<u>A neural circuit model for motor control in C.elegans</u>

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Abstract

The field of cognitive science deals with the scientific study of mind and the various processes being carried out in the mind, which are involved in interpreting the information available around us. In such a field of study, studying Brain and the nervous system becomes both essential and fundamental in nature. However, the nervous system, comprising of brain and spinal cord, functions in a very peculiar way. Its basic entity, known as nerve cell or neurons, always functions in groups. These groups are what we call as neural circuits. Generally, these ensembles specialize in processing a certain kind of information. In this project, a study of such a circuit which is responsible for motor control in <u>Caenorhabditis elegans</u> for gentle touch stimulation was carried out based on the model proposed by M Sujuki et al in their paper "A model of motor control of nematode C.elegans with neuronal circuits"(2005) and a computational model was generated. The model correctly predicted the response of the C.elegan in the gentle touch stimulation.

Introduction

Neural circuits: Neural circuit, as it sounds, is a circuit of neurons. Essentially, it is a network of interconnected neurons that specialize in performing a particular function. There are three kinds of neuron that work together to form a circuit. These are –

- Sensory neurons: These are the neurons that sense the information from the environment. They act like a sensor and convert the stimulations into a flow of ions known as neuronal current.
- Inter neurons: These are a kind of relay neurons that connect sensory neurons to other neurons present. An important function that they perform is, forming feedback loops. A feedback loop is a backward connection of a neuron that regulates inhibition or excitation in the previous neuron.
- Motor neuron: It is the effector neuron in a circuit. It ends into muscles and based on the current from sensory neurons through interneuron, relaxes or contracts the muscle fibres making the action possible.

These various kinds of neurons are joined together through chemical synapses and gap junctions. Synapses are basically axons of a neuron ending over dendrites of the successive neuron. At chemical synapses release of neurotransmitters from pre synaptic neuron opens up the ion channels in post synaptic neurons and thereby causing ions to flow through it.

Gap junctions are found at electrical synapses. Here pre and post synaptic neurons are joined together through several connecting channels or Gap junctions.

Several architectures of neural circuits are found. Two most common ones are converging and diverging. As name suggests, in a diverging circuit a single neuron branch out in many neurons whereas in converging ones several neurons eventually end in one neuron.

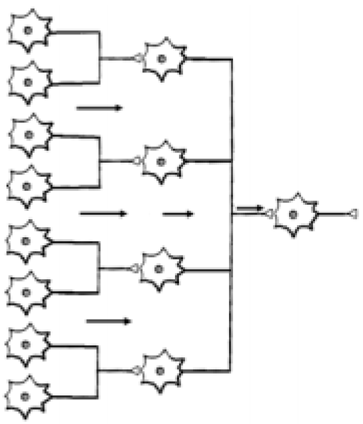

Fig: Converging Neural circuit

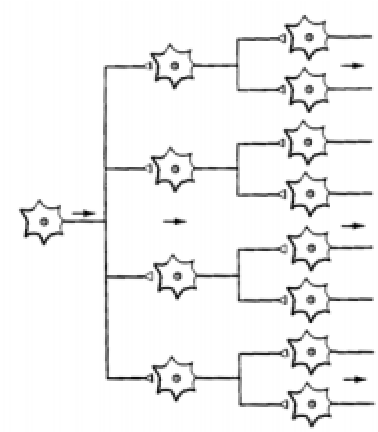

Fig: Diverging Neural circuit

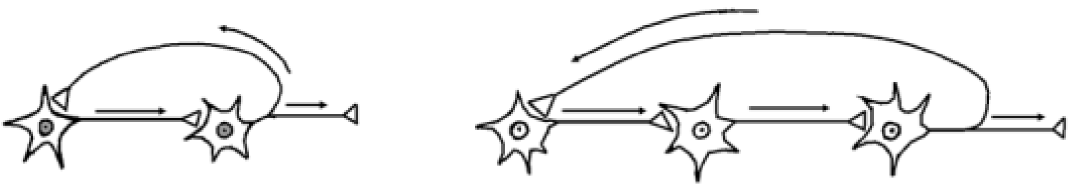

Fig: Feedback loops

(Source: http://courses.washington.edu/psych333/handouts/coursepack/ch06-Principles_of_neural_circuits.pdf)

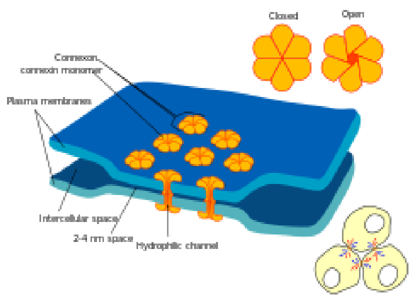

Fig: Gap junctions

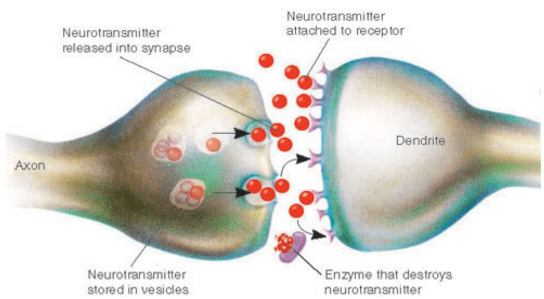

Fig: Chemical synapse

(Source: Google images)

Motor Control: As defined by Wikipedia *"Motor controls are information processing related activities carried out by the central nervous system that organize the musculoskeletal system to create coordinated movements and skilled actions".* That is, motor control is the type of information processing which results in the movement of our body. These responses or results of these processing is most easily and instantaneously visible in our actions and this makes this type of response apt for studying neural circuits in a detailed and easy way.

