Computational Neuroscience
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Week – 09
Lecture – 44

Lecture 44: Short Term Plasticity - I

Welcome. So, we are in our lectures on synaptic plasticity. And we have discussed the different types of plasticity mainly structural plasticity and synaptic plasticity and the different types within synaptic plasticity, short term and long term plasticity. So, now we get into the side of modeling and using it in models for the effects of short term plasticity or those that are temporary. So, first of all in order to see short term plasticity we had said that if we measure the post synaptic potential let us say after we pre synaptically produce a spike. So, this is I am drawing average diagram here we do this multiple times with gap in our gap and measure the post synaptic potential.

And we had said that there is some manipulation that is being done and then we are measuring again. Actually in the short term plasticity case the manipulation is simply producing another spike. And what we can see is that the synaptic strength may reduce here and then with another spike the synaptic strength may reduce even further and with another spike the synaptic strength may reduce even further and be there. But after a delay of undisturbed period we do the measurement again with a pre synaptic spike we measure the post synaptic potential and we get back our original strength.

So, this is the same as this. So, we have recovered our original strength and in between we have what we call short term depression. That is the synaptic strength is reducing with every subsequent spike. So, it is not necessary that it will happen all the time, but in general many synapses can show short term depression where subsequent spikes produce short smaller size EPSP and there is a weakening of the synaptic strength. And obviously this is also dependent on the gap between the pre the spikes in the pre synaptic site.

So, if we have many closer spikes then we can get even stronger effects of depression or if we make the spikes a pre synaptic spikes much further then we may even end up not seeing any change. So, it is dependent on how much pre synaptic activity we are seeing. So, if this is the pre synaptic activity then that essentially is going to determine the properties of the short term depression that we are observing. And similarly instead of short term depression we can also

see short term facilitation or potentiation where we do have an action potential in the pre synaptic site and we measure the EPSP size. Let us say this is height of A and the manipulation is producing another spike pre synaptically let us say in within 50 milliseconds and we see that the synaptic strength increases and then with another spike we see that the synaptic strength increases further and another spike we see increasing further.

And later on if we allow the system to remain undisturbed and measure the synaptic strength again we get back our original synaptic strength where this particular EPSP is going to be the same as the last EPSP we are seeing and hence regaining the original synaptic strength that is by measuring the post synaptic potential. So how do these actually I mean why do this happen why is some synapse facilitatory and some synapse depressive in the short term. So in order to understand that we usually explain it based on the evidence so far and the idea that there is a limited amount of resource present in the pre synaptic site and that is the limited amount of neurotransmitters present in the pre synaptic site and that may be depleted and with successive action potentials pre synaptic. So this is how it may be thought of that this is the pre synaptic terminal as you may recall that there is a synaptic vesicle that is carrying the neurotransmitter here and it is primed to be or rather it is docked to be released in the synaptic cleft that is the neurotransmitters will be released. So when there is an action potential pre synaptically we know that these neurotransmitters are released into the synaptic cleft many of them go and bind to the receptors on the post synaptic site and cause neurotransmission and after that many are left to be taken back up endocytosed into the endosomes and then back into synaptic vesicle.

So actually the we can think of this as a cyclic process we can say that the to make it simple model first we say that this pool of vesicles is the recovered pool. The pool of rather the pool of neurotransmitters in the vesicles inside the recovered pool the ones that are effectively producing the post synaptic potential that is they are being bound to neurotransmitters is called the effective pool. And the ones that are left in the synaptic cleft unused to be taken back up is called the ineffective pool or inactive pool in certain matter. And so it is a three state process that is happening so we have neurotransmitter in this which is made to be effective by going here which goes to ineffective and that is cycle back into the recovered pool. Now the steps that are involved this is they are unidirectional we do not consider that the backwards flow can happen in this process.

And the time constants of each of the steps play a crucial role in determining the entire the kinetics or even the short term plasticity. So if we think of this as a three state model that is we have the recovered pool we have the effective pool

and we have the inactive pool. So we have a time constant here let us say
$tau(RE)$ from E to I we have a time constant
$tau(EI)$ and from I to R we have a time constant of
$tau(IR)$ Now if we think of the way R is being or rather say R is changing that is dR/dt over time if this is the concentration of R. Let us say normalized concentration that is R+E+I is fixed to 1 that is the total concentration is 1 of the neurotransmitter and R,E and I are basically the fractions can be represented as normalized concentration. So this is r dr/dt so from i to r we have the process is driven by the concentration of i and it is the time constant
tau_{ir} and r is reducing due to the flow from r to e which is driven by the concentration of r and the time constant
tau_{re}.

