

Welcome!

#pod-031

Week #3, Day 1

(Reviewed by: Deepak)



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Agenda

- **Tutorial 1 (LIF Model)**
 - **3 exercises (+ bonus)**
- **Tutorial 2 (Effect of input correlations)**
 - **2 exercises (+ bonus)**
- **Tutorial 3 (Synaptic transmission)**
 - **1 exercise (+ bonus)**
- **Tutorial 4 - bonus (Spike timing dependent plasticity)**
 - **2 exercises**

Tutorial #1

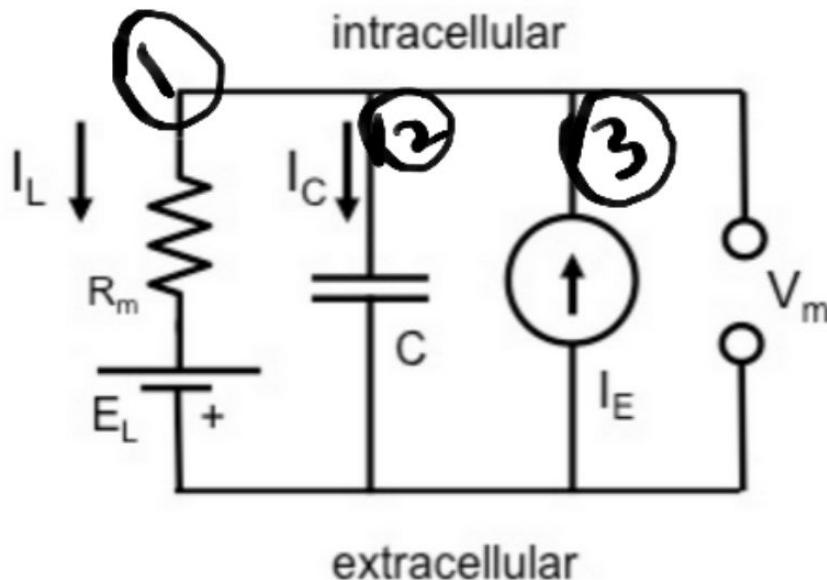
Explanations

Objective

- Implementation of realistic neuron models.
- build up/simulate a leaky integrate-and-fire (LIF) neuron model and study its dynamics in response to various types of inputs, drive the LIF neuron with external inputs, such as direct currents, Gaussian white noise, and Poisson spike trains, etc and study how different inputs affect the LIF neuron's output (firing rate and spike time irregularity)

Note: Emphasize the identifying conditions (input statistics) under which a neuron can spike at low firing rates and in an irregular manner. The reason for focusing on this is that in most cases, neocortical neurons spike in an irregular manner.

LIF Neuron Equation



Current(2) = Current(3) + Current(1)

$$C_m \frac{dV_m}{dt} = -(V_m - V_{rest})/R_m + I$$

Ref:

https://ocw.mit.edu/resources/res-9-003-brains-minds-and-machines-summer-course-summer-2015/tutorials/tutorial-2-matlab-programming/MITRES_9_003SUM15_fire.pdf

if I is strong enough that V reaches V_{th} (threshold)
 \rightarrow reset V to reset potential ($V_{reset} < V_{th}$)

voltage clamped to V_{reset} for T_{ref}

(mimics refractoriness of neuron during action potential)

if $V(t_{sp}) \geq V_{th}$: $V(t) = V_{reset}$ for $t \in (t_{sp}, t_{sp} + T_{ref}]$


 spike time when $V(t)$ has exceeded V_{th} .

θ : threshold voltage V_{th}

Δ : refractory time T_{ref}

Sub-thresholding

Sub-threshold (or *subthreshold*) refers to a stimulus that is too small in magnitude to produce an action potential in excitable cells. In general, a **sub-threshold** stimulus leads to the depolarization of the membrane, but the magnitude of the depolarization is not large enough to reach the threshold voltage.

Sub-thresholding

Sub threshold membrane potential dynamics (LIF)

$$C_m \frac{dV}{dt} = -g_L (V - E_L) + I_e$$

Diagram illustrating the components of the equation:

- C_m → membrane capacitance
- $\frac{dV}{dt}$ → membrane potential
- $-g_L$ → leak conductance
- $(\frac{1}{R})$ → leak resistance
- $(V - E_L)$ → resting potential
- I_e → external input current

÷ by g_L

$$\tau_m \frac{dV}{dt} = -(V - E_L) + \frac{1}{g_L}$$



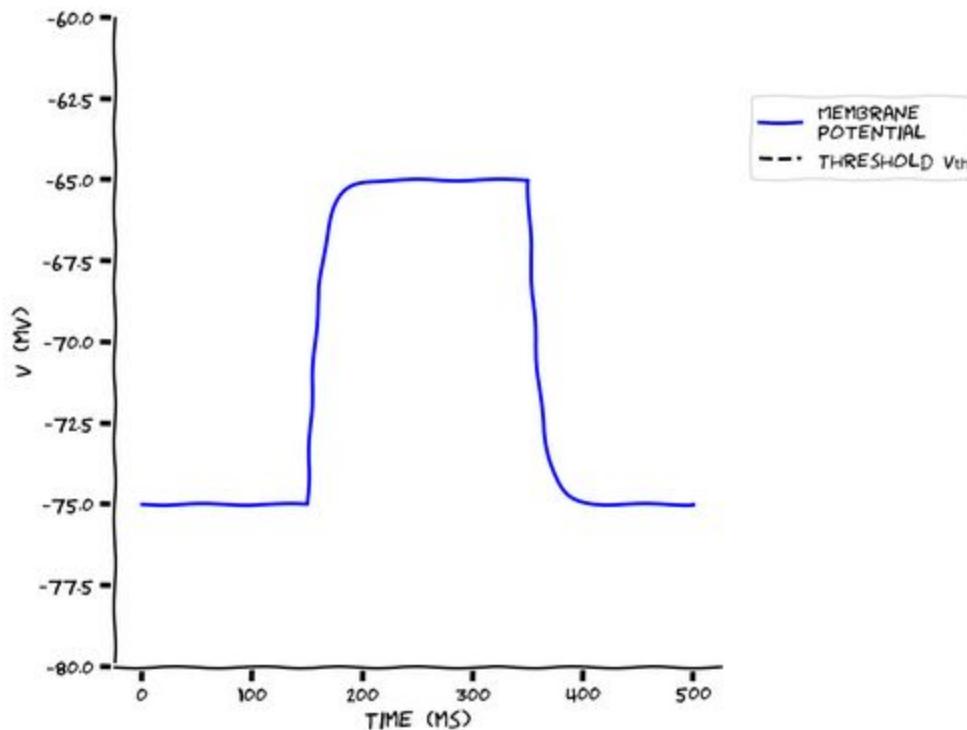
$$\frac{C_m}{g_L} \quad (\text{membrane time constant})$$

Thus, the LIF model captures the facts that a neuron:

- performs spatial and temporal integration of synaptic inputs
- generates a spike when the voltage reaches a certain threshold
- goes refractory during the action potential
- has a leaky membrane

The LIF model assumes that the spatial and temporal integration of inputs is linear. Also, membrane potential dynamics close to the spike threshold are much slower in LIF neurons than in real neurons.

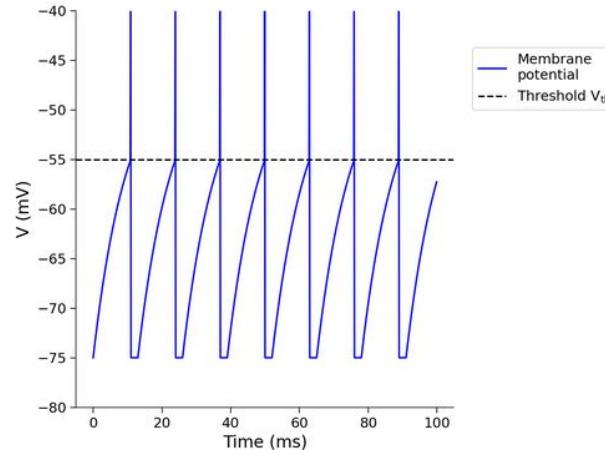
Membrane potential vs threshold



Response of an LIF model to different types of input currents

Inject direct current and white noise to study the response of an LIF neuron.

LIF neuron driven by constant current/DC(300 pA)



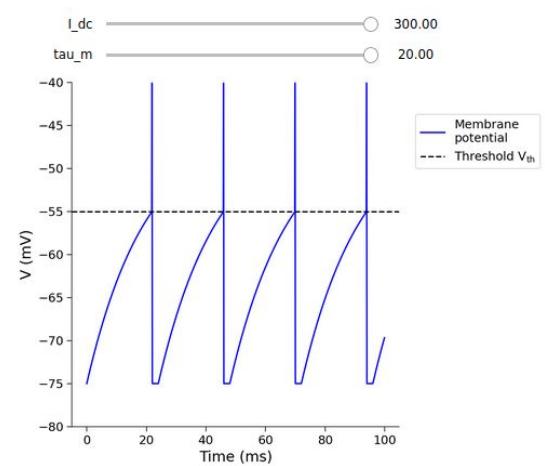
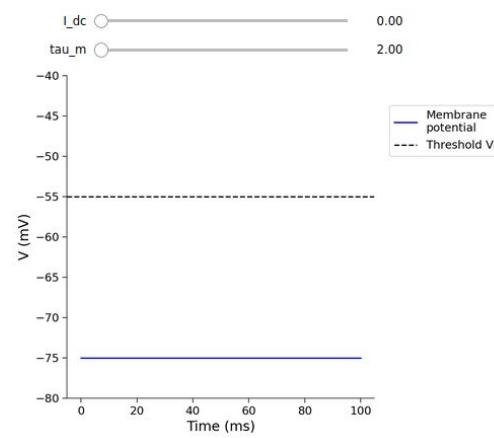
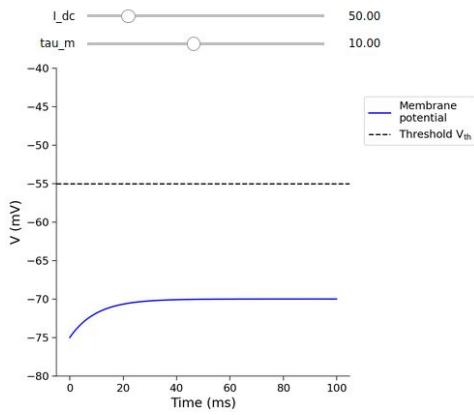
Observations

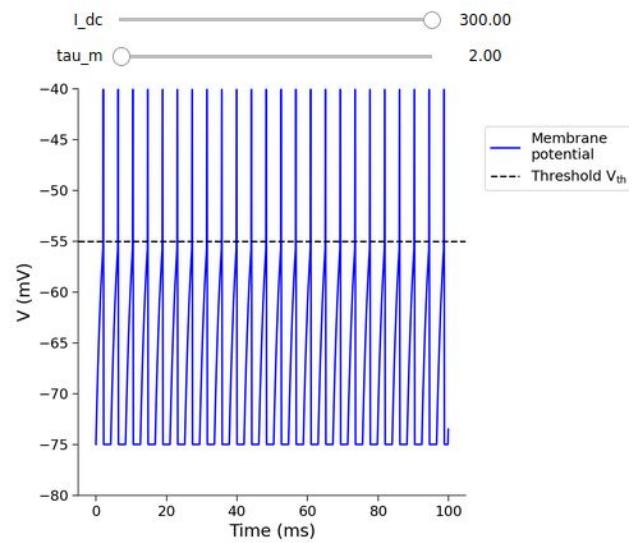
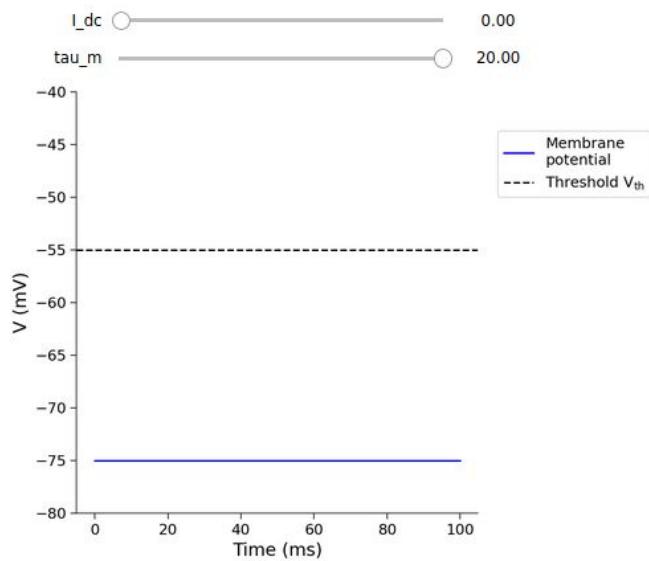
The neuron generates a spike but it's only cosmetic.

Note: In an LIF neuron, we only need to keep track of times when the neuron hit the threshold so the postsynaptic neurons can be informed of the spike.

Parameter exploration of DC input amplitude

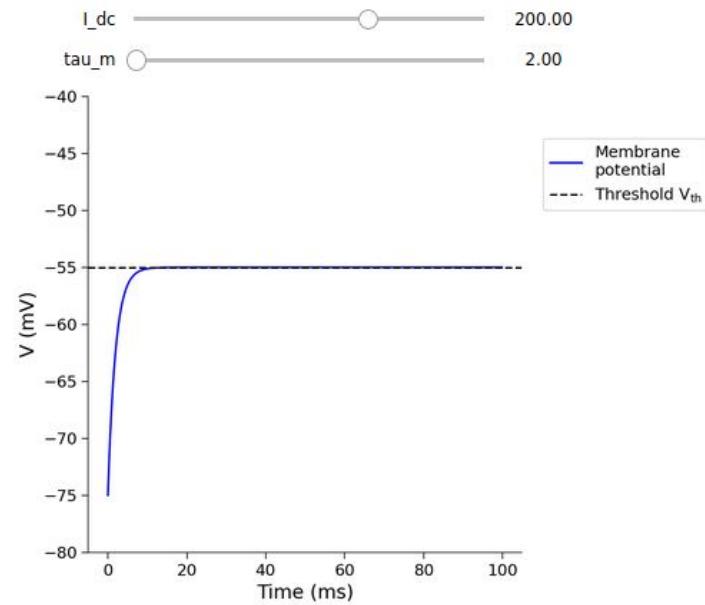
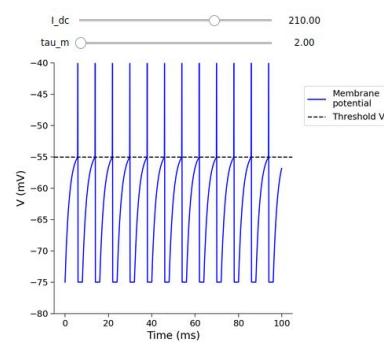
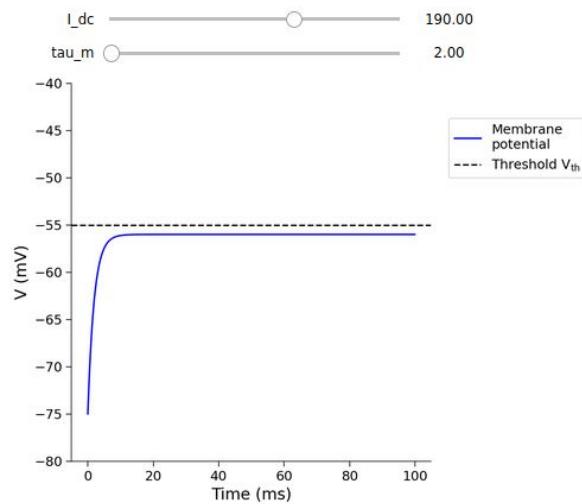
How much DC is needed to reach the threshold (rheobase current)? How does the membrane time constant affect the frequency of the neuron?





Observations

1. As we increase the current, we observe that at $210 \mu\text{A}$ we cross the threshold.
2. As we increase the membrane time constant (slower membrane), the firing rate is decreased because the membrane needs more time to reach the threshold after the reset.



gaussian white noise (GWN) current

Given the noisy nature of neuronal activity *in vivo*, neurons usually receive complex, time-varying inputs.

gaussian white noise

Additive white Gaussian noise (AWGN) is a basic **noise** model used in information theory to mimic the effect of many random processes that occur in nature. The modifiers denote specific characteristics: Additive because it is added to any **noise** that might be intrinsic to the information system.

Gaussian White noise in neurons

Neuronal noise is a general term that designates random influences on the transmembrane voltage of single neurons and by extension the firing activity of neural networks. This noise can influence the transmission and integration of signals from other neurons as well as alter the firing activity of neurons in isolation.

