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Research Article

Investigation of Factors Affecting Motif-Based Short- and Long-Term Memory Behaviour in Brain Neuron Networks

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Abstract : Learning and memory formation in living things is a subject under investigation. It is thought that the memory formed in the brain's neural network structure is closely related to the connections between neurons. Connections called "motifs" have been identified, usually consisting of three or four neurons and repeating within the neural network. The basic structure of biological memory is thought to be related to such repetitive neural connections. In this study; the effect of the structures of motifs on short- and long-term memory was examined for all triple-neuronal network motifs. We used the Hodgkin-Huxley model of neurons. Using graph theory, we generated all triple-neuron motifs. In the created motifs; the effects of synaptic inputs between neurons, types of synaptic inputs of neurons, and chemical synapse duration on short- and long-term memory were examined. From the data obtained in all triple-neural network motif models; from the structure of the motif and the type of synaptic input, we determined the status of long- and short-term memory. We classified all triple-neural network motifs for situations in which they exhibit short- and long-term memory behaviour. We show that short-term memory varies with synaptic connection duration

Keywords : Brain neural network motifs, intercellular synaptic type, short-term memory, synaptic conductivity time, long-term memory

1 Introduction

How learning occurs in living things is investigated by biological experiments and computational methods. In order to elucidate this issue, studies on neuronal connections are being made [1] Intercellular synaptic inputs are being studied [2]. The connections formed between neurons are considered to be an important factor in memory formation. In order to support these studies, studies describing neural network structures have been carried out [3]. In fact, brain neuron network connection maps of some living things have been obtained [4]–[10]. These network maps, which are also the graphical representation of dynamic systems, are used to analyse the complex structures of biological systems [5]. The behaviour of neurons forming the networks in the learning process has been followed by biological studies and important data have been obtained [11]. It has been observed in biological experimental studies that while living things are learning, new connections are established between neurons, some of which are temporary and some are permanent [12]–[18]. Changes related to the learning process have been observed in the dendrites of neurons [19]. In these studies, it was also observed that some interneuron connections detected in neuronal networks were frequently repeated within the network. These special-function subnet links are named "Network motif". [4], [6]–[8], [13], [20]–[23]. Here the term "Network motif" refers to directed subgraphs. Motifs containing such triple-neurons are common in many biological environments [1]. These network motifs are modelled by computational neuroscience studies and their roles in their environments are investigated [24], [25]. Computational neuroscience uses computational techniques to model neural networks [26]–[28]. Thus, the functions of network motifs are investigated by means of computational models [7], [19]. It is thought that biological memory systems where learning takes place include such network motifs with memory capability [15]. Neurons in triple neural network motifs are usually; are named as input, output and driver neurons [7], [29]. It is thought that especially interneuron connections are effective in the formation of long and short-term memory [30]. Short-term memory, where thinking and information processing takes place, is considered to be the most functioning part of memory [26]. It is considered that the type of synaptic input between neuron groups is effective in the functioning of short-term memory, which is one of the important parts of memory. It is thought that storing information in long-term memory is possible with permanent, functional,

biochemical and structural changes that occur in neural connections in the brain [16], [31]–[33]. Experimental studies have shown that neurons are electrically active and usually communicate via chemical synapses. Chemical synaptic communication between neurons has also been modelled mathematically [34]. In some modelling studies, the responses of motifs to stimuli have been interpreted as short- and long-term memory behaviour. In these studies; some special network motif constructs and simpler neuron models (such as the Integrate and Fire Neuron Model) are used. For the synaptic input between neurons, a noise signal was applied to the postsynaptic cell, representing signals from other neurons. In some models, the synaptic weight parameter was used to express the total synaptic input to the dendrites [7]. All these studies have not yet fully revealed how learning takes place. How long- and short-term memory formation, learning, remembering, and forgetting occur in neurons is being investigated [35]. During learning, synaptic input changes were observed between neurons. Although this suggests that connectivity is effective in learning, the occurrence of this change has not been fully explained [36]. While Biological studies investigate the adaptive changes of the brain during learning, on the other hand, computational neuroscience studies try to model the learning process. The parameters that are effective in the retention of information during and after the learning process have not been fully explained. Understanding the learning functions of the brain will benefit the diagnosis and treatment of many diseases [37]. When the motif behaviours are learned, the properties of the network environments to be obtained by motif multiplexing can also be learned [38]. Although the behaviour of some neural network motifs has been investigated, especially in connectivity studies, there is no comprehensive motif model study. In addition, in learning research; no detailed studies on motif structure, intercellular synaptic entry type and synapse duration have been performed. The findings of our study will reveal the analysis of all triple neural network motifs on the effect of connectivity in learning. Our work; it is based on the thesis that learning is directly related to the type of synaptic input and motif structures between neurons. To this end, we examined some factors that affect the short- and long-term memory behaviour of all three-neuron motifs. Using graph theory, we systematically constructed all three-neuron motifs. First, we studied the basic motif connections, which are used in many studies in the literature. In these studies, the effect of synaptic input types of neurons was revealed. Considering the findings obtained here, the memory behaviour of triple neural network motifs was studied. Motifs were evaluated considering neuron roles. In the studied motifs, after the learning information was given to the input neuron in the form of electrical signals, the electrical effect on the output neuron was examined. The persistence of the output signal (action potentials) was interpreted as long-term memory behaviour, and its temporality (ending after a while) was interpreted as short-term memory behaviour. With this approach, we examined short- and long-term memory behaviour in motifs, across all possibilities of neurons' synaptic input types. We also studied the effect of time constant variation in the interneuron chemical synapse model on short-term memory duration. The prolongation of the synapse duration was made by increasing the time constant of the model. This means that one neuron continues to excite the other.In these studies, how learning happens is evaluated in terms of connectivity. Thus, it is aimed to contribute to the solution of neurological diseases such as learning problems, forgetting, memory loss, dementia, Alzheimer's, etc. From the findings of the study, it has been shown that memory formation is highly related to the following factors:

- With the interneuron connections that form the neural network motifs,
- With synaptic input types between neurons,
- With the duration of synapse between neurons.

2 Materials and Methods

The deterministic Hodgkin-Huxley neuron modelling method used in our study is one of the most basic and successful models. Modelling was performed in the MATLAB software environment.

2.1 Modelling of Neuron and Neural Network Motifs

In our study, we used Hodgkin-Huxley's neuron model, which is frequently used in many studies, to model the neurons forming the motifs. While the neuron was modelled as a single compartment of the soma and deterministic, signal transmission between neurons was modelled as a chemical synapse [39]–[43]. Synaptic inputs between neurons; were added to the electrical model with excitatory (E) or inhibitory (I) potential values [34], [40], [44]. In triple neural network motifs, in addition to external current input to neurons, synaptic input is made from one or two neurons depending on the motif structure. The electrical models of neurons according to the inputs they receive are shown in Figure 1 [40]. Ion channels in the cell membrane of the neuron are responsible for its electrical behaviour. These channels allow the neuron to generate an action potential. E_{Na}, E_K, E_L expressions are among the parameters in the electrical solution of the model, the equilibrium potentials of the ion channels. V_m is neuron membrane voltage, V_r is neuron membrane voltage at rest, C_m is neuron membrane capacitance. $G_N a$, G_K conductivity values of sodium Na^+ and potassium K^+ channels $G_N a$, G_K, maximum conductivity in the neuron membrane, G_L is leakage current conductivity equation (16-17). In the model, for the Na^+ ion channel, three identical activations m^3 and one inactivation gate (h) and the ion K^+ is defined with four identical activations n^4 gates equation (13-15). The voltage-dependent transition rate constants between the open-and-close states of an ion channel are defined as: α_{Vm} and β_{Vm} equation (2-9). Steady-state

activation of Na^+ current is defined as m_∞, inactivation as h_∞ and steady-state activation of K^+ current is defined as n_∞ equation (10-12).The solution of the single-compartment neuron modelled with the electrical circuit shown in Fig.1-a is given in equation 1.

