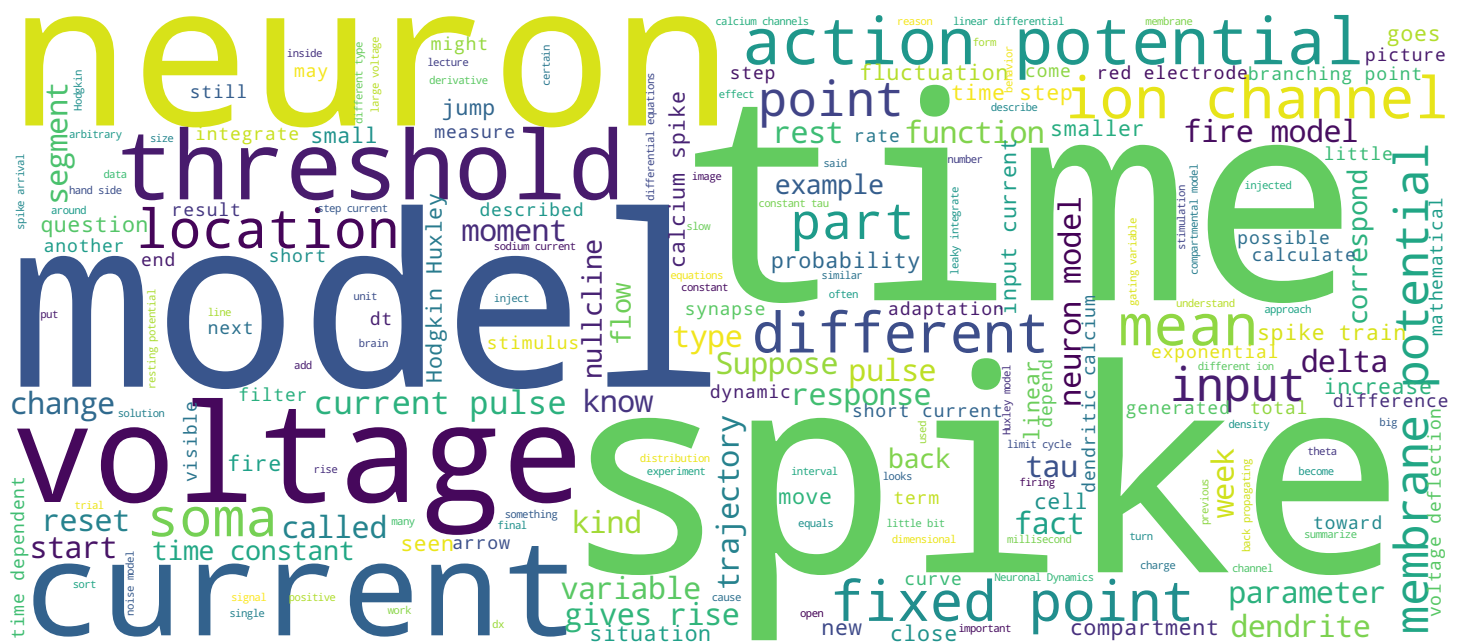


ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE



EPFL

Week 3 – part 5: Compartmental Models



✓ 3.1 Synapses

✓ 3.2 Short-term plasticity

✓ 3.3 Dendrite as a Cable

✓ 3.4 Cable equation

3.5 Compartmental Models

- active dendrites

Welcome to the final part of the third week of the class Neuronal Dynamics.