There is one missing aspect in this differential equation that we have written for dr/dt it is that all the things are not happening continuously. So r to e is only happening when there is an action potential. So when there is an action potential only then the vesicles in the inside of the presynaptic side is going to release the neurotransmitter. So this rate of reduction in r must be happening only at the time point of spikes which may be indicated by u where this u is generally 0 and will be considered to be 1 for a brief 1 millisecond period or some short delta time period and then it will go back to 0. That will essentially represent that the depolarization has happened and the calcium comes in and the recovered pool sends neurotransmitters into the effective pool.

So that is what we are representing by this u which can be taken as 1 for the spikes for that small duration. So now if I have the de/dt that is basically being increased due to the flow from the spiking that is u times r by
tau_{re} and is being reduced due to the flow from e to i and that is basically the concentration of [E] divided by
$tau(RE)$. So all are first order kinetics and using this equation we or we can also write from the diagram itself that is dI/dt is simply increasing due to E by
$tau(EI)$ and it is reducing due to the i itself going to R that is
$tau(RI)$. So now with this model if the
$tau(RE)$ is of the order of 1 millisecond this practically is of the order of 100 milliseconds and this of the order of 1000 or greater than 1000 milliseconds that is more than a second in multiple seconds that is the time constant. So this becomes the rate limiting step in the whole process that is if we have an action potential that is this u becomes 1 then r is reduced and that triggers the flow in the forward direction from r to e to i to r.

So initially all the neurotransmitter is in r where R is equal to 1 and after that

with every spike we are that R is reducing and going into E and I. However the rate of change of I that is going from I to R is extremely small because this $tau(RI)$ is very large and that basically keeps the neurotransmitter in the ineffective to the r pathway in the middle in that state. So it is in I and trying to move on to R so very little is actually being going to the recovered pool. So the reduction in the neurotransmitter is a reason for the synaptic depression to happen when we have many spikes simultaneously in a closed time period. So every for every spike we get some reduction in the in the post synaptic potential and we can actually show with this model by simulating it that there is synaptic depression.

So this synaptic depression model works very well and has been used in multiple models this with this three state model. So in fact with this idea we will be discussing one of the consequences of short term depression later on. So now there may be I mean this is only a simple model now there are many other parts of this short term depression and that has to do with the calcium that is coming in. If you recall for this u becoming 1 we actually it is based on the calcium coming in due to the spiking. So this entire model can be further modified by qualifying that u and bringing in the calcium concentration explicitly instead of making a 0 1 kind of transfer from recovery pool to the effective pool.

So in order to do that I mean the reason why we will do that is actually this above this model that we have talked about does not explain short term facilitation. Because this only can explain short term depression based on the time constants that we have discussed. And so what can we do I mean basically there is always a probability associated with the release that is the synaptic transmission is also probabilistic. And so overall neurotransmitter available may be NT but it is now being multiplied by a probability in order to be able to bring in the effect of the calcium. Because the calcium is effectively what decides the probability of release.

So actually when we have lot of activity like this in small synapses there is a build up of calcium that is the residual calcium hypothesis where due to every action potential the calcium is building up only some of the calcium is used up in releasing the vesicles releasing the neurotransmitter in vesicles. Whereas in the next action potential due to the remaining calcium and more calcium added up the calcium concentration increases and hence the probability of releasing increases. And there is an increased number of neurotransmitters released and effectively we have a larger postsynaptic potential. So if we want to go ahead and include actually show facilitation we have to go and explicitly modify that you and bring in this probability term. And there will be further other things that need to be included.

There is one more aspect here where we can have this R may be broken up into two pools and that is that has its own consequences as well where R is one is the recovered pool and then we can have another state that is a readily releasable pool that is the ones that are only readily releasable that goes into the effective state. So we can we may be there is no direct path for say as we have had in the model that we have described. But there can be a an additional stop which is the readily releasable pool. And that we will discuss along with the inclusion of the probability term and calcium concentration in our next lecture on short term depression short term plasticity.