$$C_m(dV_m)/dt = -G_L(V_m - E_L) - G_{Na}(V_m - E_{Na}) - G_K(V_m - E_K) + Iinj(t) \tag{1}$$

$$\alpha_m = (\frac{-0.1(V_m - V_r - 25)}{\exp(-(V_m - V_r - 25)/10) - 1}) \text{ whereas } V_r - V_m > 24,99 \tag{2}$$

$$\alpha_m = (\frac{-1}{\exp(-(V_m - V_r - 25)/10)}) \text{ whereas } V_r - V_m <= 24.99 \tag{3}$$

$$\beta_m = 4(\exp(-(V_m - V_r)/18)) \tag{4}$$

$$\alpha_h = 0.07(\exp(-(V_m - V_r)/20)) \tag{5}$$

$$\beta_h = (\frac{1}{1 + \exp(-(V_m - V_r - 30)/10)}) \tag{6}$$

$$\alpha_n = (\frac{0.01(V_m - V_r - 10)}{1 + \exp(-(V_m - V_r - 10)/10)}) \text{ whereas } V_r - V_m > 9.99 \tag{7}$$

$$\alpha_n = (\frac{0.1}{\exp(-(V_m - V_r - 10)/10)}) \text{ whereas } V_r - V\_m <= 9.99 \tag{8}$$

$$\beta_n = 0.125(\exp(-(V_m - V_r)/80)) \tag{9}$$

$$m_\infty(V_m) = \alpha_m(V_m)/(\alpha_m(V_m) + \beta_m(V_m)) \tag{10}$$

$$h_\infty(V_m) = \alpha_h(V_m)/(\alpha_h(V_m) + \beta_h(V_m)) \tag{11}$$

$$n_\infty(V_m) = \alpha_n(V_m)/(\alpha_n(V_m) + \beta_n(V_m)) \tag{12}$$

$$\frac{dm}{dt} = \alpha_m(V_m)(1 - m) + \beta_m(V_m)m \tag{13}$$

$$\frac{dh}{dt} = \alpha_h(V_m)(1 - h) + \beta_h(V_m)h \tag{14}$$

$$\frac{dn}{dt} = \alpha_n(V_m)(1 - n) + \beta_n(V_m)n \tag{15}$$

$$G_{Na} = \overline{G}_{Na}m^3h \tag{16}$$

$$G_K = \bar{G}_K n^4 \tag{17}$$

Neurotransmitter-activated ion channels, which are electrically excited when synaptic input arrives in the interneuron connection, are defined by time-dependent $gsyn(t)$ conductivity, as seen in equation (18) [45]. The synaptic communication current of the model we used is shown in equation (20), and the addition of the current to the electrical circuit is shown in Figure 1(d). Dynamics involving multiple synaptic inputs to a neuron, that is, multiple synapse inputs, are as shown in equation (20) [40]. Neural network motifs are created with neurons communicating with this method.

$$gsyn(t) = g_{\max}\frac{t}{\tau}e^{(1-\frac{t}{\tau})} \tag{18}$$

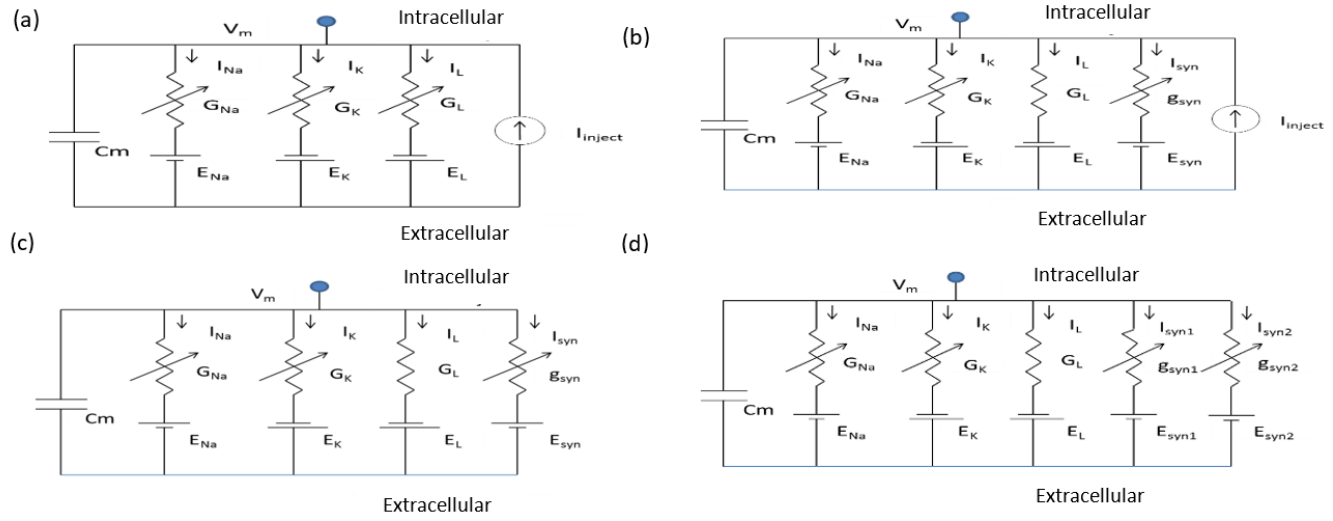

Figure 1: (a) Neuron model with only external current input. (b) Neuron model with external current input and single synaptic input. (c) Neuron model with only one synaptic input. (d) Neuron model with two synaptic inputs

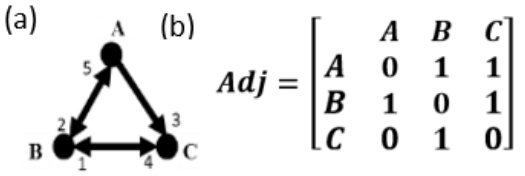

Figure 2: (a) Directed motif comprising 3-neuron and 5 links. (b) Adjacency matrix Adj.

$$I_{syn}(t) = g_{syn}(t)(V_m - E_{syn}) \tag{19}$$

$$C_m \frac{dV_m}{dt} + g_{rest} V_m + g_{syn}{}^{(1)}(t)(V_m - E_{syn}{}^{(1)}) + g_{syn}{}^{(2)}(t)(V_m - E_{syn}{}^{(2)}) + \ldots = 0 \tag{20}$$

The parameters obtained from the biological experimental studies of Hodgkin-Huxley were used in the motif models. Commonly used model parameter values $G_{Na} = 120ms/cm^2$, $G_K = 36ms/cm^2$, $G_L = 0.3ms/cm^2$, $E_{Na} = 50mV$, $E_K = -77mV$, $E_L = -54.4mV$, $C_m = 1\mu F/cm^2$, $V_r = -65mV$. In synaptic input reversal potentials were used as: $E_{syn} = -70mV$ for inhibitor (I), $E_{syn} = -10mV$ for excitatory (E), maximum synaptic conductivity $g_{\max} = 64nS$, synaptic conductivity time constant $\tau = 25ms$ [45]–[47]. For numerical solutions of Euler differential equations, the time step interval was chosen as $\Delta t = 10\mu s$. To model neuron and neural network motifs, we created simulation software using these parameters suitable for experimental studies. In our study, the Hodgkin-Huxley model, which contains more parameters and is closer to the behaviour of the neuron, was preferred for neuron modelling. In experimental studies on neurons communicating with chemical synapses; it has been observed that when the synaptic input type of the presynaptic neuron is Excitatory (E), action potentials are formed in the postsynaptic neuron. It has been observed that when the synaptic entry type is blocker (I), it prevents the formation of action potentials.

