Reduced Neuron Models

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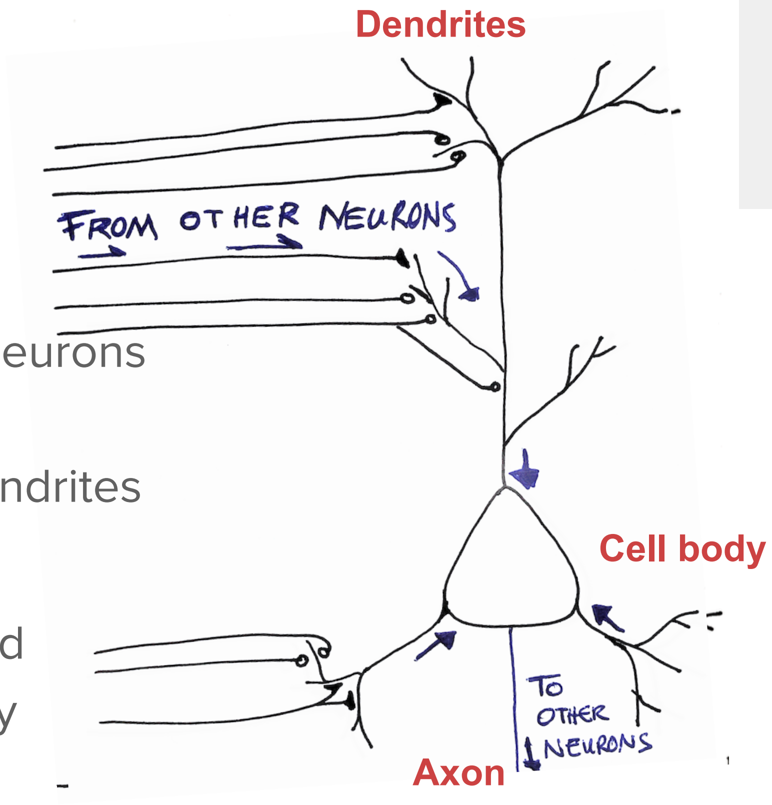
neuromatch academy

Neuronal Excitability

Steps of information processing:
- **Synapses**: connection between neurons
- **Dendrites**: receive inputs
- **Cell body**: sums currents from dendrites
- **Axon**: sends to action potentials

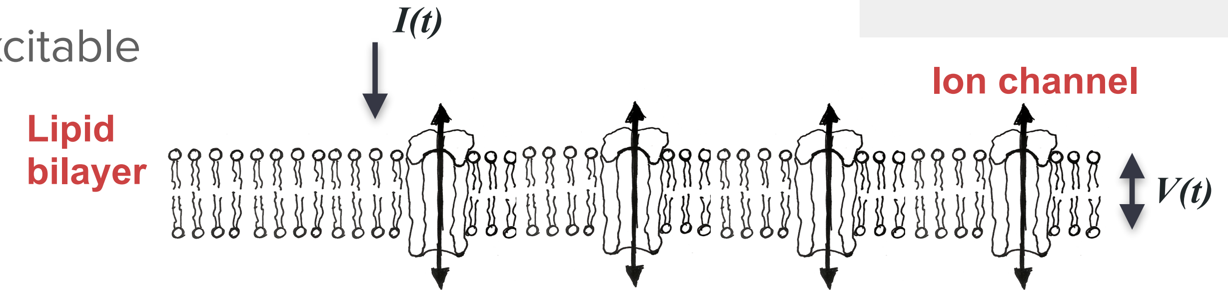
How are action potential generated given current flowing into cell body from dendrites and synapses?



Biophysical description

$I(t)$ **Current** impinging on excitable membrane patch

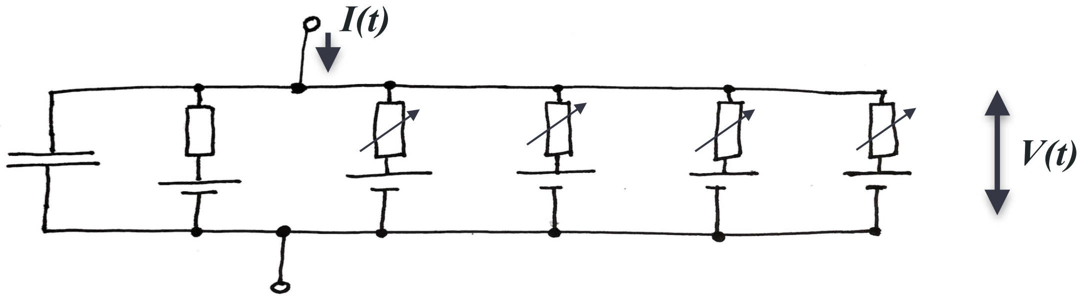
$V(t)$ Membrane **potential**



C **Capacitance** of the membrane

g_L **Conductance** of the membrane

E_L **Equilibrium potential** of 'leak'



