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Features of C. Elegans Thermosensory System

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Abstract:
To understand more complex neural systems, it is reasonable to start with analysing more simple ones. C. Elegans is a model organism for such analysis; both because of its mapped connectome and genome. Within C. Elegans, the simplest neural subsystem seems to be the thermosensory system. In this paper we analyse the neural pathway leading from thermosensory neurons down to locomotory neurons.
Although rudimentary compared to mammals, neural system of nematode C. Elegans still remains to be elucidated by neuroscientific research. The Thermosensory system of the nematode is believed to have two major thermosensory neurons, AFDL and AFDR (that are also believed to have CO2-sensory function) and supportive sensory neurons involved in other modalities but also in thermosensation - AWCL, AWCR, ASIL and ASIR. A complete neural circuitry of the thermosensory circuit is not clear yet. Although the basic circuit is known, thermosensation in C. Elegans has many features and we do not know yet in detail how thermosensation works on the level of individual neurons and synapses. The thermosensory system of C. Elegans operates at several levels. Firstly, an animal remembers at what temperature it hatched and can adjust its thermotaxis accordingly. Secondly, the nematode exhibits three major forms of thermotaxis – moving from lower temperatures towards the preferred temperature, moving from higher temperatures towards the preferred temperature and isothermal tracking – remaining in the preferred temperature range. Thirdly, the preferred temperature is adaptable; if animals are starved at a certain temperature they will adjust their preferred temperature to a different level. Fourthly, there seems to be different mechanism/circuit for extreme and for normal temperatures. Although C. Elegans is a relatively simple organism, its nervous system is still too complex for us to fully elucidate. By analysing one of the simplest C. Elegans subsystems - the thermosensory subsystem - we can still see several hurdles to be overcome before fully understanding this pathway. Researchers have been quite successful in identifying the neurons that contribute to the pathway (although there are still speculations that additional neurons may be temporarily recruited into the pathway). Although we know quite a lot about the thermosensory neurons (especially ADFL and ADFR) we are only beginning to learn about the function and the molecular underpinnings of interneurons in C. Elegans. And, at the same time, interneurons appear to be the part of the system where most of the neurocomputation happens. There are approximately 6000 synapses in the neural system of C. Elegans. Although the connectome of the worm has been mapped, we still do not know many features of individual neurons and their synapses. For example, it is still not clear what synapses are excitatory and which are inhibitory. Besides modelling studies, new experimental studies are necessary to establish the excitatory/inhibitory nature of interactions between respective neurotransmitters and their receptors.

Keywords:
Thermosensation. C. Elegans. Computational modelling.

Introduction

Although rudimentary compared to mammals, the neural system of nematode C. Elegans still remains to be elucidated by neuroscientific research. A thermosensory system of the nematode is relatively simple compared to other sensory systems of C. Elegans. It is believed to have two major thermosensory neurons; AFDL and AFDR (that are also believed to have CO2-sensory function) and supportive sensory neurons involved in other modalities but also in thermosensation – AWCL, AWCR, ASIL and ASIR.

A complete neural circuitry of the thermosensory circuit is not clear yet. Although the basic circuit is known (Mori, Ohshima, 1995; Garrity et al., 2010; Figure 1), the thermosensation in C. Elegans has many features and we do not know yet in detail how thermosensation works on the level of individual neurons and synapses.

