected processing units one may 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).*

R. ¹	Num ²	Act. Funct. ³	Thres. ⁴	AD Feat. ⁵	Prob. (%)
1	30	Logistic	0.1	-	-
2	35	H. Tang.	0.2	N.A. ⁶	75
3	35	Logistic	0.25	-	-

⁶Neuron Atrophy



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

4.3 Synaptic Loss

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

5 Conclusion

This article put forward a computational model of Alzheimer's disease based on Venn networks and Hopfield training algorithm. AD is a devastating

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

R. ¹	Num ²	Act. Funct. ³	Thres. ⁴	AD Feat. ⁵	Prob. (%)
1	20	Logistic	0.1	None	-
2	30	H. Tang.	0.2	N.A. ⁶	75
3	20	Logistic	0.25	None	-
4	30	H. Tang.	0.1	N.A. ⁶	75

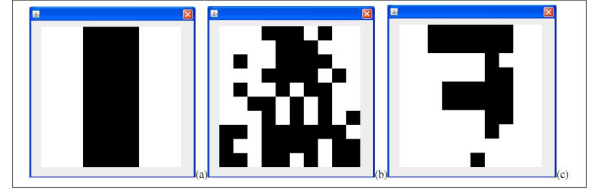


Figure 6: Simulation on neural atrophy: (a) Regular pattern of training; (b) same pattern with 30% noise; and, (c) the network response.

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,

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

R. ¹	Num ²	Act. Funct. ³	Thres. ⁴	AD Feat. ⁵	Prob. (%)
1	30	Logistic	0.1	-	-
2	35	H. Tang.	0.2	S.L. ⁷	75
3	35	Logistic	0.25	-	-

⁷Synaptic Loss

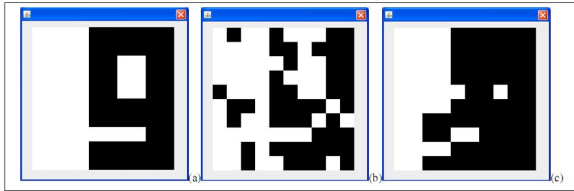


Figure 7: Simulation on synaptic loss: (a) Regular pattern of training; (b) same pattern with 20% noise; and, (c) the network response.

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 6 and 7. 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.

6 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 works to 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 her 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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