2.2 Generating All Triple-Neuron Brain Network Motifs Using Graph Theory

Graph theory is a mathematical method used to model complex biological systems. Graphs can be directed, undirected, and mixed. Directed graphs are often used to model biological neural networks. The interconnections of neurons can be described by the adjacency matrix (Adj). In this matrix, (1) shows a connection between neurons and (0) shows no connection [5], [29], [48]. The analysis of complex networks and the concept of network motifs is a subject studied in many fields of study [49], [50]. Figure 2 shows a directed graph motif and its adjacency matrix for its synaptic input directions (arrowheads). It has been found that the neuronal connectivity forming the motif is much stronger than the connections they make with other neurons. This brings to mind the idea that the motif structure is specialised for a purpose. The network motifs probably protect the behaviour they display alone when they are connected to other neurons. In all motifs, we consider (A) as the input neuron, (C) as the output neuron and (B) as the generally drive neuron (C) [7]. In our study; recognizing the input (A), output (C) and driver (B) roles of neurons, we systematically constructed all triple-neuron motifs using the adjacency matrix method of graph theory. In

$$[A_{adj}] = \begin{bmatrix} A & B & C \\ 0 & 0 & 0 \\ 0 & 0 & 1 \\ 0 & 1 & 0 \\ 0 & 1 & 1 \end{bmatrix} \quad [B_{adj}] = \begin{bmatrix} A & B & C \\ 0 & 0 & 0 \\ 0 & 0 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 1 \end{bmatrix} \quad [C_{adj}] = \begin{bmatrix} A & B & C \\ 0 & 0 & 0 \\ 0 & 1 & 0 \\ 1 & 0 & 0 \\ 1 & 1 & 0 \end{bmatrix}$$

Figure 3: An example of systematically constructing the synaptic input probabilities of three neurons.

$$[A_{adj}] = \begin{bmatrix} B & C \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 1 & 0 \\ 1 & 0 \\ \cdot & \cdot \\ \cdot & \cdot \end{bmatrix} [B_{adj}] = \begin{bmatrix} A & C \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 1 \\ 1 & 1 \\ 1 & 1 \\ 1 & 1 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 1 \\ 1 & 1 \\ 1 & 1 \\ 1 & 1 \\ 0 & 0 \\ 0 & 0 \\ \cdot & \cdot \\ \cdot & \cdot \end{bmatrix} [C_{adj}] = \begin{bmatrix} A & B \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ 1 & 0 \\ 1 & 1 \\ 0 & 0 \\ 0 & 1 \\ \cdot & \cdot \\ \cdot & \cdot \end{bmatrix}$$

Figure 4: Adjacency matrix showing intercellular synaptic inputs for all triple neuron brain network motifs.

order to derive all triple neural network motifs by graph theory, we constructed an adjacency matrix in Figure 3 for an example similar to that in Figure 2(b). Some of the connection possibilities of A, B, C neurons in the motif with each other are shown in the example below with three matrices. When three adjacency matrices are combined, each row of the resulting matrix will represent the connection of a different motif. Since a neuron will not make synaptic input to itself, the corresponding column will be zero (0) (In neural networks, the neuron does not make a synaptic link with itself). For example, there is no motif since all zeros are in the first line. The second line describes a motif that provides synaptic input of neurons ($A \rightarrow C, B \rightarrow C, C \rightarrow B$). The adjacency matrix containing all triple neuron network motif connections was created in Figure 4. The matrix is constructed as a six-input truth table. Since the neuron does not create synaptic input with itself, this column has been omitted from the matrices. All of the synaptic input possibilities that each neuron can make with the others are built into these matrices. All triple-neuron network motifs were obtained from synaptic input states of neurons in the adjacency matrix formed by combining four columns. In the first matrix, the synaptic input probabilities of neuron A with neuron B and C were created. Others were created in the same way. Synaptic input status of the neuron is indicated by (1) and not by (0). For example, case $A\begin{bmatrix}0 & 1\end{bmatrix}$, $B\begin{bmatrix}0 & 0\end{bmatrix}$, $C\begin{bmatrix}1 & 1\end{bmatrix}$; It describes a motif with synaptic inputs ($A \rightarrow C$, $C \rightarrow A$, $C \rightarrow B$). In this way, taking into account the table, all triple neuron network motifs were created. In the adjacency matrix created in the form of a 6-variable truth table, $2^6 = 64$ motifs emerge. Some of these motifs are; since it does not carry neuron A input, neuron C output, neuron B driver characteristics due to synaptic input directions, it was not evaluated. We have shown 38 different motifs suitable for the study format in Fig. 5. To facilitate analysis, we named the motifs with short names (Motif1 = MTF1), indicating the synaptic input directions with arrows. Repetitive links were combined and the rest were named sequentially (010000, 000100 etc.). Two major intercellular synaptic inputs (Basic Motif1 = BMTF1 and Basic Motif2 = BMTF2) found within all motifs were also named.

2.3 Investigation of the Effects of Connection Structure and Synaptic Input Type in Motifs on Short- and Long-Term Memory Behaviour.

The brain structures of living organisms are a complex network of connections between many neurons [17], [18], [51]. Learning is thought to be related to motifs (triple, quadruple,) that are often seen in the extensive network of neurons [51]. The short-

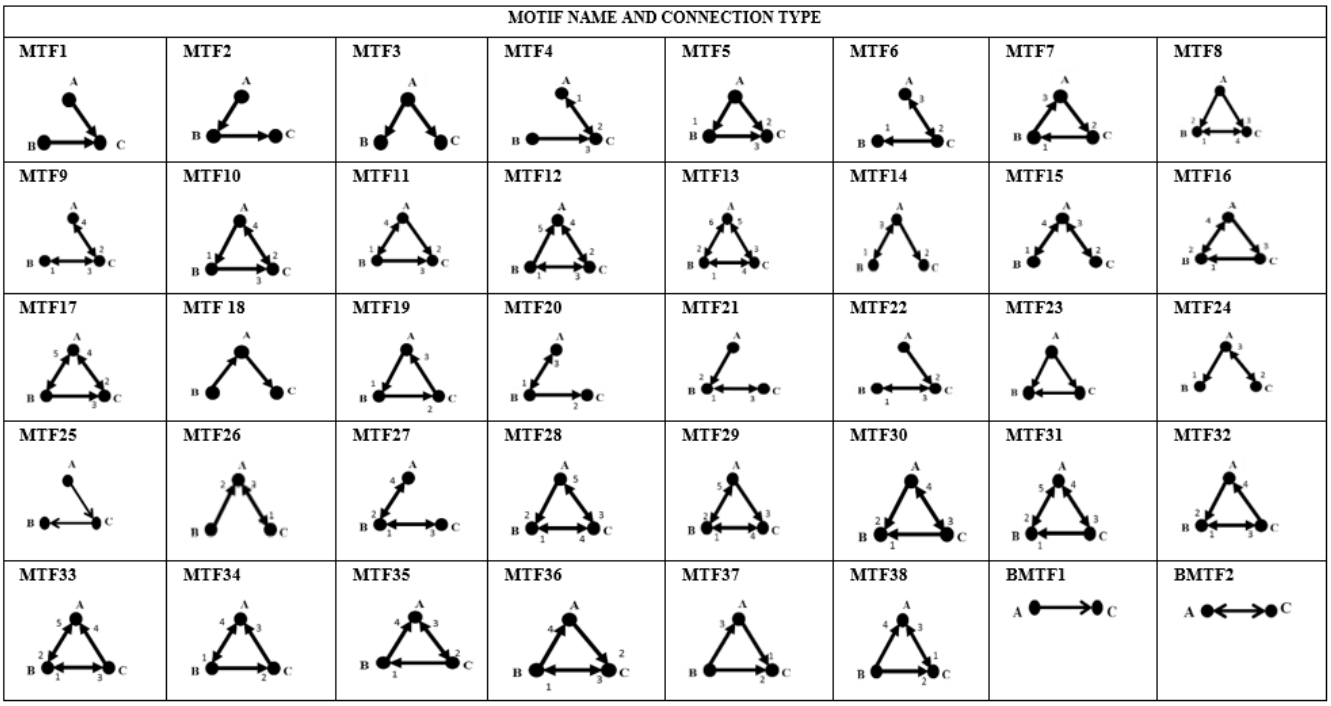

Figure 5: All directed triple neuron brain network motifs were generated using graph topology.

