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Analyzing of Alzheimer's Disease Based on Biomedical and Socio-Economic Approach Using Molecular Communication, Artificial Neural Network, and Random Forest Models

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Abstract: Alzheimer's disease will affect more people with increases in the elderly population, as the elderly population of countries everywhere generally rises significantly. However, other factors such as regional climates, environmental conditions and even eating and drinking habits may trigger Alzheimer's disease or affect the life quality of individuals already suffering from this disease. Today, the subject of biomedical engineering is being studied intensively by many researchers considering that it has the potential to produce solutions to various diseases such as Alzheimer's caused by problems in molecule or cell communication. In this study, firstly, a molecular communication model with the potential to be used in the treatment and/or diagnosis of Alzheimer's disease was proposed, and its results were analyzed with an artificial neural network model. Secondly, the ratio of people suffering from Alzheimer's disease to the total population, along with data of educational status, income inequality, poverty threshold, and the number of the poor in Turkey were subjected to detailed distribution analysis by using the random forest model statistically. As a result of the study, it was determined that a higher income level was causally associated with a lower risk of Alzheimer's disease.

Keywords: Alzheimer's disease; molecular communication; amyloid beta; socioeconomic; random forest; neural network; Turkey; number of received molecules; total population; income inequality

1. Introduction

Living organisms, especially humans, suffer from various diseases such as multiple sclerosis (MS), heart rhythm disorder, low and high levels of sugar, spinal cord paralysis, Alzheimer's Disease, and cancer, due to the deterioration in the structure of some cells or the environment (viscosity) in which molecules move [1,2]. For this reason, proper communication between cells is very important for living things [3] and many studies on this subject are required. Within this perspective, it is hoped that some artificial neuron and synapse models, or nanorobots designed to be integrated into microcircuits, can be partially used in the treatment of diseases. The use of molecular communication (MC) in the medical field is generally for the diagnosis and treatment of diseases that have no cure today. In this context, there are many studies in the literature proposing nanorobots and cell models [1,2], and electronic circuits typically designed on a chip [4]. For example, in

one study of the applications of a nanoscale, neuro-spike communication system for the nervous system, a new model inspired by digital communication systems was proposed for the development of diagnosis and treatment methods in nervous diseases [3]. As a result, it has been concluded that some incurable or difficult-to-treat nervous diseases could be treated with biologically inspired molecular communication systems, although this is not yet possible with current technology. It is thought that by creating artificial immune systems and injecting them into the body, a significant contribution can be made to the treatment of many diseases in the future [5]. These injected systems could be trained in advance, just as in a real immune system, so that some of them could be used to find pathogens in the body, and some of them used to destroy pathogens.

Today, many people around the world lose their lives as a result of various diseases. One of these is Alzheimer's disease (AD), which is usually seen in older people. It is estimated that Alzheimer's disease will affect more people as elderly populations increase. It is known that one of the causes of this disease is a peptide which is known as amyloid peptide and which accumulates inside cells. Amyloid peptide is a protein produced by cells to sustain their vital activities. However, disintegration of this protein by various enzymes, disruption of the cell structure, or protein overproduction may occur in diseases that have not yet been cured even today. The best known of these diseases is Alzheimer's, which causes forgetfulness in humans [6,7]. AD is estimated to be a disease caused by inadequate communication between cells, or by failure of individual cells. Aβ peptides are formed by the breakdown of amyloid precursor proteins (APPs), which are first type membrane proteins; by β-secretase; and γ-secretase enzymes, as shown in Figure 1 [6].
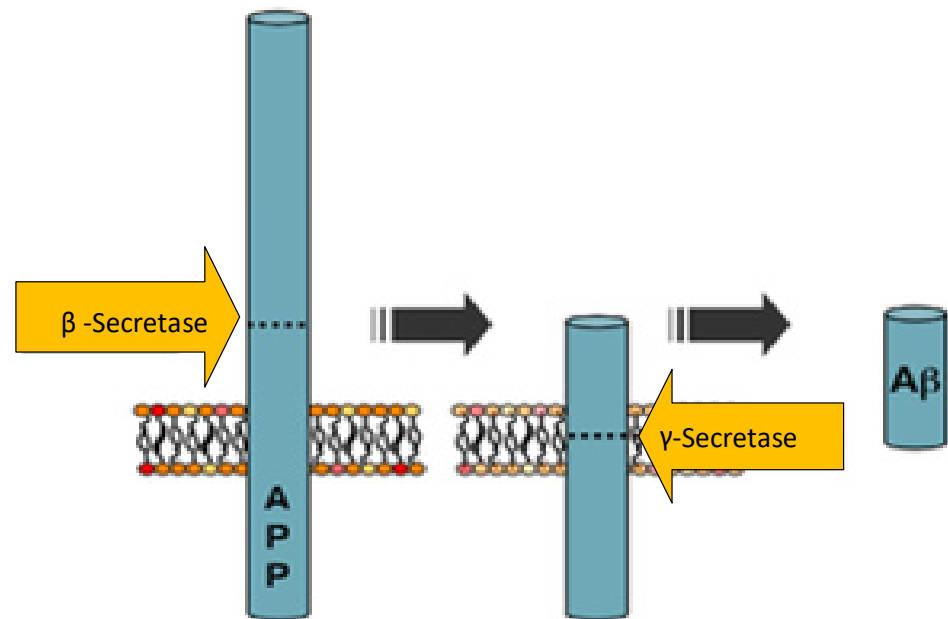

Figure 1. A symbolic figure showing how Aβ is obtained by degrading the β-secretase and γ-secretase enzymes of the APP, adapted with permission from Ref. [8].

