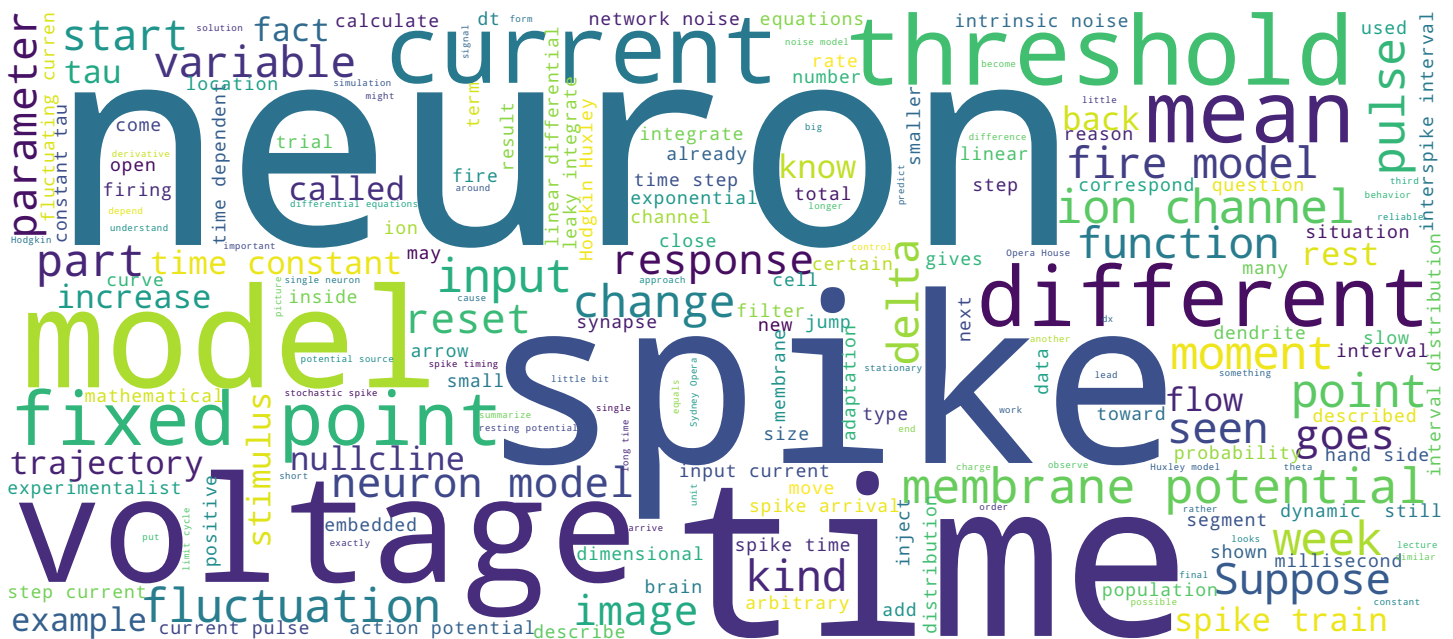


ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

EPFL, Lausanne, Switzerland

- subthreshold and superthreshold



EPFL



Week 5 – part 2 : Sources of Variability



✓ 5.1 Variability of spike trains

- experiments

5.2 Sources of Variability?

- Is variability equal to noise?

5.3 Three definitions of Rate code

- Poisson Model

5.4 Stochastic spike arrival

- Membrane potential fluctuations

5.5. Stochastic spike firing

- subthreshold and superthreshold

In part one of week five, we have seen that membrane potentials show fluctuations. We have seen that spike timing is not reliable. And the question arises-- what are the sources of this variability? What is the source of the fluctuations?