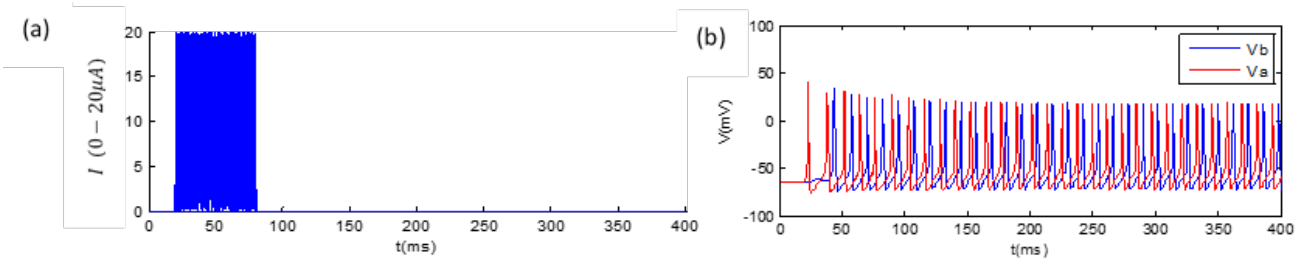

Figure 6: (a) Uniformly distributed random current applied externally to the A neuron. (b) Action potentials generated in A and B neurons when the neurons have synaptic input type (AB-EE).

and long-term memory behaviour of several triple- and quadruple-neuron network motifs has been investigated [52]. In studies conducted in this area, models with fewer parameters have been preferred in terms of ease of processing to model neuron [7], [53]. In previous studies, short- and long-term memory behaviour of some motifs comprising three neurons was investigated. In these studies, it has been shown that neurons form short- or long-term memory depending on the type of synaptic input. In the action potential graphs seen in the motif output cell, it is assumed that the motifs that continue to produce the output signal after the external current stimulus to the input neuron is interrupted show long-term memory behaviour. Graphic images that generate output signals for a while after the external current warning is interrupted are also considered as short-term memory [7]. By modelling this behaviour in our study, we examined memory behaviours in all possibilities of excitatory-inhibitory states of synaptic inputs of neurons, of all motifs obtained by graph theory. For this purpose, we examined the short- and long-term memory formation states of all motifs in Table 1 for these possibilities. To better evaluate the effect of motifs on the memory behaviour of the intercellular connection pattern and the type of synaptic input of the neurons (Excitatory-E, $E_{syn} = -10mV$ Inhibitor-I, $E_{syn} = -70mV$, we studied the basic motif (BMTF2) in Fig. 5. In BMTF2 basic connection; neuron A is modelled with the circuit in Figure 1(b) and neuron B is modelled with the circuit in Figure 1(c). Neuron A receives both external stimulation current and synaptic input from neuron B. B neuron only receives synaptic input from A neuron. In the experiments, the uniformly distributed random current form, which is shown in Fig.6.(a) and represents the total excitation from the dendrites to the soma, can be used as the external input current. When the synaptic input types of A and B neurons are selected as excitatory (AB - EE), action potentials continue to occur in both A and B neurons, although the external current input is cut off. A time shift (phase difference) occurs between the voltages V_a and V_b seen in Fig. 6.(b). This is because neurons A and B have reciprocal synaptic inputs and both types of synaptic input are excitatory. In the same structure; when the synaptic input type is (AB -EI), (AB-IE) and (AB-II), action potential generation ends when the external current input is cut off. When only one of

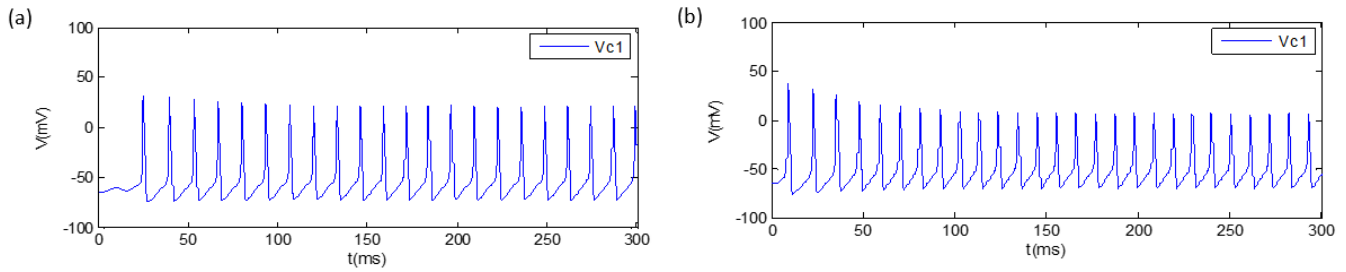

Figure 7: In MTF1 motif, external current input ($10\mu A$- DC); (a) when applied to A neuron only, ($A \rightarrow C$, E) action potentials generated in C neuron (b) When applied to both A and B neurons, (AB, EE) action potentials generated in C neuron.

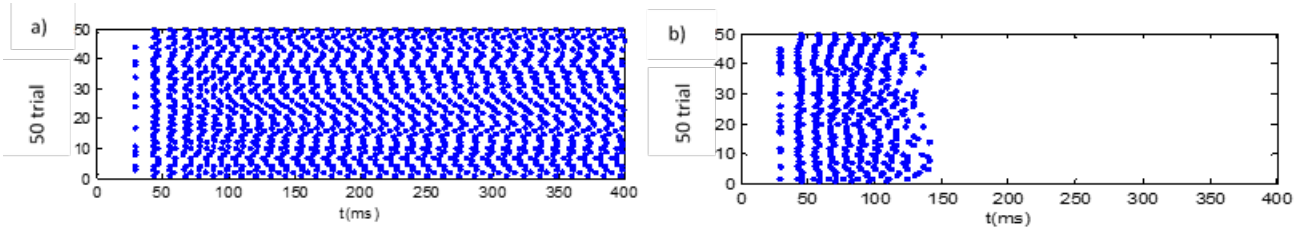

Figure 8: When the external current in Figure 3(a) is applied to the A neuron in the MTF8 motif; (a) raster plots of action potentials generated in C neuron in each of 50 trials when synaptic input types (ABC-EEE), (b) raster plots of action potentials generated in C neuron in each of 50 trials when synaptic input types (ABC-EEI) are present.