APPs are known to be produced by many cells of living things, but precursor proteins produced by nerve cells in the brain cause Alzheimer's disease [6,7]. Although it is not yet known what causes this disease, experimental studies on mice have shown that the peptide Aβ 40–42 inhibits the transfer of information from the transmitter cell to the receiver cell with more accumulation between neurons than normal [9]. As a result of experimental studies, it has been suggested that Aβ peptides are present both inside and outside of the neuron cells of healthy people at a certain rate, and that this is necessary for neuron cell function [10]. The most common example of this is that Aβ peptides play an active role in the formation of synapses and memory structures of living things.

There are some studies in the literature about the accumulation of Aβ peptides in neuron cells causing many diseases such as Alzheimer's, and how to prevent this accumulation. For example, in [10], a review of the literature on the function of Aβs in nerve cells was conducted. As a result of this study, it was concluded that Aβs in the neuron and in the synaptic space contribute to the formation of neuron cells and memory structures of living organisms, as well as to the death of neurons and memory loss. As a result of experimental studies, the effect of Aβs on nerve cells was found to be positive amongst young and middle-aged people, but the effect was observed as negative in those of older age. This negative effect is known to result from the disruption of N-methyl-D-aspartic acid (NMDA) receptors, α7-nicotinic acetylcholine receptors (α7-nAChR), mitochondrial Aβ alcohol dehydrogenase (ABAD) and cyclophilin D in neuron cells of Aβs. It has also been suggested that Aβ peptides are associated with tension-controlled Ca^{+2} and K^+ channels, NMDA and amino-3-hydroxy-5-methyl-isoxazolepropionic acid (AMPA) glutamate receptors in the cell membrane [9–11]. In order to demonstrate this, studies [12–14] showed that intracellular Ca^{+2} content was higher in Alzheimer's patients than in nonpatients. This shows that there is a relationship between Aβ and Ca^{+2} ion production. There are also studies in the literature claiming that an increased amount of Aβ disrupts the structure of the synapse. In [15], an analytical study was performed on the effect of high levels of Aβ peptides found inside and outside the cell on the synaptic ion release of the neuron. In this study, a model which analyzes the effect of Aβ on the probability of Ca^{+2} and K^+ ion release in synapse is proposed based on many previous experimental studies. For this study, a mathematical model which produces action potential was first developed; then, the information obtained from the synapses of living mice was compared with information obtained from the model. For comparison, synaptic release changes in intact mice and in diseased mice with a large amount of Aβ in their neurons were examined. It has been emphasized that an increased amount of Aβ in nerve cells affects ion release of pre-synaptic neurons, and this effect is especially notable in the CA3–CA1 synaptic region. In [16], it is proposed that the amount of Aβ accumulated outside the cell disrupts the structure of the synapse, which, in contrast to the inside of the cell, affects the vesicle release of the neuron. In this study, Aβ peptides accumulated between neurons were shown to cause death of post-synaptic neurons by a new imaging technique called array tomography. Many analyzes were performed experimentally on real mice using this technique. It is reported that post-synaptic neuron density varies with increasing amounts of Aβ, which in turn affects the synapses. As a result, it has been claimed that the amount of Aβ accumulated in the synapse disrupts the function of neurons and causes spine accumulation. In [17], it is claimed that the Aβ peptides attached to the cell membrane disrupt the structure of the synapse by causing diseases such as oligomeric dysfunction and destruction. In [14], the relationship between Aβ and Ca^{+2} levels of neurons was experimentally investigated by inserting synthetic Aβ 25–35 or Aβ 1–40 and Ca^{+2} inhibitors into the endoplasmic reticulum. As a result, it is claimed that an increased amount of Aβ increases the level of released Ca^{+2}, which leads to the death of the neuron cell, so that Alzheimer's disease can be treated if the Ca^{+2} level can be controlled. In another experimental study, the effects of intracellular and extracellular Aβs in the 3xTg-AD transgenic model, a model of Alzheimer's disease, were investigated in mice. As a result of these experiments, it is claimed that Aβs accumulated outside the cell consist of the same Aβs accumulated inside the cell [13]. Looking at the literature examining the effect of Aβ on neuron cells and on Alzheimer's disease, the questions of how and where the Aβ peptides that cause this disease accumulate, and how the disease is actually caused, have not yet been clearly answered [13]. However, there are many studies showing that the presence of the amyloid peptide, which is known to cause Alzheimer's disease, is affected by varying education levels within a society and, additionally, by socioeconomic factors such as income inequality and the elderly population proportion [18,19]. Many recent community-based Alzheimer's disease prevalence and incidence studies have found a direct correlation between lower levels of education and the risk of Alzheimer's disease [18]. On the other hand, it is stated in a novel study that

Aβ pathology and AD are related with respect to cognitive abilities, and the ability of forms of Aβ and tau protein in combination to drive healthy neurons into a diseased state. Aβ peptides and tau proteins consistently accumulate in the frontal and/or parietal lobes, and cause alterations in the frontal lobe which impact memory and error-driven learning in individuals who have a high risk of dementia [20]. In addition, an overview of the anatomical–functional interplay between the prefrontal cortex and heart-related dynamics in human emotional conditioning (learning) has been carried out, and a theoretical model constructed to conceptualize these psychophysiological processes. A neuro–visceral integration model of fear conditioning that can be impaired in the context of psychiatric disorder is therefore proposed in [21]. In another study, the role of the prefrontal cortex in fear conditioning on a neurophysiological level was investigated [22]. In this study, using a short-time Fourier transform and instantaneous spectral estimates taken from a point process modeling approach, a unique frequency domain study of heart rate was carried out to gain greater insight into the physiological basis of fear learning. There are also some studies about novel pharmaceutical approaches with respect to dementia [23] and neurogenic inflammation [24]. In these studies, the emerging evidence supporting the involvement of neurogenic inflammation and neuropeptides in the pathophysiology of migraine are discussed, and the most recent advances in preclinical research as well as novel therapeutic approaches to the disease are presented.