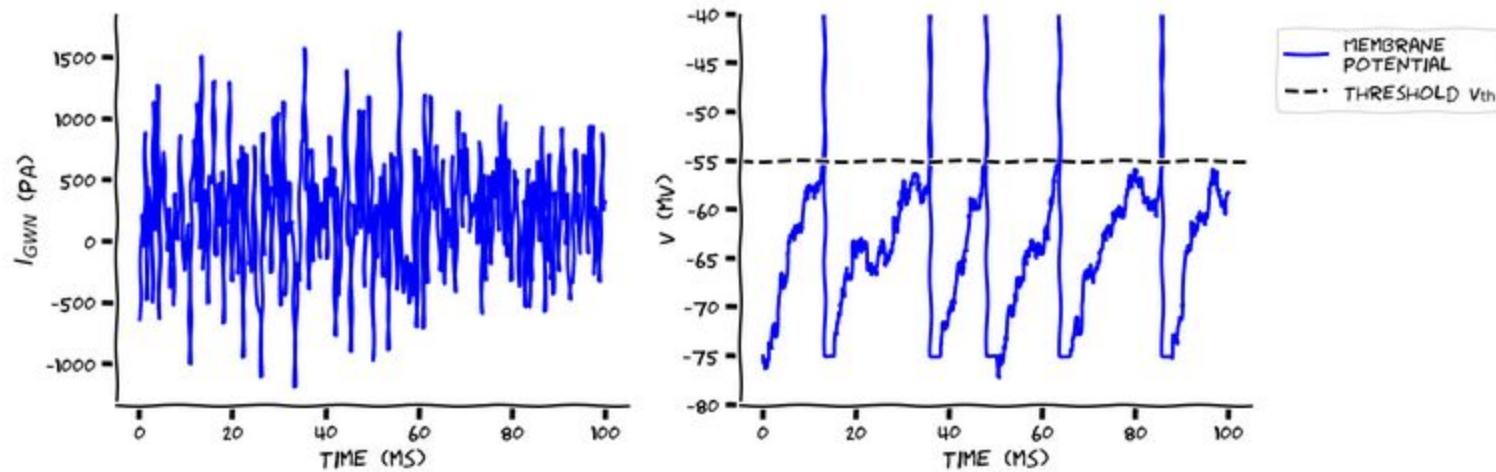
investigate neuronal response when LIF neurons receive gaussian white noise
↳ $\xi(t)$

mean : $E[\xi(t)] = M = 0$

autocovariance : $E[\xi(t) \xi(t + \tau)] = \sigma_\xi^2 \delta(\tau)$

describes only fluctuations of input received by neuron

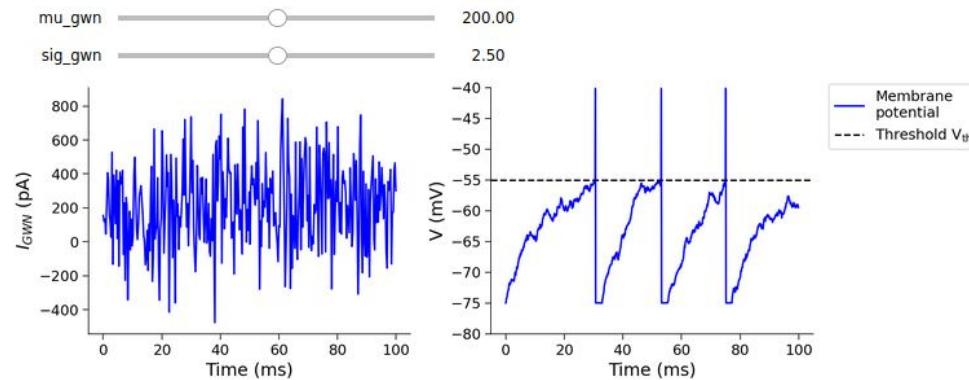
Non 0 mean $\Rightarrow M = \text{DC input}$ (any input into cell)

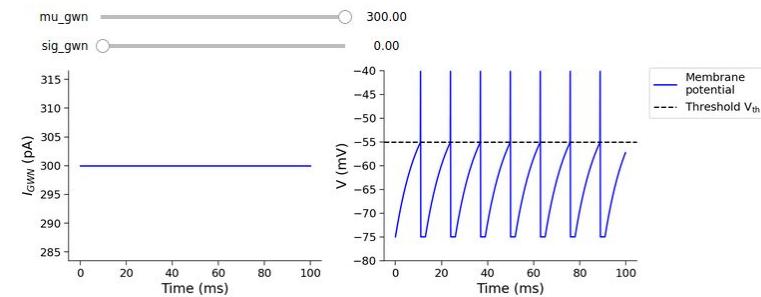
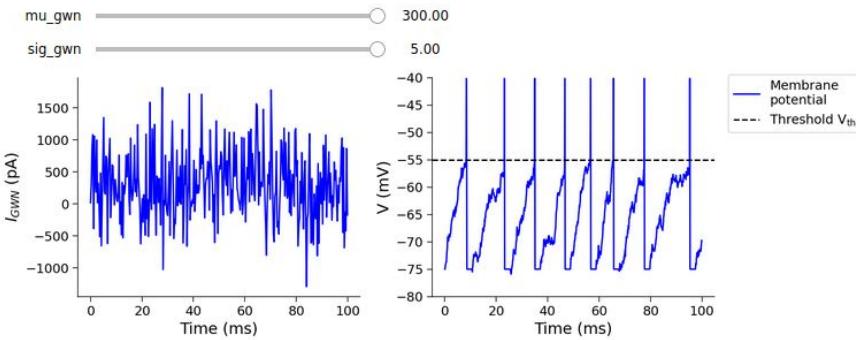
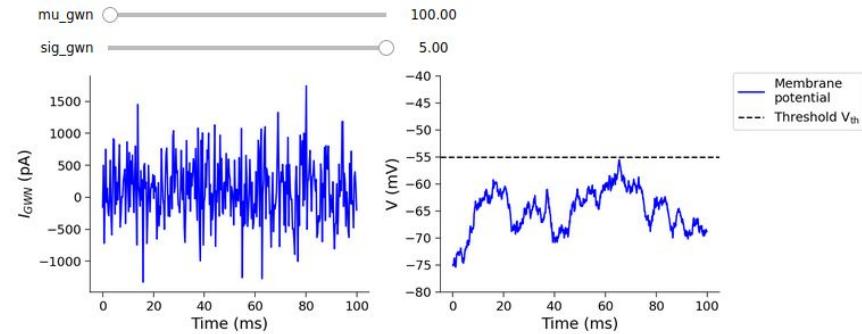
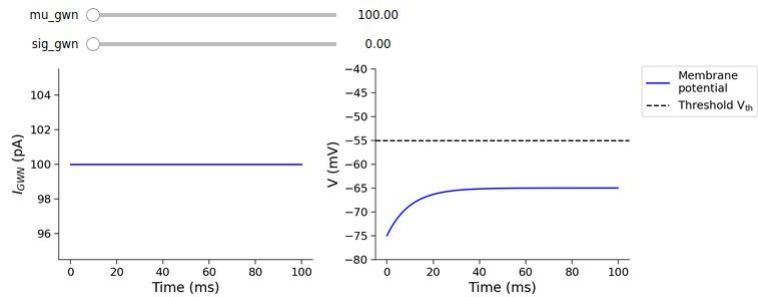


LIF NEURON VISUALISATION FOR NOISY INPUT

The mean of the GWN is the amplitude of DC. Indeed, when $\sigma = 0$ (fluctuation size), GWN is just a DC.

How does σ of the GWN affect the spiking behavior of the neuron.





Observations

- *how does the minimum input (i.e. μ) needed to make a neuron spike change with increase in σ ?*

If we have bigger current fluctuations (increased sigma), the minimum input needed to make a neuron spike is smaller as the fluctuations can help push the voltage above threshold.

- *how does the spike regularity change with increase in σ ?*

The standard deviation (or size of current fluctuations) dictates the level of irregularity of the spikes; the higher the sigma the more irregular the observed spikes.

Food for thought

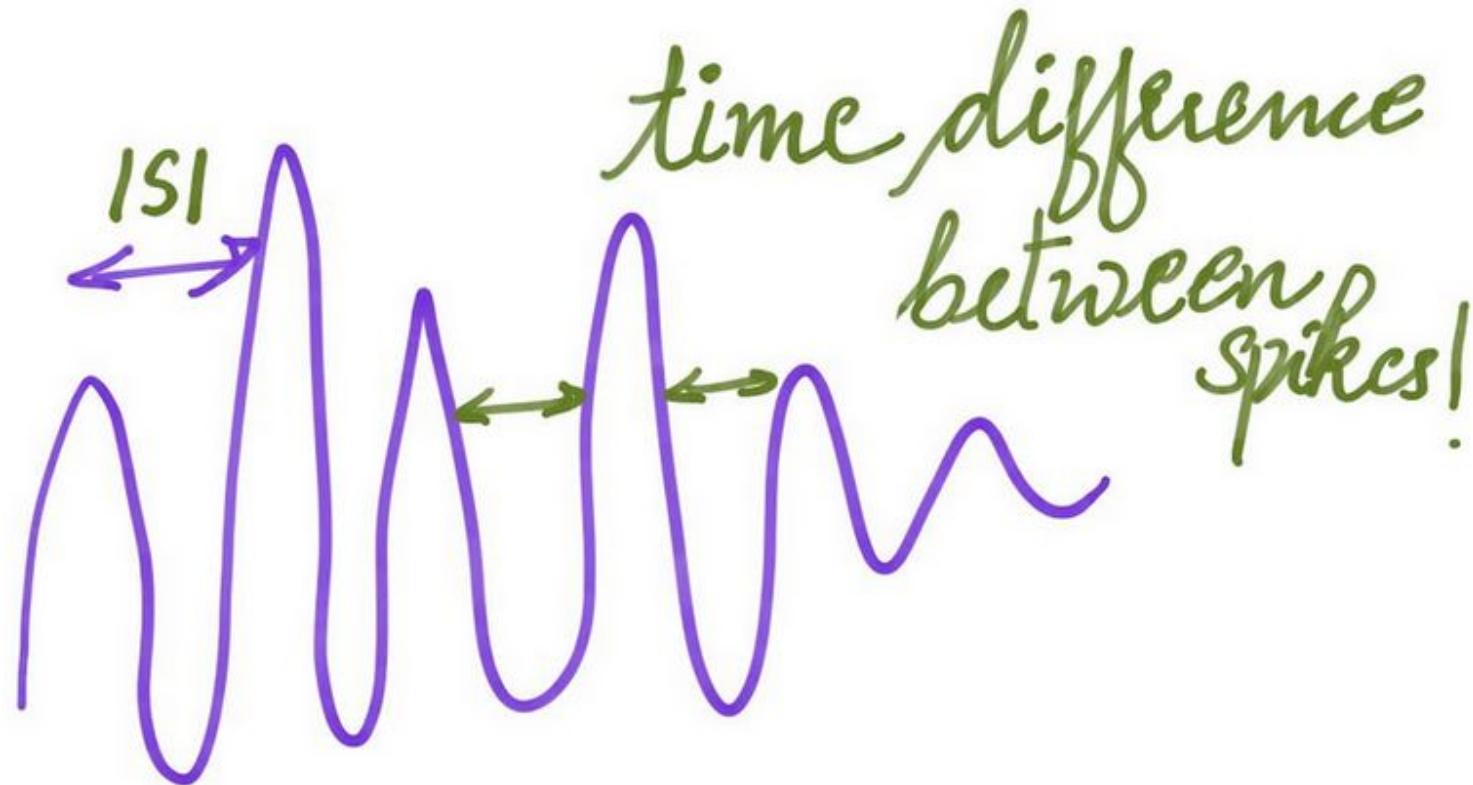
AS WE INCREASE THE INPUT AVERAGE (μ) OR THE INPUT FLUCTUATION (σ), THE SPIKE COUNT CHANGES. HOW MUCH CAN WE INCREASE THE SPIKE COUNT, AND WHAT MIGHT BE THE RELATIONSHIP BETWEEN GWN MEAN/STD OR DC VALUE AND SPIKE COUNT?

INPUT-OUTPUT TRANSFER FUNCTION

WE HAVE SEEN ABOVE THAT WHEN WE INJECT DC, THE NEURON SPIKES IN A REGULAR MANNER (CLOCK LIKE), AND THIS REGULARITY IS REDUCED WHEN GWN IS INJECTED. THE QUESTION IS, HOW IRREGULAR CAN WE MAKE THE NEURONS SPIKING BY CHANGING THE PARAMETERS OF THE GWN?

SPIKE REGULARITY CAN BE QUANTIFIED AS THE COEFFICIENT OF VARIATION (CV) OF THE INTER-SPIKE-INTERVAL (ISI):

Inter-spike intervals (ISI)



Input output transfer function / F1 curve
 plotting output firing rate as a function of GWN mean/DC value

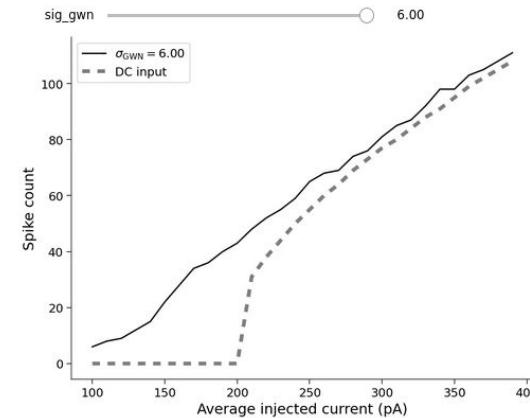
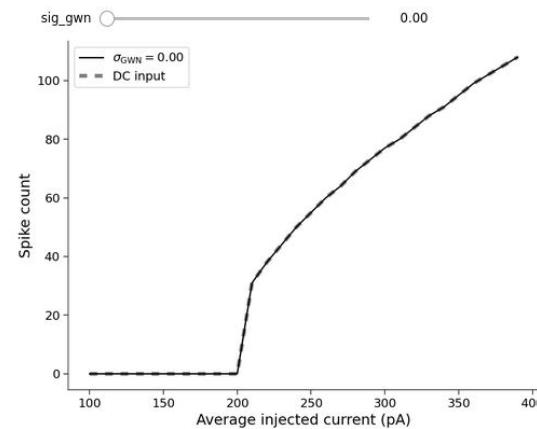
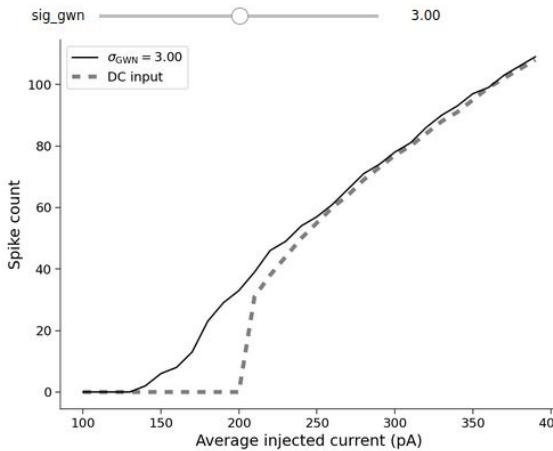
Spike regularity
 quantified as coefficient of variation of interspike interval
 (CV_{ISI})

$$CV_{ISI} = \frac{\text{std}(ISI)}{\text{mean}(ISI)}$$

Poisson train: high irregularity $[CV_{ISI}=1]$
 regular processes $[CV_{ISI}=0]$ as $\text{std}(ISI)=0$

How does the $f-I$ curve of the L-L7 neuron change as we increase the σ of the GWN?

$f-I$ curve is stochastic and the results will vary from one trial to another.