C.elegans: C.elegans or *Caenorhabditis elegans* are free living roundworms(nematodes) that belong to the phylum *Nemathelminthes.* They are transparent and about 1mm in length. They are typically found in temperate soil environments.

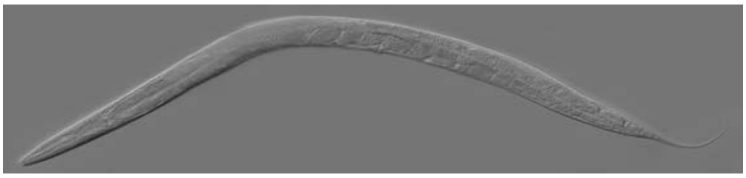

Fig: Caenorhabditis elegans

Now, to study a neural circuit it is important to choose a circuit which is reliable and is well known. The nervous system and neural circuits of C.elegans serve this purpose very well. They have been widely studied and characterized ever since 1986 when J. G. White in his paper "*The structure of the nervous system of the nematode Caenorhabditis elegans*" presented the first detailed structure of nervous system of this organism.

The nervous system of C.elegans is very simple. Comprising of just about 300 neurons, it is broadly divided into two parts – the somatic and the pharyngeal nervous system. These two mainly differ in their topologies and communicate with each other via a single pair of neurons called the RIP neurons.

The Somatic nervous system consists of 282 neurons and constitutes the main functioning part. The Pharyngeal nervous system just contains 20 neurons. These neurons are connected by around 6400 synapses 900 gap junctions and 1500 neuro - muscular junctions.

Another important feature about the Nervous system of C.elegans that makes it suitable for studying neural circuits is that the reliable data for its neural connections and their characteristics is also readily available. Various sites like "*WORMATLAS"* and "*Database of Synaptic Connectivity of C. elegans for Computation"* maintain an updated record of such data.

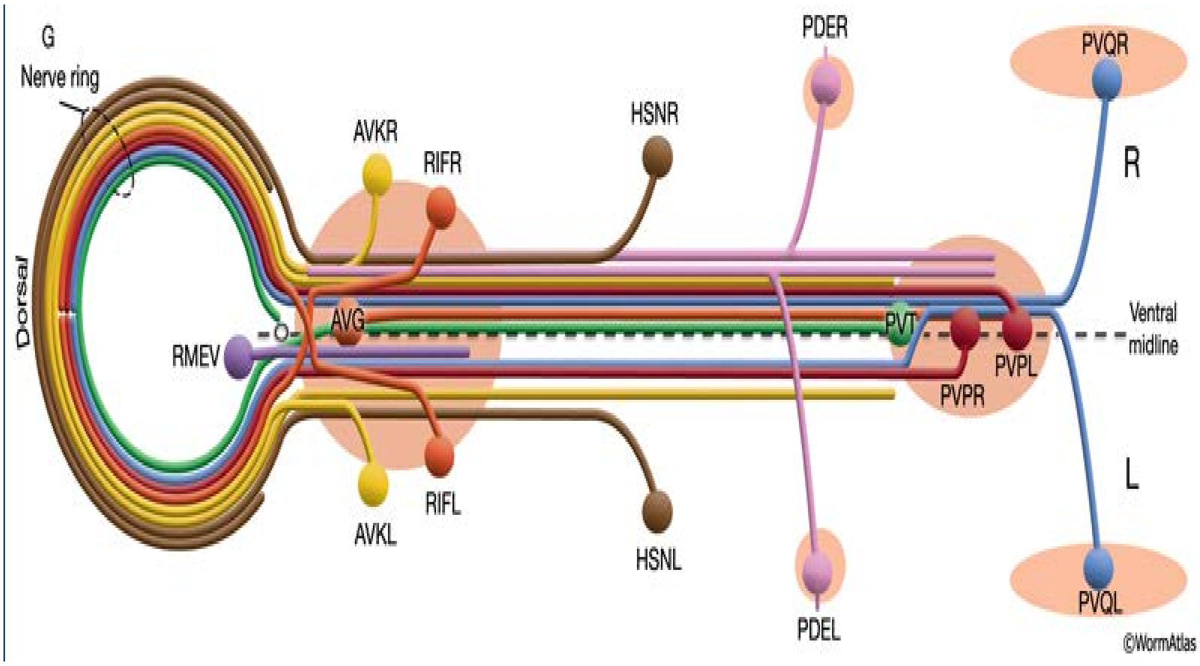

Fig: Main sensory system of C.elegans

(Source: http://www.wormatlas.org/hermaphrodite/nervous/Neuroframeset.html)

Methods

Obtaining neural circuit for gentle touch stimulations: From the paper "*The structure of the nervous system of the nematode Caenorhabditis elegans*" by J. G. White et al (1986) it was found that 18 neurons are involved in the gentle touch stimulation response. These 18 neurons comprise of 6 sensory neurons, 12 inter neurons and 2 motor neurons.