Numerous epidemiological studies have focused on identifying protective factors against Alzheimer's disease, which also represent potential components of cognitive reserve. In this context, one of the most frequently studied determinants is education, along with socioeconomic status closely associated with educational levels. Epidemiological studies consistently report that higher education is associated with a lower risk of Alzheimer's disease. Many studies have shown that people with less education have a higher risk of Alzheimer's disease [25–28]. Various processes have been proposed to explain this link. The author of [29] argued that increasing synaptic density in the neocortical association cortex could improve brain reserves. Stern et al. expanded on the cognitive reserve hypothesis by considering the potential benefits of mental engagement across the entire lifespan, and found that professional achievement and educational success may reduce the risk of Alzheimer's disease [25]. Only a few studies have found links between adult occupational socioeconomic level and the occurrence of Alzheimer's disease. Evans et al. discovered that all of the socioeconomic status markers studied (education, occupational prestige, and income) predicted the onset of Alzheimer's disease [30]. Manual work, especially when it includes the creation of commodities, has been linked to an increased risk of clinical Alzheimer's disease [31]. There are also studies about risk factors, pathogenesis, and structural and functional changes associated with neurodegeneration in AD [32–34], the genetic, clinical, and biochemical data of individual patients [35], searching for peripheral biomarkers in neurodegenerative diseases [36] and gut microbiota regulation and their implication in the development of neurodegenerative disease [37,38]. In [39], the pathophysiological basis and biomarkers of AD pathology, and molecular signs of neural inflammation in neurodegenerative diseases are investigated. In [39,40], the roles of hub and spoke regions in theory of mind in early AD and frontotemporal dementia are studied. In [40], the etiological factors behind neurodegenerative disease are explored. There are also some studies which consider age-related impairments of the ability to process contextual information and to regulate responses to threat, finding that structural and physiological alterations in the prefrontal cortex and medial temporal lobe determine cognitive changes in advanced old age that can eventually cause patterns of cognitive dysfunctions observed in patients with AD/MCI [22].

Recently, with the spread of nanotechnology, the number of publications on molecular communication has been increasing. Many researchers have proposed new methods and techniques so that nanotechnology can be used more effectively in various fields such as medical science and nanorobotics. Such methods are typically used to solve intercellular communication problems. For example, in digital communication systems, hardware-based

antennas are used to more effectively transmit information from the transmitter to the receiver, while molecular-based antennas are used in molecular communication systems. There are some studies of molecular-based antenna models in the literature [41–43]. In study [41], on the probability of molecules successfully reaching the receiver, a simulation-based analytical study was carried out and a proposed system was tested and analyzed. For this study, the receptors on the receiver in biological organisms were considered as molecular antennas and the probability of molecules released from the transmitter successfully reaching the receiver was analyzed by changing the size of the receptors and the density on the receiver. As a result of the analysis, it was discovered that smaller-size receptors with the same density on the receiver take up the released molecules with a higher probability of success. In the study of [42], a ligand–receptor model was proposed by the researchers who sought to obtain capacity increase in this proposed model by using the Markov chain model. In study [43], oriented receiver models, which for molecular communication systems are claimed to be equivalent of antennas for digital communication systems, were studied.

There are also many applied studies and research related to MC. Specific areas of research include the use of MC for medical applications [44,45], the control and sensing of chemical reactions [46], molecular communication with computational biology [47], the use of nanorobots in the diagnosis and treatment of diseases by injection into the human body [48], communication between nanorobots [49], and thermoluminescence applications for physics [50]. In addition, the use of molecules trained for medical applications [51], the application on lab-on-a-chip systems where small labs on a chip are used [52], and directed drug delivery [5] are all reported examples of molecular communication applications.

In our previous studies, we proposed molecular communication-based models used to increase communication quality between the receiver and the transmitter by changing of system and environment parameters [53,54], by the use of deep learning algorithms [55] and by mobile bio-inspired structures [56].

To the best of the authors' knowledge, although all of these studies are biomedically-based, there has been no multidisciplinary study in which socioeconomic status is included when considering solutions to a health problem using MC and neural network methods. Moreover, past studies have only looked at the primary occupation of individual subjects, not all periods of employment. Furthermore, no research has been carried out on the relationship between social mobility (between different socioeconomic levels) and the risk of Alzheimer's disease in old age.

In this study, firstly, a molecular communication model that has the potential to be used in the diagnosis of Alzheimer's disease—which is one of these communication-related diseases—is proposed and its results analyzed with an artificial neural network (ANN). Secondly, we consider the ratio of people suffering from Alzheimer's disease to the parameters of total population, educational status, income inequality, poverty threshold, and the number of the poor., A detailed distribution analysis for Turkey was carried out using the random forest model. The aim of this study was to use the proposed ANN and MC models for diagnosing Alzheimer's disease and for predicting the number of received molecules which are related to Aβ. Another aim of this study was to emphasize the relationships between Alzheimer's disease and parameters which affect this disease directly using the random forest model, after socioeconomic analysis is carried out. It will then be possible to determine, finally, which parameters exert the more important influences upon this disease.