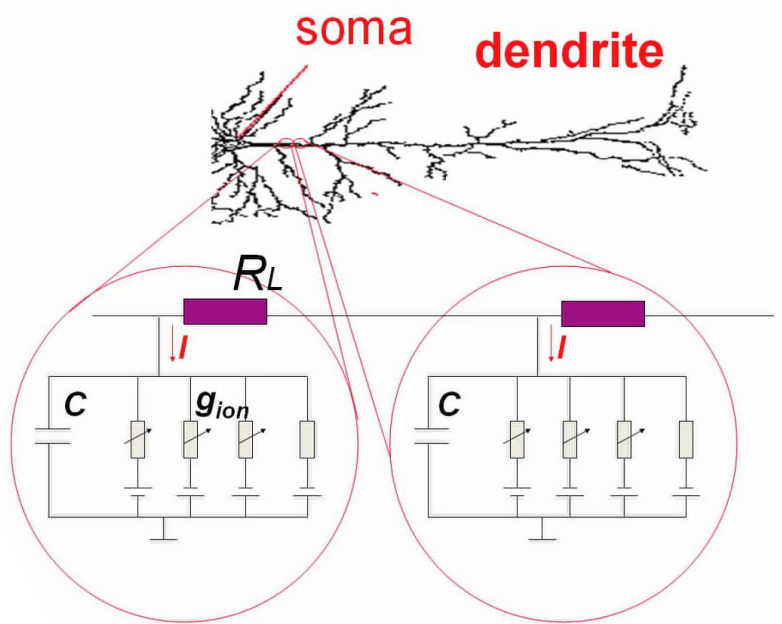
Notes

Summary



0m 04s

Neuronal Dynamics – 3.5. Compartmental models



In the previous two parts, we started off with a segmented dendrite, and then we took the continuum limit. We said the segment size gets smaller and smaller, and finally we arrived at a partial differential equation, which could include all sorts of ion channels. However, for practical analytical solution, most often we have to go back to positive dendrites and that's what we did in Part 4. Now, if you have ion channels with interesting dynamics spread out all over the dendrite, and it turns out it's much better just to simulate directly the discrete model. And this is called a compartmental model of a neuron, or a compartmental neuron model.

Notes

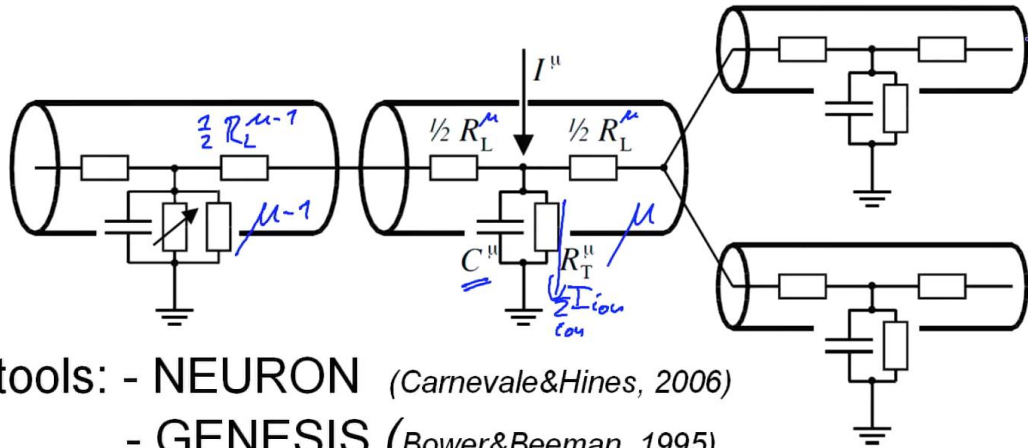
Summary



0m 09s

Neuronal Dynamics – 3.5. Compartmental models

$$\frac{u(t, \mu-1) - u(t, \mu)}{0.5(R_L^\mu + R_L^{\mu-1})} - \frac{u(t, \mu) - u(t, \mu+1)}{0.5(R_L^\mu + R_L^{\mu+1})} = C^\mu \frac{d}{dt} u(t, \mu) + \sum_{ion} I_{ion}(t, \mu) - I^\mu(t)$$



Software tools: - NEURON (Carnevale&Hines, 2006)
- GENESIS (Bower&Beeman, 1995)