The sensory neurons belonged to the classes ALM, AVM, PLM, PVM. These classes are defined based on the position of sensory neurons in the elegan body. Similarly, inter neurons belonged to classes PVC,AVD,LUA,AVA,AVB.

The two motor neurons were responsible for excitation in anterior and posterior parts of the bodies.

These information were fed into the "*Database of Synaptic Connectivity of C. elegans for Computation"* and the data for synaptic and gap junction connectivity was obtained. Also a diagram for neural connectivity in C.elegans was generated to form a basis for generation of the neural circuit model.

Once the diagram was obtained computational modelling of neurons and then final circuit was done.

Synaptic connectivity Data

resynaptic neuron class	(A) somatic nervous system						(B) pharyngeal nervous system sources of data are the figures in [2]		
	(A-1) sources of data are the figures in [1]			(A-2) sources of data are the tables and the text in [1]					
	connection	**chemical synapse**	**gap junction**	**connection**	**chemical synapse**	**gap junction**	**connection**	**chemical synapse**	**gap junction**
ALM	ALML(se) --> AVDR(in) ALML(se) --> AVM(se) ALML(se) --> PVCL(in) ALML(se) --> PVCR(in) ALMR(se) --> AVDR(in) ALMR(se) --> AVM(se) ALMR(se) --> PVCR(in)	1 0 4 2 0 0 3	0 1 0 0 1 1 0	no data	-	-	no data	-	-
AVA	AVAL(in) --> AVAR(in) AVAL(in) --> LUAL(in) AVAR(in) --> AVAL(in) AVAR(in) --> LUAL(in) AVAR(in) --> LUAR(in)	0 1 0 1 3	1 1 1 0 0	AVA(in) --> AVA(in) AVA(in) --> AVB(in) AVA(in) --> AVD(in) AVA(in) --> LUA(in) AVA(in) --> PVC(in)	3 2 2 5 28	4 0 0 0 10	no data	-	-
AVB	AVBL(in) --> AVBR(in) AVBR(in) --> AVBL(in)	0 0	2 2	AVB(in) --> AVA(in) AVB(in) --> AVB(in) AVB(in) --> AVD(in)	27 2 3	0 1 0	no data	-	-
AVD	AVDL(in) --> AVM(se) AVDL(in) --> LUAL(in) AVDR(in) --> ALMR(se) AVDR(in) --> LUAL(in)	0 1 0 2	1 0 1 0	AVD(in) --> AVA(in) AVD(in) --> AVB(in) AVD(in) --> AVD(in) AVD(in) --> AVM(se) AVD(in) --> LUA(in) AVD(in) --> PVC(in)	70 1 2 0 3 1	0 0 0 1 0 0	no data	-	-
AVM	AVM(se) --> ALML(se) AVM(se) --> ALMR(se) AVM(se) --> AVBL(in) AVM(se) --> AVBR(in) AVM(se) --> AVDL(in) AVM(se) --> PVCL(in) AVM(se) --> PVCR(in)	0 0 6 6 0 4 6	1 1 0 0 1 0 0	AVM(se) --> AVD(in)	0	1	no data	-	-
LUA	LUAL(in) --> AVAL(in) LUAL(in) --> AVAR(in) LUAL(in) --> AVDL(in) LUAL(in) --> AVDR(in) LUAR(in) --> AVAL(in) LUAR(in) --> AVAR(in) LUAR(in) --> AVDL(in) LUAR(in) --> AVDR(in) LUAR(in) --> PLMR(se) LUAR(in) --> PVCR(in)	5 5 4 2 3 7 1 3 0 3	1 0 0 0 0 0 0 0 1 0	LUA(in) --> AVA(in) LUA(in) --> AVD(in) LUA(in) --> PLM(se) LUA(in) --> PVC(in)	20 7 0 3	0 0 2 0	no data	-	-
PLM	PLMR(se) --> LUAR(in)	0	1	PLM(se) --> AVA(in) PLM(se) --> AVD(in) PLM(se) --> LUA(in) PLM(se) --> PVC(in)	5 5 0 1	0 0 2 2	no data	-	-
PVC	PVCL(in) --> AVAR(in) PVCL(in) --> AVBL(in) PVCL(in) --> AVBR(in) PVCL(in) --> AVDL(in)	2 4 12 3	0 0 0 0	PVC(in) --> AVA(in) PVC(in) --> AVB(in) PVC(in) --> AVD(in) PVC(in) --> LUA(in)	14 4 4 1	10 0 0 0	no data	-	-

