Cognition and its Computation
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Lecture - 59
Topics in Current Research - IV

Welcome. So, we are continuing with our last week's lectures on open questions of cognition and computation. So, so far we have discussed more from a theoretical point of view, the first two points.

And, then in the third open questions lecture, we talked more about the connectome and how the neurons are organized between each other, how they are connected with each other and how they ultimately function together if and probably how we can gain access to all that information from the brain with newer technologies from of recording from the brain and knowing about the connectivity pattern in the brain and so on.

So, those were more on the side of mathematical theory and technological advancements like deciphering the connectome requires technological advances. But, there are many other questions which are more grounded in biology. Well, I mean to ultimately in future to completely understand those questions, we will probably be requiring newer and newer technologies and that is going to help us understand these better. So, one of the things that we have not at all discussed in this course is the role of glial cells.

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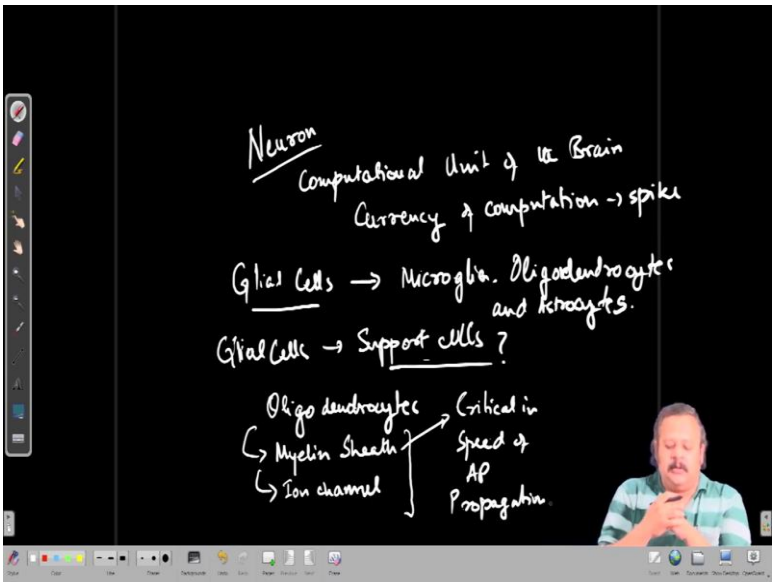

So, in the brain so, as in initially we had told you that the course is mainly based on computation by neurons and this is we say the computational unit of the brain. And, we also said that the currency of computation is the spike. This is the event, the all or none event that is communicated across from one neuron to another across synapses. And, the belief is that this activity of spiking patterns in in over population of neurons is ultimately what leads to perception or which is involved in cognition.

However, a much larger number or group of cells in the brain are glial cells and these are mainly of three types. They are the microglia, the oligodendrocytes and astrocytes. So, depending on species, the relative proportions of each within the glial cells and the relative proportions of glial cells and neurons vary across species. In the rodent actually the glial cells are less than the number of neurons, but in other many species the glial cells hugely outnumbered the number of neurons.

So, but very little has I mean over the past 50 years or so, the amount of in information that has been generated about how neurons functions, how neurons compute, how sensory stimulus is encoded in a neuron; these kind of questions have been pursued almost exclusively with very little attention to the possible role of glial cells in computation. So, now, gradually with more and more evidence the scientists are starting to believe that actually even the glial cells have a role in learning and cognition and memory, I mean aspects all aspects of cognition.

So, although the efforts effort towards understanding the role has been limited. Whatever little effort has been given has produced a wealth of knowledge, because this is totally unscratched area or rather scantily scratched area and a lot remains to be discovered. We really understand very little about the role of glial cells in overall computation.

So, we will discuss a little bit of what we know and which provides compelling evidence that forces, the current community in neurosciences and cognitive sciences to rethink many of the things that have to do with computation or many of the models that have been developed for a plasticity, many of the models that have been developed of networks and they require some additional aspects, the role that the glial cells play.

So, before some point of time, I mean even maybe few tens of years ago it was believed that the glial cells are support cells and are essentially there to provide nutrition for the neurons, for the neurons to do the work and they only provided the nutrients. Well, that is I mean definitely they provide nutrients in many ways and are involved in lots of metabolism of neurotransmitters and synthesis of neurotransmitters and so on.

However, glial cells the role is definitely not only that. We know now that particularly if we think of oligodendrocytes; so, oligodendrocytes are the cell types that actually produce the myelin sheath around the axon. And, these also pack the ion channels required at the node of run v a to have the action potential be generated again and again as the action potential travels to the synaptic terminal. And, this action potential itself is the biggest difference between the glial cells and the neurons.

So, the glial cells themselves do not produce action potentials or they do not communicate with the electrical impulses or spikes or action potentials, that we call and that we have devoted most of our efforts into understanding that is action potentials of neuron and how that plays a role in computation. But, if you think of the myelin sheath and the ion channels on the node of run v a, that allow the action potential to propagate and the myelin sheath is critical in determining the speed of the action potential propagation.

So, as we know that as we have talked about, there is a lot of evidence of synchronization across many many neurons, across different structures, may be even far away. And, in that case the timing of the action potentials become crucial and for the

timing to be maintained at a particular manner, the speed or of the action potential across the axon from one neuron to the other has to be maintained at the proper level.