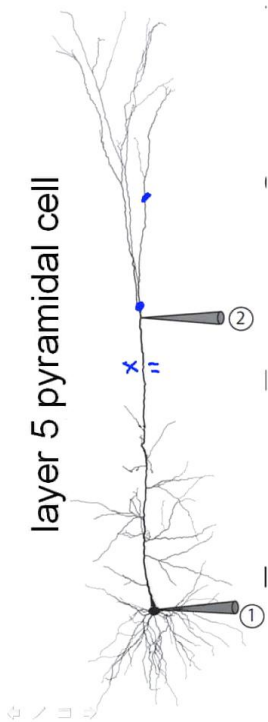
So here's the picture. This is one segment. It has a certain size. And this is my segment with index mu. So this would be the longitudinal assistance in segment mu. And I put half of it left to the branching point and the other half right off the branching point. Now, different compartments will talk to each other. And if I look at this compartment here, which would have the index mu minus 1, then I can rewrite the equation of part 3. And the total longitudinal resistance has now two compartments. One is the resistance associated with compartment mu and the other one is the resistance associated with compartment mu minus 1. The reason to keep this separate is that it could be that the resistance here is slightly different. Be it because the segment size is different. Be it because properties of the membrane change from one segment to the other. Then I have for each compartment the capacitance and I have my different ion currents that correspond to a global resistance voltage dependent gating variable-dependent resistance. So this is the sum of all the ion channel types. Now with this model, we can take the spatial structure of a neuronal dendrite seriously and also include branching points. So this dendrite may split up in two branches, which are described by separate sequences of segments that are coupled to the main part of the dendrite and so forth.

Notes

Summary

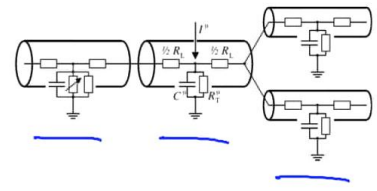


Neuronal Dynamics – 3.5. Model of Hay et al. (2011)



Morphological reconstruction

- Branching points
- 200 compartments ($\leq 20\mu m$)
- spatial distribution of ion currents



Sodium current (2 types)

- $I_{Na,transient}$ HH-type (inactivating)
- I_{NaP} persistent (non-inactivating)

Calcium current (2 types and calcium pump)

Potassium currents (3 types, includes I_M)

Unspecific current

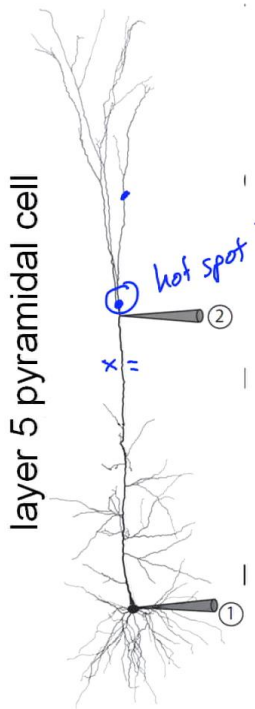
With this kind of approach, it's possible to give a rather detailed image of the anatomical structure of the dendrite. This is an image of a layer 5 pyramidal cell. And you see many, many branching points. Here, the main dendrite splits up in two or three sub-branches. Here, there are lateral branches. Now, it's possible to do a morphological reconstruction anatomy of the dendritic tree and translate this into a compartmental neuron model of the type that I have just described, including branching points. For a dendrite of this size, it's not unusual to use, say, 200 compartments. Each compartment would correspond to a little segment which is worth less than 20 meters. Now, not all segments must have the same type of ion channels. They can be active ion channels. They can be just positive ion channels. And the type of ion channels that are here at this location might be different from the location here or from the location there. There's a model of Hay et al of such a layer 5 pyramidal cell, which includes different type of sodium currents. One is of the Hodgkin-Huxley type. It's an inactivating current. But then there's also the persistent sodium current, which is non-inactivating.