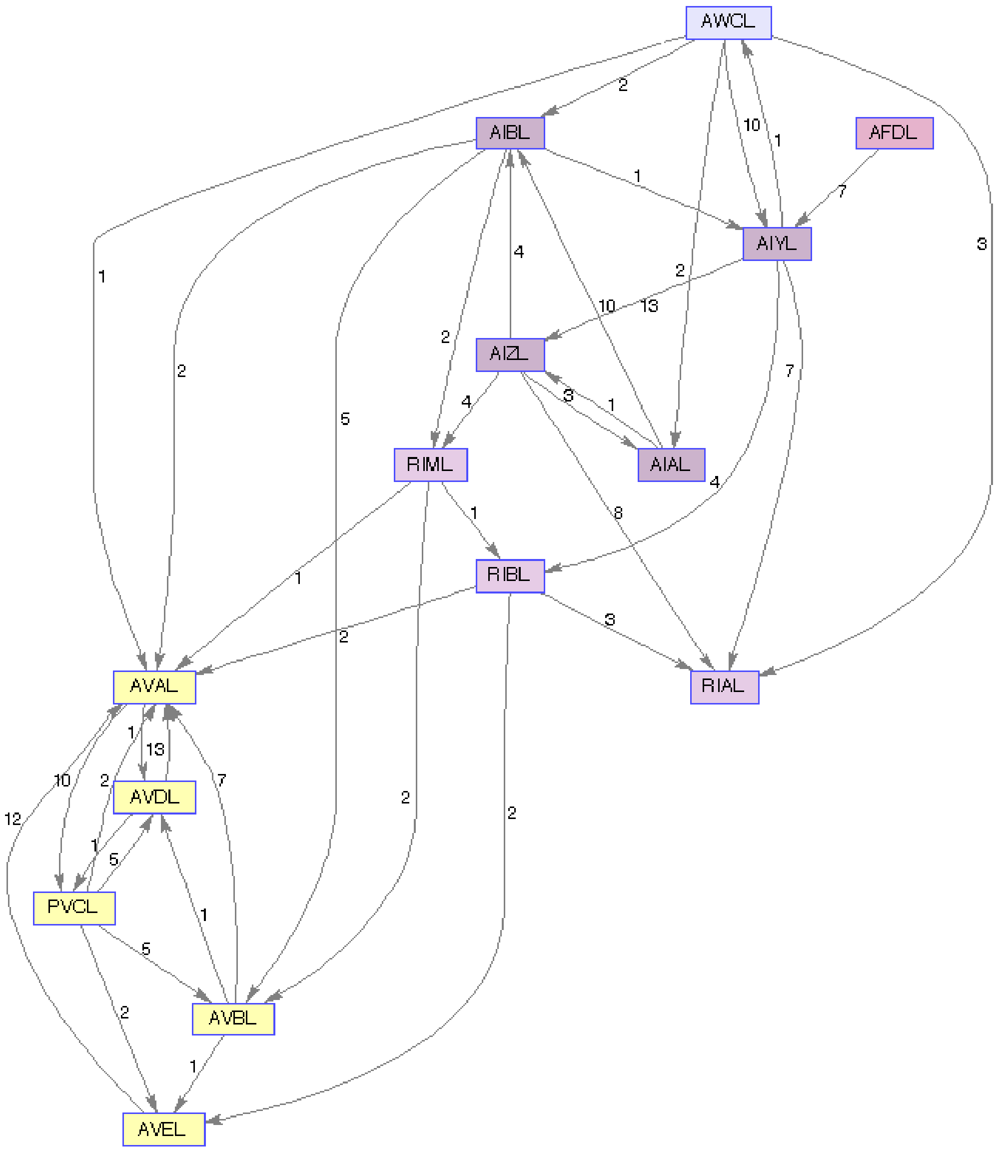

Figure 1: Neural pathways involved in the transmission of thermal signals down to locomotory command interneurons in C. Elegans. Starting from thermosensory neurons (AFDL, AWCL), flowing through the first- and second-level interneurons towards neurons responsible for

movement (yellow). Only L – neurons from the left part of the body are shown. Numbers denote number of synapses. Data from White et al., 1986, wormatlas.org .

Functions of C. Elegans thermosensory system

The thermosensory system of C. Elegans operates at several levels. Firstly, an animal remembers at what temperature it hatched and can adjust its thermotaxis (movement towards or away from a source of heat or cold) accordingly. Secondly, the nematode exhibits three major forms of thermotaxis – moving from lower temperatures towards the preferred temperature, moving from higher temperatures towards the preferred temperature and isothermal tracking – remaining in the preferred temperature range. Thirdly, the preferred temperature is adaptable – if animals are starved at a certain temperature, they will adjust their preferred temperature to a different level. Fourthly, there seems to be different mechanism/circuit for extreme and for normal temperatures (Garrity et al., 2010).

Thermosensory pathway of C. Elegans

Now let us look more closely at some of the neural mechanisms that result in the functions described above.