I mean because a synchronized event across multiple neurons; let us say if we want to integrate information by synchronization or coincidence detection which is a common phenomena across different modalities of inputs coming in onto a particular neuron. So, that they are all associated together, that requires precise time matching across them and that requires precise timing of the action potentials and hence the speeds along the axon of the neurons.

So, as you can see the myelin sheath, the oligodendrocytes may make the myelin sheath thicker or thinner and that essentially will determine how fast the action potential will flow. So, they are thus in this way the glial cells can bring about a huge change in a circuitry, in terms of the timing of the spikes. It may lead to total lack of plasticity or it may produce plasticity in a way that by synchronizing events across different regions of the brain.

So, how these are controlled? We have we do not have a very good idea about. So, what kind of signals are there that the oligodendrocyte gets in order to play the role of controlling the amount of myelin to be packed around the particular axon is an open question. Similarly, there are many other open questions as to do with the microglia.

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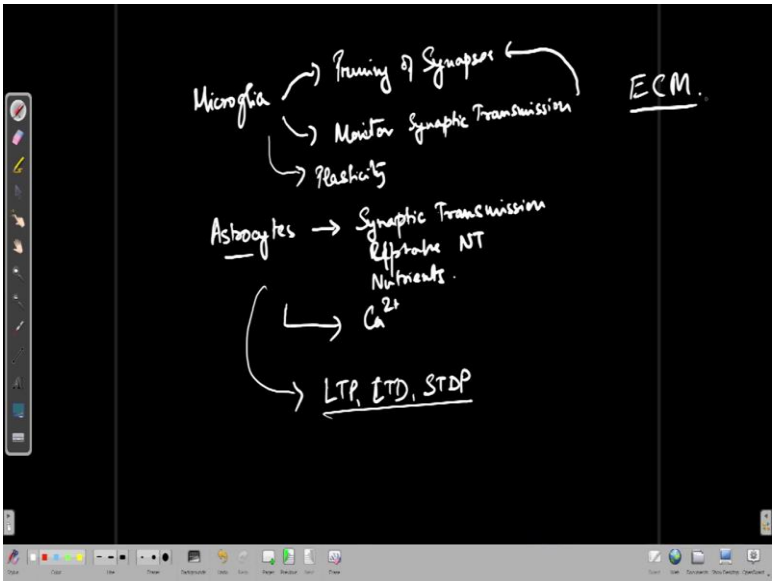

So, as we know the microglia, now the evidence suggests that they are involved in pruning of synapses. So, actually what some evidence suggests is that they monitor the synaptic transmission, like how much neurotransmitter is traveling across by a particular signal. And, with that they ultimately prune synapses and are critical essentially in plasticity so, microglia.

So, basically this is direct role in plasticity that actually we do not even think about and how they can influence the plasticity. We not we do not hopefully understand and how it will influence the plasticity at different kinds of synapses is yet another question. So, along with that astrocytes which are also equally critical; so, they are definitely involved in synaptic transmission itself.

They are involved in re uptake or uptake of neurotransmitters from the synaptic cleft, they also actually provide nutrients to the neurons and they actually respond to stimuli with a calcium signal. So, with the imaging studies to photon imaging studies, there have been some studies with in the visual system which shows that actually just like neurons around it, the astrocytes calcium levels increase and in a tuned manner.

They have essentially a tuning in the calcium response to the orientation columns or orientation oriented bar stimulus which is surprising, which was very very surprising when it was first found out. And, since then the there has been a lot of research and actually that begs many many questions as to how astrocytes play a role in the computation and coding encoding of stimuli even if possible. And, they are also directly involved in LTP, LTD and synaptic spike timing dependent plasticity.

So, in all these forms the astrocytes play a big role. So, while the microglia communicate between each other with neurotransmitters and also with neurons with neurotransmitters and with other molecules, they are not at all they are not the kind that produce spikes and communicate through electrical impulses. So, what those communication signals are very scantily understood, that they must have some way of organizing things.

So, basically if we think of a spatial integration of synapses and neurons together, the microglia or rather the entire glial cells have a huge role to play in terms of combining spatially everything together and putting together connections and actually pruning them or even removing the synapses. So, a lot of evidence suggests that. So, in terms of the a

theoretical understanding of or rather even just the biological understanding is scanty of how these processes work.

And obviously, the one last important finding that I will talk about will I think convince you why these are extremely important. So, the extracellular matrix has an important role to play which is called the ECM: Extra Cellular Matrix, that is the outside region in the brain and it is mainly controlled by the glial cells. And so, in humans the astrocytes are much much more complicated with very large very intricate processes involved in the I mean in the interaction with the surrounding neurons.

And so, if we compare that with the rodent, the complexity of the processes of the astrocytes are much less. So, in an experiment where some or a part of the mouse astrocytes were replaced by human astrocytes in a chimeric model, they basically showed that these mice had faster learning more plasticity. So, now that; obviously, begs the question how these things happen? And, these are really open for research and probably very very important questions to be answered in the near future or in the longer term future depending on how many people approach it and or get lucky early on ok.

Thank you.