Notes

Summary

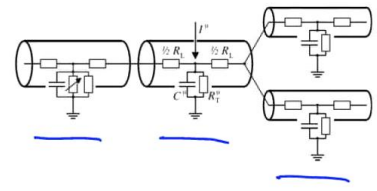


Neuronal Dynamics – 3.5. Model of Hay et al. (2011)



Morphological reconstruction

- Branching points
- 200 compartments ($\leq 20\mu m$)
- spatial distribution of ion currents



'hotspot'

Ca currents

Sodium current (2 types)

- $I_{Na,transient}$ HH-type (inactivating)
- I_{NaP} persistent (non-inactivating)

✗ Calcium current (2 types and calcium pump)

Potassium currents (3 types, includes I_M)

Unspecific current

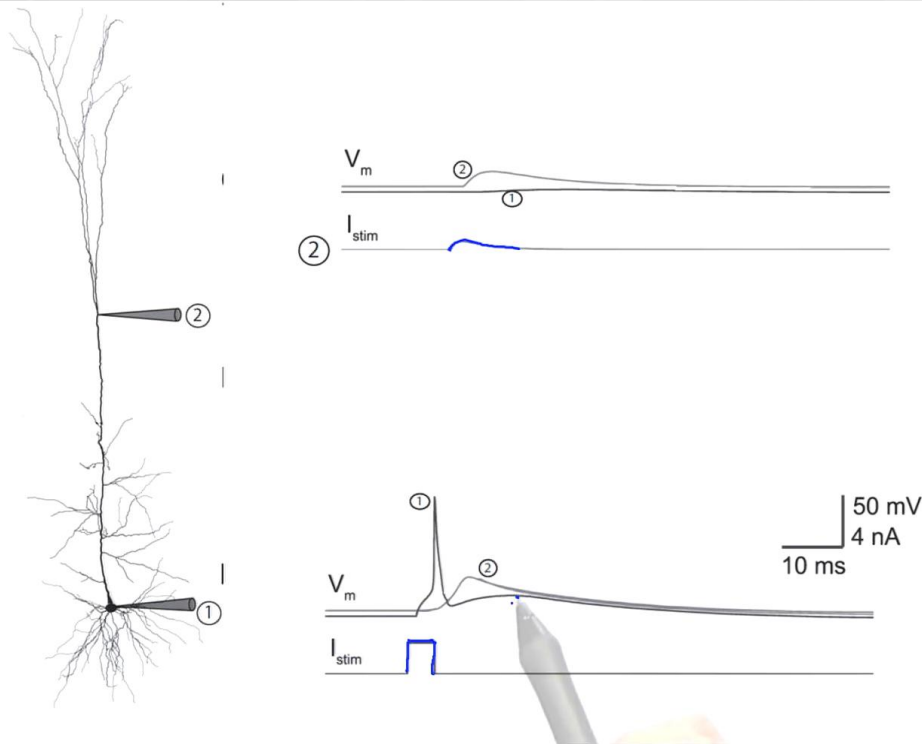
There are additional calcium channels, two different types of calcium channels, and a calcium pump. There are potassium currents, some of these depend on calcium, others don't. And there might be also some unspecific current. Now, the spatial distribution of these different ion channel types is not uniform across the dendrite, but some of the ion channels-- in particular, the calcium channels, have a higher density at some singular spots that are called the hot spots of the model.

Notes

Summary



Neuronal Dynamics – 3.5. Active dendrites: Model



Hay et al. 2011,
PLOS Comput. Biol.

Now, this model can be stimulated at various locations, and you can also record at various locations. Suppose that in the model, a current is injected at location 2. This current has some time course, and this time course was chosen so as to reflect the typical input current that would arise due to synaptic stimulation. Now, if you measure at the same location the voltage, this is what you would see, a transient increase and slow decrease of the voltage, which reflects the stimulating current. If at the same time you measure the voltage at the soma at location 1, you hardly see any deflection at all. The picture is different if the stimulation is given at the soma. Here, the simulation consists of a short current pulse strong enough to excite an action potential. This action potential is visible as a voltage peak at the soma, but it's also visible at this other location, at location 2. And there it gives a voltage deflection. Now, because of this voltage deflection at location 2, there is a slight bump later on again at location 1. The fact that you see the action potential that's sent out here-- that would be the action potential going out an axon, measured at the soma.