Notes

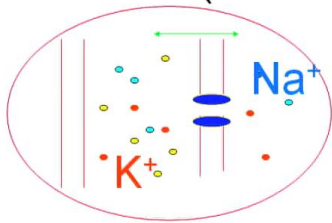
Summary



0m 04s

Neuronal Dynamics – 5.2. Sources of Variability

- Intrinsic noise (ion channels)



- Finite number of channels
- Finite temperature

✎ ✏ 📄 ➡

One potential source is that there's intrinsic noise in each neuron. We have seen that ion channels open and close and that the number of ion channels embedded in the membrane is limited. The brain is at 37 degrees temperature. At finite temperature with a finite number of channels, we expect some stochastic effects.

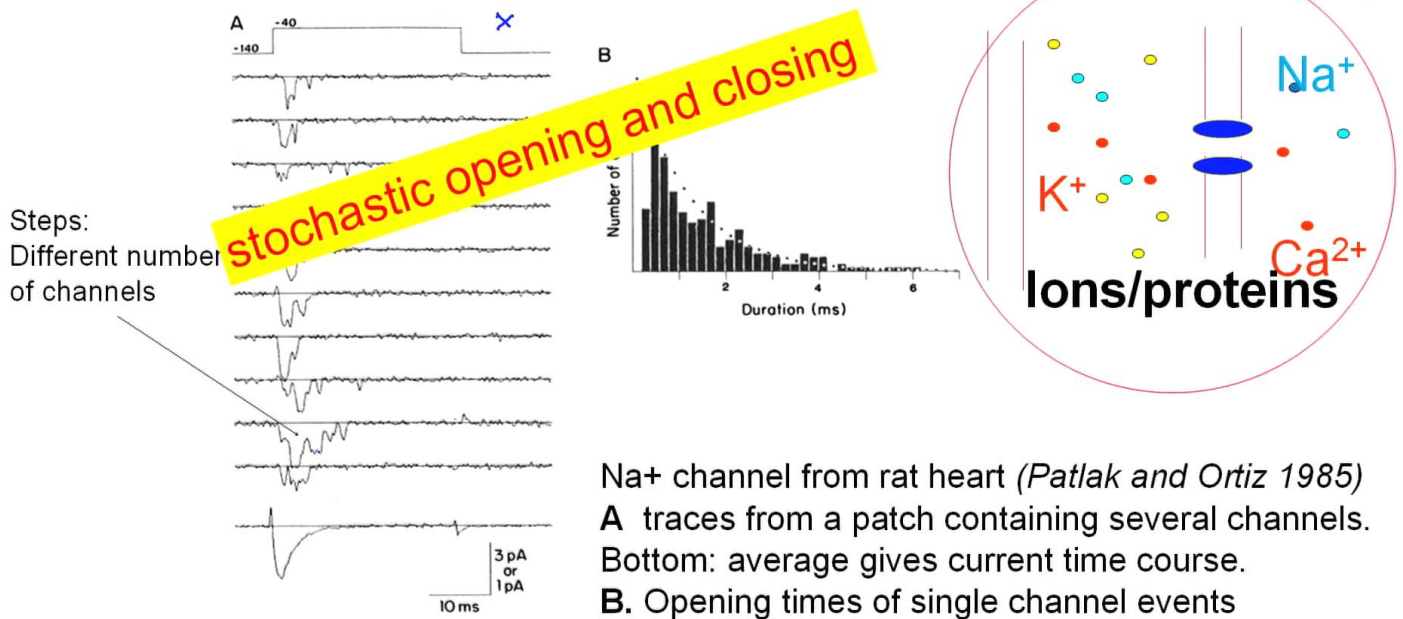
Notes

Summary



0m 23s

Review from 2.5 Ion channels



Indeed, in recordings of ion channels, we see that if the same stimulus is presented several times-- the stimulus is up here-- then in the first trial, ion channel opens here, goes down, goes down, goes up again. In a later trial, the opening might be bigger. There are these fluctuations. The steps correspond to different numbers of ion channels that are open. But the important point here is that the opening and closing of ion channels is visible in the membrane. And it shows up as fluctuations in the iron current flowing through the set of channels.