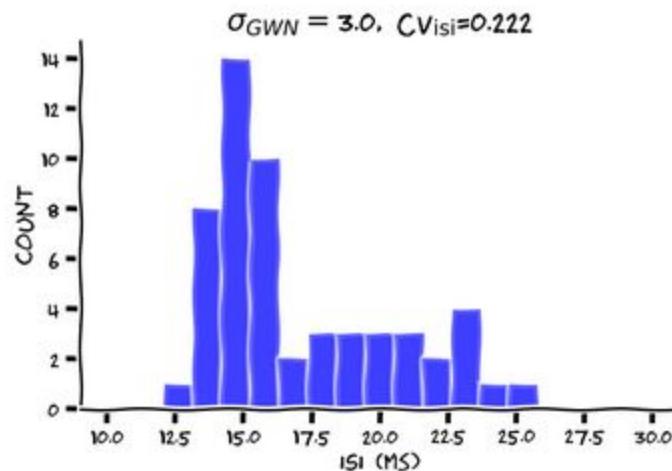
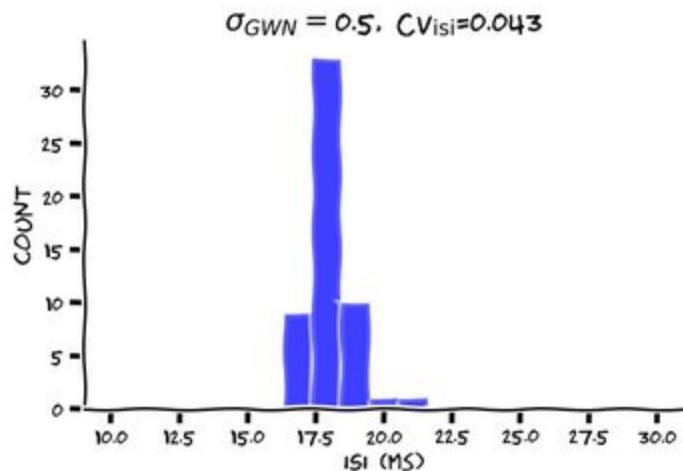
Observations

If we use a DC input, the F-I curve is deterministic, and we can find its shape by solving the membrane equation of the neuron. If we have GWN,

as we increase the sigma, the F-I curve has a more linear shape, and the neuron

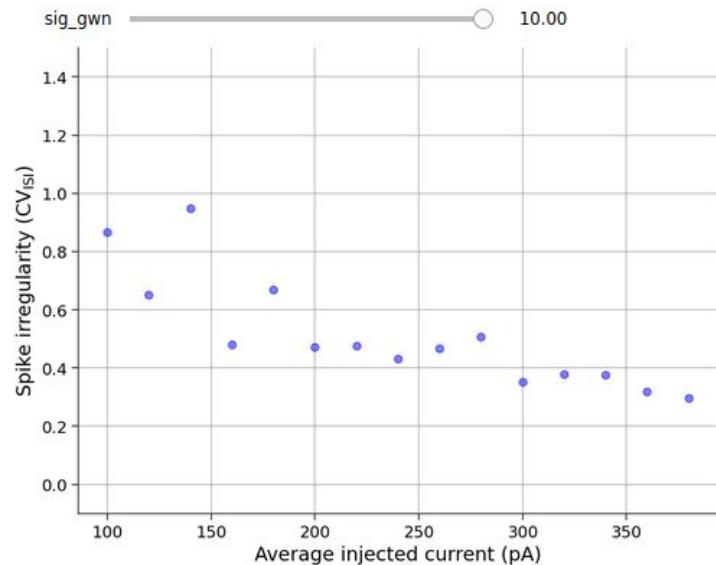
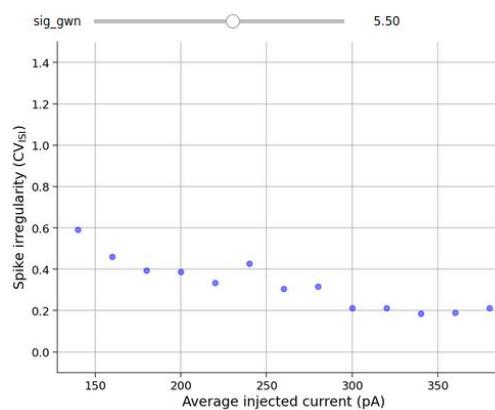
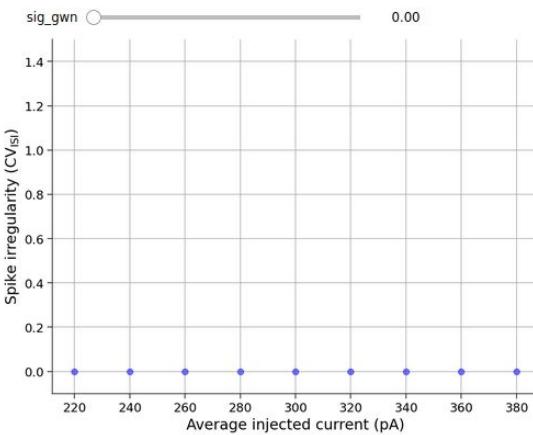
reaches its threshold using less average injected current.

F-I curve becomes smoother while increasing the amplitude of the fluctuation (σ). In addition, the fluctuation can also change the irregularity of the spikes



Food for thought

we see that the CV of inter-spike-interval (ISI) distribution depends on σ of GWN. What about the mean of GWN, should that also affect the CV ISI? If yes, how? Does the efficacy of σ in increasing the CV ISI depend on μ ?



Food for thought #1

- Does the standard deviation of the injected current affect the F-I curve in any qualitative manner?

Yes, it does. With DC input the F-I curve has a strong non-linearity but when a neuron is driven with GWN, as we increase the sigma the non-linearity is smoothed out. Essentially, in this case noise is acting to suppress the non-linearities and render a neuron as a linear system.

- Why does increasing the mean of GWN reduce the CVISI?

When we increase the mean of the GWN, at some point effective input mean is above the spike threshold and then the neuron operates in the so called mean-driven regime -- as the input is so high all the neuron does is charge up to the spike threshold and reset. This essentially gives almost regular spiking.

Food for thought #2

- If you plot spike count (or rate) vs. CV_{ISI} , should there be a relationship between the two?

In an LIF, high firing rates are achieved for high GWN mean. Higher the mean, higher the firing rate and lower the CV_{ISI} . So you will expect that as firing rate increases, spike irregularity decreases. This is because of the spike threshold.

For a Poisson process there is no relationship between spike rate and spike irregularity.

Mathematical neuron process

Mathematically, a spike train is a Point Process. One of the simplest models of a sequence of presynaptic pulse inputs is the Poisson process. We know that given temporal integration and refractoriness, neurons cannot behave as a Poisson Process, and Gamma Process gives a better approximation. Assume that the incoming spikes are following Poisson statistics.

Poisson process

a Poisson point process is a type of random mathematical object that consists of points randomly located on a mathematical space

- has independent increments; and
- the number of events (or points) in any interval of length t is a Poisson random variable with parameter (or mean) λt

Generation of Poisson type spike trains

Generation of Poisson process (method #1)

- with rate λ

probability of finding event in time window }
 with sufficiently small length Δt }

$$P(N=1) = \lambda \Delta t$$

\Rightarrow each time window generates uniformly distributed random variable $r \in [0, 1]$

generate Poisson event when $r < \lambda \Delta t$

\Longrightarrow allows generation of Poisson distributed spikes in online manner

Generation of Poisson process (method #2)

interval $t_{k+1} - t_k$ between Poisson events
with rate λ follows exponential distribution

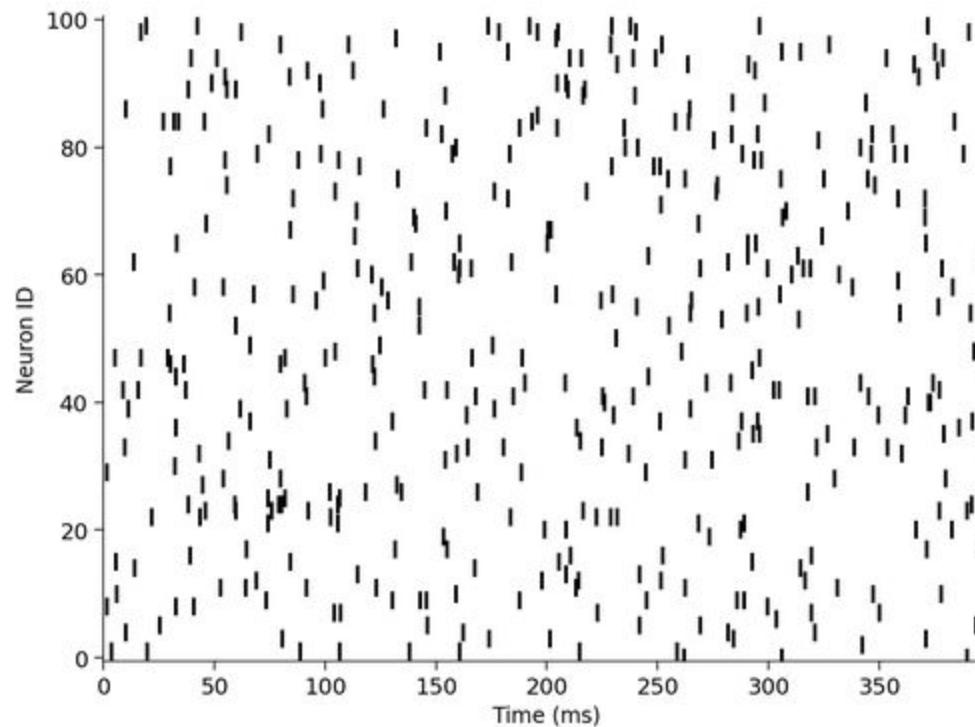
$$P(t_{k+1} - t_k < t) = 1 - e^{-\lambda t}$$

We only need to generate 1 set of exponentially distributed variables $\{s_k\}$ to obtain timing of Poisson events

$$t_{k+1} = t_k + s_k$$

\Rightarrow generate all future spikes @ once.

Poisson Generator to mimic presynaptic spike trains



Poisson process - properties

- The ratio of the mean and variance of spike count is 1
- Inter-spike-intervals are exponentially distributed
- Spike times are irregular i.e. $C(VS) = 1$
- Adjacent spike intervals are independent of each other.

Tutorial #1 bonus Explanations

Orenstein-Uhlenbeck Process

When a neuron receives spiking input, the synaptic current is Shot Noise -- which is a kind of colored noise and the spectrum of the noise determined by the synaptic kernel time constant. That is, a neuron is driven by **colored noise (filtered white noise)** and not **GWN**.

Ornstein-Uhlenbeck Process

temporally correlated input current

modeled as - Ornstein Uhlenbeck process $\eta(t)$

low pass filtered GWN with time constant T_m

$$T_m \frac{d}{dt} \eta(t) = \mu - \eta(t) + \sigma_n \sqrt{\frac{2T_m}{\pi}} \xi(t)$$

where $E[\eta(t)] = \mu$

$$\text{autocovariance: } \eta(t) \eta(t+\tau) = \sigma_\eta^2 e^{-|t-\tau|/T_m}$$

Gamma process

Gamma process is a random process with independent gamma distributed increments.

Thus jumps whose size lies in the interval $[x, x+dx]$ occur as a Poisson process with intensity $v(x) dx$.

O1 process

Gaussian noise

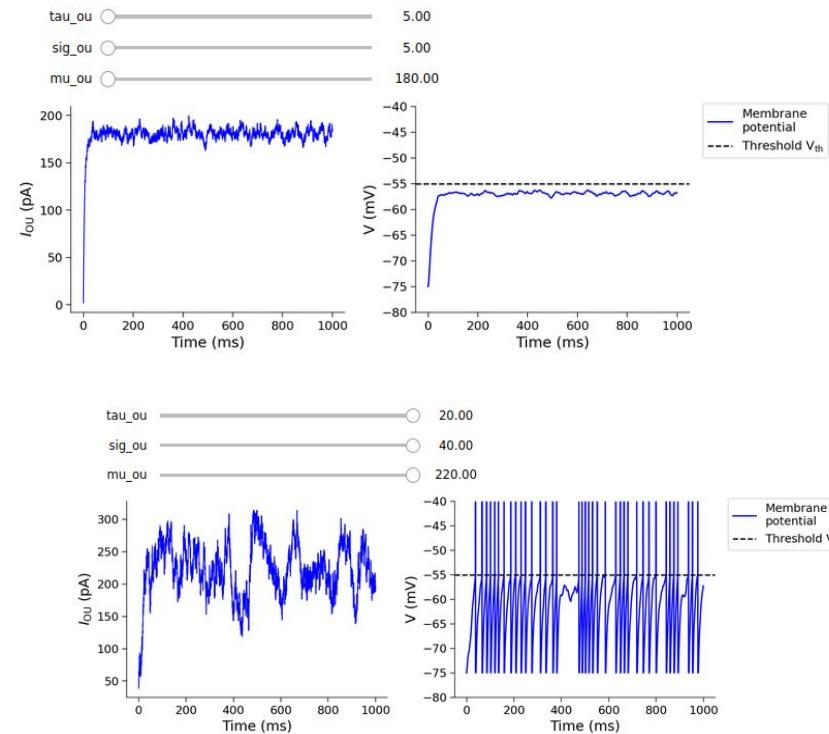
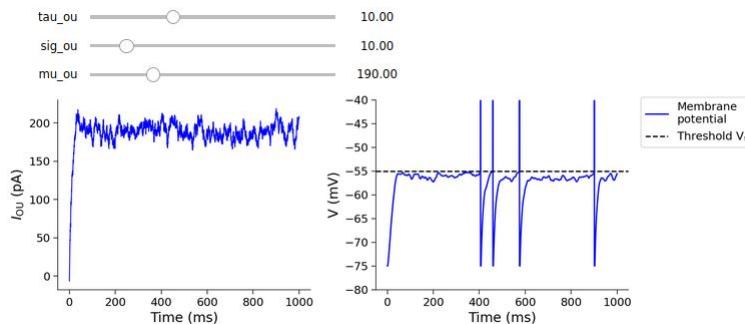
Any kind of filtered noise signal can be called 'colored noise', which is just to say that it is not a pure white noise. In audio, the most common color encountered is 'pink noise': Realized as sound, white noise sounds like the hiss of an untuned FM radio, or the background noise on a cassette tape player.

O2: low pass filter

LPF

A **low-pass filter** (LPF) is a **filter** that **passes** signals with a **frequency lower** than a selected cutoff **frequency** and attenuates signals with frequencies higher than the cutoff **frequency**. The exact **frequency** response of the **filter** depends on the **filter** design.

how a neuron responds to a noisy current that follows the statistics of an OU process.



Generalized Integrate-and-Fire models

IIF model is not the only abstraction of real neurons. Other models:

extended generalized leaky integrate-and-fire: <https://www.frontiersin.org/articles/10.3389/fninf.2018.00088/full>

Adaptive exponential integrate and fire patterns: <https://neuronaldynamics.epfl.ch/online/Ch6.html>

Exponential integrate and fire: https://en.wikipedia.org/wiki/Exponential_integrate-and_fire

Adaptive Exponential Integrate-and-Fire: <https://neuronaldynamics.epfl.ch/online/Ch6.SI.html>

Hodgkin–Huxley model: https://en.wikipedia.org/wiki/Hodgkin%E2%80%93Huxley_model

Spiking Neural network: https://en.wikipedia.org/wiki/Spiking_neural_network

Food for thought

- How does the OU type input change neuron responsiveness?
- What do you think will happen to the spike pattern and rate if you increased or decreased the time constant of the OU process?

In a limiting case, when the time constant of the OU process is very long and the input current is almost flat, we expect the firing rate to decrease and neuron will spike more regularly. So as the OU process time constant increases, we expect firing rate and CV_ISI to decrease, if all other parameters are kept constant.

Tutorial #2

Explanations

Objective

- use the leaky integrate-and-fire (LIF) neuron model to study how they transform input correlations to output properties (transfer of correlations).
- inject correlated GWN in a pair of neurons to measure correlations between the spiking activity of the two neurons and study how the transfer of correlation depends on the statistics of the input, i.e. mean and standard deviation.

Correlations/Synchrony

Correlation or synchrony in neuronal activity can be described for any readout of brain activity.

In the simplest way, correlation/synchrony refers to coincident spiking of neurons, i.e., when two neurons spike together, they are firing in synchrony or are correlated. Neurons can be synchronous in their instantaneous activity, i.e., they spike together with some probability. However, it is also possible that spiking of a neuron at time t is correlated with the spikes of another neuron with a delay (time-delayed synchrony).

Origins of correlation/synchrony

- Common inputs, i.e., two neurons are receiving input from the same sources. The degree of correlation of the shared inputs is proportional to their output correlation.
- Pooling from the same sources. Neurons do not share the same input neurons but are receiving inputs from neurons which themselves are correlated.
- Neurons are connected to each other (uni- or bi-directionally): This will only give rise to time-delayed synchrony. Neurons could also be connected via gap-junctions.
- Neurons have similar parameters and initial conditions.

Implications of synchrony

When neurons spike together, they can have a stronger impact on downstream neurons. Synapses in the brain are sensitive to the temporal correlations (i.e., delay) between pre- and postsynaptic activity, and this, in turn, can lead to the formation of functional neuronal networks ~ the basis of unsupervised learning. Synchrony implies a reduction in the dimensionality of the system. In addition, correlations, in many cases, can impair the decoding of neuronal activity.

study the emergence of correlations

A simple model to study the emergence of correlations is to inject common inputs to a pair of neurons and measure the output correlation as a function of the fraction of common inputs to investigate the transfer of correlations by computing the correlation coefficient of spike trains recorded from two unconnected LlF neurons, which received correlated inputs.

input current to LIF neuron

($i = 1, 2$)

$$\frac{I_i}{g_L} = \mu_i + \sigma_i (\sqrt{1-c} \xi_i + \sqrt{c} \xi_c)$$

common to
all neurons

temporal avg
of current

independent
for each
neuron

variance of
total input

c : controls fraction of common & independent inputs.