	PVCL(in) --> AVDR(in) PVCL(in) --> PVCR(in) PVCR(in) --> AVAL(in) PVCR(in) --> AVAR(in) PVCR(in) --> AVBL(in) PVCR(in) --> AVBR(in) PVCR(in) --> AVDL(in) PVCR(in) --> AVDR(in) PVCR(in) --> LUAR(in) PVCR(in) --> PVCL(in)	2 2 1 3 5 6 2 1 1 1	0 1 0 0 0 0 0 0 0 1	PVC(in) --> PLM(se) PVC(in) --> PVC(in)	0 1	2 4			
PVM	no data	-	-	PVM(se) --> AVM(se) PVM(se) --> PVC(in)	1 2	0 0	no data	-	-
	Total[*]	118	10	Total[*]	217	24	Total[*]	0	0

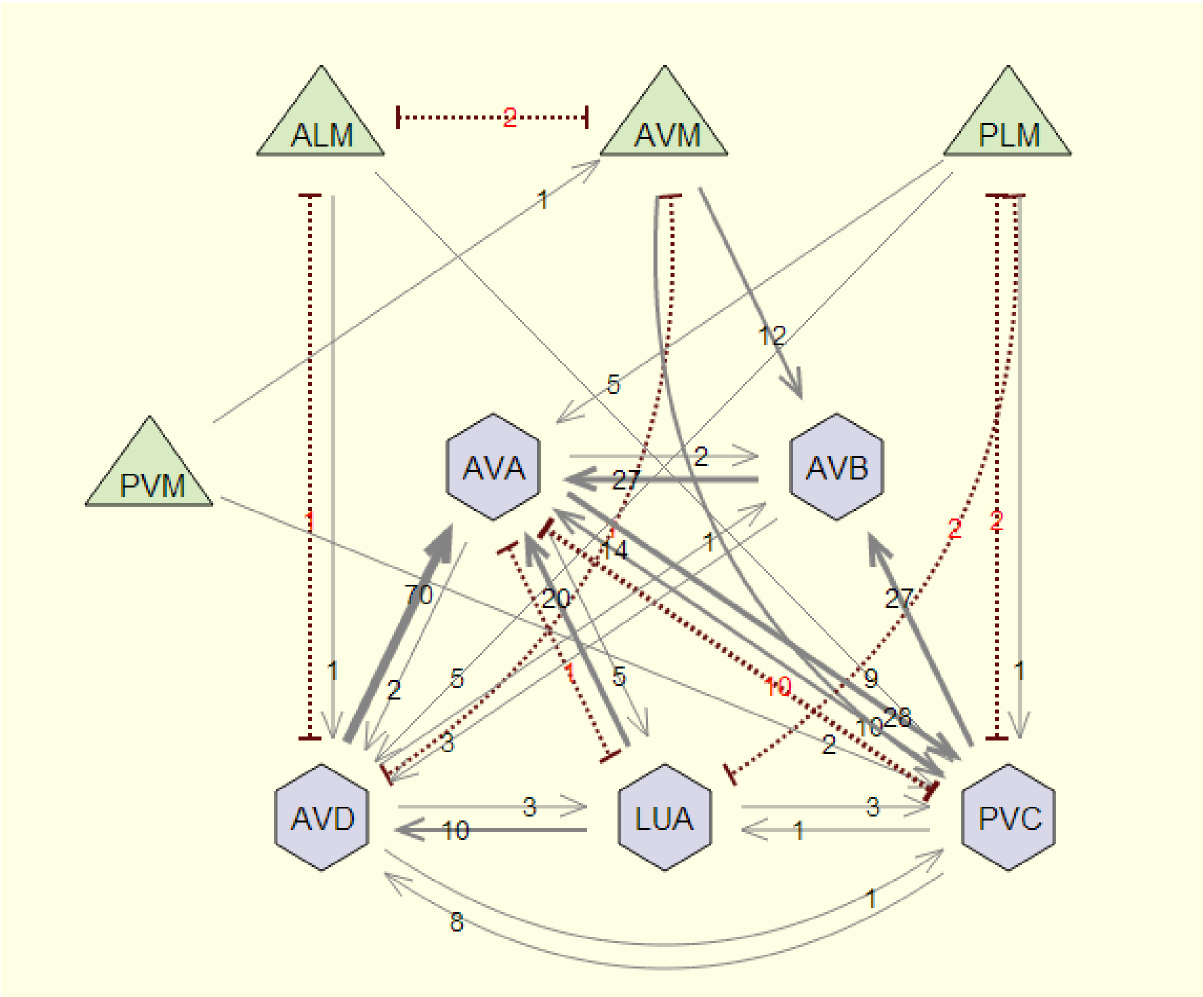

Fig: Wiring Diagram for the given connectivity data.