the A or B neurons is stimulated by an external direct current (DC) input ($10\mu A$ - DC), an action potential occurs in the neuron. These action potentials, which are formed in the A or B neuron under the influence of the external current, are transmitted to the C neuron as synaptic input (AB-EE). Thus, a sequence of action potentials is observed in the C neuron at a frequency of f=68Hz, shown in Figure 7(a). When both neurons A and B are stimulated by external direct current input, action potentials are generated in both neurons. Thus, the action potentials of the two neurons are transmitted simultaneously to the C neuron as synaptic input (AB-EE), and the action potential sequence is observed in the C neuron at a frequency of f=72Hz, shown in Figure 7(b). The reason for the increase in frequency is that the neuron receives more than one synaptic input. When A and B neurons have synaptic input type (AB-EI, etc.) to C neuron; as one of them is excitatory (E) and the other is inhibitor (I), the inputs cancel each other's effect. Thus, no action potential occurs in the C neuron. With these studies; we have examined the effect of intercellular connection type and synaptic input type. This study was carried out for all motifs in Fig. 5. As an example, we have shown the studies on the motif we named MTF8 in Fig. 5. First synaptic input type for all neurons in the motif were selected as excitatory (E) (ABC-EEE). The current shown in Figure 6(a) is applied to neuron A as an external current. The same application was repeated 50 times to show the difference in the action potential generation time in the C neuron. This difference is due to the randomness of the external current applied to the input neuron. Fig. 8. (a) shows a raster graph showing the action potential generation times in one line for each of the 50 trials. This graphical representation is the preferred method for describing short- and long-term memory behaviour. When the stimulus current is random and uniformly distributed, the time of the current magnitude that will generate the action potential is variable. Such a current application is for modelling that the neuron has been excited externally by an electrical signal of random time and magnitude. Although the external current application was cut off after 80ms, action potentials continued to occur in neuron C as seen in Fig. 8. (a). This is interpreted as the motif exhibiting long-term memory behaviour. In the same motif, action potentials continued to be produced in the C neuron for 60ms after the external current application, when the neurons stimulus types (ABC-EEI) were made. This, seen in Figure 8(b), is interpreted as the short-term memory behaviour of the motif. For other possibilities of warnings, these applications were repeated. In these excitation states (ABC-III, IIE, IEI, IEE, EII, EIE) the motif did not show both memory behaviours. We performed these applications for all motifs in Fig. 5. From the results obtained, the situations in which the motifs show memory behaviour were determined and shown in Fig. 9. in the conclusion part.

2.4 Investigation of the Effect of Change in Chemical Synapse Conductivity Function Time Constant Parameter on Short-term Memory Time

The time constant parameter of the synaptic conductivity function $gsyn(t)$ (equation 18) in intercellular synaptic input, the model is associated with the synaptic input duration. This function is defined with a time-dependent exponential function so that the sum of the impulses coming to the dendrites creates an action potential in the neuron. Synaptic input current $I_{syn}(t)$; is the product of the conductivity value $gsyn(t)$ and the difference $V_m - E_{syn}$ of the cell membrane voltage V_m and the synaptic excitation threshold voltage E_{syn} (equation 19). As can be seen here, as the time constant of the conductivity value increases,

Motif Name	Synaptic Input Type				F	Motif Name	Synaptic Input Type					F	Motif Name	Synaptic Input Type					F	Motif Name	Synaptic Input Type						F	Motif Name	Synaptic Input Type						F
	1	2	3	4			1	2	3	4	5			1	2	3	4	5			1	2	3	4	5	6			1	2	3	4	5	6	
MTF30	E	E	E	E	75	MTF20	E	E	E			69	MTF19	E	E	E			69	MTF13	E	E	E	E	E	E	75	MTF28	E	E	E	E	E		79
	E	I	E	E	75	MTF21	E	E	E			69	MTF22	E	E	E			78		E	E	E	E	E	I	78		E	E	E	E	I		77
	I	E	E	E	69	MTF34	E	E	E	E	E	69	MTF4	E	E	E			74		E	E	E	E	I	E	78		E	I	E	E	E		69
	I	I	E	E	69	MTF7	E	E	E			74		E	E	I			75		E	E	E	E	I	I	78		E	I	E	I	E		74
MTF8	E	E	E	E	83		E	E	I			75	MTF24	E	E	E			74		E	E	E	I	E	E	66		I	I	E	E	E		74
MTF11	E	E	E	E	80	MTF27	E	E	E	E		70		I	E	E			70		E	E	I	E	E	E	69		I	I	E	I	E		74
MTF6	E	E	E		69		E	E	E	I		70	MTF36	E	E	E	E		74		E	E	I	E	E	I	75	MTF12	E	E	E	E	E		79
	I	E	E		69	MTF29	E	E	E	E	E	81		E	E	E	I		74	MTF17	E	E	E	E	E		83		E	E	E	E	I		69
MTF26	E	E	E		79		E	E	E	E	I	75	MTF15	E	E	E	E		69										E	E	E	I	E		77
	E	E	I		69	MTF14	E	E	E			69		I	E	E	E		74		E	I	E	E	I		68		E	E	E	I	I		75
MTF32	E	E	E	I	69		E	E	I			74		I	E	E	I		69		I	E	E	E	E		78		E	I	E	E	E		69
	E	E	E	E	69		E	I	E			73	MTF35	E	E	E	E		69		I	E	E	E	I		78		E	I	E	E	I		69
MTF10	E	E	E	E	80	MTF38	E	E	E	E		75		I	E	E	E		79		I	E	I	E	E		74		E	I	I	E	E		69
	I	E	I	E	79		E	E	E	I		74		I	E	E	I		69		I	E	I	E	I		74		E	I	I	E	I		78
	I	E	E	E	74		E	I	E	E		79	MTF16	E	E	E	E		79	MTF31	E	E	E	E	E		69	MTF33	E	E	E	E	E		63
MTF9	E	E	E	E	75		E	I	I	E		77		E	I	E	E		79		E	I	E	E	E		69		E	E	E	E	I		69
	E	E	E	I	74									I	E	E	E		69		E	I	E	E	I		78		E	E	E	I	E		69
	I	E	E	E	74									I	I	E	E		84		I	E	E	E	E		80		E	E	E	I	I		69
	I	E	I	E	74																I	I	E	E	E		78		I	I	E	E	E		78
TMTF_2	E	E			79																I	I	E	E	I		69		I	I	E	E	I		69

Figure 9: Of the motifs in Fig.5., those showing long-term memory behaviour; (numbers above motifs indicate synaptic input, numbers in the figure indicate synaptic input type) representation of neurons with probabilities of synaptic input types and frequency of action potential produced in neuron C

the exponential decay time of the conductivity gets longer. The larger the time constant of the function, the longer a synaptic input state occurs between neurons. Time constant variation has been studied with simpler models in a few four-cell motifs in the literature [7]. In these modelling studies; the synaptic conductivity time constant has been shown to affect short-term memory duration in appropriate Motifs [53]. While chemical synapses are formed between neurons, physical changes occur in dendritic spines [54]. In our study; we examined the effect of synaptic conductivity time constant variation on short-term memory duration in triple-neuron motif models. For the appropriate motifs in Fig. 10., we show that the short-term memory duration changes with the change of the neurons communication function time constant. In the experiments in the first chapters, the time constant value of the interneuron synaptic conductivity function in the motifs was taken as $\tau = 25ms$. In this part of our study, we examined the short-term memory duration of the neuron at certain values by making the time constant (τ) variable. Studies in this section were carried out on the MTF8 motif.

3 Results

3.1 Identification of Triple Neuron Network Motifs, which are Long-Term Memory

We studied the effect of all probabilities of the intercellular synaptic input types (E or I) on memory behaviour in all motifs seen in Fig. 5. For all motifs, we repeated the work described in section 2.3. These motifs were simulated for all intercellular synaptic input type possibilities, and their long-term memory status was shown in Fig. 9. . Fig. 9. also shows the frequency (f) of the continuous action potential signal formed in the C output neuron. It is seen that the action potential frequency is close to each other in different motives and situations. If the output neuron receives more than one synaptic input, due to the motif structure, the output signal frequency is slightly increased. We have placed this in the table to express the continuity of the signal. With the synaptic flexibility in the learning process, when such synaptic input types occur between neurons, it is considered that the information is stored for the long-term. This study also revealed that intercellular connectivity and synaptic entry type play a very important role in motif analysis. Findings from this part of the study revealed a common feature of triple-neuronal network motifs displaying long-term memory behaviour. It has been determined that the intercellular connections of these motifs form a closed loop (in the form of A-C or A-B-C) reaching the output neuron. In the case of appropriate intercellular synaptic input type, such a loop-forming motif connection can retain information long-term even if the total synaptic input applied to the A neuron is interrupted. Among the motifs in Fig. 5., those with long-term memory are shown in Fig. 9. Examples of those listed in Fig. 9. are MTF30; 4 synaptic entries in the order in the figure (EEEE, EIEE, IEEE, IIEE) become long-term memory, MTF13; the 6 synaptic inputs, in the order in the figure (EEEEEE, EEEEEI, EEEEIE, EEEEII, EEEIEE, EEIEEE, EEIEEI), become long-term memory. There is no special order for motifs in the figure.