Biophysical description

$I(t)$ **Current** impinging on excitable membrane patch

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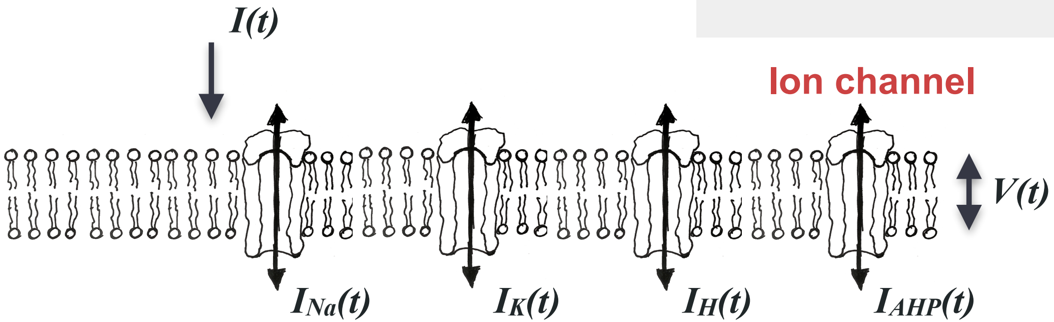


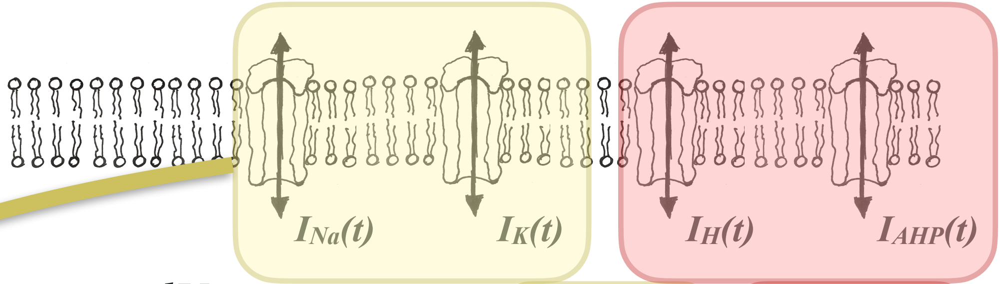
C_m **Capacitance** of the membrane

g_L **Conductance** of the membrane

E_L **Equilibrium potential** of 'leak'

$$I = C\frac{dV}{dt} + g_L(V - E_L) + I_{Na} + I_K + I_H + I_{AHP}$$

Leaky Integrate-and-Fire



$$I = C_m \frac{dV}{dt} + g_L(V - E_L) + \boxed{I_{Na} + I_K} + \boxed{I_H + I_{AHP}}$$

Replace by a threshold for spike emission

Followed by a reset to a fixed potential

Ignore for now:

Action of ion channels other than stereotypical action potential generation

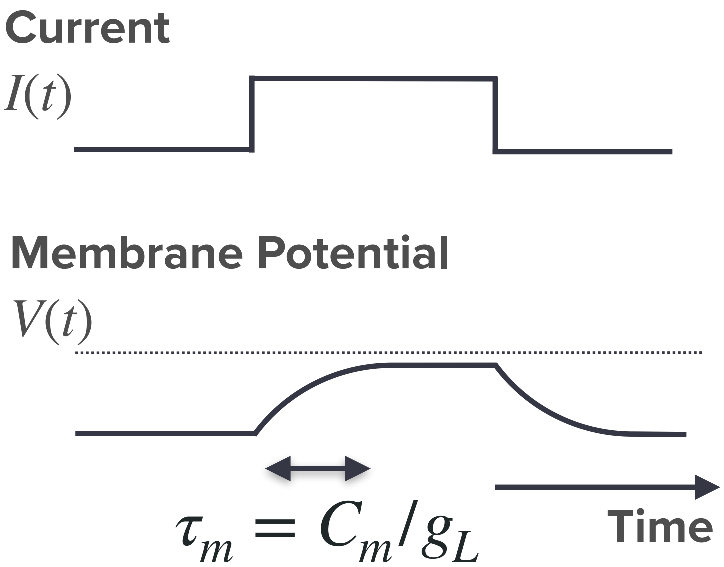
Leaky Integrate-and-Fire (LIF)

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

If $V(t) = V_{th}$ then $V(t + \Delta) = E_L$

Subthreshold current step: Exponential relaxation to a steady-state.

$$V(t) = (\frac{I}{g_L} + E_L)\left[1 - e^{-t/\tau_m}\right]$$

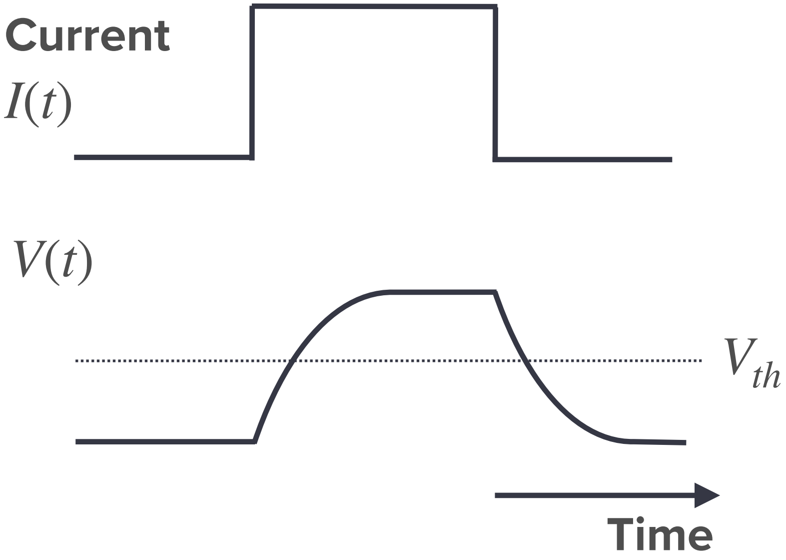


Leaky Integrate-and-Fire (LIF)