($0 \leq c \leq 1$)

Sample correlation coefficient r_{ij} = $\frac{\text{cov}(I_i, I_j)}{\sqrt{\text{var}(I_i)} \sqrt{\text{var}(I_j)}}$

(Sample pearson correlation coefficient)

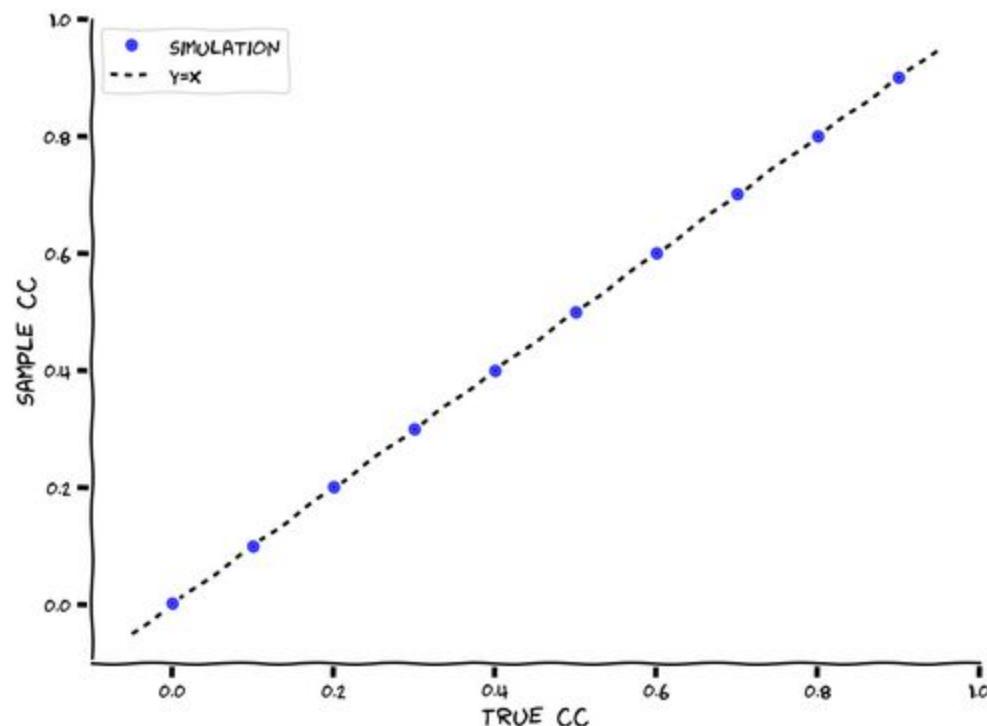
used to compute correlation b/w any 2 time series (input currents)

$\text{cov}(I_i, I_j) = \sum_{k=1}^L (I_i^k - \bar{I}_i)(I_j^k - \bar{I}_j)$

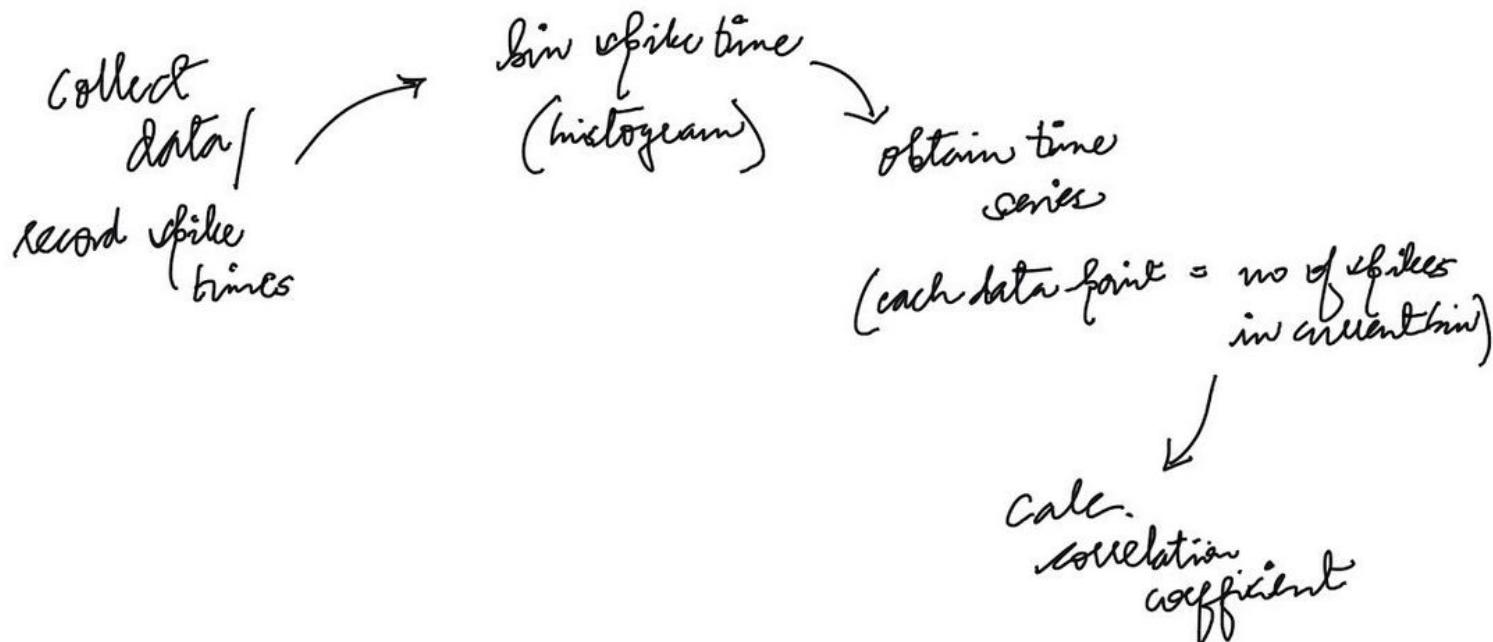
time bin

$\text{var}(I_i) = \sum_{k=1}^L (I_i^k - \bar{I}_i)^2$

current i @ time $k \cdot dt$



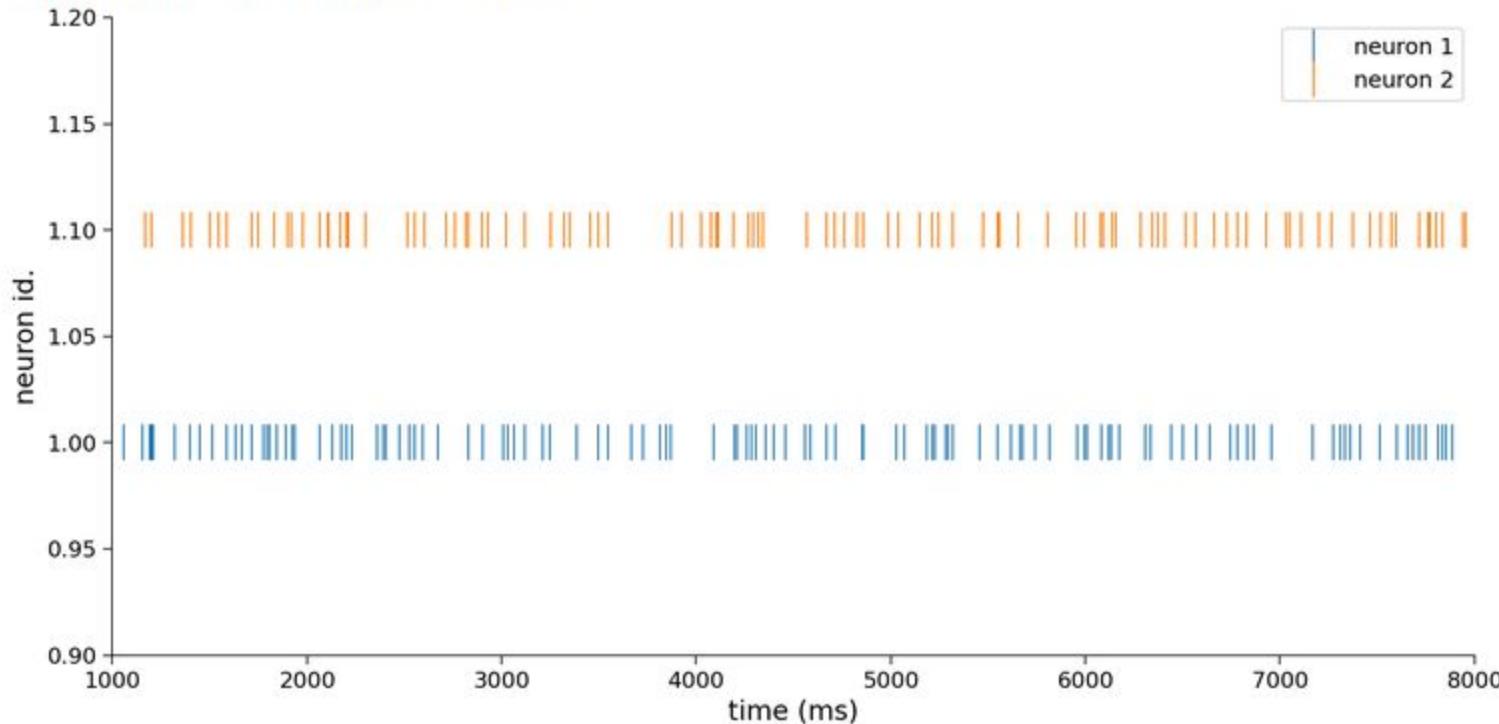
Estimate correlation coefficient (Algorithm)



Simulation time = 0.05 min

Input correlation = 0.3

Output correlation = 0.07832830696226945



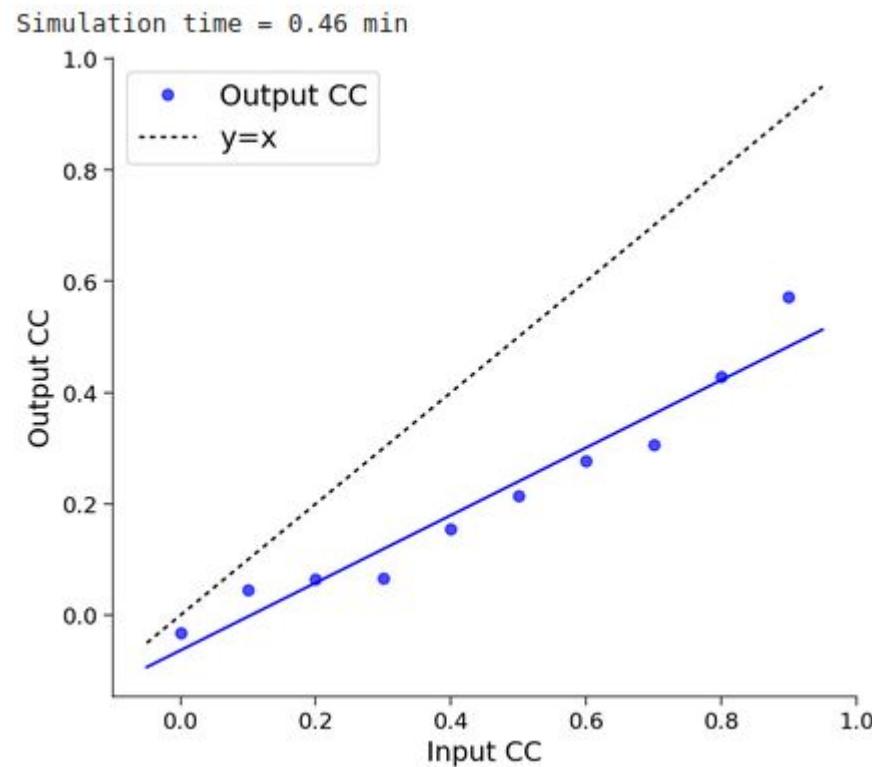
Food for thought

- Is the output correlation always smaller than the input correlation? If yes, why?
- Should there be a systematic relationship between input and output correlations?

Observations

- output correlation is smaller than input correlation
- output correlation varies linearly as a function of input correlation.

While the general result holds,
this relationship might change depending on
the neuron type.

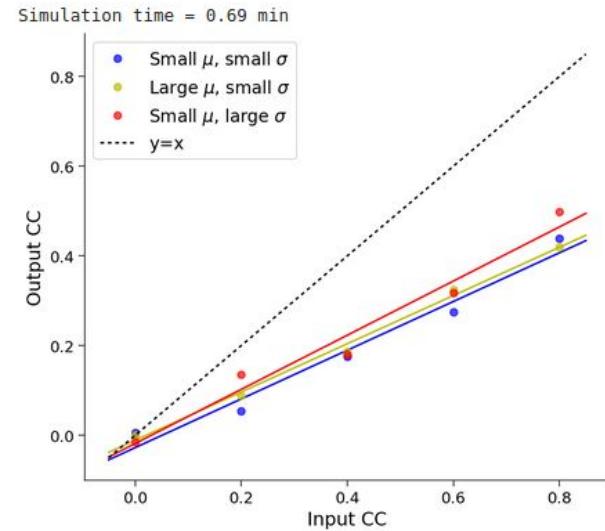


Correlation Transfer function

plot of input correlation vs. output correlation is called the **correlation transfer function** of the neurons. (can be taken as the input/output transfer function of LIF neurons for correlations, instead of the transfer function for input/output firing rates (i.e., F-I curve)).

The correlations transfer function appears to be linear.

What would you expect to happen to the slope of the correlation transfer function if you vary the mean and/or the standard deviation of the GWN?



Observations

Which part of the input current distribution is transferred to the spiking activity?

Intuitive understanding is difficult but this relationship arises due to non-linearities in the neuron F-I curve. When F-I curve is linear, output correlation is independent of the mean and standard deviation. But this relationship arises even in neurons with threshold-linear F-I curve.

Campbell theorem

mean and the variance of the synaptic current depends on the spike rate of a Poisson process.

Campbell theorem

$$\mu_{\text{syn}} = \lambda J \int P(t) dt$$

Shape of postsynaptic current
 as a function of time
 amplitude of postsynaptic current

$$\sigma_{\text{syn}}^2 = \lambda J \int P(t)^2 dt$$

firing rate of poisson input

Therefore, when we varied μ and/or σ of the GWN, we mimicked a change in the input firing rate. Note that, if we change the firing rate, both μ and σ will change simultaneously, not independently.

Here, since we observe an effect of μ and σ on correlation transfer, this implies that the input rate has an impact on the correlation transfer function.

FOOD FOR THOUGHT

- What are the factors that would make output correlations smaller than input correlations? (Notice that the colored lines are below the black dashed line)
- What does it mean for the correlation in the network?
- How do results obtained from injection of GWN apply to the case where correlated spiking inputs are injected in the two LIFs? Will the results be the same or different?

Observations

1. Anything that tries to reduce the mean or variance of the input e.g. mean can be reduced by inhibition, sigma can be reduced by the membrane time constant. Obviously, if the two neurons have different parameters that will decorrelate them. But more importantly, it is the slope of neuron transfer function that will affect the output correlation.
2. These observations pose an interesting problem at the network level. If the output correlation are smaller than the input correlation, then the network activity should eventually converge to zero correlation. But that does not happen. So there is something missing in this model to understand origin of synchrony in the network.
3. For spike trains, if we do not have explicit control over mu and sigma. And these two variables will be tied to the firing rate of the inputs. So the results will be qualitatively similar. But when we think of multiple spike inputs two different types of correlations arise.

Summary

WORKED ON ZERO TIME LAG CORRELATION.

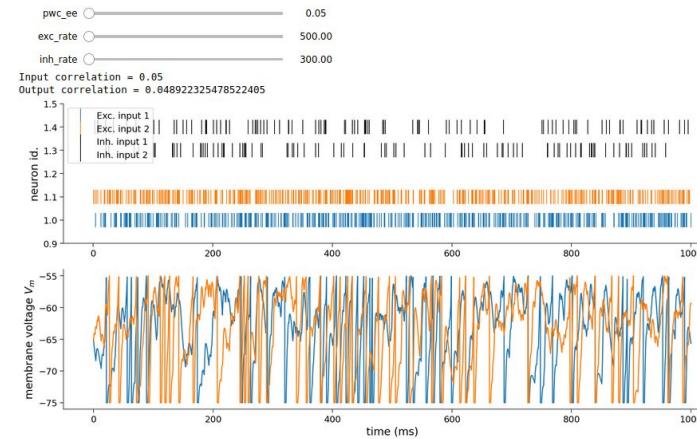
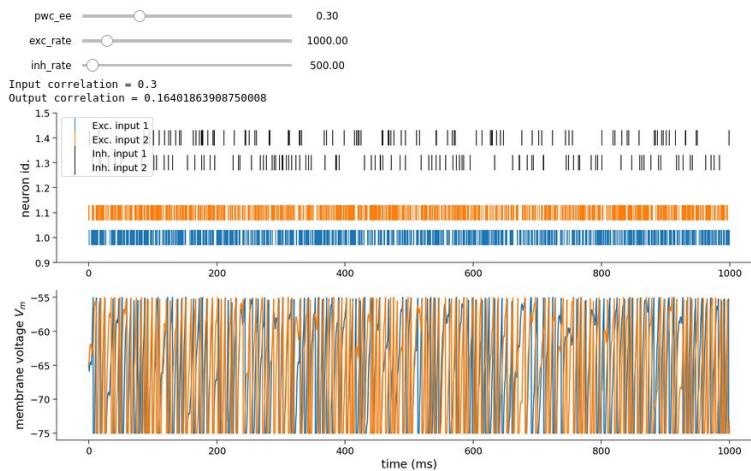
RESTRICTED ESTIMATION OF CORRELATION TO INSTANTANEOUS CORRELATIONS.