2. Materials and Methods

2.1. Molecular Communication and Artificial Neural Network-Based Analysis of Alzheimer's Disease

In order to model and verify the communication mechanism of nanoscale systems, intensive studies have been carried out recently on the development of new communication techniques inspired by nanoscale electrochemical communication systems used by living

things. This phenomenon, where chemical signals are used as carriers in information transfer, is known as MC. In this study, molecules are used as carriers for signal transmission between transmitters and receivers of nano or micro sizes in systems of molecular communication by diffusion. For the motion of these molecules in the diffusion medium, system modeling was carried out based on the Brownian motion principle. In the proposed model, to simulate the movement of carrier molecules, the simulation time is divided into small time steps and a random motion is added to each of the three dimensions in each successive time step, with the motion of the molecules performed in 3D. According to these dynamics, the total displacement of the dispersed molecule for a time step (Δt) in n-dimensional space can be found as follows [57,58]:

$$(\Delta x_i, \Delta y_i, \Delta z_i) = N(0, 2D\Delta t) \quad i = 1, 2, 3 \ldots.., \tag{1}$$

where $\Delta x_i, \Delta y_i$, and Δz_i refer to position of nanomachines of size i, D denotes the diffusion coefficient and N is the Gaussian (normal) random variable.

It is known that molecules reaching the receiver through the channel are absorbed by chemical reactions or directly by the receptors and taken into the receptor [59]. The molecules reaching the receptors are referred to as the first successful hitting. The formula for the probability of this first successful hitting of a molecule transmitted at time t in a 3-dimensional medium is as follows:

$$f_{hit}^{3D}(t) = \frac{r_r}{d + r_r} \, erfc\left(\frac{d}{\sqrt{4Dt}}\right) = \frac{r_r}{d + r_r} \frac{d}{\sqrt{4\pi Dt^3}} e^{-\frac{d^2}{4Dt}} \tag{2}$$

where r_r and d refer to the radius of the receiver and the distance from the transmitter to the receiver surface, respectively. The multiplying rate of molecules up to time t can be obtained by integrating Equation (2) over time. In this study, a pure diffusion channel method was used for the movement of nanomachines (NMs) in a fluid medium [60]. The movement and information transfer of these information molecules in the channel environment can only be achieved by using molecular communication methods. The proposed MC model consists of a point transmitter, a spherical receiver, carrier molecules, and receptors on the receiver, as shown in Figure 2. Carrier molecules are used as information carriers between transmitter and receiver. First, the receiver is placed at the origin (0, 0, 0) in the 3-dimensional plane and the transmitter is randomly placed at a distance d from the receiver in the 3-dimensional plane, as shown in Figure 2. After the molecules are released into the environment, they spread according to Brownian motion, until they reach the receiver. The spherical receiver uses receptors with radius of r_r to absorb information molecules as shown in Figure 2 [53]. If a molecule collides with one of these receptors on the surface of the receiver, the receiver absorbs it. If a molecule enters the receiver without hitting any of the receptors, this molecule is considered as not received [41]. In a previous molecular communication-based study for the diagnosis and treatment of Alzheimer's disease, amyloid beta peptides were randomly placed in the channel environment as shown in Figure 2 [61]. As a result of the study, it was observed that the amount of this peptide, which was found to be closely related to Alzheimer's disease, was directly affected by the communication between the transmitter and the receiver.

2.2. Socioeconomic Status Analysis of Alzheimer's Disease

In Turkey, many people are struggling with Alzheimer's disease. As far as it is known, there are 300,000 Alzheimer's patients in Turkey and the proportion of people who suffer as a result of this disease is increasing day by day in Turkey and around the world. In order to overcome this problem, many people, especially those researchers working in the medical field, have carried out various studies. However, although the treatment of this disease is not known yet, intensive research continues to be carried out by researchers working in the fields of medicine, engineering, and the social sciences. Alzheimer's disease, which was analyzed in terms of medical and engineering sciences in the previous section,

will now be examined in terms of socioeconomic parameters which are widely used as a binding indicator in health studies [62,63]. Thus, it is hoped to guide future diagnosis and prognosis for this disease, which has no treatment yet.
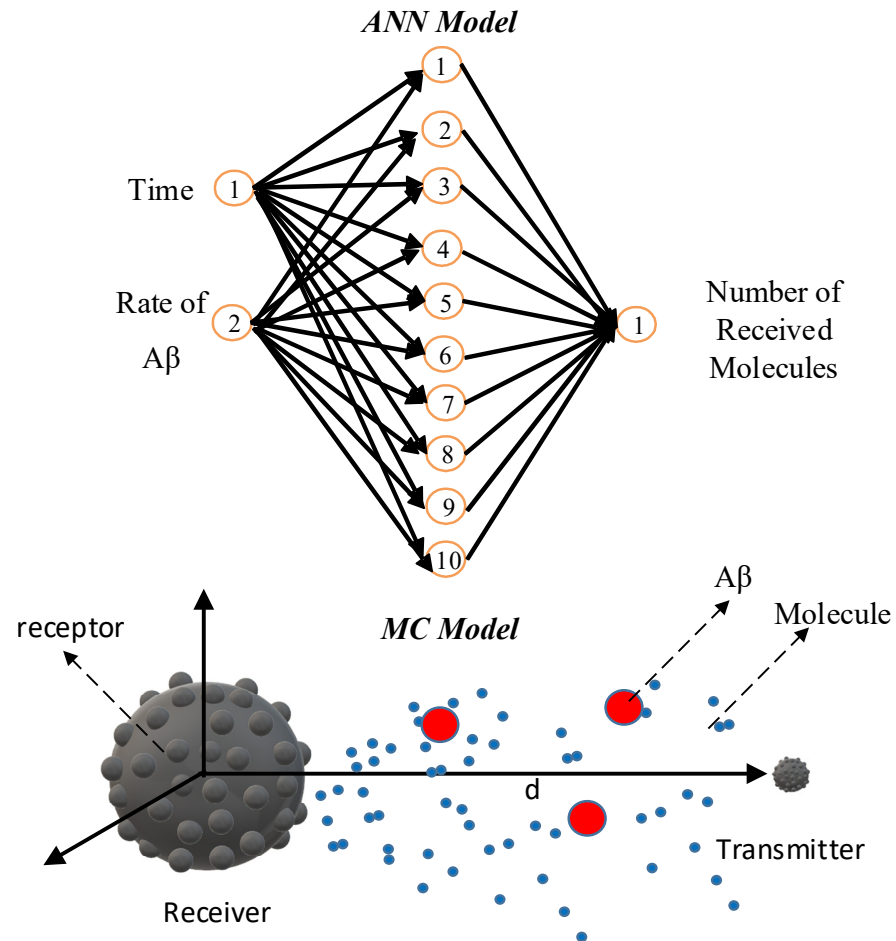

