Cognition and its Computation
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Lecture - 58
Topics in Current Research - III

Welcome, continuing on with our lectures on open questions very important aspect of neuroscience and cognition has to do with how different regions are connected with each other and particularly if we go more into the micro circuit level how different neurons or different types of neurons are connected with each other and their functional properties. So, this is an extremely difficult problem to be able to determine the entire connectivity atlas so to speak.

On a broad scale Allen Brain Institute has taken up the problem in the mouse and in and they have actually presented a great deal of systematic and organized connectivity atlas of the mouse brain, but it is still at the level of broad and gross region wise connectivity. Definitely that is the point to start.

But in order to be able to fully comprehend perception and how cognition comes into play it probably becomes very important to be able to understand the entire connectome or be able to determine the entire connectome that is how the different neurons are connected with each other. And also be able to measure activity of the neurons during a particular behaviour or during a perceptual task.

So, from the statement it; obviously, shows that it is extremely difficult, especially if you are thinking of the human brain with some 80 billion neurons or 100 billion neurons and trillions of synapses we it will be probably never possible to be able to get the connectome.

So, the idea is that has been taken up is basically to look into lower species, lower in the sense of evolution evolutionarily lower that is systems or organisms that have fairly simple nervous system with fewer number of neurons that are tractable fewer number of synapses that can be easily observed and we are able to measure activity from the entire nervous system simultaneously.

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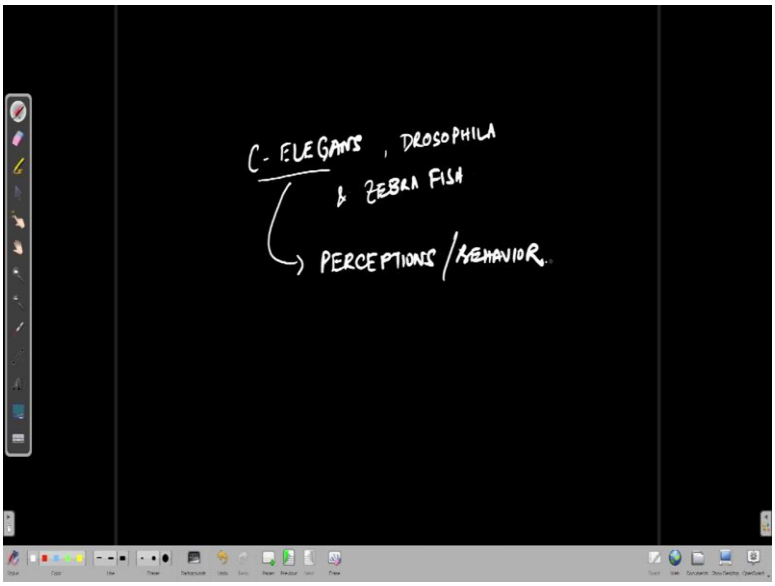

So, people have been working along those lines in the C elegans also in the Drosophila and zebra fish, where in particularly in the C. elegans it is a handful of neurons in the 100 around a slightly over 300 neurons in the male and hermaphrodite species of the C elegans.

And there are handful of synapses also in the 100s to 1000s and the entire connectome is more tractable and based on such species experiments on those we can gradually come up with principles of perception related to how connectivity and activity of the different types of neurons are involved in providing the perception.

So, there will be a slight disconnect in the sense of what we mean by perception or behaviour in these particular organisms versus you know what we mean or what the different kinds of behaviour are in humans, but it is it will be instructive if we can get the entire connectome in some of these species may be even the mouse and also be able to active measure activity of all the neurons simultaneously. We would from there we would be able to conclude and make connections or correlations with behaviour and the activity.

And given the current state of the art where we can actually manipulate activity with optogenetics or chemo genetics in neurons of particular types, at a particular position and so on. We can then gradually ask the causal the question the questions about causality

that is whether one particular neuron is involved in a behaviour or not or one particular type of neuron in a particular location or region is involved in a behaviour or not.

And from these we can draw parallels with human behaviour it may seem a stretch, but that is how most of the experimental studies have provided grounds for examination in the humans and there are lots of parallels in terms of cognition and learning and memory that we know from species like C elegans, Drosophila, zebra fish and mice, other rodents and also humans and what the parallels are.

So, if we think of the different types of neurons and the different specificity of connectivity we know that other than the environment the genome plays a huge role in terms of the structural the basic structural connections in the nervous system or in the brain. And most of the genome is conserved and there are analogous elements in the different species very and which are now well established and well understood..

So, along those lines it would be possible to connect the different elements to the human stage and while there are complicated behaviorus and cognitive aspects that are related to humans and not so much in the other species, but certain basic aspects of behaviour are still common.

For example, if we talk of maternity, if we talk of visual perception in terms of something moving in the visual space and we paying attention to the particular object in a visual field or detecting certain vibrations, the principles of transduction are conserved, the representation could I mean we do not know that yet many of them could definitely be conserved because the elements involved from the genome aspects from the genetics are very very similar and highly analogous..

So, by when we talk of the connectome definitely an open question is to how can we create the let us say the mouse connectome, find out how exactly the connections form between the different types of neurons in the different regions. And also we want to be able to measure the activity of all the neurons possibly simultaneously.

Measuring activity is of course, very difficult from deeper structure inside the brain at a single resolution given the current state of the art. So, an open question of course, added on to this is can we measure can we come up with methodologies to be able to measure activity at single neuron resolution from deeper structures in the brain.

I mean probably it would not be possible in the human in the long future in the may be in the 50 years coming you never know, but it is an open question whether we can do it in the human or not, maybe it would be possible in the mouse which has a much smaller brain and there we can also manipulate the activity. So, we can actually see the exact changes that occur because of the manipulations in terms of activity in the entire network and how that is correlated with the observed behaviour.

So, people have taken up the ideas from FMRI or functional magnetic resonance imaging or the principles in FMRI and also in terms of if near infrared imaging and we are getting closer in terms of being able to measure activity of single neurons may be deeper inside the brain, but currently in terms of temporal resolution and spatial resolution we are still ways off.

Of course, with FMRI by reducing the region of interest to a very small region we can probably get very high resolution images, but still the temporal resolution is poor. Similarly, with MEG or magneto encephalography we can get very high temporal resolution; however, the spatial resolution still is a mess.

So, methodology is required to be developed where we can actually approach the problem of measuring activity at single neuron resolution from the entire brain. And of course, methodologies like clarity where you can actually remove or make the tissue transparent.

So, recently there have been methods where people have been able to remove the fatty tissue from the entire brain and so, the entire brain becomes very transparent and now if you have fluorescent proteins marking different types of neurons and synopses from those images we can actually get the connectome that is how the different types of neurons are connected with each other in the different regions even at a micro scale..

So, such developments in techniques are have to go in hand with these kind of open questions about the connectome and single neuron measures of activity and how that can be related to perception and behaviour and establishing causation of that causal roles of activity with behaviour.

So, with this open question I will conclude this particular lecture on the connectome and the ability to measure single neuron activity simultaneously from the entire brain as one of the key open areas in Cognition and Computation.

Thank you.