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

If $V = V_{th}$ then $V(t + \Delta) = E_L$

Suprathreshold current step:



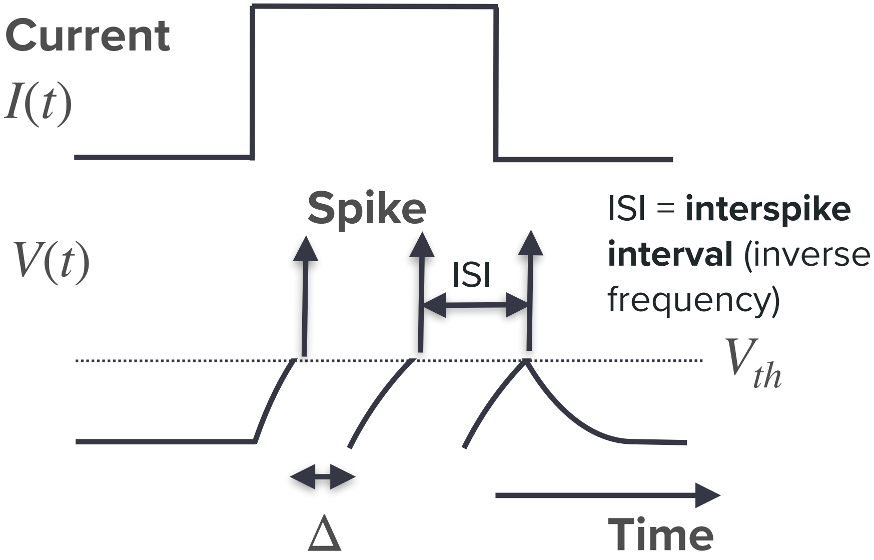
Leaky Integrate-and-Fire (LIF)

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

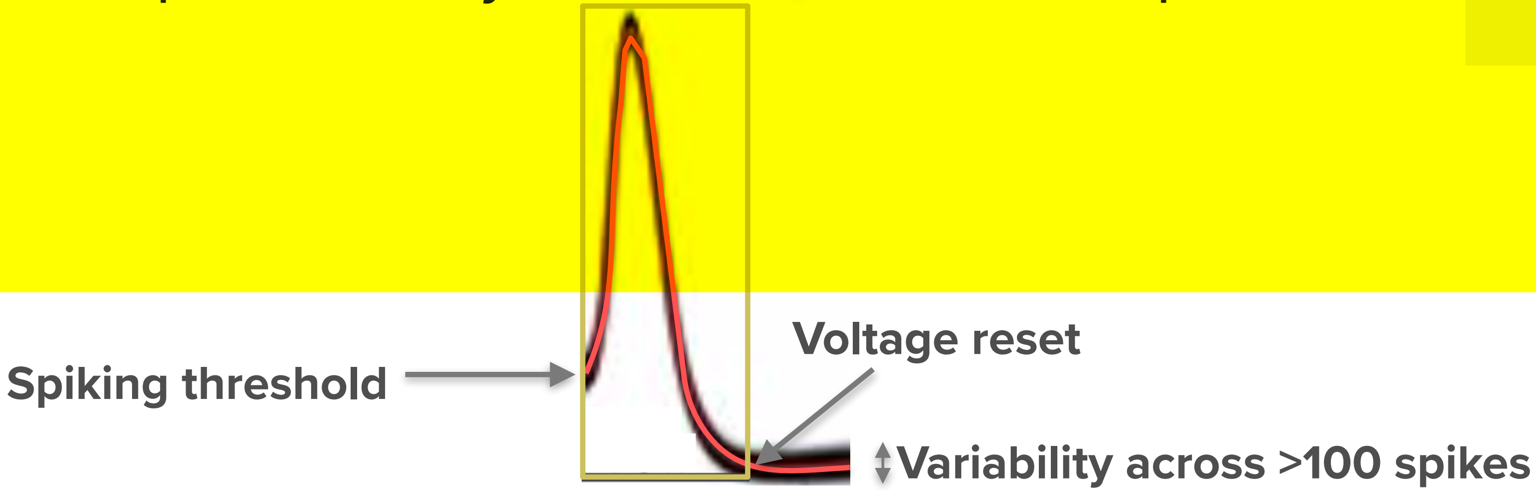
If $V = V_{th}$ then $V(t + \Delta) = E_L$

Suprathreshold current step:

Regular firing



Do Spikes Always Have the Same Shape?