Motif Name	Synaptic Input Type				ap	Motif Name	Synaptic Input Type					ap	Motif Name	Synaptic Input Type					ap	Motif Name	Synaptic Input Type						ap	Motif Name	Synaptic Input Type						ap
	1	2	3	4			1	2	3	4	5			1	2	3	4	5			1	2	3	4	5	6			1	2	3	4	5	6	
MTF8	I	E	E	E	10	MTF19	E	E	I			9	MTF28	I	I	E	E	I	10	MTF29	I	E	E	E	E		13	MTF13	E	E	I	E	I	E	8
	I	I	E	E	9	MTF20	E	E	I			9		I	I	E	I	I	8		I	E	E	E	I		10		E	E	I	E	I	I	8
	I	I	E	I	9	MTF22	I	E	E			8		E	I	E	I	I	8		E	I	E	I	I		8		E	E	I	I	I	E	9
MTF38	E	I	I	E	9	MTF36	I	E	I	E		8	MTF34	E	E	I	E		8		I	E	E	E	E		12		E	E	I	I	I	I	8
MTF5	E	E	E		11	MTF26	E	I	I			8	MTF35	E	E	E	I		10		I	E	E	E	I		9		E	I	E	E	E	I	11
MTF6	I	E	I		10	MTF15	E	E	E	I		9	MTF33	E	I	I	I	I	8		I	I	E	E	I		8		E	I	E	E	I	E	9
MTF7	I	E	E		8		I	E	E	I		8		I	E	E	E	E	8	MTF31	E	E	E	I	E		8		E	I	I	E	I	E	9
	I	E	I		8		E	E	I	E		8	MTF17	E	E	E	E	I	13		E	I	E	I	E		8		E	I	I	E	I	I	8
MTF9	I	E	I	I	8	MTF11	E	E	E	I		12		E	E	E	I	E	12		E	I	E	I	I		9		E	I	I	I	I	E	8
MTF30	E	I	E	I	9		I	E	E	E		8		E	E	E	I	I	11		I	E	E	E	I		8								
	I	E	E	I	9		I	E	I	E		8		I	E	E	I	E	9		I	E	E	I	E		8								
MTF4	E	E	E		9		I	E	I	I		9		I	E	E	I	I	8		I	I	E	I	E		8								
	E	E	I		8	MTF12	E	I	E	I	I	8		I	E	I	I	E	9		I	I	E	I	I		8								

Figure 10: Of the motifs in Fig. 5., those showing short-term memory behaviour; (numbers above motifs indicate synaptic input, numbers in the figure indicate synaptic input type) representation of neurons with probabilities of synaptic input types and the number of Action Potentials (AP) produced in neuron C.

Table 1: Chemical synaptic conductivity model, effect of time constant variation on short-term memory time.

Synaptic conductivity time constant $\tau(ms)$	Short-term memory duration (ms)	Number of action potentials
5	-	-
10	-	-
20	30	3
25	35	5
30	60	6
35	88	8
40	110	9
50	127	11

3.2 Identification of Triple Neuron Network Motifs, which are Short-Term Memory

All the motifs in Fig. 5. were analysed in terms of short-term memory behaviour by the methods described above. In some motifs; we observed that depending on the synaptic type, the action potentials formed in the output neuron C continued for a while, although the external current stimulus to the input neuron (A) was ended. This situation evaluates motifs as short-term memory behaviour. It refers to the retention of information for a while after the warning. Fig. 10. shows motifs that create short-term memory. Additionally, it shows the number of action potentials generated in neuron C to express the excitation situations of the neuron s and the retention time of the information. This study revealed the effect of connection and stimulus type on short-term memory formation in all three-neuron motifs.

3.3 The Effect of the Change in the Time Constant Parameter of the Conductivity Function of the Chemical Synaptic Communication Model between Neurons on Short-Term Memory Behaviour

The duration and number of action potentials formed in the C neuron were examined for different time constant values from the studies performed by changing the time constant of the chemical synaptic conductivity function. For this, the case study was carried out on the MTF8 motif model in Fig. 5. For the different values of the synaptic conductivity time constant (τ) seen in Table 1, the external current input in Fig. 6. (a) was applied to the neuron (A). The short-term memory time, as measured by the action potentials that continue to be produced in the C neuron after the external current input is interrupted, is shown in Table 1. From these data; it is seen that with increasing values of synaptic conductivity time constant, the duration and number of action potentials that occur at the output of the motif increase after external current input. This change prolongs the short-term memory time.

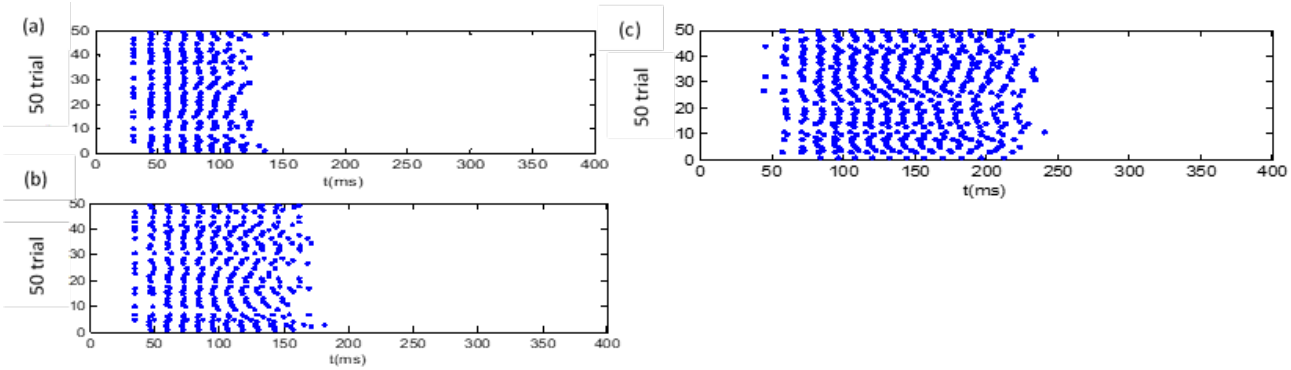

Figure 11: Raster plots of action potentials formed in the C neuron for (a) $(\tau = 25ms)$ **(b)** $(\tau = 35ms)$ **(c)** $(\tau = 50ms)$ **as a result of experiments repeated 50 times for each of the synaptic conductivity time constant** $((\tau))$ **values in the MTF8 motif.**

In this section, the variation of short-term memory duration with time constant is graphically shown. From the studies done in MTF8; the short-term memory times of neurons at different values of the synaptic communication time constant (stimulus types IEEE) are shown in Fig. 11. This situation can also be evaluated as an increase in synapse strength during learning. It can be seen from the figures that as the time constant increases, the information retention time also increases.