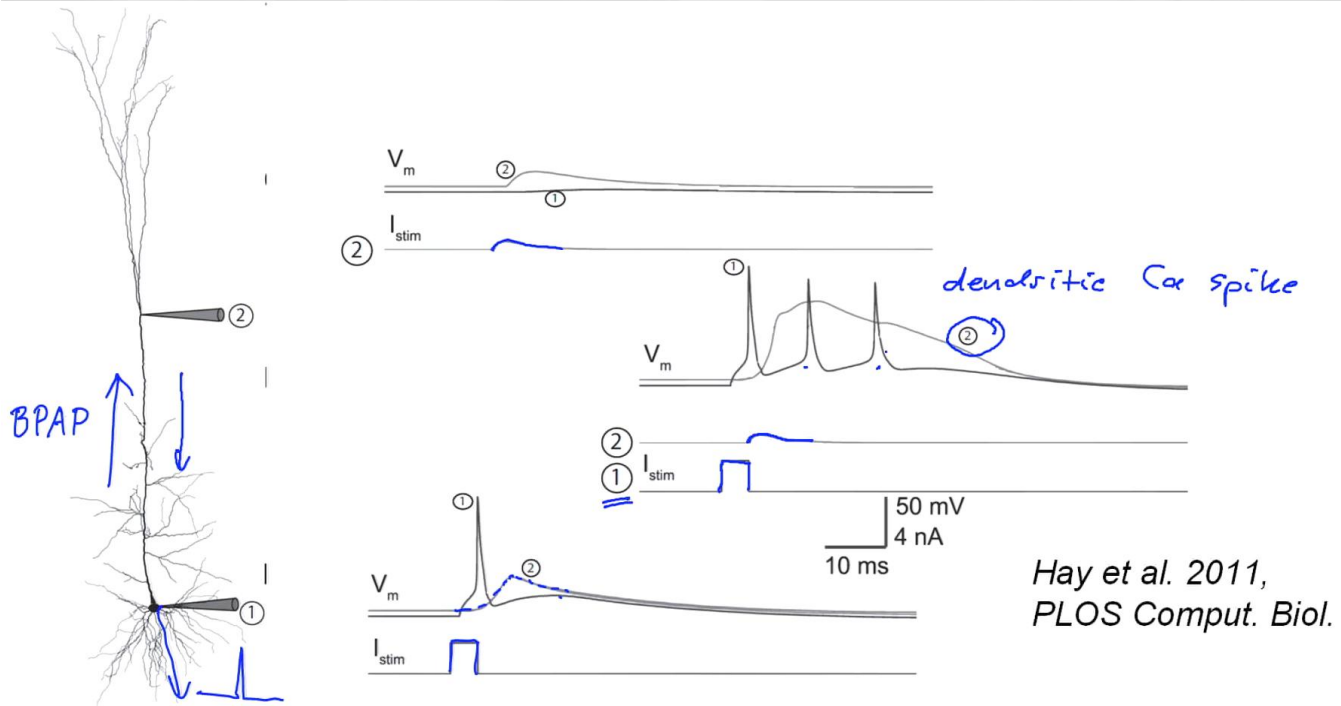
Notes

Summary



5m 50s

Neuronal Dynamics – 3.5. Active dendrites: Model



This action potential, basically, travels backwards up the dendrite. And that's why it's visible here at location two. This is a back-propagating action potential, which is broader than the sharp, narrow action potential at the soma. Now, let's combine the simulation with a short current pulse at location 1 with a stimulation of a weak synaptic-type input at location 2. Now, because of this first spike at the soma, we have a back-propagating potential, which gives rise to this initial peak. But the initial peak combined with a synaptic stimulation gives enough calcium transient so that in the end you see a big voltage detour measured at the synapse-- at the electrode number 2. This large voltage detour corresponds to a dendritic calcium spike that is fairly broad in this situation here. Now, the dendritic calcium spike will influence the voltage at the soma so that there another two action potentials are generated.