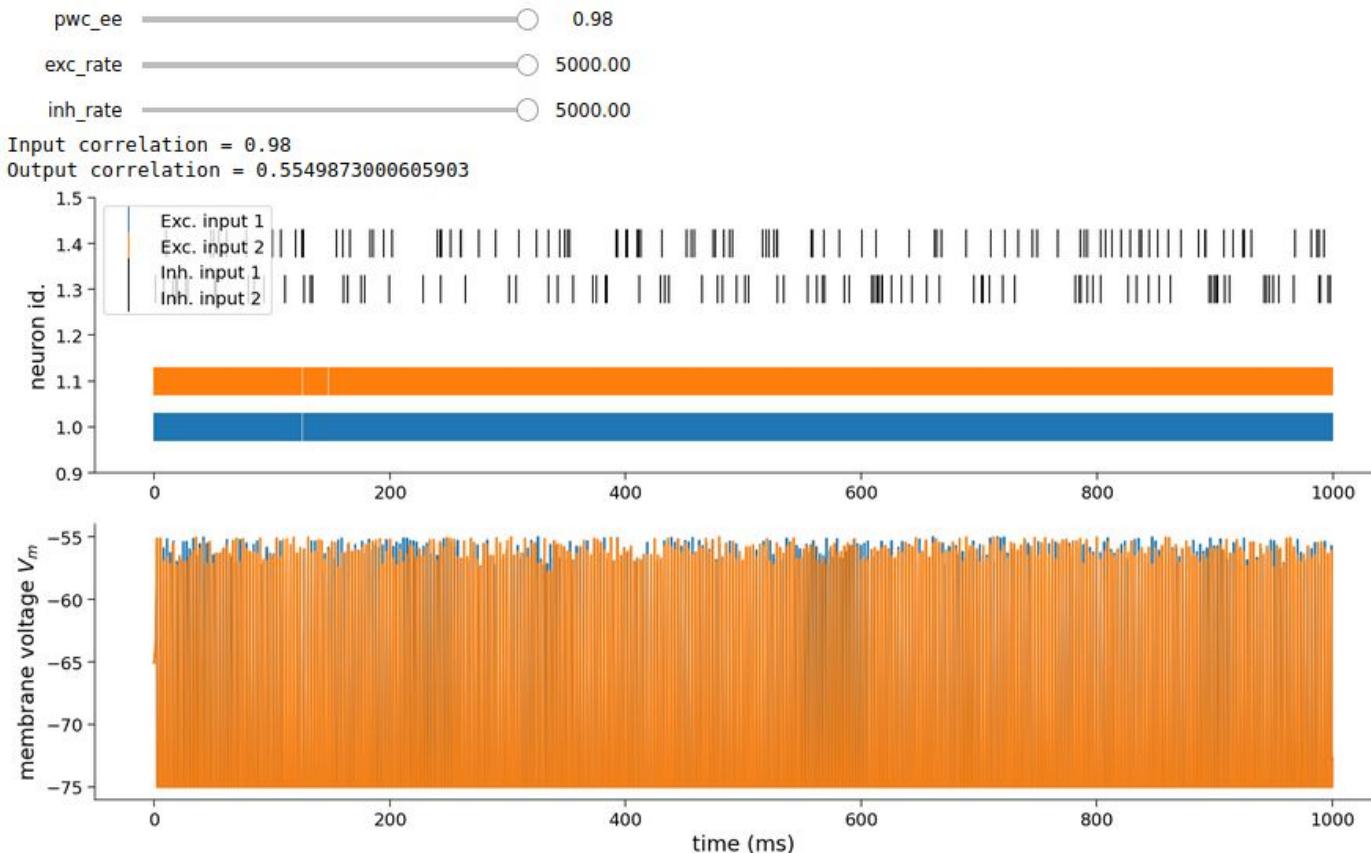
TIME-LAGGED CORRELATION => ESTIMATE THE CROSS-CORRELOGRAM OF THE SPIKE TRAINS AND FIND OUT THE DOMINANT PEAK AND AREA UNDER THE PEAK TO GET AN ESTIMATE OF OUTPUT CORRELATIONS.

Tutorial #2 bonus Explanations

CORRELATED SPIKE INPUT TO AN LIF NEURON

For simplicity, the correlation between inhibitory spike trains is set to 0.01.





Tutorial #3

Explanations

OBJECTIVE

Synapses connect neurons into neural networks or circuits. Specialized electrical synapses make direct, physical connections between neurons.

- focus on **chemical synapses**, which are more common in the brain. These synapses do not physically join neurons. Instead, a spike in the presynaptic cell causes a chemical, or neurotransmitter, to be released into a small space between the neurons called the synaptic cleft. Once the chemical diffuses across that space, it changes the permeability of the postsynaptic membrane, which may result in a positive or negative change in the membrane voltage.
- study how excitation and inhibition affect the patterns in the neurons' spiking output
- model chemical synaptic transmission and study some interesting effects produced by **static synapses** and **dynamic synapses** (weight is always fixed.)
- extend to model **dynamic synapses** -- whose synaptic strength is dependent on the recent spike history: synapses can either progressively increase or decrease the size of their effects on the post-synaptic neuron, based on the recent firing rate of its presynaptic partners. This feature of synapses in the brain is called **Short-Term Plasticity** and causes synapses to undergo Facilitation or Depression.
- simulate static synapses and define mean- or fluctuation-driven regimes
- study how a change in pre-synaptic firing history affects the synaptic weights (i.e., PSP amplitude)

Simulate synaptic conductance dynamics

Synaptic input *in vivo* consists of a mixture of **excitatory** neurotransmitters, which depolarizes the cell and drives it towards spike threshold, and **inhibitory** neurotransmitters that hyperpolarize it, driving it away from spike threshold. These chemicals cause specific ion channels on the postsynaptic neuron to open, resulting in a change in that neuron's conductance and, therefore, the flow of current in or out of the cell.

This process can be modelled by assuming that the presynaptic neuron's spiking activity produces transient changes in the postsynaptic neuron's conductance ($g_{syn}(t)$). Typically, the conductance transient is modeled as an exponential function.

Conductance transients generated using simple ordinary differential equation (ODE)

$$\frac{dg_{syn}(t)}{dt} = \bar{g}_{syn} \sum_k \delta(t - t_k) - g_{syn}(t)/\tau_{syn}$$



synaptic weight

(max conductance elicited
by each incoming spike)

synaptic
time constant

by Ohm's law: (converts conductance changes to current)

reverse potential

$$I_{syn}(t) = g_{syn}(t)(V(t) - E_{syn})$$

Colored Noise

The reversal potential E_{syn} determines the direction of current flow and the excitatory or inhibitory nature of the synapse.

Thus, incoming spikes are filtered by an exponential-shaped kernel, effectively low-pass filtering the input. In other words, synaptic input is not white noise, but it is, in fact, colored noise, where the color (spectrum) of the noise is determined by the synaptic time constants of both excitatory and inhibitory synapses.

total synaptic current

$$I_{\text{syn}}(v(t), t) = -g_E(t)(v - E_E) - g_I(t)(v - E_I)$$

membrane potential dynamics of LIF Neuron
under synaptic current drive

$$I_m \frac{dV(t)}{dt} = - (V(t) - E_L) - \frac{g_E(t)}{g_L} (V(t) - E_E) - \frac{g_I(t)}{g_L} (V(t) - E_I) + \frac{I_{\text{inj}}}{g_L}$$

external current injected

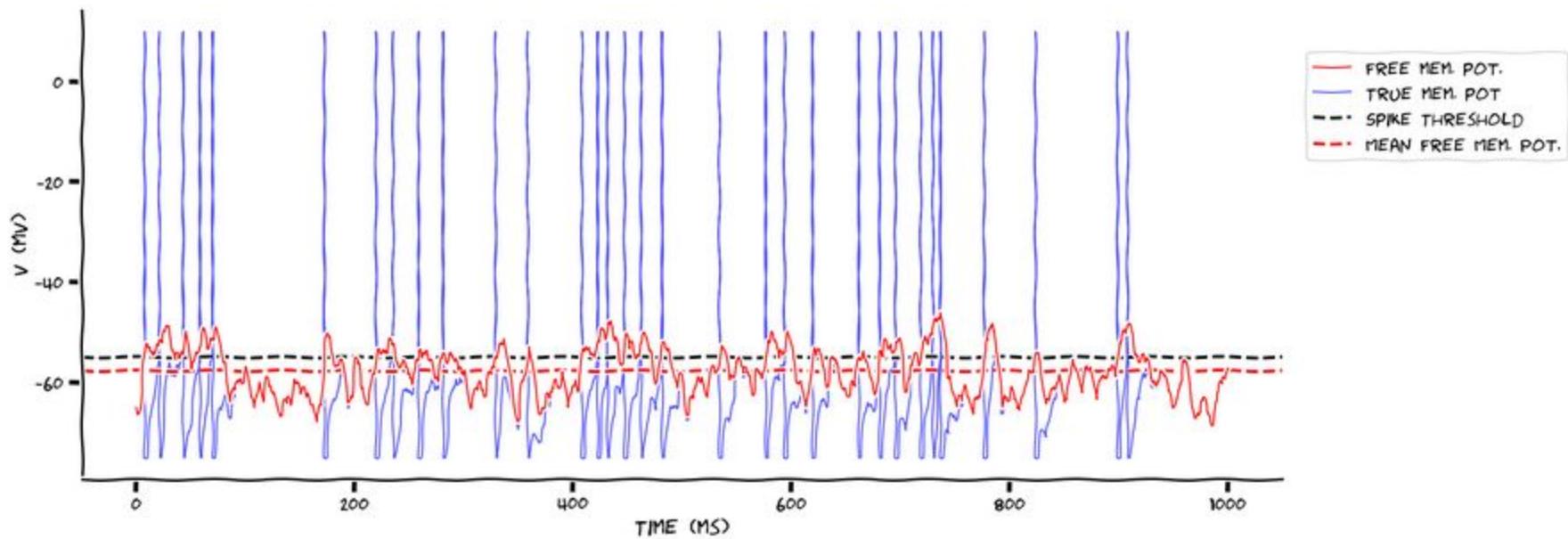
excitatory
inhibitory
conductance
reversal potentials

Output of a single neuron (spike count/rate and spike time irregularity) changes when we stimulate the neuron with DC and GWN. The simplest model of input spikes is given when every input spike arrives independently of other spikes, i.e., we assume that the input is Poissonian.

#TASK: study how the neuron behaves when it is bombarded with both excitatory and inhibitory spikes trains -- as happens *in vivo*.

Measure the mean free membrane potential

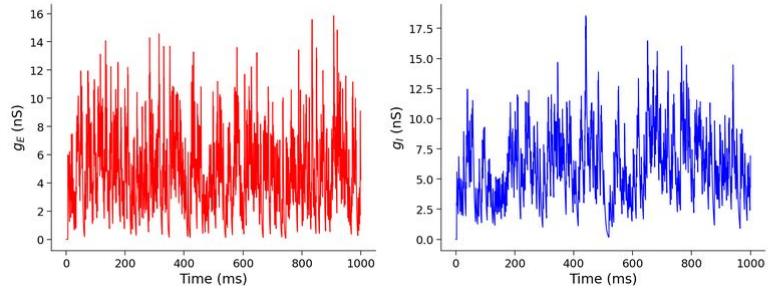
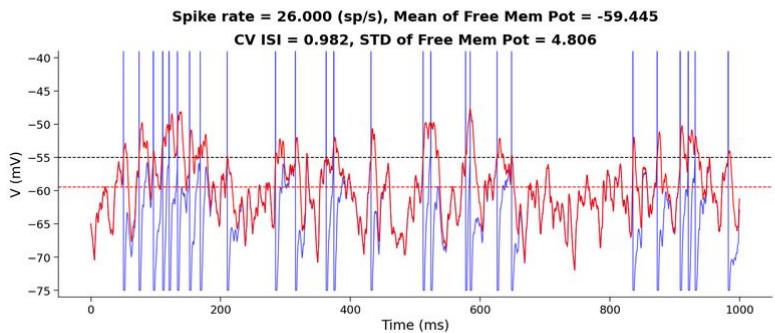
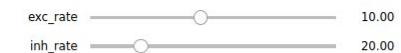
- SIMULATE THE CONDUCTANCE-BASED LIF NEURON WITH PRESYNAPTIC SPIKE TRAINS GENERATED BY A POISSON_GENERATOR WITH RATE 10 Hz FOR BOTH EXCITATORY AND INHIBITORY INPUTS. HERE, WE CHOOSE 80 EXCITATORY PRESYNAPTIC SPIKE TRAINS AND 20 INHIBITORY ONES.
- CV ISI CAN DESCRIBE THE IRREGULARITY OF THE OUTPUT SPIKE PATTERN.
- INTRODUCE A NEW DESCRIPTOR OF THE NEURON MEMBRANE, I.E., THE FREE MEMBRANE POTENTIAL (FMP) -- THE MEMBRANE POTENTIAL OF THE NEURON WHEN ITS SPIKE THRESHOLD IS REMOVED.
- ALTHOUGH THIS IS COMPLETELY ARTIFICIAL, CALCULATING THIS QUANTITY ALLOWS US TO GET AN IDEA OF HOW STRONG THE INPUT IS.



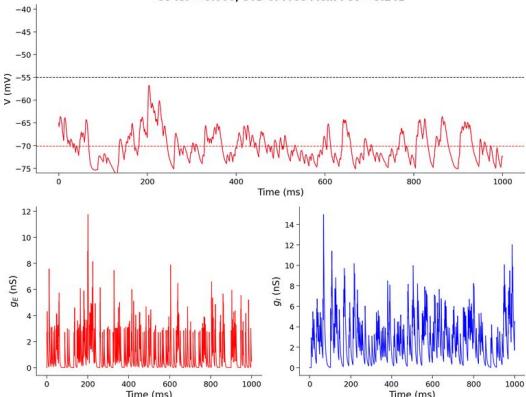
Conductance-based LIF with different E/I input

- VARYING RATIO OF EXCITATORY TO INHIBITORY INPUTS CHANGES THE FIRING RATE AND THE SPIKE TIME REGULARITY
- VARY THE STRENGTH AND/OR THE NUMBER OF THESE CONNECTIONS AS WELL.
- MEAN FREE MEMBRANE POTENTIAL (RED DOTTED LINE) AND ITS LOCATION WITH RESPECT TO THE SPIKE THRESHOLD (BLACK DOTTED LINE).
- DEVELOP A HEURISTIC ABOUT THE MEAN OF THE FMP AND SPIKE TIME IRREGULARITY (CVSI)

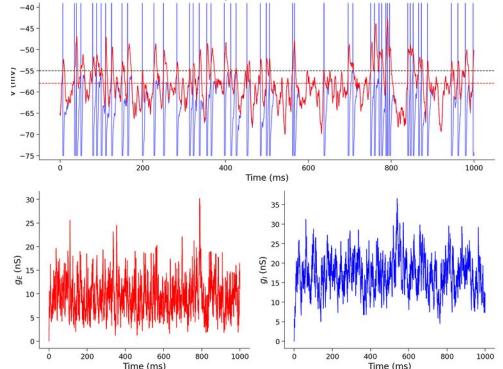
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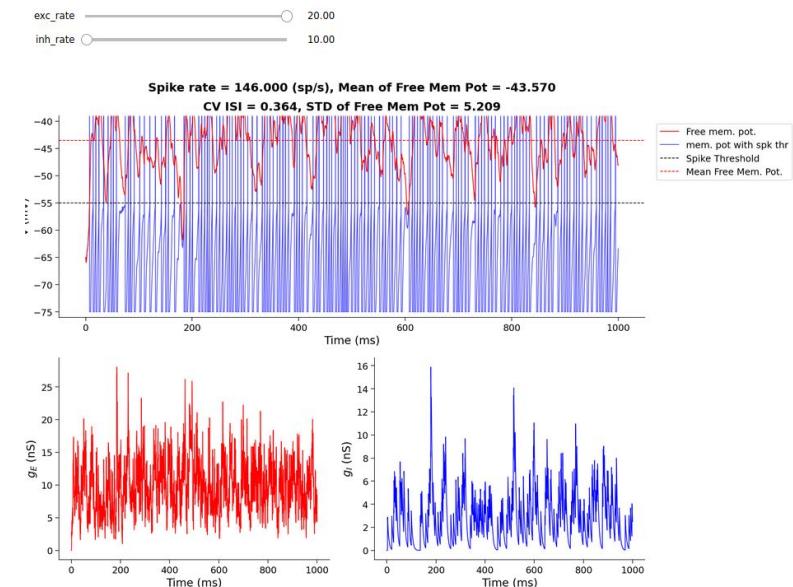
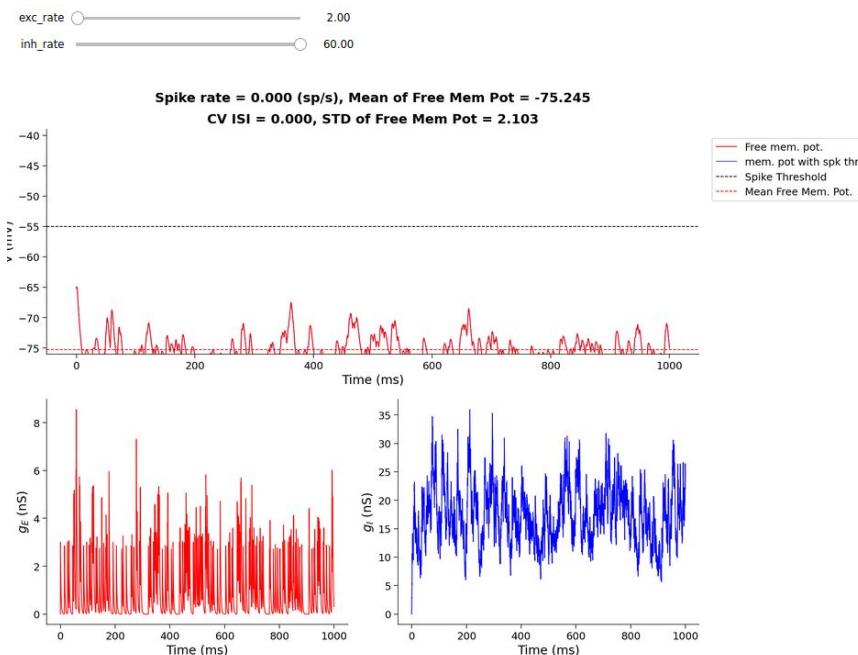


Spike rate = 0.000 (sp/s), Mean of Free Mem Pot = -70.160
CV ISI = 0.000, STD of Free Mem Pot = 3.241



Spike rate = 49.000 (sp/s), Mean of Free Mem Pot = -57.953
CV ISI = 0.768, STD of Free Mem Pot = 4.434





MEAN-DRIVEN AND FLUCTUATION-DRIVEN REGIMES

- note that when the mean FMP is above spike threshold, the fluctuations in the FMP are rather small, and the neuron spikes in a fairly regular fashion. This regime, where the mean FMP is above the spike threshold, is called **mean-driven regime**
- When the mean FMP is below the spike threshold, the fluctuations in the FMP are large, and the neuron's spikes are driven by these fluctuations. As a consequence, the neuron spikes in more Poisson-like fashion. This regime, where the mean FMP is below the spike threshold, and spikes are driven by the fluctuations, is called **fluctuation-driven regime**.