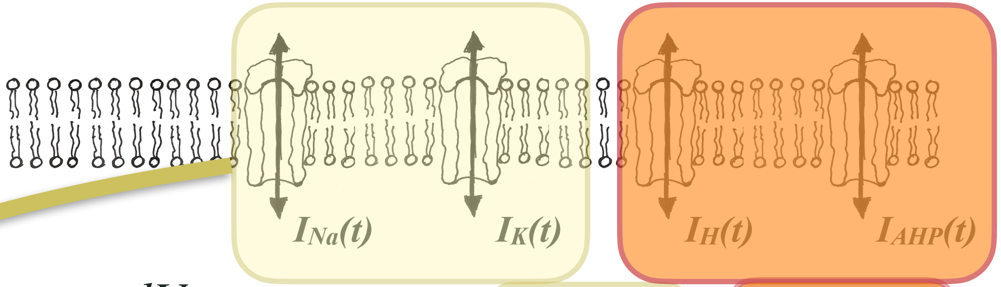


Yes. Spikes follow stereotypical time course within 1-2 ms of onset.

Notable **exception**: spikes late in a high-frenquency burst.

Figure modified from: Mensi et al. *J. Neurophys.* (2012)

Generalized Integrate-and-Fire



$$I = C\frac{dV}{dt} + g_L(V - E_L) + \boxed{I_{Na} + I_K} + \boxed{I_H + I_{AHP}}$$

Replace by a threshold for spike emission

Followed by a reset to a fixed potential

Ignore for now:

Action of ion channels other than stereotypical action potential generation

Approximate with linear dynamics

Generalized Integrate-and-Fire (GIF)

$$C_m \frac{dV}{dt} = -g_L(V - E_L) - \boxed{\sum_k} w_k + I \qquad \tau_k \frac{dw_k}{dt} = a_k(V - E_L) - w_k$$

Linearized subthreshold current

If $V = V_{th}$ then $V(t + \Delta) = E_L$

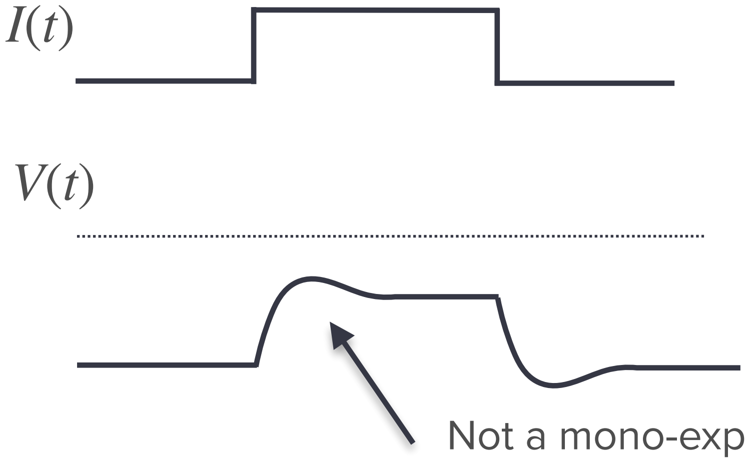
Linear dynamics

a_k: sub-threshold coupling of k'th current.

τ_k: time scale of k'th current

Generalized Integrate-and-Fire (GIF)

Current

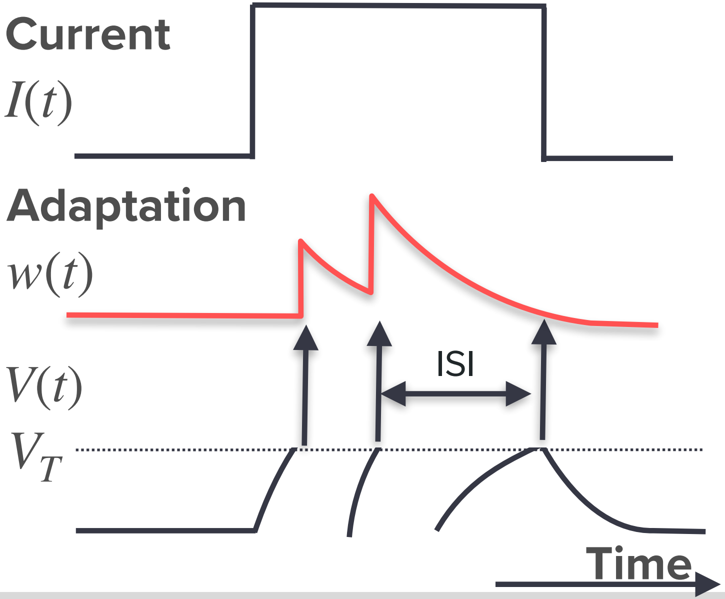


Not a mono-exponential relaxation

Linearized sub-threshold currents can capture some non-mono-exponential features

Generalized Integrate-and-Fire (GIF)

Spike-frequency adaptation



Almost all cells show some spike-frequency adaptation

Modeled by adding a **spike-triggered inhibitory current** with linear dynamics

Generalized Integrate-and-Fire (GIF)

$$C_m \frac{dV}{dt} = -g_L(V - E_L) - \boxed{\sum_k w_k} + I \qquad \tau_k \frac{dw_k}{dt} = a_k(V - E_L) - w_k$$

$$\boxed{\text{If } \; V = V_{th} \; \text{ then } \quad V(t+\Delta) = E_L} \qquad w_k(t+\Delta) = w_k + b_k$$

Linearized spike-triggered current

b_k: spike-triggered jump in k'th current.