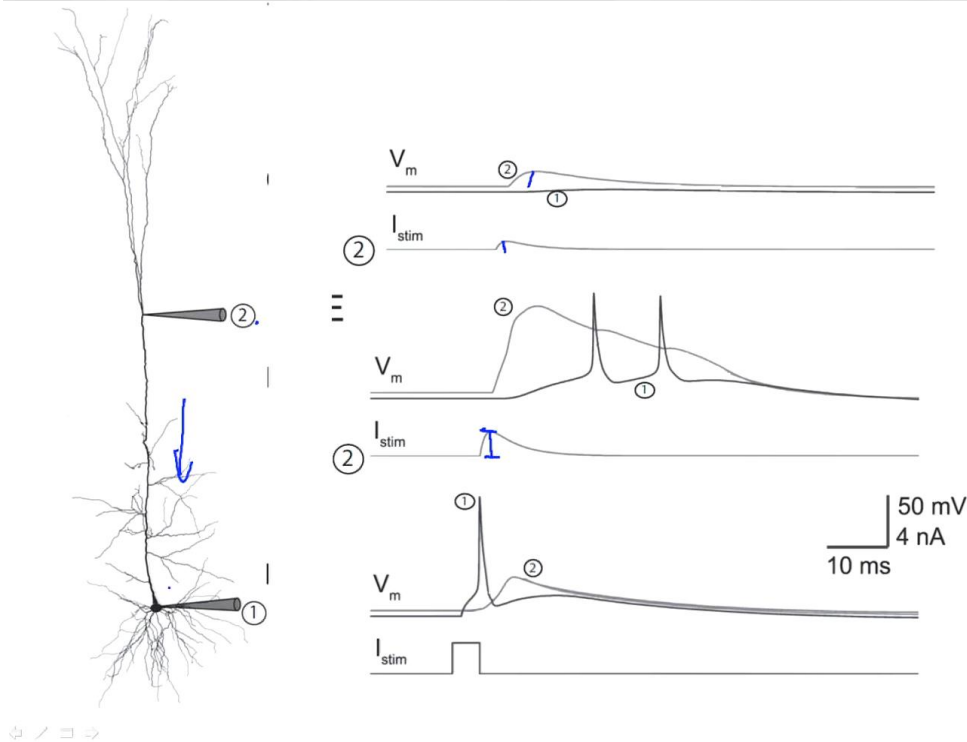
Notes

Summary



7m 39s

Neuronal Dynamics – 3.5. Active dendrites: Model



Hay et al. 2011,
PLOS Comput. Biol.