Firstly, we have to realise that thermal inputs to C. Elegans sensory neurons are not linear. C. Elegans is mostly in motion, turning its head to the sides. Thus, temperature sensed by the thermosensory neuron is oscillating. $Ca2+$ dynamics in the AFD neuron seems to be phase-locked with oscillations in the temperature of the environment (Clark et al., 2006). When a sudden increase or decrease in temperature happens, it is also followed by changing AFD $Ca2+$ levels which then slowly recover to previous values.

It means the worm can detect subtle as well as more pronounced changes in temperature and relay them further down the nervous system. However, it is yet not clear how interneurons deal with this information.

Kuhara et al. (2011) suggest that generally there are three modes in which C. Elegans operates. Cryophilic behaviour is thought to be independent of the AFD – AIY circuit. Thermophilic behaviour seems to be mediated by weak sensory signal from AFD, inducing strong response in AIY. Normal thermotaxis is believed to be mediated by a strong thermosensory signal from AFD resulting in a weak response in AIY. This inverse signalling is due to the existence of both excitatory and inhibitory pathways from AFD to AIY; where excitatory pathway is believed to be stronger than the inhibitory.

It is still not clear what synapses in C. Elegans are excitatory and which are inhibitory. Different kinds of neurotransmitters have differing effects on many types of neuroreceptors in C. Elegans. Besides, it seems that the neurotransmitter system in C. Elegans is more complicated than previously thought. For example, besides conventional excitatoy ACh cation channels, also inhibitory ACh anion channels are expressed in C. Elegans (Pereira et al., 2015, Putrenko et al., 2005). As for GABA neurotransmitters, spillover transmission phenomenon may bring about effects previously not accounted for (Gendrel et al., 2016, Jobson et al., 2015).

Narayan et al. (2011) studied the synapse between AFD and AIY and believe that it mostly transmits the signal from AFD to AIY without much computation. AIY then integrates inputs from various sensory neurons – mainly thermosensory AFG, gustatosensory ASE and odorsensory AWA (Tsalik, Hobert, 2003). It is still unclear how does AIY integrate these inputs. If all the inputs act in unison, that is, if all of them drive the animal towards the same motor action, it will be enough for AIY just to sum the inputs. However, if the inputs from various sensory modalities bring conflicting information to the worm, it is not clear how it decides.

AIY does not have direct connection to locomotory command neurons. It seems to work primarily via second-level interneuron RIB (Tsalik, Hobert, 2003). (Tsalik and Hobert also suggest similarly structured parallel pathway via AIZ and RIM). RIB then connects to AVA and AVE, locomotory command neurons. Locomotory system of C. Elegans seems to work via a bistable switch, alternating between forward and backward movements (Tsalik, Hobert, 2003, Karbowski, 2008).

Discussion

Although C. Elegans is a relatively simple organism, its nervous system is still too complex for us to fully elucidate. By analysing one of the simplest C. Elegans subsystems - the thermosensory subsystem, we can still see several hurdles to be overcome before understanding this pathway in full detail. Researchers have been quite successful in identifying the neurons that contribute to the pathway (although there are still speculations that additional neurons may be temporarily recruited into the pathway).

Although we know quite a lot about the thermosensory neurons (especially ADFL and ADFR) we are only beginning to learn about the function and the molecular underpinnings of interneurons in C. Elegans. At the same time, interneurons appear to be the part of the system where most of the neurocomputation happens.

There are approximately 6000 synapses in the neural system of C. Elegans. The connectome of the worm has been mapped, however we still do not know many features of individual neurons and their synapses. For example, it is still not clear what synapses are excitatory and which are inhibitory. To model the flow of signals in the neural network of C. Elegans, this information is vital. Besides modelling studies that could infer the nature of synapses from the function microcircuits should exhibit, new experimental studies are necessary to establish the excitatory/inhibitory nature of interactions between respective neurotransmitters and their receptors.

To conclude, C. Elegans neural network seems to be an ideal model system for understanding how neural systems work. It is at the same time complex enough to account for rich behaviours of the worm and simple enough for us to be able, after much time and effort, to understand in full detail.

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