Notes

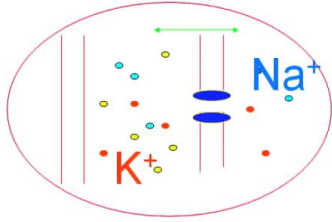
Summary



0m 54s

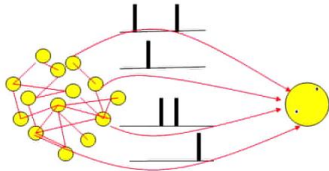
Neuronal Dynamics – 5.2. Sources of Variability

- Intrinsic noise (ion channels)



- Finite number of channels
- Finite temperature

-Network noise (background activity)



- Spike arrival from other neurons
- Beyond control of experimentalist

————— Check intrinsic noise by removing the network

So this is a first noise source. There's a finite number of ion channels that run at finite temperature. This leads to intrinsic noise in the neuron. However, there is also another potential source of noise. And that's what I call network noise. Neurons are embedded in the network of many, many other neurons. And let's just pull one of these neurons out of the network. And this neuron will receive input from all the other neurons. The other neurons send out their spikes. Spikes will arrive at different moments in time. The exact spike timing of the other neurons is beyond the control of the experimentalist. An experimentalist can, for example, stimulate visual cortex by presenting an image-- say, the image of the Sydney Opera House. However, he cannot control what each individual neuron receives from other neurons-- other neurons that send spikes over the synapses to the neuron and from which the experimentalist is recording. Now, in order to find out whether network noise is important, the first step is to remove the network noise, and to remove the network noise by isolating a neuron.