Food for thought

- How much can you increase the spike pattern variability? Under what condition(s) might the neuron respond with Poisson-type spikes? Note that we injected Poisson-type spikes.

We can push the neuron to spike almost like a Poisson neuron. Of course given that there is a refractoriness it will never spike completely like a Poisson process. Poisson type spike irregularity will be achieved when mean is small (far from the spike threshold) and fluctuations are large. This will be achieved when excitatory and inhibitory rates are balanced -- i.e. ratio of exc and inh. spike rate is constant as you vary the inout rate.

- Link to the balance of excitation and inhibition: one of the definitions of excitation and inhibition balance is that mean free membrane potential remains constant as excitatory and inhibitory input rates are increased. What do you think happens to the neuron firing rate as we change excitatory and inhibitory rates while keeping the neuron in balance?

Firing rate will increase because fluctuations will increase as we increase exc. and inh. rates. But if synapses are modelled as conductance as opposed to currents, fluctuations may start decrease at high input rates because neuron time constant will drop.

dynamics of excitatory STP:

$$\frac{d\mu_E}{dt} = -\frac{\mu_E}{\tau_f} + \mu_0 (1 - \mu_E^-) \delta(t - t_{sp})$$

time constant

fraction/probability
before spike
determines increment of
n produced by spikes

$$\frac{dR_E}{dt} = \frac{1 - R_E}{\tau_d} - \mu_E^+ R_E^- \delta(t - t_{sp})$$

overall of the
times (k)

$$\frac{dg_E(t)}{dt} = -\frac{g_E}{\tau_E} + \bar{g}_E \mu_E^+ R_E^- \delta(t - t_{sp})$$

transmission
after spike.

max. excitatory
conductance.

synapses whose weight change in some input conditions.

Short-term plasticity (STP) is a phenomenon in which synaptic efficacy changes over time in a way that reflects the history of presynaptic activity. Two types of STP, with opposite effects on synaptic efficacy, have been experimentally observed. They are known as Short-Term Depression (STD) and Short-Term Facilitation (STF).

The mathematical model (*for more information see [here](#)*) of STP is based on the concept of a limited pool of synaptic resources available for transmission (R), such as, for example, the overall amount of synaptic vesicles at the presynaptic terminals. The amount of presynaptic resource changes in a dynamic fashion depending on the recent history of spikes.

Following a presynaptic spike, (i) the fraction u (release probability) of the available pool to be utilized increases due to spike-induced calcium influx to the presynaptic terminal, after which (ii) u is consumed to increase the post-synaptic conductance. Between spikes, u decays back to zero with time constant T_f and R recovers to 1 with time constant T_d .

Depression and Facilitation

The interplay between the dynamics of u and R determines whether the joint effect of uR is dominated by depression or facilitation. In the parameter regime of $\tau_d \gg \tau_f$ and for large U_0 , an initial spike incurs a large drop in R that takes a long time to recover; therefore, the synapse is STD-dominated. In the regime of $\tau_d \ll \tau_f$ and for small U_0 , the synaptic efficacy is increased gradually by spikes, and consequently, the synapse is STF-dominated. This phenomenological model successfully reproduces the kinetic dynamics of depressed and facilitated synapses observed in many cortical areas.

Euler numerical integration method
(calculation of each derivative at step n)

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$$d\mu_E = \frac{-\mu_E[t]}{T_f} dt + \nu_0 (1 - \mu_E[t]) \cdot \text{sp-or-not}[t+dt]$$

$$dR_E = \frac{1 - R_E[t]}{T_d} dt - \mu_E[t+dt] R_E[t] \cdot \text{sp-or-not}[t+dt]$$

$$dg_E = -g_E[t] dt + \bar{g}_E \mu_{\bar{c}}[t+dt] R_E[t] \cdot \text{sp-or-not}[t+dt]$$

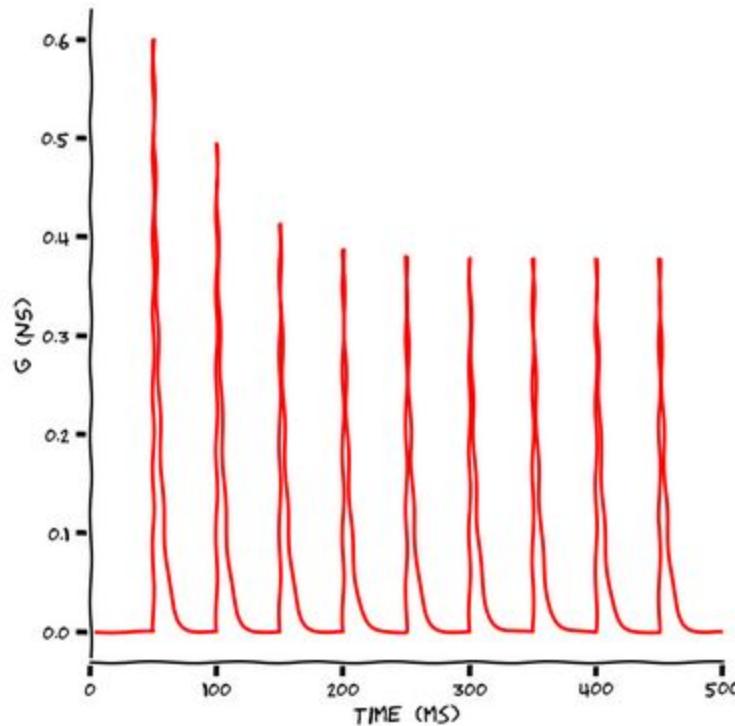
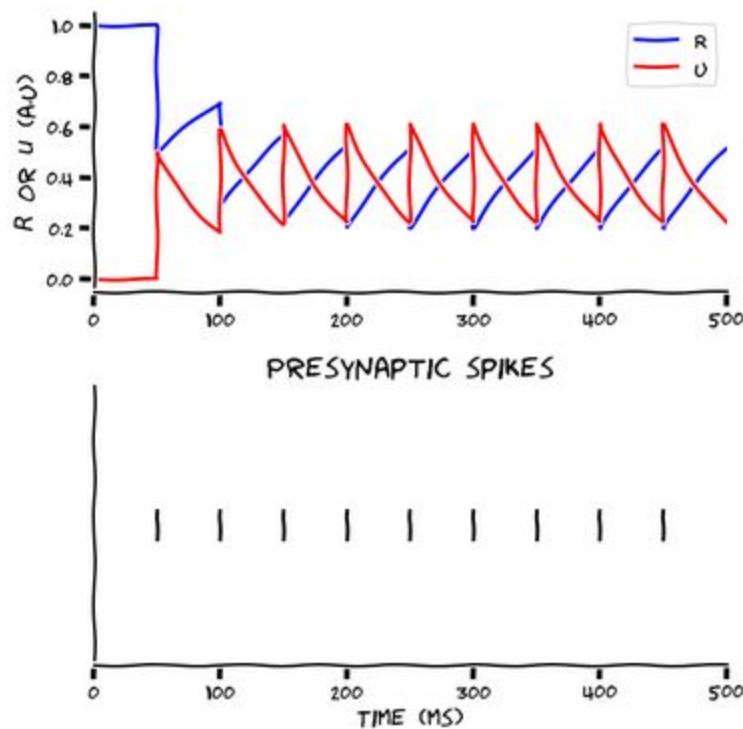
$$\text{sp-or-not} = \begin{cases} 1 & \text{if spikes in time window } dt \\ 0 & \text{otherwise} \end{cases}$$

Updating values.

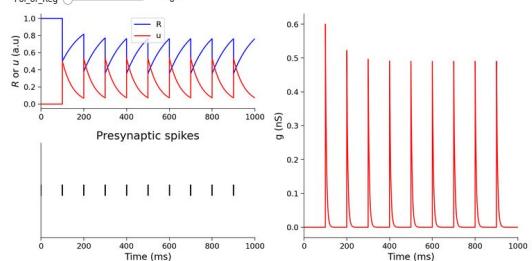
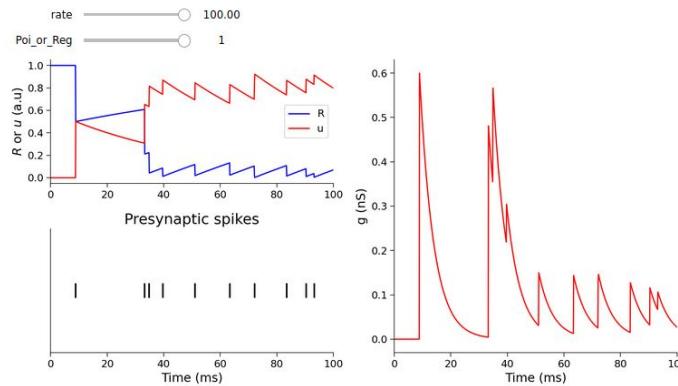
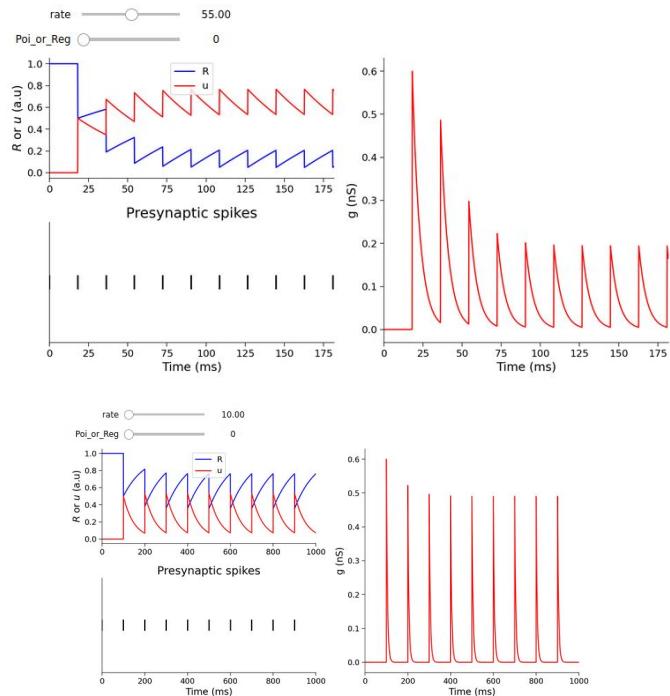
$$\mu_E[t+dt] = \mu_E[t] + d\mu_E$$

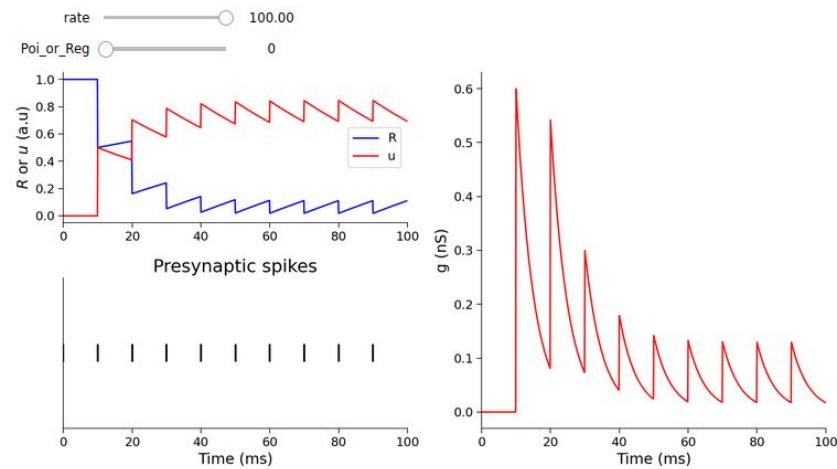
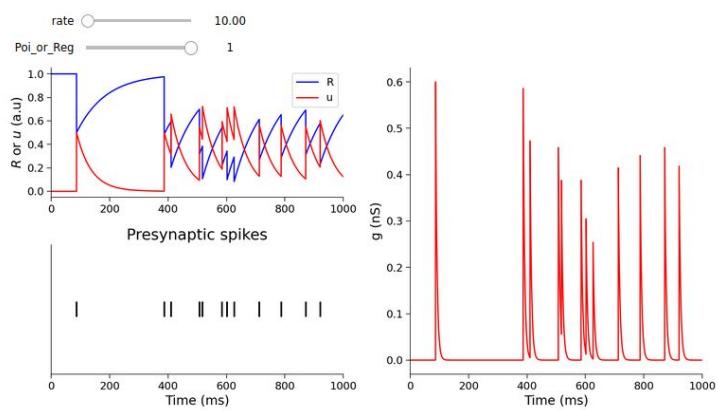
$$R_E[t+dt] = R_E[t] + dR_E.$$

$$g_E[t+dt] = g_E[t] + dg_E$$



Short-term synaptic depression (STD) changes for different firing rates of the presynaptic spike train and how the amplitude synaptic conductance g changes with every incoming spike until it reaches its stationary state.





Observations

Increasing the input rate, we decrease the synaptic efficacy, i.e., the synaptic conductance decreases. This is the case for both Poisson or a regular spiking input.

In case of regular spiking, the synaptic conductance reaches a steady state. This will not happen in the case of Poisson type spikes.

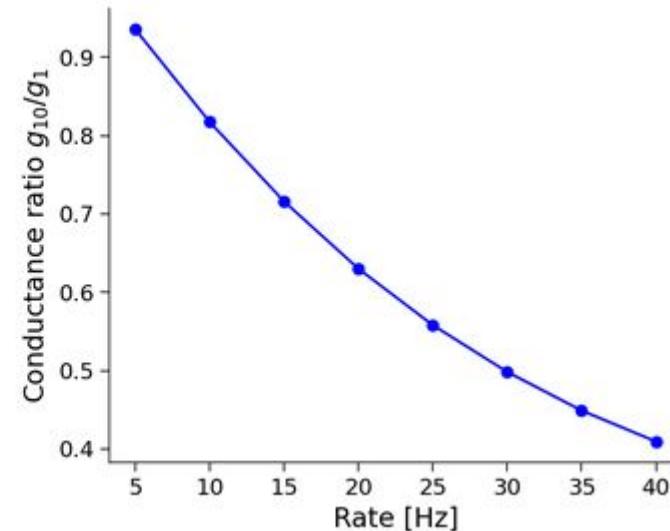
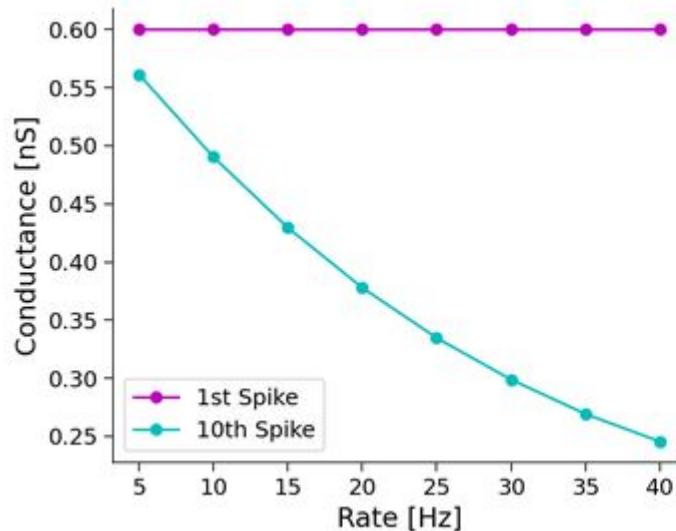
Synaptic depression and presynaptic firing rate

- experimental values of the PSP amplitude produced by a connection between two neocortical excitatory neurons (PSP amplitude depends on the spike history, and therefore on the spike rate of the presynaptic neuron.)
- study how the ratio of the synaptic conductance corresponding to the first and 10th spikes change as a function of the presynaptic firing rate (experimentalists often take the ratio of first and second PSPs).