Modelling a single neuron: For modelling a single neuron reference from the paper *"A model of motor control of nematode C.elegans with neuronal cicuits"* by Michiyo Suzuki et al(2005) was taken. In this paper considering various factors for a neuron like its position in the elegan body, sensitivity towards excitation and input and output range of activity Sujuki et al have proposed the following mathematical characteristic of a single neuron. All the parameters of this characteristic model have been tested and adjusted using the real coded genetic algorithm.

$$O_n = \frac{C_n}{1+\exp(-A_n(I_n - B_n))}$$

Mathematical characteristic of a single neuron

Here O_n is the output current, I_n is the input current, A_n is inclination with output function B_n is value of the stimulation input at which the output of the neuron takes a central value and C_n is the stimulation reception sensitivity.

Using this characteristic as a basis a MATLAB model for single neuron was made and subsequently the model for sensory layer involved in the gentle touch stimulation was completed.

Modelling interneurons: While sensory neurons get excited directly by the stimulation, the interneurons are excited by sensory neurons. Each sensory neuron forms synapse with one or more interneurons which also form synaptic connections among themselves. Also, it is important to note that the chemical synapses have a transfer strength i.e the current passing in the presynaptic neuron is not completely transferred to the post synaptic neuron but only a part of it is transferred, moreover, chemical synapse are not bilateral i.e strength of synapse from neuron 1 to neuron 2 is not the same as strength of synapse from neuron 2 to neuron 1.

Gap junctions on the other hand are easier to handle. They are bilateral (strength from 1 to 2 is same as strength from 2 to 1) and transfer almost all the current flowing through them.

To decide the input current for an interneuron with multiple synaptic and gap junctions, neural network model was used. Each synapse was provided with a weight. The calculation of theses weights was based on the assumption that current in each neuron is divided equally in all its axons. With this assumption

$$w_{n,i} = 1/(\text{number of neurons with which neuron n forms synapse}) .$$

$w_{n,i}$ is the weight of synapses from neuron n.

Similarly, weight of gap junctions was decided. The gap junctions were considered as chemical synapses with equal wigthage in both directions, so

Weight of gap junction = ½(Weight of synapse of a neuron)

Also,

$$w_{i,j} \neq w_{j,i} \text{ however } g_{i,j} = g_{j,i}$$

$g_{i,j}$ is the weight of gap junction.

Once the weight were decided, based on the neural network model, Interneuron input current was decided to be calculated as

$$I_n = w_{a,n}I_a + w_{b,n}I_b + w_{c,n}I_c + g_{d,n}I_d + g_{e,n}I_e$$

To model the feedback connections, the first output (output at t = 0) of the preceding neuron was calculated without taking into account the feedback current and the subsequent outputs were calculated by considering the feedback current.

After modelling the sensory and interneurons, motor neurons were modelled in the same way as interneurons and then the complete circuit was generated.

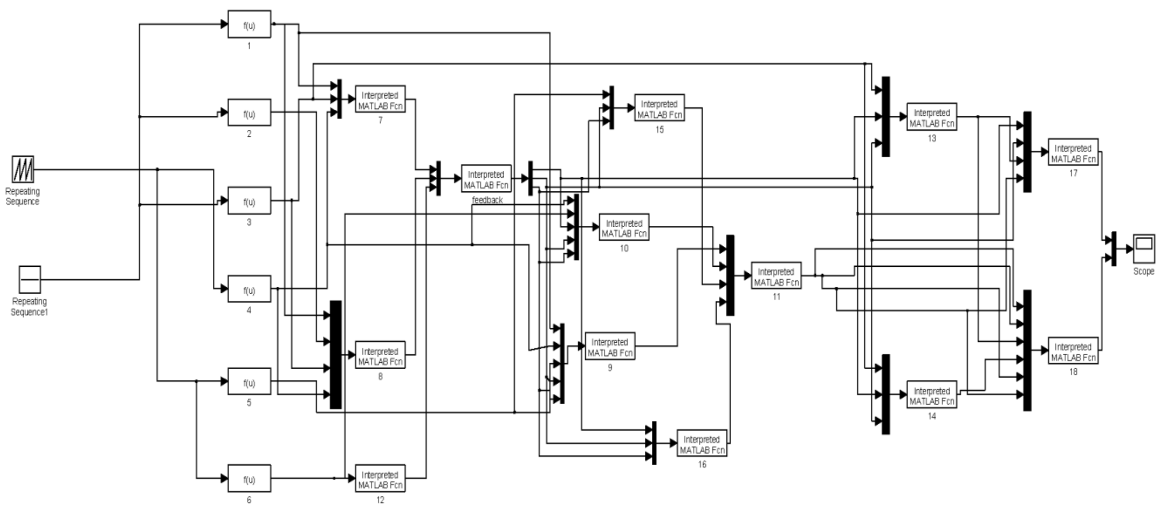

Fig: Final neural circuit model

Results

Recording for functioning of circuit at various stages of development was done. These recordings ensured the proper functioning of each of the component of the circuit. These recordings are depicted below.