Figure 2. Proposed MC and ANN models.

2.3. Random Forest Model

The random forest methodology is used to solve two types of problems: building a prediction rule in a supervised learning problem; and evaluating and ranking variables based on their ability to predict the answer. Random forest, in common with neural networks and some other classifiers, is nonlinear. It is commonly used to sort nonlinearly separable data. The latter is accomplished by using the random forest algorithm's variable importance measures, which are automatically produced for each predictor. Random forest variable importance models, in particular, are thought to be successful at identifying predictors involved in interactions; that is, predictors that can only predict response in conjunction with one or more other predictors [64,65].

A random forest is a set of tree predictors $h(x, \theta_k)$, $k = 1, \ldots K$ where x represents the observed input (covariate) vector of length p and θ_k represents independent and identically distributed (*iid*) random vectors. As previously stated, we here concentrate on regression problems with a numerical outcome, Y. However we do also identify certain classification (categorical outcome) issues. The observed (training) data are considered to have been drawn independently from the joint distribution of (X,Y) and consist of $n(p + 1)$-tuples $(x_1, y_1), \ldots, (x_n, y_n)$.

The unweighted average over the collection is the random forest prediction for regression: $h(x) = (1/K) \sum_{k=1}^{K} h(x; \theta_k)$. As $k \rightarrow \infty$ the law of large numbers provides

$$E_{X,Y}\left(Y - \bar{h}(X)\right)^2 \rightarrow E_{X,Y}(Y - E_\theta h(X; \theta))^2 \quad (3)$$

The value on the right is the prediction (or generalization) error for the random forest, labeled PE_t^*. Because of the convergence described in (3), random forests do not overfit. We then define the average prediction error for a single tree $h(X; \theta)$ as follows:

$$PE_t^* = E_\theta E_{X,Y}(Y - h(X; \theta))^2 \quad (4)$$

We now assume that the tree is unbiased for all, i.e., $EY = E_X h(X; \theta)$. Then,

$$PE_f^* \leq \bar{\rho} PE_t^* \quad (5)$$

where $\bar{\rho}$ is the weighted correlation between the residuals $Y - h(X; \theta)$ and $Y - h(X; \theta')$ for independent variables θ, θ'. The inequality (5) identifies what is needed for precise random forest regression: (i) there is a low correlation between the residuals of different forest tree members; and (ii) the individual trees have a low prediction error. Furthermore, it is expected that the random forest will reduce the individual tree error, PE_t^*, by a significant factor. As a result, the injected randomization aims for low correlation [65–67].

In this study, six different parameters which are income, population, education, poverty threshold, population aged 65+, and number of the poor are considered with respect to the ratio of people suffering from Alzheimer's disease to show which parameters affect the rate of death from Alzheimer's disease more.

3. Results

In this study, first of all, the effect of the proposed MC model on the number of received molecules was analyzed for different values of the ratio of Aβ present in the medium as shown in Figure 3. All analyzes were performed taking into account only the receptors on the receiver. If a molecule was received by the receiver without touching any of the receptors, then that molecule was not taken into account [41]. As seen in Figure 2, some spherical objects were placed into the environment randomly to represent Aβ. After the molecules were emitted from transmitter to receiver, is the latter was checked at each time step of the simulation if it moved without touching any Aβ to obtain a more biological result. Molecules received by the receiver without touching any Aβ were not taken into account. The ratio of Aβ was also considered during the analysis by noting the number of Aβs in the environment to obtain a more statistical result. After obtaining the number of received molecules for different Aβ ratios, the system was analyzed by ANN so that the system could easily test for different Aβ ratios in the future.