Notes

Summary



1m 47s

Neuronal Dynamics – 5.2 Variability in vitro

neurons are fairly reliable

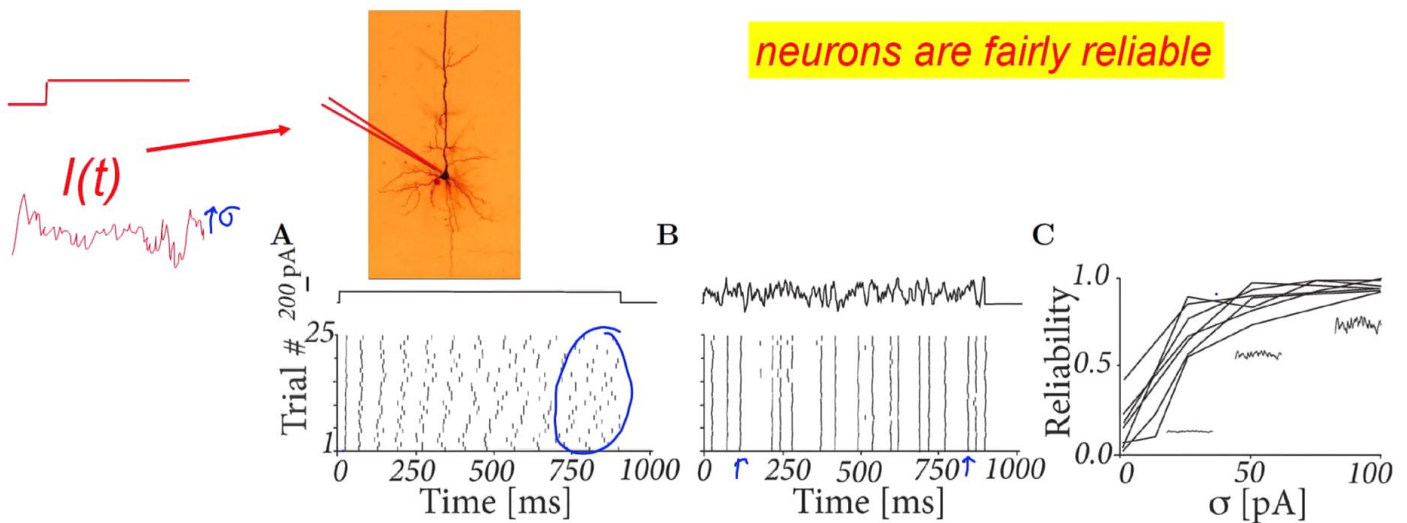


Image adapted from
Mainen & Sejnowski 1995

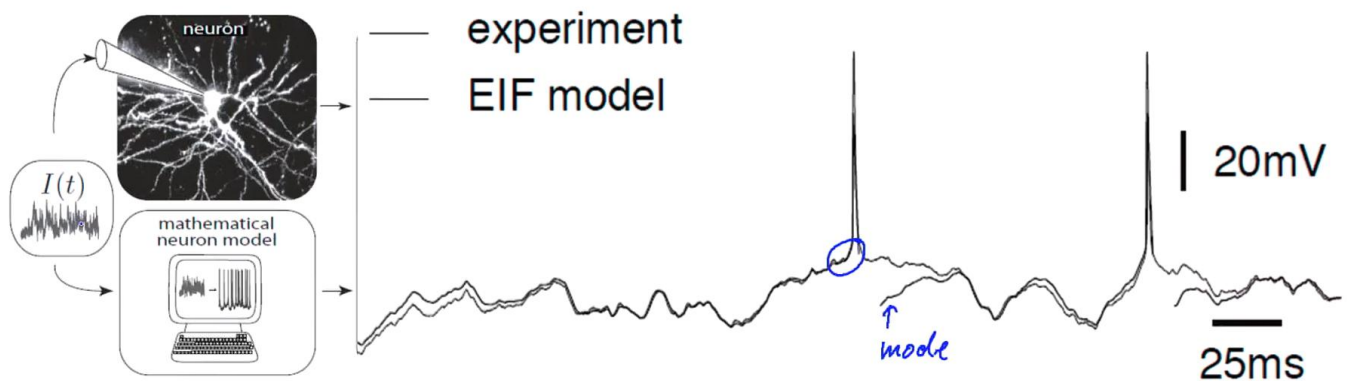
And that leads back to in vitro recordings. Suppose we inject a step current into a single neuron. Then you see that the first spike is very reliable in all the 25 trials shown here. However, later spikes-- they are not reliable at all. On the other hand, if you inject a strongly fluctuating current into the same neuron, then you see that all spikes occur fairly reliably. So if you increase the size of the fluctuations-- so the size of the fluctuations is σ . If you increase σ , then the reliability increases as well. And already for fairly small amount of fluctuations, the neuron is quite reliable.

Notes

Summary



REVIEW from 4.5: How good are integrate-and-fire models?



Badel et al., 2008

- Aims:
- predict spike initiation times
 - predict subthreshold voltage

only possible, because neurons are fairly reliable

⌂ / ☐ ➡

Thus, neurons are fairly reliable. And that means we can attempt to predict spike times, as we did already in week one and in week four. The reason that our model-- the model is this trace here-- that our model can predict the spike times on new input currents that were not used for parameter optimisation-- the reason that this is possible is exactly that neurons themselves are very fairly reliable.

Notes

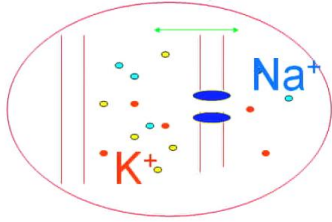
Summary



4m 15s

Neuronal Dynamics – 5.2. Sources of Variability

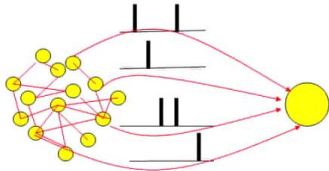
- Intrinsic noise (ion channels)



- Finite number of channels
- Finite temperature

small contribution!

- Network noise (background activity)



- Spike arrival from other neurons
- Beyond control of experimentalist

Check network noise by simulation!

Thus, we may conclude that the intrinsic noise plays only a small contribution in the case that the neuron is stimulated with a fluctuating current. Now, the fluctuating current represents what the neuron is expected to see when it's embedded in the brain network. And neuron inside the brain is not going to be stimulated naturally by a step current, but rather, by some kind of fluctuating current, or more precisely, a fluctuating conductance. So we can exclude a big contribution from intrinsic noise. Then the question is is this image of a network noise really realistic? And we can check this by simulations.