Also, the **threshold is allowed to jump** up after every spike and decay to a baseline.

Accuracy of Reduced Models

To validate the neuron model we inject in-vivo-like current in neuron and try to **predict precise spike timing** (+/- 4 ms) using a mathematical neuron model.

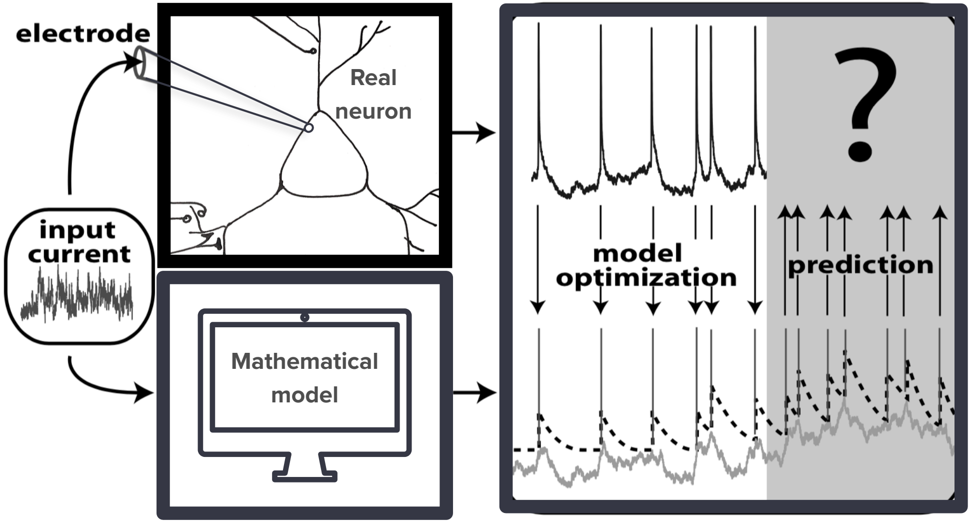
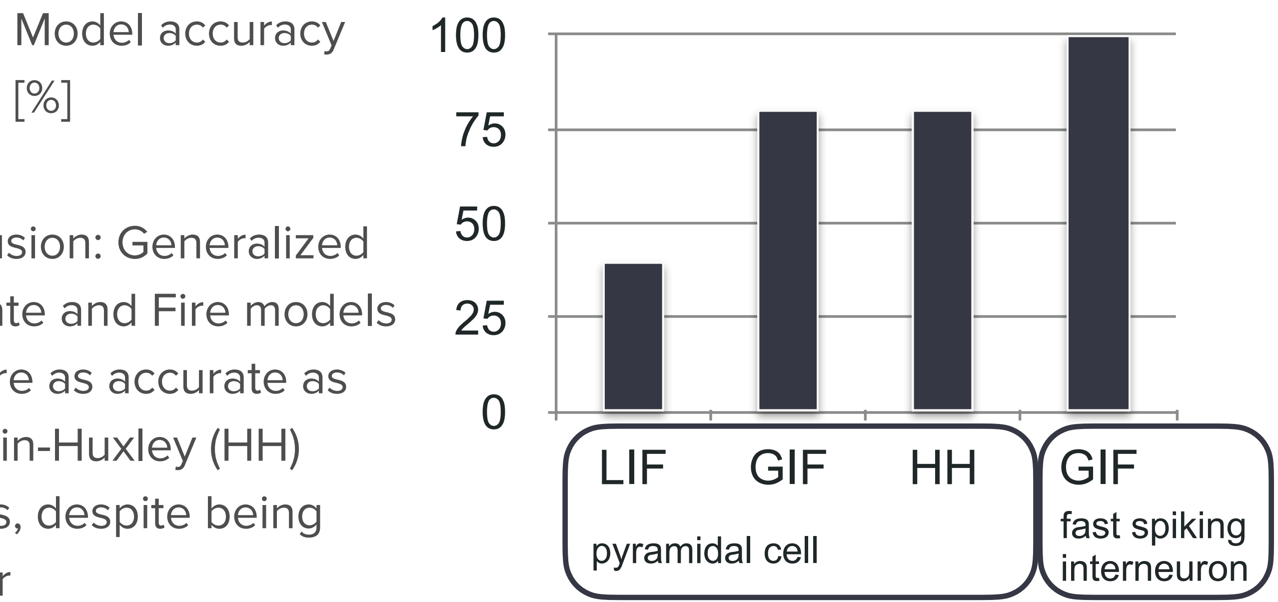


Figure modified from: Gerstner, Kistler, Naud and Paninski *Neuronal dynamics* (2014)