As can be seen in Figure 3, as the Aβ ratio increases, the number of received molecules decreases in both the proposed MC and ANN models. This situation has been interpreted in this way in the medical field. In tissue samples taken from Alzheimer's patients, a proven link has been identified between the increased numbers of Aβs and the progression of the disease. This shows that the proposed model works correctly. In addition to Figure 3, some results of MC and ANN models with respect to Aβ ratios are also given in Table 1. As can be seen in Table 1, the number of received molecules decreases with increasing levels of Aβ, as expected. The highest number of 65 molecules was obtained with an Aβ ratio of zero for the MC model and the lowest number of 0 molecules was obtained with an Aβ ratio of 0.05 for both MC and ANN models. The results of the ANN and MC models are given below.
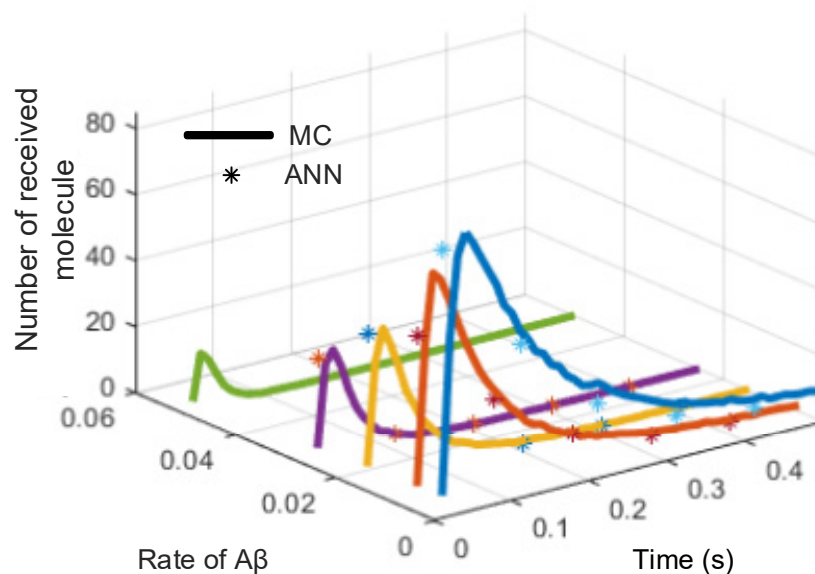
Figure 3. Comparison of the results obtained from the MH and ANN models for different Aβ ratios (yellow line for rate of Aβ = 0.05, yellow line for rate of Aβ = 0.025, yellow line for rate of Aβ = 0.015, yellow line for rate of Aβ = 0.005, yellow line for rate of Aβ = 0).

Table 1. Number of received molecules with respect to rate of Aβ for both MC and ANN models.

Time (s)	Number of Received Molecules									
	Rate of Aβ = 0		Rate of Aβ = 0.005		Rate of Aβ = 0.015		Rate of Aβ = 0.025		Rate of Aβ = 0.05	
	MC	ANN	MC	ANN	MC	ANN	MC	ANN	MC	ANN
0	0	0	0	0	0	0	0	0	0	0
0.1	65	63	45	46	24	23	20	19	0	0
0.2	40	42	25	27	15	16	7	8	2	1
0.3	20	21	8	7	3	4	2	2	1	1
0.4	8	7	3	3	1	1	0	0	0	0

The results obtained from the two models were then compared to show that the results from the proposed MC and ANN models were close to each other, and very low residual values of around ±1 (difference between ANN and MC) were obtained, as illustrated in Figure 4. Although very low residual results were obtained from the two models, the residual values obtained for an Aβ ratio of zero were higher than for other Aβ ratios.

For the socioeconomic status analysis of Alzheimer's disease, the age group proportions of the elderly population of Turkey in 2015 and 2020 are given in Figure 5. The proportion of elderly people in Turkey in recent years is given in Table 2. It can be seen from the table that the elderly population of Turkey has increased over time, and this has affected the numbers of elderly people who have Alzheimer's disease. The table shows that total population and rates of increase in the population aged 65+ have both increased, and numbers of deaths on account of Alzheimer disease have also risen, because the prevalence of this disease increases with increasing rates of elderly people within populations.