Notes

Summary



4m 47s

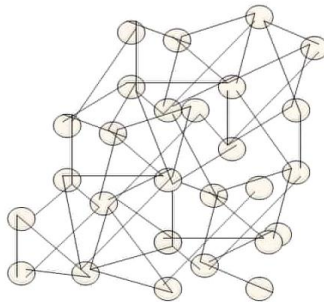
Neuronal Dynamics – 5.2 Sources of Variability



Brain

The Brain: a highly connected system

High connectivity:
systematic, organized in local populations
but **seemingly random**



Distributed architecture

10^{10} neurons

10^4 connections/neurons

5m 31s

So the brain is highly connected. There are connection patterns. Different areas across the brain are more strongly connected to each other than other areas. However, locally, the connectivity looks more or less random.

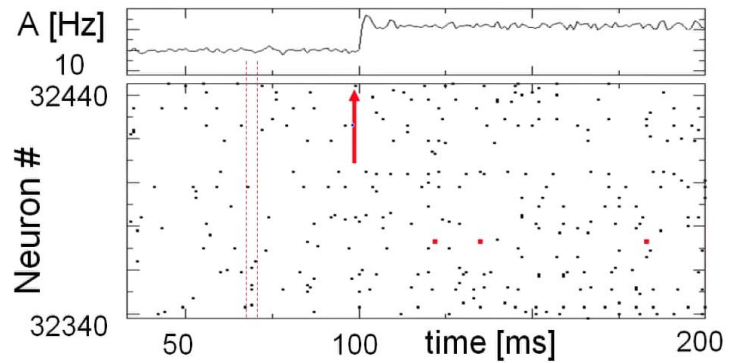
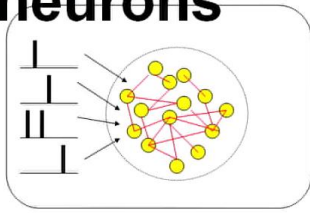
Notes

Summary



5m 31s

Random firing in a population of LIF neurons



Brunel, J. Comput. Neurosc. 2000
Mayor and Gerstner, Phys. Rev E. 2005
Vogels et al., 2005

Population

- 50 000 neurons ✕
- 20 percent inhibitory
- **randomly connected**



So let's simulate such a local population of neurons with random connectivity. And to do so, we use leaky integrate-and-fire models, the neuron model that we have seen in week one. We have 50,000 neurons in total. 20% of these are inhibitory. The remaining ones are excitatory. And the connectivity between these neurons is random. Now, what you see is that at any moment in time, different neurons fire. The activity pattern, this spike pattern, looks more or less random. Now, this population is not isolated. It will receive spike input from other populations.

Notes

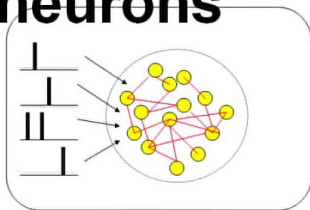
Summary



5m 52s

Random firing in a population of LIF neurons

neurons

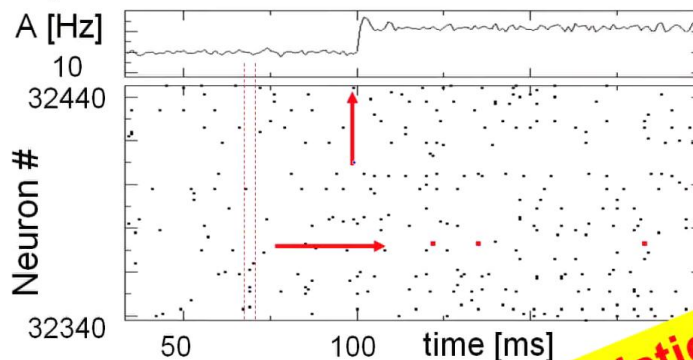


input { low rate
high rate

Population

- 50 000 neurons ✕
- 20 percent inhibitory
- **randomly connected**

Brunel, J. *Comput. Neurosc.* 2000
 Mayor and Gerstner, *Phys. Rev E.* 2006
 Vogels et al., 2005