Accuracy of Reduced Models

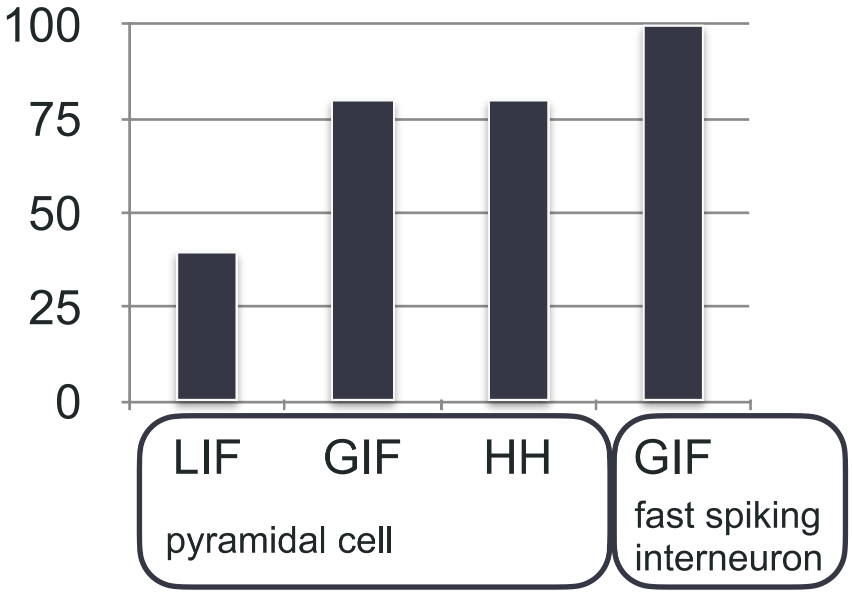


Conclusion: Generalized Integrate and Fire models (GIF) are as accurate as Hodgkin-Huxley (HH) models, despite being simpler

Conclusion

Integrate-and-fire models form an **approximation** to the complex dynamics of real neurons.

Generalized Integrate-and-fire models attain **high accuracy** by taking into account **adaptive** features



Further information

Textbooks:
Gerstner, Kistler, Naud and Paninski, *Neuronal Dyanmics* (2014)
Tuckwell, *Introduction to theoretical neurobiology vol 1 & 2* (1988)
Dayan and Abbott, *Theoretical Neuroscience* (2001)

GIF and extensions:
Richardson, Brunel, Hakim *Journal of Neurophysiology* (2003)
Fourcaud-Trocme et al. *Journal of Neuroscience* (2003)
Mensi *et al. Journal of Neuorphysiology* (2011)
Pozzorini *et al. Nature Neuroscience* (2013)
Mensi et al. *PLoS Computational Biology* (2016)

GIF accuracy:
Pillow et al. *Journal of Neuroscience,* (2005)
Pillow et al. *Nature* (2008)
Jolivet et al. *J Neuroscience Methods* (2009)
Naud and Gerstner, *Science* (2011)
Teeter et al. *Nature Communications* (2018)