A classification of the elderly population of Turkey by educational level is also given in Table 3. It is seen from the table that, while the proportion of illiterate people has decreased, the proportion of those with a higher level of education has increased. We therefore conclude that education level does not have a major effect on Alzheimer's disease.
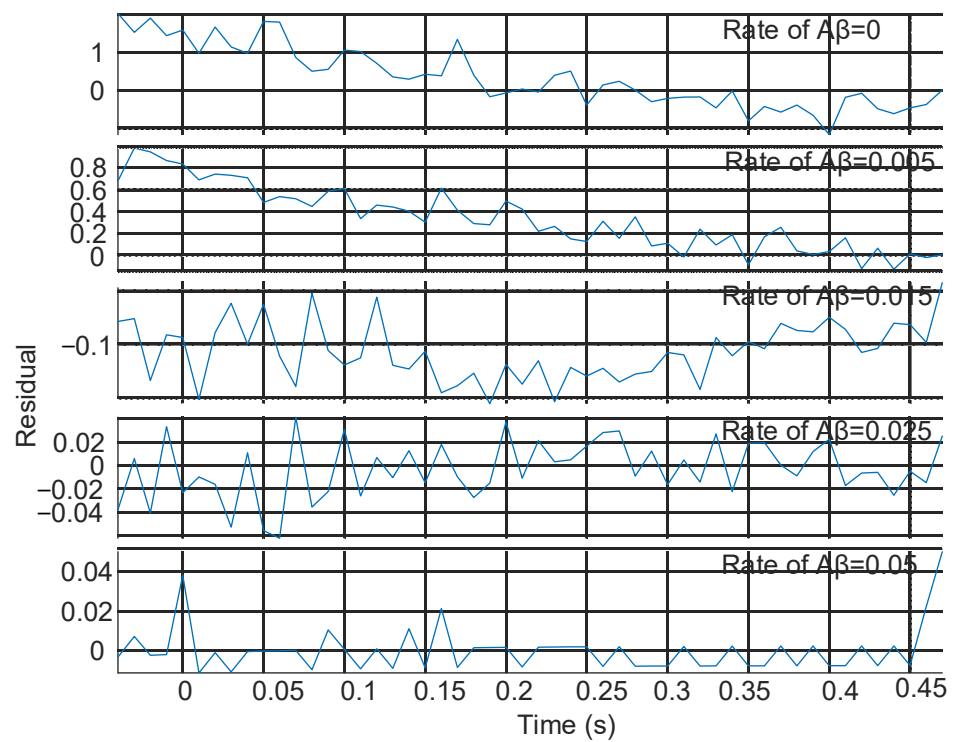
Figure 4. Residual plots giving the errors between MC and ANN for different Aβ ratios.
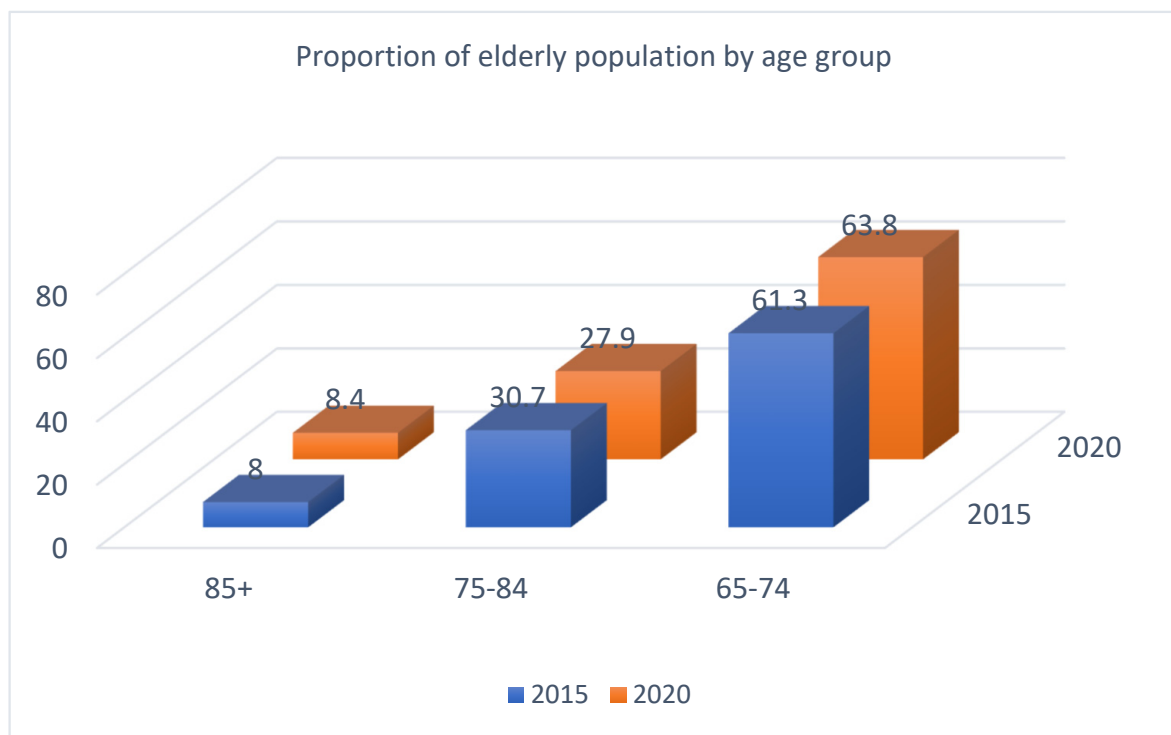

Figure 5. Proportion of elderly population by age group, 2015, 2020 for Turkey, adapted with permission from Ref. [68].

Table 2. Elderly population ratio in Turkey by year, adapted with permission from Ref. [69].

Year	Total Population	Rate of 65+ (%)	Death from Alzheimer (65+)	Gender	
				Male	Female
2015	78,741,053	8.2	12,059	4786	7273
2016	79,814,871	7.9	13,051	5061	7990
2017	80,810,525	8.1	13,642	5252	8390
2018	82,003,882	8.8	13,859	5257	8602
2019	83,154,997	8.9	13,498	5049	8449

Table 3. Elderly population and proportion of elderly population by educational level for Turkey, adapted with permission from Ref. [68].

Educational Level	2015 (%)	2016 (%)	2017 (%)	2018 (%)	2019 (%)
Illiterate	21.9	20.8	19.6	18.3	16.9
No school completed	18.9	18.2	17.5	16.8	15.9
Primary school	43.0	43.7	44.5	45.0	45.5
Junior high school or equivalent/primary education	5.2	5.6	6.0	6.5	7.3
High school or equivalent	5.6	5.9	6.3	6.8	7.5
Higher education	5.4	5.8	6.2	6.6	7.0

We think that a more important factor is early diagnosis and application of disease treatment methods with respect to the individual person. Although the proportion of elderly people in Turkey is low, the rate of Alzheimer's amongst the elderly Turkish population is high. We think also that the physiology and stress levels of people are very important factors affecting this disease. We note that the rates of Alzheimer's disease are higher in the west of Turkey, and this may depend on the physiology of the people in that region.