**Network of deterministic
leaky integrate-and-fire:
'fluctuations'**

And the spike input will change at some point. Say, a new image is shown. After the image of the Sydney Opera House, it's now image of the Pisa Tower. And the inputs, the spike arrivals, the rate of spike arrivals to this population of neurons changes. And what you see is that the neurons emit more spikes, but it's still a random pattern. So what's shown up here is an average across the whole population of neurons. And this Activity A is the population activity that will be formally introduced in the next lecture. This was the moment when we switched from one image to the next image. And this population responds stronger to the second image. Now, this is a population picture. An experimentalist will look at one neuron at a time.

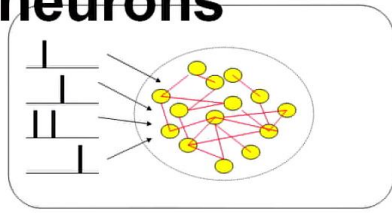
Notes

Summary



6m 45s

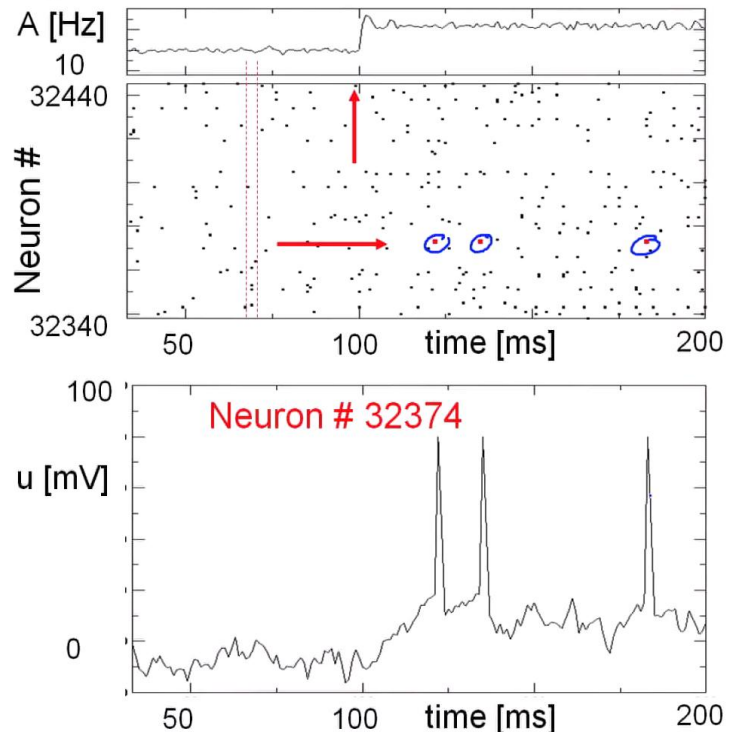
Random firing in a population of LIF neurons



input {
- low rate
- high rate

Population

- 50 000 neurons
- 20 percent inhibitory
- **randomly connected**



So let's focus on one of the neurons-- say this neuron here, neuron number 32,374, one of the many neurons. And you see here that this neuron has to emitted spikes at three moments in time. And suppose we can do a intracellular recording of our model neuron so that we see the membrane potential fluctuations. These membrane potential fluctuations look not very different to those that we see in in vivo data. And then we have occasional spikes. Spikes are rare events.