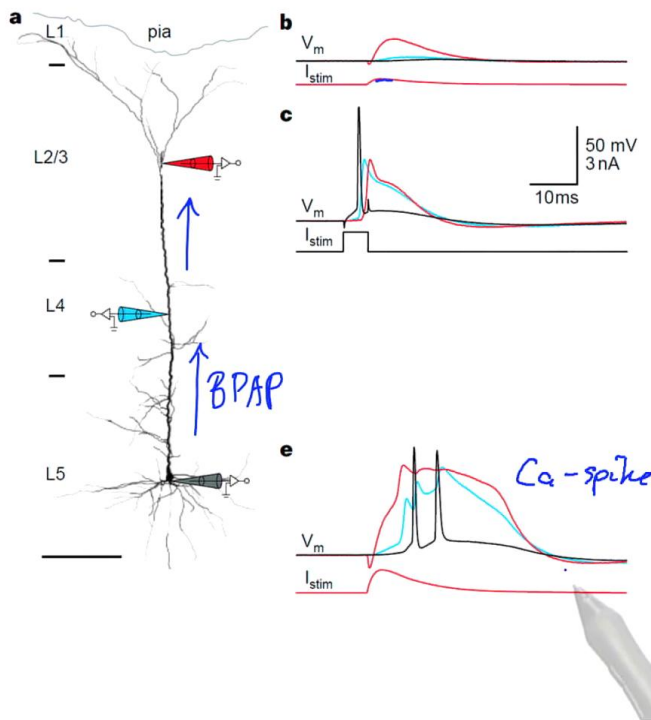
The dendritic calcium spike does not need stimulation at soma. You can also just give a stronger current pulse at this dendritic location. And this alone gives rise to this strong pulse. This alone gives rise to this strong voltage deflection. If you compare the little pulse causing a little voltage deflection, the stronger pulse is maybe two or three times bigger but the voltage deflection is at least five times larger than over here. So it's a more than linear reaction of the dendrite to the stronger stimulation. And this calcium detour, in the end, gives rise to additional action potentials measured down here at the soma.

Notes

Summary



Neuronal Dynamics – 3.5. Active dendrites: Experiments



BPAP:

backpropagating action potential

Dendritic Ca spike:

activation of Ca channels

Larkum, Zhu, Sakman
Nature 1999

Now, is this all an artifact of the model? No, quite the contrary. In fact, the model was designed, the parameters of the ion channel distribution was fitted so as to reproduce experimental results of the group of Mathew Larkum. Here is an experimental situation. Current is injected at this location, at the dendritic location through the red electrode. And you see the stimulating current, the voltage at this location. We also see a reduced voltage measured down here, and hardly anything at the black electrode. Now, the second experiment is you give a current pulse at the soma. The soma responds with this sharp action potential. The sharp action potential travels back and you see a response at the blue electrode and a little bit later at the red electrode. This is important because this tells you it's really traveling backwards up the dendrite. Now, if you give a stronger current pulse at the red electrode, then you see this large voltage reflection at the red electrode which is the dendritic calcium spike visible as a large transient of the voltage. Now, this calcium spike gives rise to a voltage increase at the soma, which eventually gives rise to a sequence of two action potentials measured with a black electrode at the soma.

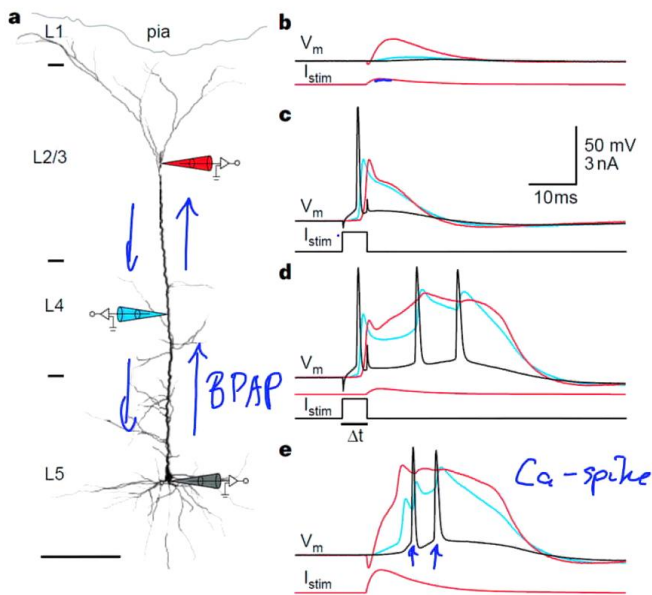
Notes

Summary

10m 36s



Neuronal Dynamics – 3.5. Active dendrites: Experiments



BPAP:

backpropagating action potential

Dendritic Ca spike:

activation of Ca channels

Ping-Pong:

BPAP and Ca spike

Larkum, Zhu, Sakman
Nature 1999



You can combine a weak stimulation in the red electrode with a current injection here, and the combination of action potentials traveling backwards contributing to the generation of culture spikes traveling forward towards the soma give rise to a ping-pong behavior, so that the single current pulse injected here gives rise to a whole burst of three action potentials and not just a single one.