For computational efficiency, we assume that the presynaptic spikes are regular. -> single trials

STD conductance ratio with different input rate

As we increase the input rate the ratio of the first to tenth spike is increased, because the tenth spike conductance becomes smaller. This is a clear evidence of synaptic depression, as using the same amount of current has a smaller effect on the neuron.

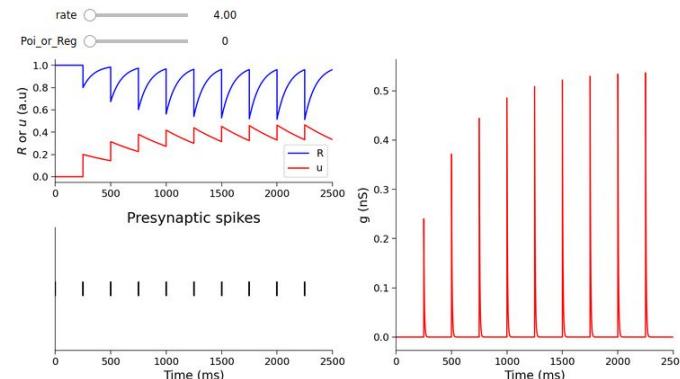
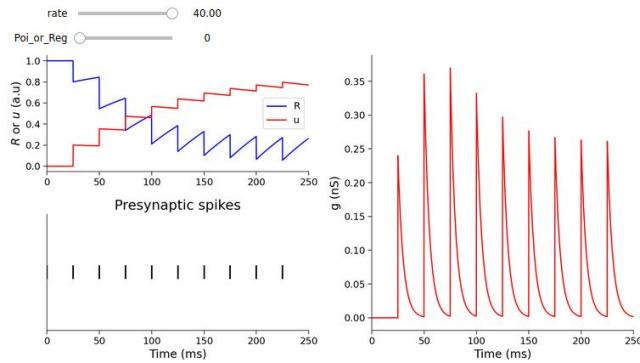
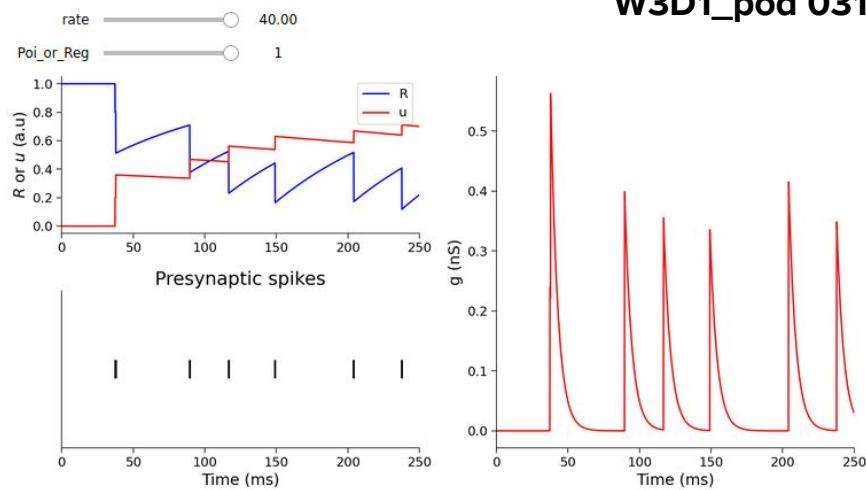
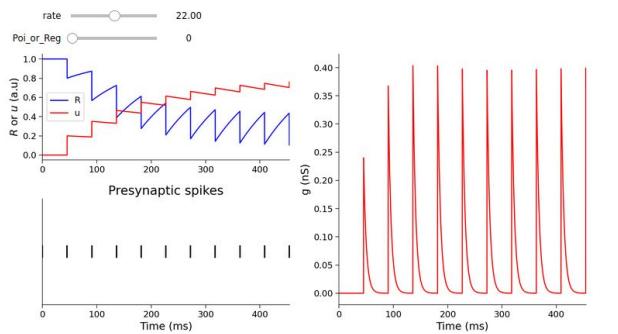


Short-term synaptic facilitation (§ 27)

- for STD, $V_0=0.5$, $\tau_{ad}=100.$, $\tau_{af}=50.$
- for STP, $V_0=0.2$, $\tau_{ad}=100.$, $\tau_{af}=750.$

How does the synaptic conductance change as we change the input rate? What do you observe in the case of a regular input and a Poisson type one?

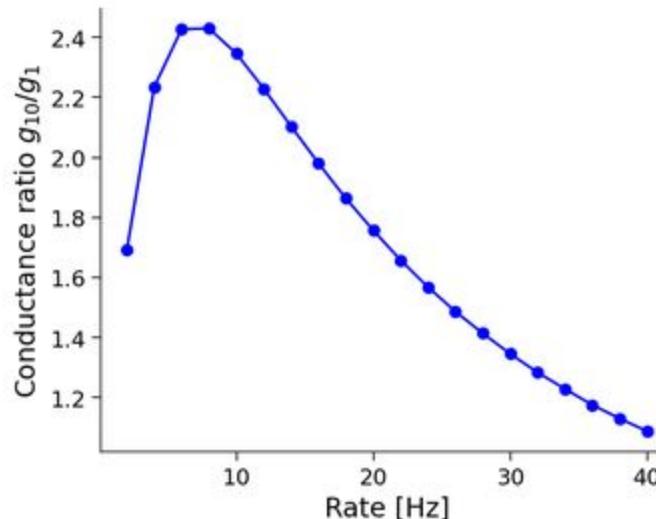
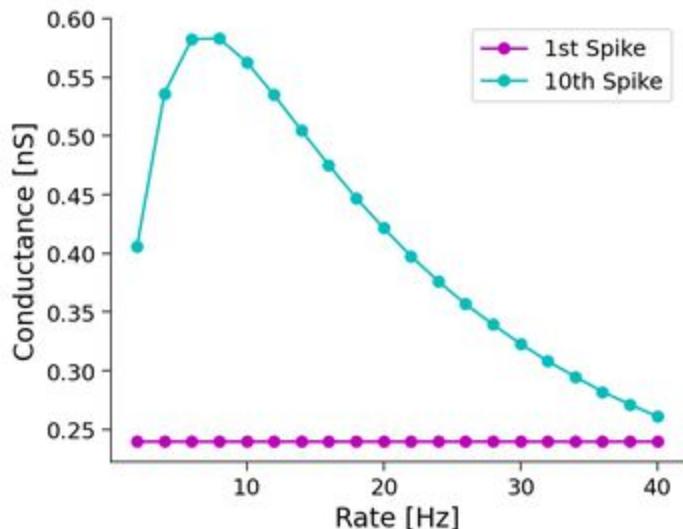
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- ▼ Synaptic facilitation and presynaptic firing rate

Here, we will study how the ratio of the synaptic conductance corresponding to the 1st and 10th spike changes as a function of the presynaptic rate.

[16] STF conductance ratio with different input rates



FOOD FOR THOUGHT

Why does the ratio of the first and tenth spike conductance changes in a non-monotonic fashion for synapses with STF, even though it decreases monotonically for synapses with STD?

Because we have a facilitatory synapses, as the input rate increases synaptic resources released per spike also increase. Therefore, we expect that the synaptic conductance will increase with input rate. However, total synaptic resources are finite. And they recover in a finite time. Therefore, at high frequency inputs synaptic resources are rapidly deleted at a higher rate than their recovery, so after first few spikes, only a small number of synaptic resources are left. This results in decrease in the steady-state synaptic conductance at high frequency inputs.

Summary

- modelling conductance-based synapses and also how to incorporate short-term dynamics in synaptic weights.
- static synapses and how excitation and inhibition affect the neuronal output
- mean- or fluctuation-driven regimes
- short-term dynamics of synapses (both facilitation and depression)
- study how a change in presynaptic firing history affects the synaptic weights!

Tutorial #3 Bonus Explanations

CONDUCTANCE-BASED LIF WITH STP

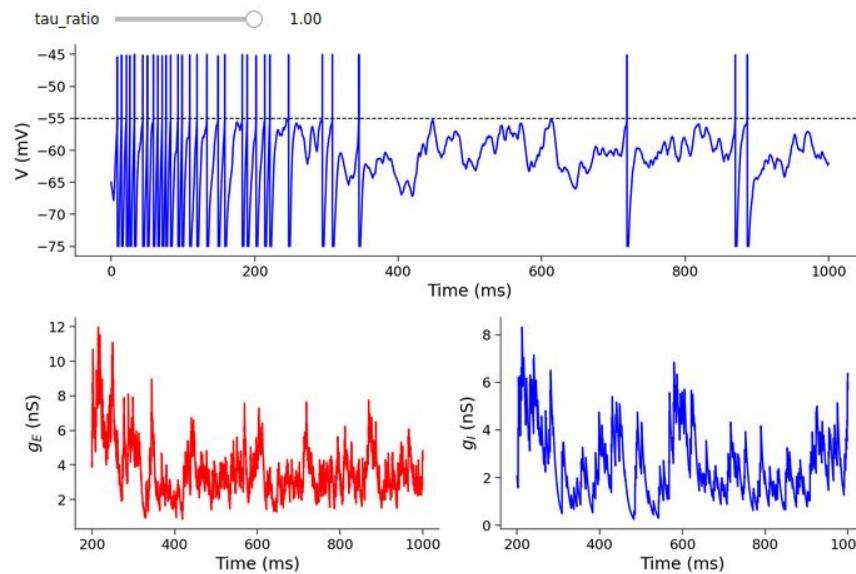
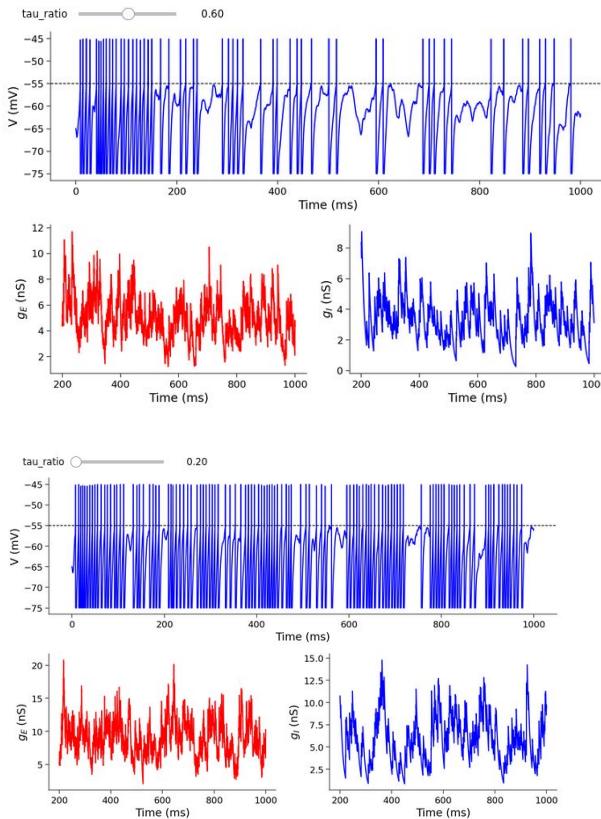
- presynaptic firing rate affects the presynaptic resource availability and thereby the synaptic conductance.
- while the synaptic conductances are changing, the output of the postsynaptic neuron will change as well.
- put the STP on synapses impinging on an LIF neuron and see what happens.

simulation of a postsynaptic neuron with 10 synapses driven by Poisson type spike trains

ASSUME THAT BOTH EXCITATORY AND INHIBITORY SYNAPSES SHOW SHORT-TERM DEPRESSION.

CHANGE THE NATURE OF SYNAPSES AND STUDY HOW SPIKE PATTERN VARIABILITY CHANGES

TAU_D = 500*TAU_RATIO (ms) AND TAU_F = 300*TAU_RATIO (ms).



OBSErvATIONS

- vary the tau ratio we are increasing τ_{mE} and τ_{mI} i.e. by increasing tau ratio we are increasing the synaptic depression. The effect is same on both Exc and Inh conductances. This is visible as a clear decrease in the firing rate of the neuron from 300-400ms onwards.
- It is curious that while both excitatory and inhibitory conductances have depressed but output firing rate has still decreased.

There are two explanations of this:

1. excitation has depressed more than the inhibition from their starting values.
2. because synaptic conductances have depressed, membrane fluctuation size has decreased.

LIKELY EXPLANATIONS

because synaptic conductances have depressed, membrane fluctuation size has decreased.

If depression at these synapses is closely matched, the balance between excitation and inhibition, and hence the overall gain of the circuit, will be relatively constant. On the other hand, if depression differs at these synapses, then the gain of the circuit may shift during repetitive stimulation.

If depression is more prominent at inhibitory than excitatory synapses, the gain will increase with increasing activity, whereas if depression is more prominent at excitatory than inhibitory synapses, the gain will decrease.

So, depression of synaptic conductances with membrane fluctuation size seems more likely.

ref: <https://www.jneurosci.org/content/19/11/4293>

STP Synapse Parameter Exploration

Vary the parameters and observe the spiking pattern of the postsynaptic neuron.

Will the neuron show higher irregularity if the synapses have STP? If yes, what should be the nature of STP on static and dynamic synapses, respectively?

#TASK: Calculate the CVSI for different tau_ratio after simulating the LIF neuron with STP

Functional implications of short-term dynamics of synapses

As you have seen above, if the firing rate is stationary, the synaptic conductance quickly reaches a fixed point. On the other hand, if the firing rate transiently changes, synaptic conductance will vary -- even if the change is as short as a single inter-spike-interval. Such small changes can be observed in a single neuron when input spikes are regular and periodic. If the input spikes are Poissonian, then one may have to perform an average over several neurons.

Tutorial #4

Explanations

Objectives

- focus on building a model of a synapse in which its synaptic strength changes as a function of the relative timing (i.e., time difference) between the spikes of the presynaptic and postsynaptic neurons, respectively. This change in the synaptic weight is known as **spike-timing dependent plasticity (STDP)**.
- build a model of synapse that show STDP
- study how correlations in input spike trains influence the distribution of synaptic weights
- model the presynaptic input as Poisson type spike trains. The postsynaptic neuron will be modeled as an LIF neuron
- assume that a single postsynaptic neuron is driven by N presynaptic neurons. That is, there are N synapses, and we will study how their weights depend on the statistics or the input spike trains and their timing with respect to the spikes of the postsynaptic neuron.

biphasic exponentially decaying function.

The phenomenology of STDP is generally described as a biphasic exponentially decaying function.

instantaneous change in weights

$$\Delta w = A_+ e^{(t_{pre} - t_{post})/\tau_+}$$

max

strengthening
if $t_{post} > t_{pre}$

$$\Delta w = -A_- e^{-(t_{pre} - t_{post})/\tau_-}$$

min

weakening
if $t_{post} < t_{pre}$

change in synaptic weight

A : Synaptic modification

(occurs when timing difference between
presynaptic / postsynaptic spikes ~ 0)

T : determine ranges of pre to post synaptic interpike intervals
over which synaptic strengthening / weakening occurs.
 $\Delta w > 0$ (postsynaptic neuron spikes after presynaptic neuron).

This model captures the phenomena that repeated occurrences of presynaptic spikes within a few milliseconds **before** postsynaptic action potentials lead to long-term potentiation (LTP) of the synapse, whereas repeated occurrences of presynaptic spikes **after** the postsynaptic ones lead to long-term depression (LTD) of the same synapse.

$$\Delta t = t_{\text{pre}} - t_{\text{post}}$$

for simplicity -
 $L_i = L_- = L_{\text{stdp}}$

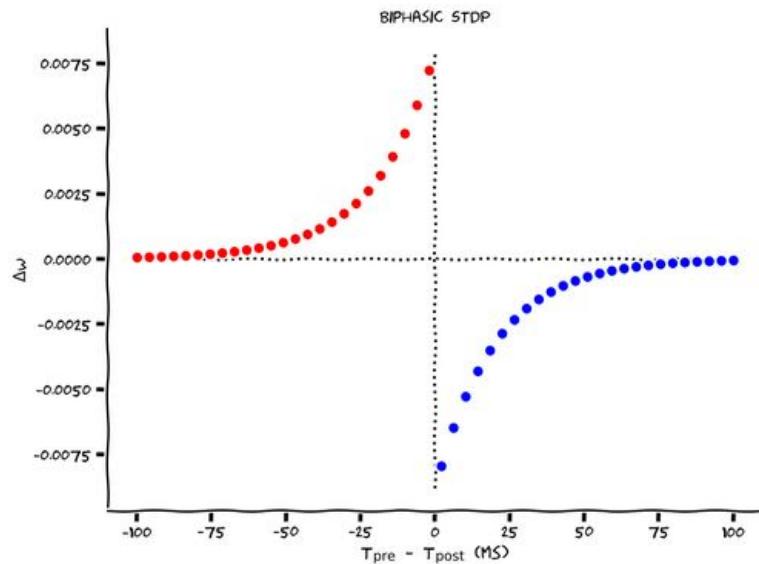
timing of post
 synaptic spike

timing of presynaptic spike

latency between
 pre & post
 synaptic

COMPUTE THE STDP CHANGES ΔW

VISUALIZE THE STDP KERNEL, WHICH DESCRIBES HOW MUCH THE SYNAPTIC WEIGHT WILL CHANGE GIVEN A LATENCY BETWEEN THE PRESYNAPTIC AND POSTSYNAPTIC SPIKES.