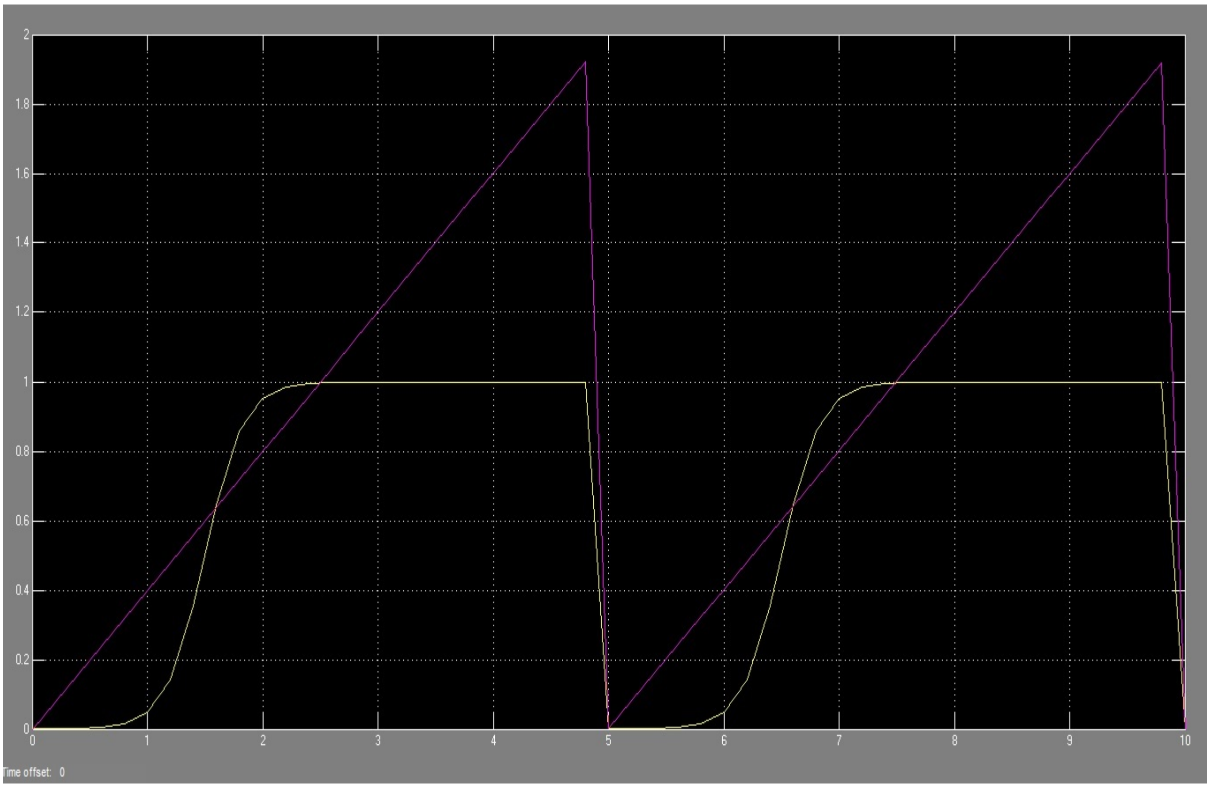

Fig: Recordings from a single neuron in two consecutive stimulations

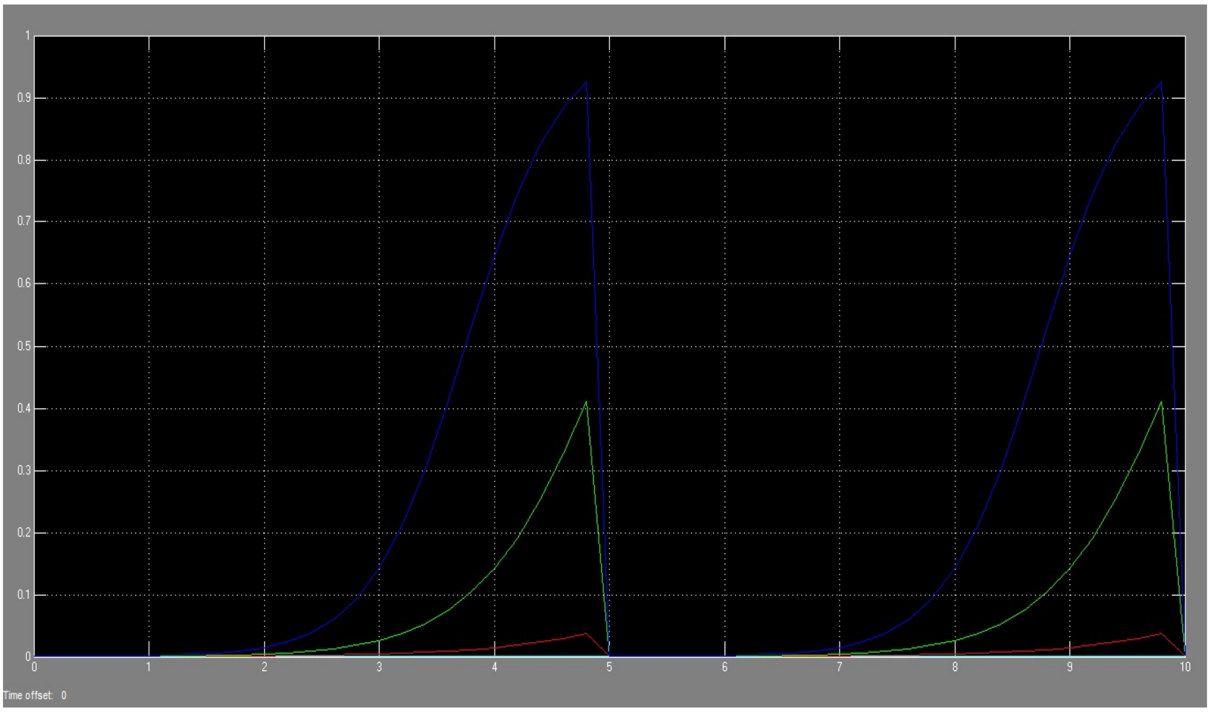

Fig: Recording from six sensory neurons in anterior touch (left) and posterior touch (right)

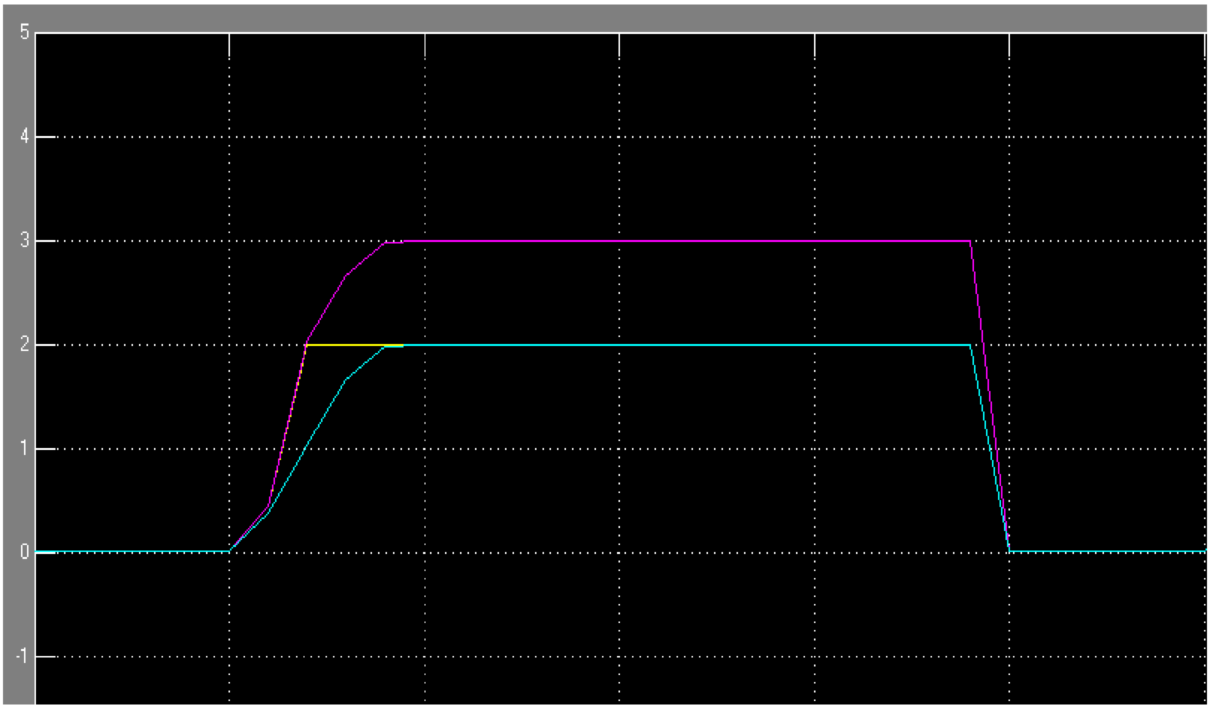

Fig: Output of six sensory neurons connected with first three interneurons

Finally, the outputs for anterior and posterior touch were recorded. In gentle touch stimulation the established response of C.elegans is that the part being touched retreats first and then a recoil motion is followed as depicted in the figure below. Such a response will require a current in anterior motor neuron and then a lagged current in posterior motor neuron (in case of anterior touch). Indeed, the developed model produced such a response.