The Statistics of Neuronal Responses

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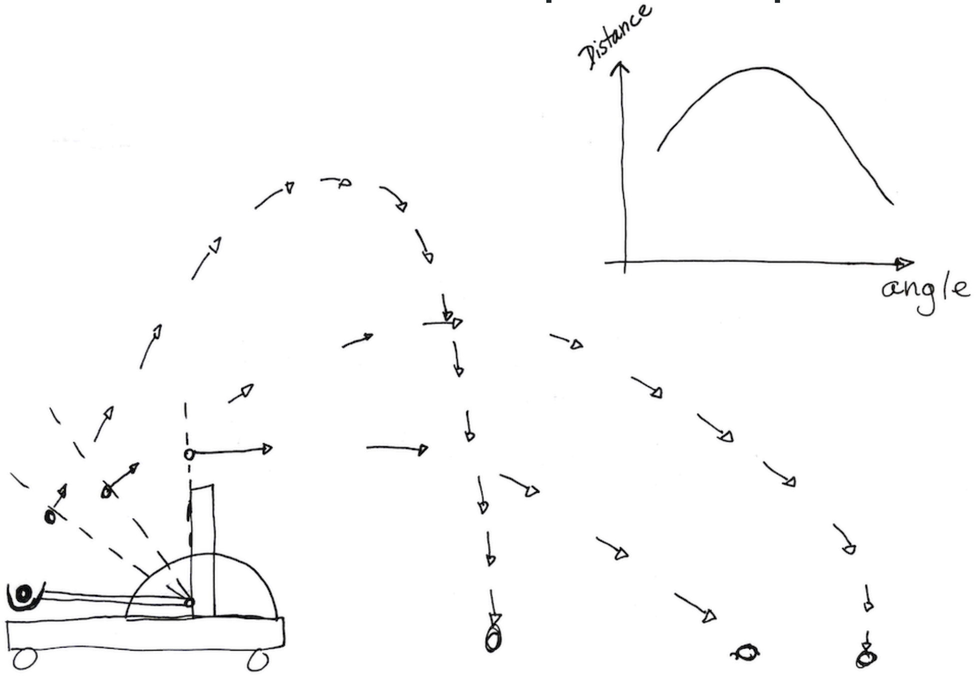
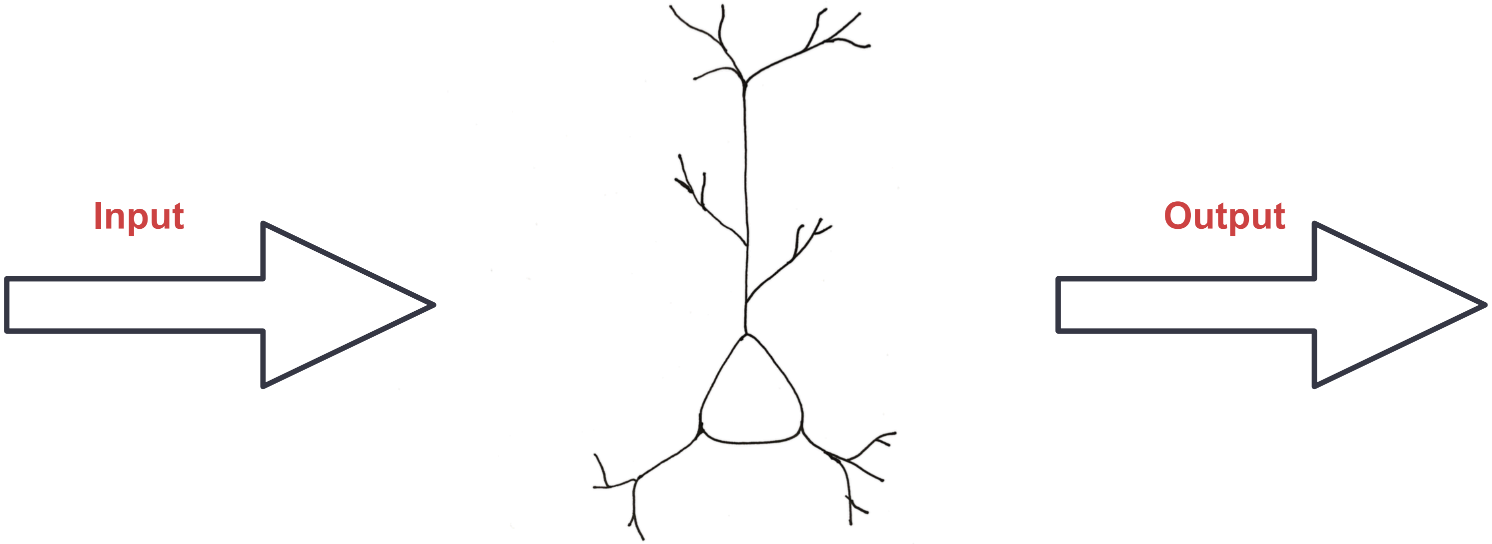
Characterization of the Input-Output Function

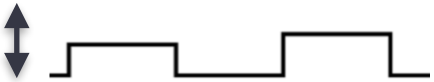


Characterization of the Input-Output Function

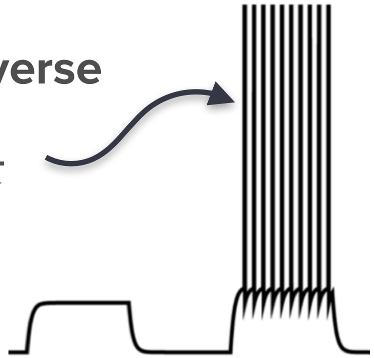


Leaky Integrate and Fire - Constant Input

Current I



Firing Frequency as inverse interspike interval: $\frac{1}{ISI}$



Input

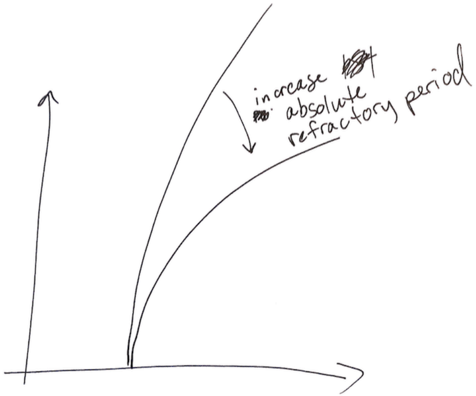
$$C\frac{dV}{dt} = -g_L(V - E_L) + I$$

If $V = \theta$ then $V(t + \Delta) = V_r$

Output

Leaky Integrate and Fire - Constant Input

Firing frequency $\frac{1}{ISI}$

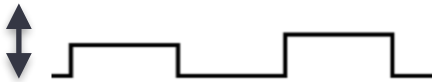


Current I

Missing:
Formula

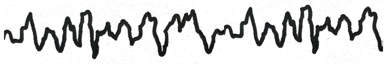
Leaky Integrate and Fire - Noisy Input

Current I



+

Noise ξ



Firing Frequency as inverse of average interspike interval: $\dfrac{1}{\langle ISI \rangle}$