Finally, the method of random forest was used for the parameters of elderly population, per capita income inequality, education level, poverty threshold and number of the poor with respect to of various Alzheimer disease indicators to show which variables affects AD more statistically. The random forest method determines the correlation between the total number of deaths from Alzheimer's disease with the socioeconomic status by using different determining factors. Socioeconomic status is thought to be associated with Alzheimer's disease. However, the reason for this was not directly explained by previous studies. Wang et al. examined the effect of socioeconomic status on Alzheimer's disease using Mendelian randomization and determined whether there was a causal protective effect of income on the risk of developing Alzheimer's disease. Their results showed that higher household income level was causally associated with lower risk of Alzheimer's disease. Under Mendelian randomization assumptions, the results suggested some evidence of a causal relationship between household income and risk of Alzheimer's disease, which could provide potential prevention strategies for the disease [70,71]. Among the six different variables used in our study, it can be seen that income is the variable that most affects the number of deaths from Alzheimer's disease, as shown in Figure 6. In a similar way to previous findings in the literature, it is seen that lower income increases the number of deaths in this disease. Researchers have often emphasized that the incidence of Alzheimer's disease increases with age. This study found that an age in excess of 65 years is the second-most important variable that affects Alzheimer's disease. Other parameters such as population, education, poverty threshold and number of the poor affect Alzheimer's disease only minimally or not at all.
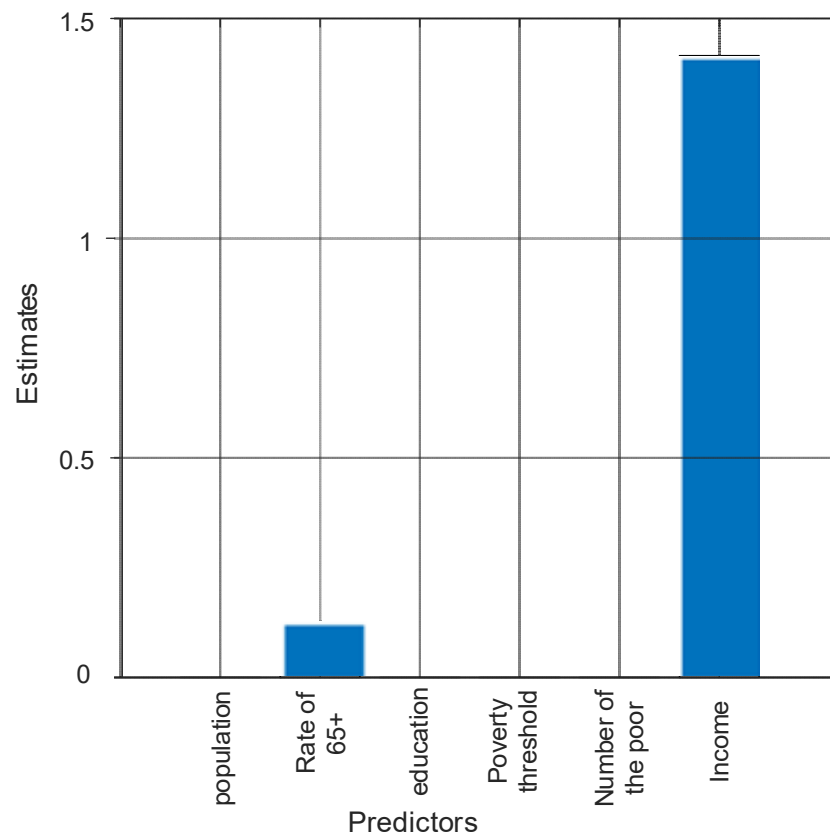
Figure 6. The importance of elderly population, per capita income inequality, education level, poverty threshold and number of the poor parameters of various Alzheimer disease indicators.

4. Conclusions

In this study, firstly, two new MC and ANN models of Aβs causing Alzheimer's disease in a fluid medium were proposed to increase the number of MMs in the receiver and to predict some unknown values of MMs. In contrast to the existing literature, the MC and ANN models were used together. Receptors were also considered in this study to increase realism with respect to biological living cells. The number of received molecules was highest when the Aβ ratio in the medium was the lowest. The highest result of 65 molecules was obtained with an Aβ ratio of 0 for the MC model and the lowest result which of 0 molecules was obtained with an Aβ ratio of 0.05 for both MC and ANN models, as shown in Table 1. After obtaining the number of molecules received for different values of the Aβ ratio, the number of molecules received by ANN was analyzed and the results were compared. After results of ANN and MC models were obtained, an error analysis was carried out to compare both models scientifically using residual theory. Although very low residual results were obtained from the comparison of ANN and MC models, residual values for an Aβ ratio of zero were higher than for other Aβ ratios. Secondly, the population of people aged 65[+] in Turkey, and the rate of this population's growth by year were investigated. It can be seen from Table 2 that the population of elderly people in Turkey has increased over time. This increase also affects the number of Alzheimer's disease sufferers because it is known that Alzheimer's is generally an older people's disease. The proportions of the elderly population of Turkey by educational level for Turkey were also investigated in this study, as shown in in Table 3. Unfortunately, Turkey shows a high percentage rise in cases of Alzheimer's disease and new treatment methods should be tried and government should propose new solutions for these patients. Finally, the method of random forest was used for the parameters of elderly population, per capita income inequality, education level, poverty threshold and number of the poor with respect to various Alzheimer's disease indicators to show which variable affects AD more statistically.

Among the six different variables used in our study, it was found that income was the variable that most affects the number of deaths from Alzheimer's disease, as shown in Figure 6. In line with the existing literature, we found that lower income increases the number of deaths from this disease.

5. Limitations and Future Directions

In the future, this study could be built upon by taking into consideration factors such as differing regions, lifestyles and eating and drinking habits of different population groups. The information thus obtained might be used for the better diagnosis and treatment of Alzheimer's disease and contribute to the overall economy of our country. More biological models might also be proposed to increase the reality of the system, such as mobile and spherical transmitter and receiver models of the same radius. By such means, the number of received molecules could be increased for higher ratios of Aβs in the environment and this could be used for treatment of AD. However, it should be noted that current technology in this subject has some limitations when applying such theoretical and simulation models to real biological cells because of inconsistencies between them at very low nanoscales.

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