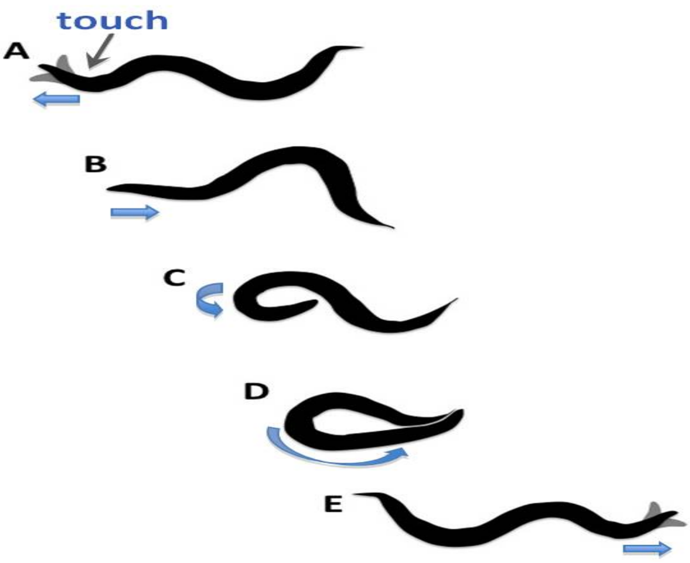

Fig: Gentle touch response of c.elegans

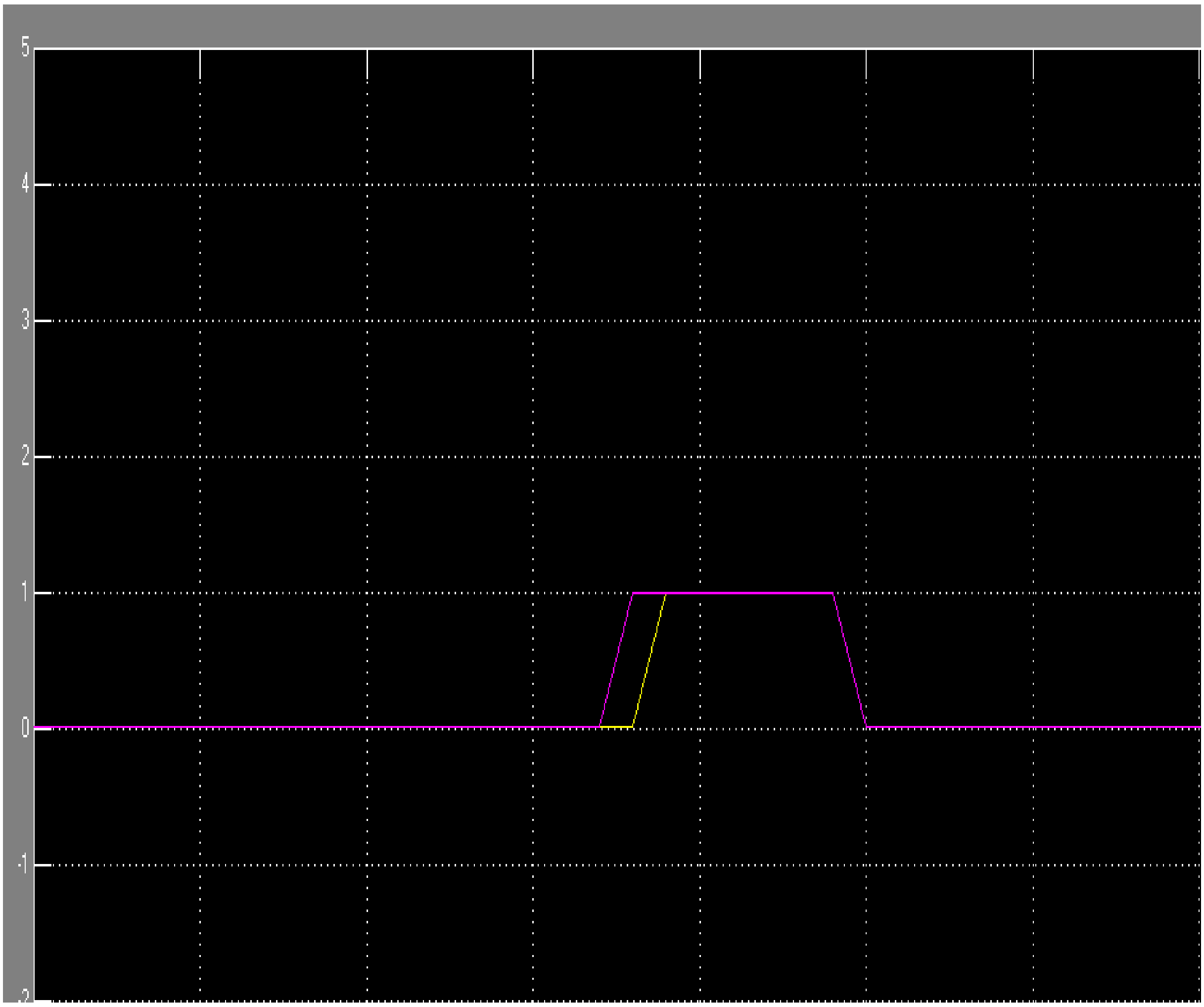

Fig: Final Output

Conclusion

Clearly, the model showed that a simulation in anterior motor neuron of the C elegans is followed by a simulation in the posterior motor neuron which correctly depicts the response of the C elegan in gentle touch stimulation.

Although the chemistry and genetics of cell have not been included in this model, but such an integral model might prove very useful in various types of cognitive and behavioural studies.

Producing such a model for higher organisms will give new insight into the working of their nervous system.

References

[1] www.wormatlas.org/hermaphrodite/nervous/Neuroframeset

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