4 Discussion

This study is about how learning occurs in brain neuronal networks, which are made up of complex connections. For this purpose, we generated all tri-neuronal network motifs using graph topology. All created motifs were eliminated considering their ability to form interneuron connections. In our study, we focused on the effect of the structure of motifs, the type of synaptic input of neurons, and the time constant of synaptic conductivity on short- and long-term memory behaviour. From the studies on motifs, all motifs showing long- and short-term memory behaviour were determined by considering the types of interneuron synaptic input. In addition, the effect of synaptic conductivity time constant in the chemical synapse model between neurons on short-term memory time was investigated. In the literature; there are studies on several motifs, of which the triple neuron connection is specific. In our study, we methodically obtained all of the three-neural interconnection possibilities in neural networks using graph topology. Some of the motifs obtained; it was removed from the work list because it did not contain three neurons and did not create an input and output neuron state due to the synaptic input direction. Thus, we constructed all the motif possibilities suitable for the neuronal network structure. In Fig. 5., 38 motif models suitable for these features are shown. Triple neural network motif structures were determined, suitable for the studies to be carried out in neural networks. We examined the short- and long-term memory status of the motifs obtained. In triple neural network motifs, one neuron input, one neuron output, and one neuron drive are considered. In the experiments, an external current is applied to the input neuron and the behaviour of the output neuron is examined. If the output neuron continues to generate signals even though the external current input is interrupted, the motif is considered to be long-term memory. If the output neuron generates a signal for some time after the external current input is interrupted, the motif is considered short-term memory. To conduct these experiments, we created separate models for each motif in Fig. 5. with Matlab software. The neurons that make up the motif, according to the interneuron connection structure; the software was modelled as a neuron with only external current input, only one synaptic input, both external current input and one synaptic input, two synaptic inputs, or no input applied. We used the Hodgkin-Huxley model for neurons. The synaptic input type probabilities (E,I) of the neurons were tested for each motif and the action potential generation status of the output neuron (C) was observed in each case. In the results obtained, the states of producing a continuous action potential were obtained and the states of being long-term memory were determined. All cases are shown in Fig. 9. Likewise, after the input current is cut off, short-term memory states that produce action potentials in the output neuron for a while were determined. All cases are shown in Fig. 10. During learning, changes occur in synaptic inputs between neurons. In addition, physical changes occur in the dendritic spines, which are in the connection from the axon tip to the dendrites, in the postsynaptic neuron section. These changes are thought to be significantly related to memory. These spines undergo changes in the form of growth during the learning process. We modelled this growth state by changing the time constant within the synaptic conductivity model. Thus, the memory time of the motif, which has short-term memory characteristics, is extended depending on the time constant. We studied this study on a motif, which is short-term memory, at different values of the time constant. The obtained results are shown in Table 1 and Fig. 11. During learning; the effects of connections between neurons, direction and type of synaptic input (E,I) on memory formation were examined. In the studies conducted in this area, a limited number of motifs have been studied. In most of the studies, neuron models with fewer parameters were preferred. In our study, the Hodgkin-Huxley neuron model, which successfully represents neurons with more parameters, was preferred and all tripartite neuronal network motifs were studied. In some studies, noise signals are generally used instead of synaptic inputs.

In our study, if the cell membrane voltage exceeds a certain threshold value as a result of interneuron communication, synaptic input to the neuron, an action potential is modelled. This is more realistic. Likewise, the effect of neurotransmitters emitted in the space between neurons making chemical synapses on the postsynaptic neuron was modelled as excitatory or inhibitory. For this, two different level voltage values of the equilibrium voltage E_syn, which constitutes of the synaptic input current, were used ($E \rightarrow E_{syn} = 10V$, $I \rightarrow E_{syn} = -70V$). All motifs and necessary conditions showing long-term memory behaviour are shown in Fig. 9. All the motives and necessary conditions showing short-term memory behaviour are also presented in Fig. 10. Especially the significant effect on short-term memory behaviour; it has been shown that besides the type of connection, the synaptic input types of neurons have suitable possibilities. In the studies, short-term memory duration was studied in quad neuron network motifs. In our study, this time change was modelled with the synaptic input time constant. This situation was evaluated as a prolongation of the learning process. The effect, which also expresses the physical change in the postsynaptic region, extended the information retention time. We demonstrated this for various values on a motif. In the neuron model we used, the deterministic model was preferred for the ion channels of neurons. The cell membrane is considered homogeneous. However, evaluating the randomness of the ion channels and considering the heterogeneous structure of the cell membrane will create a more realistic model. While the action potential is forming in the neuron, the arrival of new synaptic inputs can be prevented (the refractory period). In the three-neuronal motif structure we created; larger network connections can be created by multiplexing the input, output, driver neurons. Neural coding can be studied on these models.

Authors' Contributions

AT applied the cell software with the determined model, developed the software for the model and network motif structure. He performed all the experiments and analyzed the motifs. TK conducted pattern identification studies on cell modeling and determined motif analysis methods. All authors read and approved the last article.

Competing Interests

We declare that there is no conflict of interest between the authors and with any institution in the study.

Ethical Approval

When our study is a simulation study, it does not require ethical approval since both human and/or animal studies are not done.

References

[1] R. Milo, S. Shen-Orr, S. Itzkovitz, N. Kashtan, D. Chklovskii, and U. Alon, "Network motifs: Simple building blocks of complex networks," *Science*, vol. 298, no. 5594, pp. 824–827, 2002.
[2] S. Song, P. J. Sjöström, M. Reigl, S. Nelson, and D. B. Chklovskii, "Correction: Highly nonrandom features of synaptic connectivity in local cortical circuits," *PLOS Biology*, vol. 3, no. 10, 2005.
[3] H. Kugler, S.-J. Dunn, and B. Yordanov, "Formal analysis of network motifs," *bioRxiv*.
[4] O. Sporns and R. Kötter, "Motifs in brain networks," *PLOS Biology*, vol. 2, 2004.
[5] R. J. Prill, P. A. Iglesias, and A. Levchenko, "Dynamic properties of network motifs contribute to biological network organization," *PLOS Biology*, vol. 3, no. 11, 2005.
[6] S. Song, P. J. Sjöström, M. Reigl, S. Nelson, and D. B. Chklovskii, "Highly nonrandom features of synaptic connectivity in local cortical circuits," *PLOS Biology*, vol. 3, no. 3, 2005.
[7] C. Li, "Functions of neuronal network motifs," *Phys. Rev. E*, vol. 78, no. 3, p. 037101, 2008.
[8] C. Bargmann and E. Marder, "From the connectome to brain function," *Nature methods*, vol. 10, pp. 483–90, 2013.
[9] M. D. Humphries, "Dynamical networks: Finding, measuring, and tracking neural population activity using network science," *Network Neuroscience*, vol. 1, no. 4, pp. 324–338, 2017.
[10] S. Fornari, A. Schäfer, M. Jucker, A. Goriely, and E. Kuhl, "Prion-like spreading of alzheimer's disease within the brain's connectome," *Journal of The Royal Society Interface*, vol. 16, p. 20190356, 2019.
[11] M. De Roo, P. Klauser, P. Méndez, L. Poglia, and D. Muller, "Chapter 11 spine dynamics and synapse remodeling during ltp and memory processes," *Progress in brain research*, vol. 169, pp. 199–207, 2008.
[12] E. Bruel-Jungerman, S. Davis, and S. Laroche, "Brain plasticity mechanisms and memory: A party of four," *The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry*, vol. 13, pp. 492–505, 2007.
[13] D. Chao-Yi, J. Lim, Y. Nam, and C. Kwang-Hyun, "Systematic analysis of synchronized oscillatory neuronal networks reveals an enrichment for coupled direct and indirect feedback motifs," *Bioinformatics*, vol. 25, no. 13, pp. 1680–1685, 2009.
[14] B. Albensi, *ISynaptic Plasticity: New Research*, 2009.
[15] M. Mayford, S. Siegelbaum, and E. Kandel, "Synapses and memory storage," *Cold Spring Harbor perspectives in biology*, vol. 4, no. 13, 2012.
[16] N. Chenkov, H. Sprekeler, and R. Kempter, "Memory replay in balanced recurrent networks," *PLOS Computational Biology*, vol. 13, no. 1, pp. 1–36, 2017.
[17] M. T. Owens and K. D. Tanner, "Teaching as brain changing: Exploring connections between neuroscience and innovative teaching," *CBE—Life Sciences Education*, vol. 16, no. 2, p. fe2, 2017.
[18] J. Hennig, E. Oby, D. Losey, A. Batista, B. Yu, and S. Chase, "How learning unfolds in the brain: toward an optimization view," *Neuron*, vol. 109, 2021.
[19] O. Atay, A. Doncic, and J. M. Skotheim, "Switch-like transitions insulate network motifs to modularize biological networks." *Cell systems*, vol. 32, pp. 121–132, 2016.
[20] J.-R. Kim, Y. Yoon, and K.-H. Cho, "Coupled feedback loops form dynamic motifs of cellular networks," *Biophysical journal*, vol. 94, pp. 359–65, 2008.
[21] H. Koeppl and S. Haeusler, "Motifs, algebraic connectivity and computational performance of two data-based cortical circuit templates," in *Proceedings of the sixth International Workshop on Computational Systems Biology*, 2009, p. 4.
[22] L. Peris, M. Bisbal, J. Martínez-Hernández, Y. Saoudi, J. Jonckheere, M. Rolland, M. Sebastien, J. Brocard, E. Denarier, C. Bosc, C. Guerin, S. Gory-Fauré, J. C. Deloulme, F. Lanté, I. Arnal, A. Buisson, Y. Goldberg, L. Blanchoin, C. Delphin, and A. Andrieux, "A key function for microtubule-associated-protein 6 in activity-dependent stabilisation of actin filaments in dendritic spines," *Nature Communications*.