Keeping track of pre- and postsynaptic spikes

Since a neuron will receive numerous presynaptic spike inputs, in order to implement STDP by taking into account different synapses, keep track of the pre- and postsynaptic spike times

equation for each postsynaptic neuron .

$$\tau_- \frac{dM}{dt} = -M$$

when postsynaptic neuron spikes -

$$M(t) = M(t) - A_-$$

Teaches number of presynaptic spikes over timescale τ_-

for each presynaptic neuron

$$\tau_p \frac{dP}{dt} = -P$$

when presynaptic neuron spikes.

$$P(t) = P(-) + A_t$$

The variables $\mathcal{M}(t)$ and $\mathcal{P}(t)$ are very similar to the equations for the synaptic conductances, i.e., $g_i(t)$, except that they are used to keep track of pre- and postsynaptic spike times on a much longer timescale. Note that, $\mathcal{M}(t)$ is always negative, and $\mathcal{P}(t)$ is always positive. You can probably already guess that \mathcal{M} is used to induce STD and \mathcal{P} to induce STP because they are updated by \mathcal{A}^- and \mathcal{A}^+ , respectively.

Important note:

$\mathcal{P}(t)$ depends on the presynaptic spike times. If we know the presynaptic spike times, \mathcal{P} can be generated before simulating the postsynaptic neuron and the corresponding STDP weights.

Visualization of P

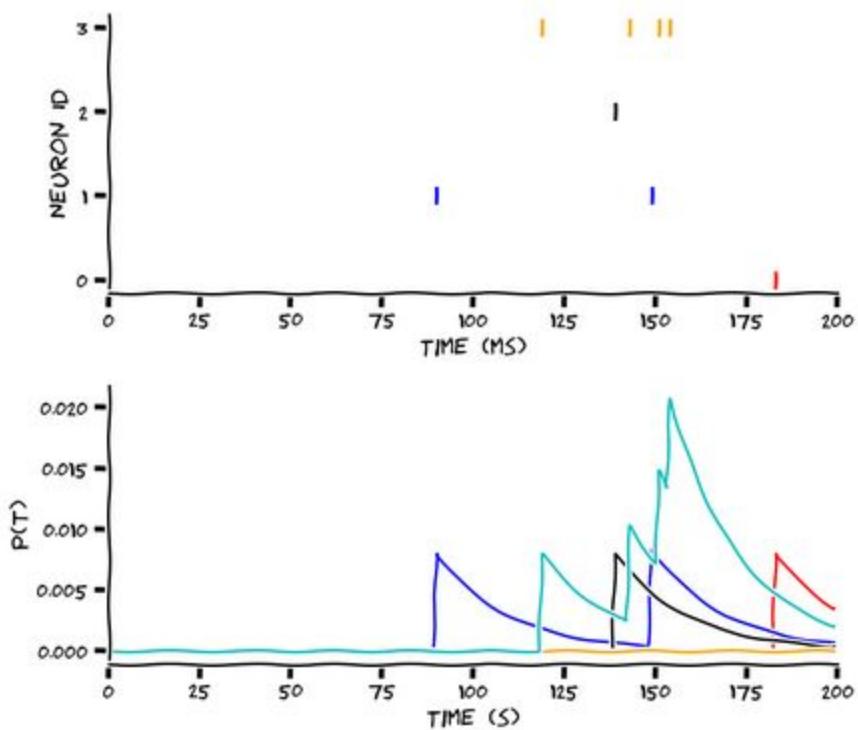
consider a scenario in which there is a single postsynaptic neuron connected to N presynaptic neurons. For instance, we have one postsynaptic neuron which receives Poisson type spiking inputs from five presynaptic neurons. We can simulate P for each one of the presynaptic neurons.

dynamics of membrane potential in LIF model

$$\frac{dp}{dt} = -\frac{dt}{T_+} P(t) + A_+ \cdot \text{sp.-or.-not}[t + dt]$$

in time step dt
 $P(t)$ will decrease
 by an amt of $\frac{dt}{T_+} P(t)$

↳ if presynaptic spike arrives
 $P(t)$ will instantaneously increase by an amt of A_+ .



Implementation of STDP

Finally, to implement STDP in spiking networks, we will change the value of the peak synaptic conductance based on the presynaptic and postsynaptic timing, thus using the variables $P(t)$ and $M(t)$. Each synapse i has its own peak synaptic conductance ($g^+ i$), which may vary between $[0, g^+ \text{max}]$, and will be modified depending on the presynaptic and postsynaptic timing.

postsynaptic neuron spikes,
peak conductance of EACH synapse is updated:

$$\bar{g}_i = \bar{g}_i + p_i(t) \bar{g}_{max} \cdot t^i$$

 tracks time since last spike
of i th pre-synaptic neuron &
is always positive.

if pre synaptic spikes before postsynaptic,
peak conductance increases.

When i th presynaptic neuron elicits a spike
corresponding peak conductance updated as :

$$\bar{g}_i = \bar{g}_i + M(t) \bar{g}_{\max}$$

tracks time since last
postsynaptic potential \rightarrow is
always negative

if postsynaptic neuron spikes shortly before presynaptic,
peak conductance decreases

Connect N presynaptic neurons to single postsynaptic neuron through N poisson type spikes.

Assumption: All inputs are excitatory.

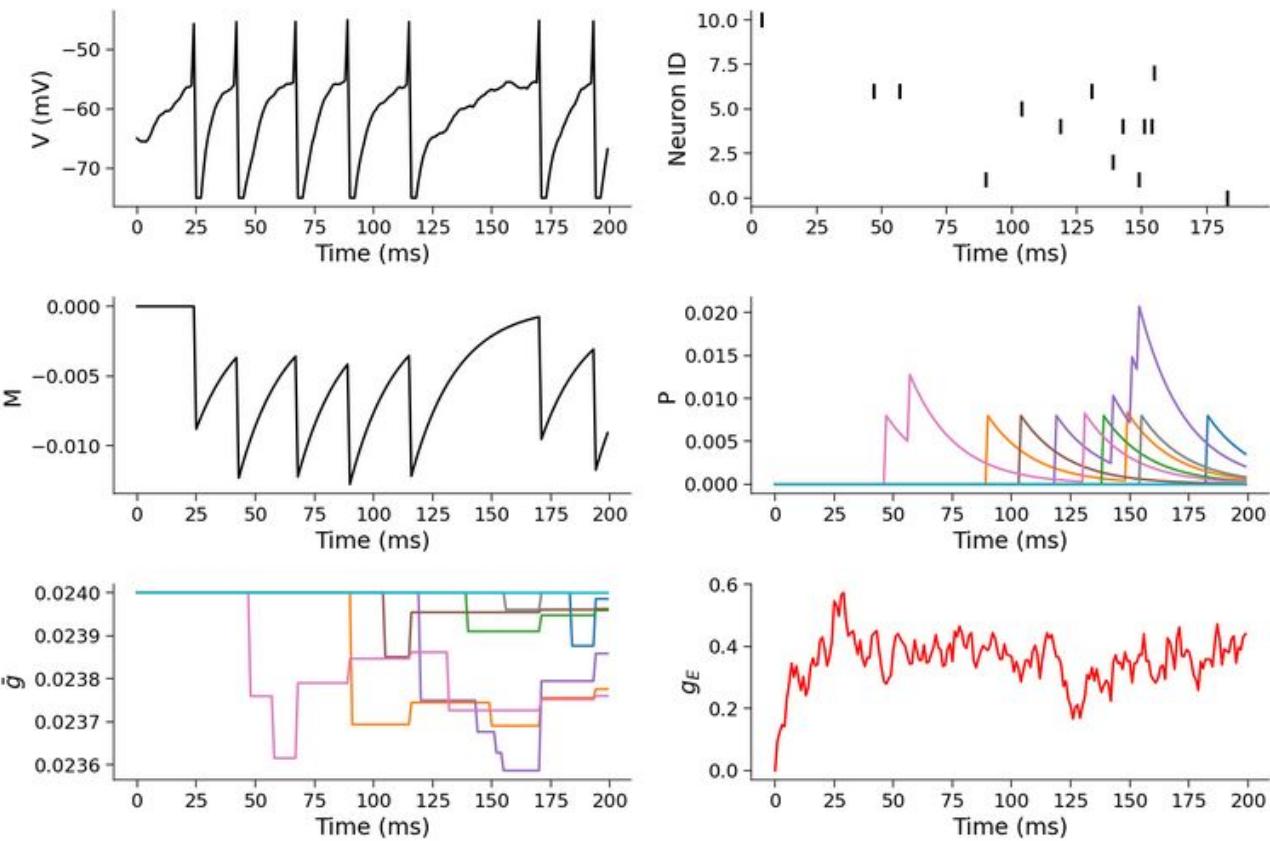
model postsynaptic neuron as a LIF neuron receiving only excitatory inputs

$$I_m \frac{dV}{dt} = -(V - E_L) - g_E(t)(V(t) - E_E)$$

total excitatory synaptic conductance.

$$g_E(t) = \sum_{i=1}^N g_i(t)$$

While simulating STDP,
it is important to make sure
that g_i never goes outside
of its bounds.



Food for thought

- In the above, even though all the presynaptic neurons have the same average firing rate, many of the synapses seem to have been weakened? Did you expect that?

Yes. Because

- a. area under the STDP curve is negative
- b. synapses are set to their maximum possible weight.
- c. presynaptic neurons have a variance in their firing rates because of Poisson nature

- Total synaptic conductance is fluctuating over time. How do you expect g_E to fluctuate if synapses did not show any STDP like behavior?

g_E will fluctuate even when synapses do not show any STDP because of the Poisson nature but with STDP, there will be bigger fluctuations as synaptic weight will vary on spike by spike basis.

- Do synaptic weight ever reach a stationary state when synapses show STDP?

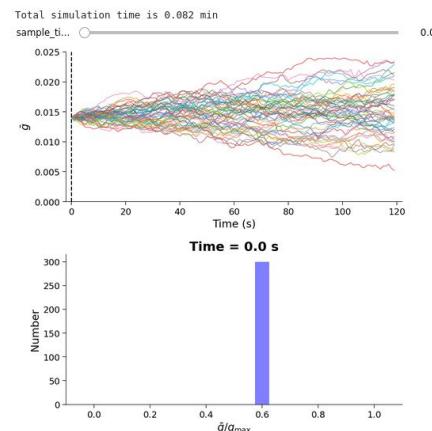
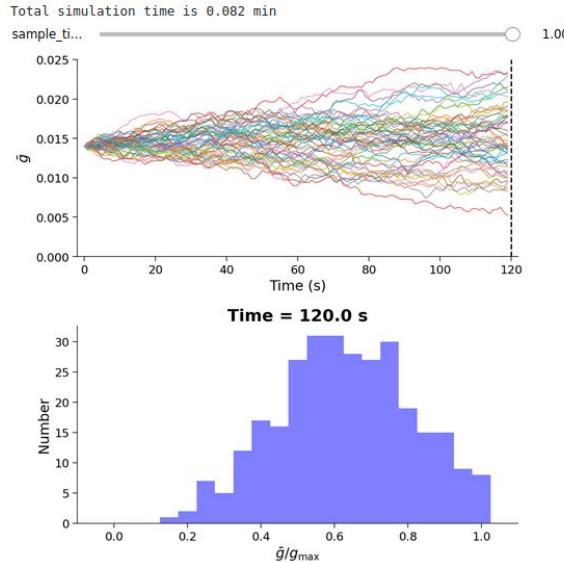
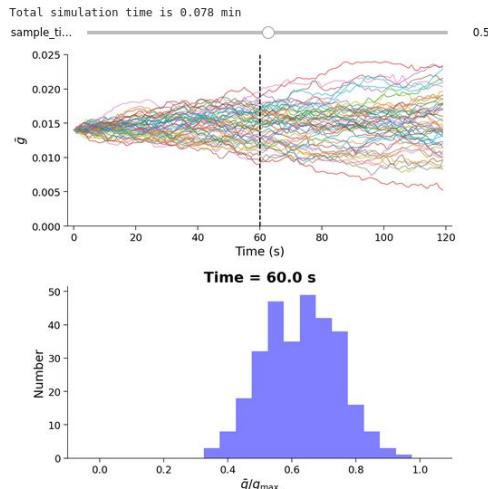
Individual synaptic weight will always fluctuate but the synaptic weight distribution will reach a steady state.

Distribution of synaptic weight

What is the distribution of the synaptic weights when synapses show STDP?

In fact, it is possible that even the synaptic weight distribution itself is a time-varying quantity. So, find how the distribution of synaptic weights evolves as a function of time.

To get a better estimate of the weight distribution and its time evolution, increase the presynaptic firing rate to 15 Hz and simulate the postsynaptic neuron for 120s.



INCREASE THE FIRING RATE (I.E., 30 Hz) OF PRESYNAPTIC NEURONS, AND INVESTIGATE THE EFFECT ON THE DYNAMICS OF SYNAPTIC WEIGHT DISTRIBUTION.

AS WE INCREASE THE INPUT FIRING RATE, MORE SYNAPSES MOVE TO THE EXTREME VALUES, EITHER GO TO ZERO OR TO MAXIMAL CONDUCTANCE. USING 15Hz, THE DISTRIBUTION OF THE WEIGHTS AT THE END OF THE SIMULATION IS MORE LIKE A BELL-SHAPED, SKEWED, WITH MORE SYNAPSES TO BE POTENTIATED. HOWEVER, INCREASING THE FIRING RATE, IN EARLY TIMES, ALMOST ALL SYNAPSES UNDERGO DEPRESSION, AND THEN ONLY A FEW ESCAPE AND THEY BECOME POTENTIATED.

Effect of input correlations

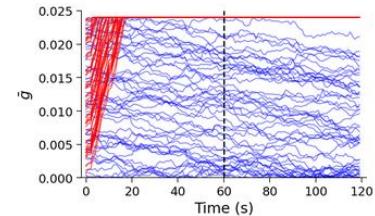
Assume that the input population was uncorrelated.

What happens if presynaptic neurons were correlated?

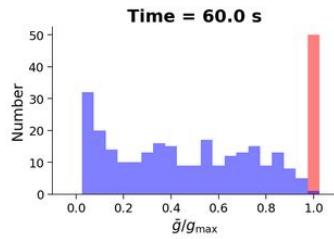
TASK: modify the input such that first L neurons have identical spike trains while the remaining inputs are uncorrelated. This is a highly simplified model of introducing correlations.

Total simulation time is 0.076 min

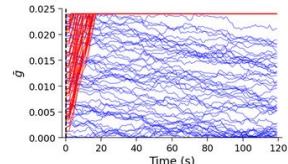
sample_t... 0.50



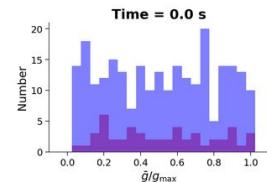
Correlated input
Uncorrelated input



Total simulation time is 0.076 min
sample_t... 0.00

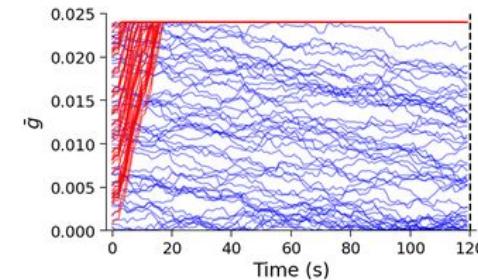


Correlated input
Uncorrelated input

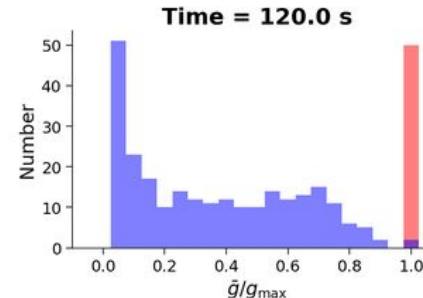


Total simulation time is 0.076 min

sample_t... 1.00



Correlated input
Uncorrelated input



Why do weights of uncorrelated neurons decrease when synapses show LTD?

Above, we notice that the synapses of correlated neurons (which spike together) were almost unaffected, but the weights of other neurons diminished. Why does this happen?

The reason is that the correlated presynaptic neurons have a higher chance of eliciting a spike in the postsynaptic neurons and that create a pre \rightarrow post pairing of spikes.

FOOD FOR THOUGHT

- *Modify the code above and create two groups of correlated presynaptic neurons and test what happens to the weight distribution.*
The two groups will compete to get to stronger synaptic values
- *How can the above observations be used to create unsupervised learning? Could you imagine how we have to train a neuronal model enabled with STDP rule to identify input patterns?*
STDP provides a basis of unsupervised learning as these synapses are sensitive to input correlations. So if the input data has any temporal correlation the neuron will become responsive to those correlated events
- *What else can be done with this type of plasticity?*
You can for circuit motifs in an otherwise unstructured network. The simplest function circuit we can make is a feedforward chain.

Summary

Using presynaptic inputs as Poisson type spike trains

- build a model of synapse that shows IDP.
- study how correlations in input spike trains influence the distribution of synaptic weights and effect of correlated inputs on the synaptic strength!