Notes

Summary

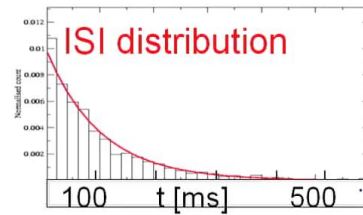
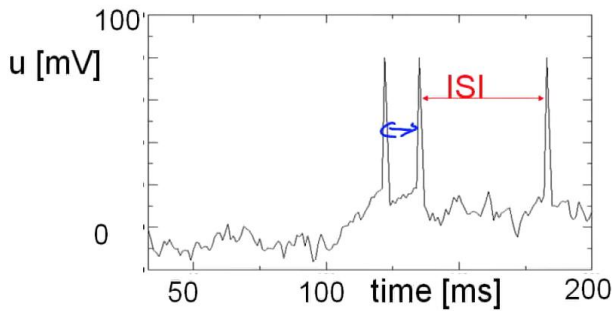


7m 46s

Neuronal Dynamics – 5.2. Interspike interval distribution

- Variability of interspike intervals (ISI)

here in simulations,
but also *in vivo*



Variability of spike trains:
broad ISI distribution

Brunel,
J. Comput. Neurosc. 2000
Mayor and Gerstner,
Phys. Rev E. 2005
Vogels and Abbott,
J. Neuroscience, 2005

Let's look at these spikes. The spikes have intervals. And this interval is longer than the first interval here. So if you observe a single neuron for a long time, you will see a distribution of interspike intervals. It's called an ISI distribution. While very, very short intervals of two milliseconds are possible because of refractoriness, if we look at longer intervals, we see a broad distribution of interspike intervals. The variability of spike trains manifests itself as a broad interspike interval distribution despite the fact that the stimulus-- say, a picture of the Sydney Opera House-- is stationary. It's presented for a long time. Now, what I've shown here are results from simulations of a network of leaky integrate-and-fire neurons. But the same kind of observations and measurements can be also made *in vivo*.

Notes

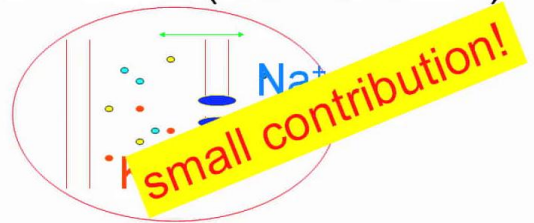
Summary



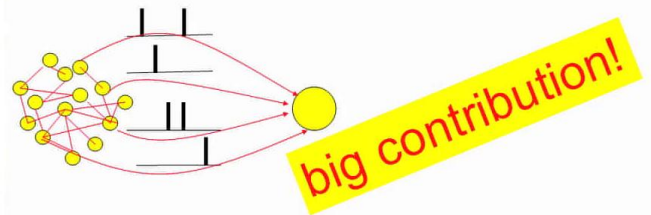
8m 24s

Neuronal Dynamics – 5.2. Sources of Variability

- Intrinsic noise (ion channels)



-Network noise



So let's summarize. Neurons show fluctuations. These fluctuations have two different potential sources. The first one is intrinsic noise. Intrinsic noise seems to be a small contribution. The bigger contribution arises from the fact that a neuron is embedded in a brain network where it receives stochastic spike arrivals from many other neurons. And interestingly, a deterministic network of leaky integrate-and-fire neurons with random connectivity can reproduce the fluctuations of membrane potentials and the broad interspike interval distributions that experimentalists have observed in vivo.

Notes

Summary



9m 36s

Neuronal Dynamics – Quiz 5.1.

A- Spike timing in vitro and in vivo

- ☐ Reliability of spike timing can be assessed by repeating several times the same stimulus
- ☐ Spike timing in vitro is more reliable under injection of constant current than with fluctuating current
- ☐ Spike timing in vitro is less reliable under injection of constant current than with fluctuating current
- ☐ Spike timing in vitro is more reliable than spike timing in vivo
- ☐ Nothing is known about spike timing in humans in vivo

B – Interspike Interval Distribution (ISI)

- ☐ An isolated deterministic leaky integrate-and-fire neuron driven by a constant current can have a broad ISI
- ☐ A deterministic leaky integrate-and-fire neuron embedded into a randomly connected network of integrate-and-fire neurons can have a broad ISI
- ☐ An isolated deterministic Hodgkin-Huxley model as in week 2 driven by a constant current can have a broad ISI

Please take a moment to look at the quiz before you go on to lecture number three.

Notes

Summary



10m 26s