[23] D. Braha, ''Patterns of ties in problem-solving networks and their dynamic properties,'' *Scientific Reports*, vol. 10, p. 18137, 2020.
[24] S. Patra and A. Mohapatra, ''Application of dynamic expansion tree for finding large network motifs in biological networks,'' *PeerJ*, vol. 7, p. e6917, 2019.
[25] E. Martorana, G. Micale, A. Ferro, and A. Pulvirenti, ''Establish the expected number of induced motifs on unlabeled graphs through analytical models,'' *Applied Network Science*, vol. 5, p. 58, 2020.
[26] M. Arbib, *The Handbook of Brain Theory and Neural Network*, 2003.
[27] D. Basset and E. Bullmor, ''Small-world brain networks,'' *The Neuroscientist : a review journal bringing neurobiolog, neurology and psychiatry*, vol. 12, pp. 512–23, 2007.
[28] B. Danielle and B. Edward, ''Small-world brain networks revisited,'' *The Neuroscientist*, vol. 23, 2016.
[29] H. Schwöbbermeyer, *Network Motifs*. John Wiley and Sons, Ltd, 2008.
[30] N. Borovok, E. Nesher, Y. Levin, M. Reichenstein, A. Pinhasov, and I. Michaelevski, ''Dynamics of hippocampal protein expression during long-term spatial memory formation,'' *Molecular and Cellular Proteomics*, vol. 15, p. mcp.M115.051318, 2015.
[31] A. Spiegler, E. C. A. Hansen, C. Bernard, A. R. McIntosh, and V. K. Jirsa, ''Selective activation of resting-state networks following focal stimulation in a connectome-based network model of the human brain,'' *eNeuro*.
[32] A. Mirisis, A. Alexandrescu, T. Carew, and A. Kopec, ''The contribution of spatial and temporal molecular networks in the induction of long-term memory and its underlying synaptic plasticity,'' *AIMS Neuroscience*, vol. 3, pp. 356–384, 2016.
[33] R. Staudemeyer and E. Morris, ''Understanding lstm – a tutorial into long short-term memory recurrent neural networks,'' 2019.
[34] J. Keener and J. Sneyd, *Cellular Homeostasis*. Springer New York, 2009, pp. 49–119.
[35] B. F. Grewe, J. Gründemann, L. J. Kitch, J. A. Lecoq, J. G. Parker, J. D. Marshall, M. C. Larkin, P. E. Jercog, F. Grenier, J. Z. Li, A. Lüthi, and M. J. Schnitzer, ''Neural ensemble dynamics underlying a long-term associative memory,'' *Nature*, vol. 543, pp. 670 – 675, 2017.
[36] N. S.R., I. Boybat, M. Gallo, E. Eleftheriou, A. Sebastian, and B. Rajendran, ''Experimental demonstration of supervised learning in spiking neural networks with phase-change memory synapses,'' *Scientific Reports*, vol. 10, 2020.
[37] Z. Harper and C. Welzig, ''Exploring spatiotemporal functional connectivity dynamics of the human brain using convolutional and recursive neural networks,'' 2019, pp. 1–6.
[38] T. Gorochowski, C. Grierson, and M. Di Bernardo, ''Organization of feed-forward loop motifs reveals architectural principles in natural and engineered networks,'' *Science Advances*, vol. 4, p. eaap9751, 2018.
[39] D. Schachinger, ''Simulation of extracellularly recorded activities from small nerve formations in the brain,'' 2003.
[40] P. Dayan and L. F. Abbott, *Theoretical neuroscience: computational and mathematical modeling of neural systems*. MIT press, 2005.
[41] E. M. Izhikevich, *Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting*. The MIT Press, 2006.
[42] Z. Tian and D. Zhou, ''Library-based fast algorithm for simulating the hodgkin-huxley neuronal networks,'' 2021.
[43] T. Zhongqi and Z. Douglas, ''Design fast algorithms for hodgkin-huxley neuronal networks,'' 2021.
[44] S. Navlakha, Z. Bar-Joseph, and A. Barth, ''Network design and the brain,'' *Trends in Cognitive Sciences*, vol. 22, 2017.
[45] J. M. Bower, D. Beeman, J. M. Bower, and D. Beeman, ''Compartmental modeling,'' *The Book of GENESIS: Exploring Realistic Neural Models with the GEneral NEural SImulation System*, pp. 7–15, 1998.
[46] W. Gerstner and W. M. Kistler, 2002.
[47] J. Wang, J. Geng, and X. Fei, ''Two-parameters hopf bifurcation in the hodgkin–huxley model,'' *Chaos, Solitons and Fractals*, vol. 23, no. 3, pp. 973–980, 2005.
[48] L. Meng and J. Xiang, ''Brain network analysis and classification based on convolutional neural network,'' *Frontiers in Computational Neuroscience*, vol. 12, 2018.
[49] L. J. Boaz, R. R. A., K. Xiangnan, K. Sungchul, K. Eunyee, and R. Anup, ''Graph convolutional networks with motif-based attention,'' in *Proceedings of the 28th ACM International Conference on Information and Knowledge Management*, New York, NY, USA, 2019, p. 499–508.
[50] K. Patrick, P. Karin, S. Achim, and M. Claus, ''Recurrence resonance in three-neuron motifs,'' *Frontiers in Computational Neuroscience*, vol. 13, p. 64, 2019.
[51] P. Sabyasachi and M. Anjali, ''Application of dynamic expansion tree for finding large network motifs in biological networks,'' *PeerJ*, vol. 7, p. e6917, 2019.
[52] ——, ''Disjoint motif discovery in biological network using pattern join method,'' *IET Systems Biology*, vol. 13, no. 5, pp. 213–224, 2019.
[53] H. Li, C. Liu, and J. Wang, ''Memory and computing function of four-node neuronal network motifs,'' in *Proceeding of the 11th World Congress on Intelligent Control and Automation*, 2014, pp. 5818–5823.
[54] L. Peris, M. Bisbal, and e. Martínez-Hernández, ''A key function for microtubule-associated-protein 6 in activity-dependent stabilisation of actin filaments in dendritic spines,'' *Nature Communications*, vol. 9, 2018.