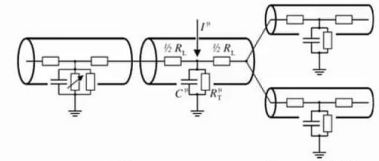
Notes

Summary



12m 35s

Neuronal Dynamics – 3.5. Compartmental models



Dendrites are more than passive filters.

- Hotspots
- BPAPs
- Ca spikes

Compartmental models

- can include many ion channels
- spatially distributed
- morphologically reconstructed

BUT

- spatial distribution of ion channels difficult to tune

In summary, dendrites are not just passive. They have active properties. They have calcium currents that can generate calcium spikes that are visible as large voltage transients. Active dendrites permit back-propagating action potentials so that if an action potential is generated at a soma, the information about the action potential is available all over the dendrite. Compartmental models can model all these different aspects of active dendrites. However, compartmental models are difficult to tune because you often don't know where along the dendrite, where to put the different ion channels at each density.

Notes

Summary



13m 11s

Neuronal Dynamics – Quiz 3.5 *Multiple answers possible!*

BPAP

- ☐ is an acronym for BackPropagatingActionPotential
- ☐ exists in a passive dendrite
- ☐ travels from the dendritic hotspot to the soma
- ☐ travels from the soma along the dendrite
- ☐ has the same duration as the somatic action potential

Dendritic Calcium spikes

- ☐ can be induced by weak dendritic stimulation
- ☐ can be induced by strong dendritic stimulation
- ☐ can be induced by weak dendritic stimulation combined with a BPAP
- ☐ can only be induced by strong dendritic stimulation combined with a BPAP
- ☐ travels from the dendritic hotspot to the soma
- ☐ travels from the soma along the dendrite

With this, I would like to close this week. Please take some time for the homework and for the quiz, and here is the literature going with Week 3.

Notes

Summary



14m 05s

Neuronal Dynamics – week 3 – Reading

Reading: W. Gerstner, W.M. Kistler, R. Naud and L. Paninski, *Neuronal Dynamics: from single neurons to networks and models of cognition*. Chapter 3: *Dendrites and Synapses*, Cambridge Univ. Press, 2014
OR W. Gerstner and W. M. Kistler, *Spiking Neuron Models*, Chapter 2, Cambridge, 2002
OR P. Dayan and L. Abbott, *Theoretical Neuroscience*, Chapter 6, MIT Press 2001

References:

M. Larkum, J.J. Zhu, B. Sakmann (1999), *A new cellular mechanism for coupling inputs arriving at different cortical layers*, *Nature*, 398:338-341
E. Hay et al. (2011) *Models of Neocortical Layer 5b Pyramidal Cells Capturing a Wide Range of Dendritic and Perisomatic Active Properties*, *PLOS Comput. Biol.* 7:7
Carnevale, N. and Hines, M. (2006). *The Neuron Book*. Cambridge University Press.
Bower, J. M. and Beeman, D. (1995). *The book of Genesis*. Springer, New York.
Rall, W. (1989). *Cable theory for dendritic neurons*. In Koch, C. and Segev, I., editors, *Methods in Neuronal Modeling*, pages 9{62, Cambridge. MIT Press.
Abbott, L. F., Varela, J. A., Sen, K., and Nelson, S. B. (1997). Synaptic depression and cortical gain control. *Science* 275, 220–224.
Tsodyks, M., Pawelzik, K., and Markram, H. (1998). Neural networks with dynamic synapses. *Neural Comput.* 10, 821–835.

✎ ✂ ✕ ✖

Looking forward to seeing you again next week.

Notes

Summary



14m 19s