Input

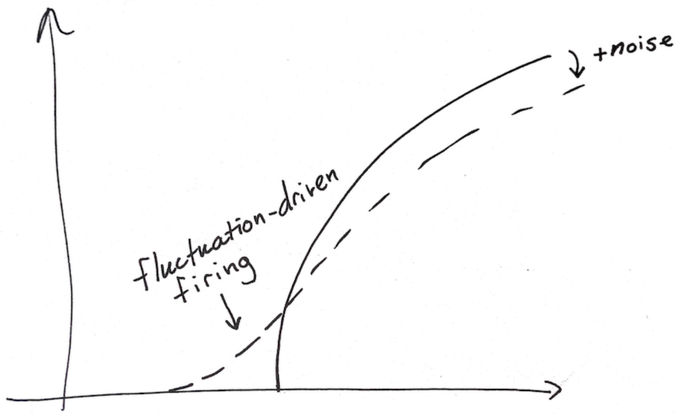
$$C\frac{dV}{dt} = -g_L(V - E_L) + I + \xi$$

If $V = \theta$ then $V(t+\Delta) = V_r$

Output

Leaky Integrate and Fire - Noisy Input

Firing frequency $\dfrac{1}{\langle ISI \rangle}$



Current $\boldsymbol{I}$

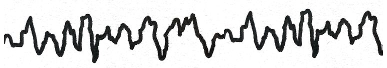
Missing: Formula

Leaky Integrate and Fire - Noisy Input

Current I

+

Noise ξ



CV $\dfrac{\sigma_T}{\langle ISI \rangle}$

Input

$$C\frac{dV}{dt} = -g_L(V - E_L) + I + \xi$$

If $V = \theta$ then $V(t + \Delta) = V_r$

Output

Leaky Integrate and Fire - Noisy Input

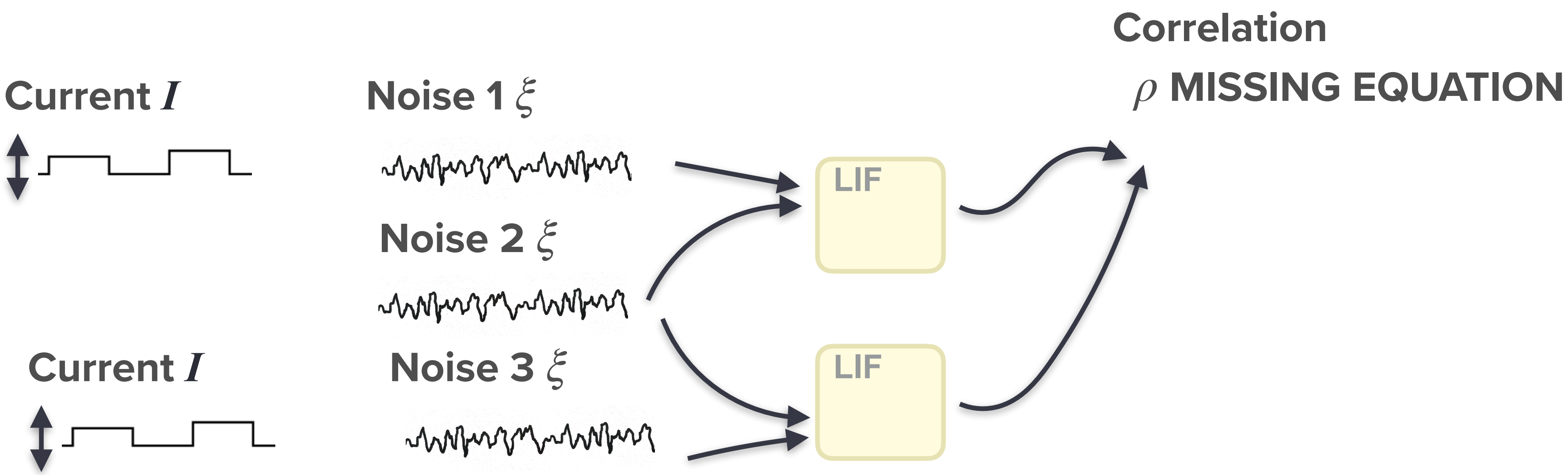
CV $\frac{\sigma_T}{\langle ISI \rangle}$

Missing:

Formula

Current I

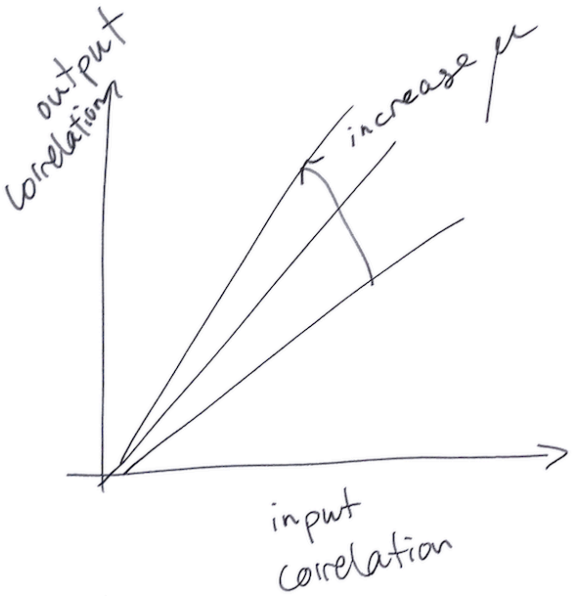
Correlation of Pairs



Correlation of Pairs

Correlation

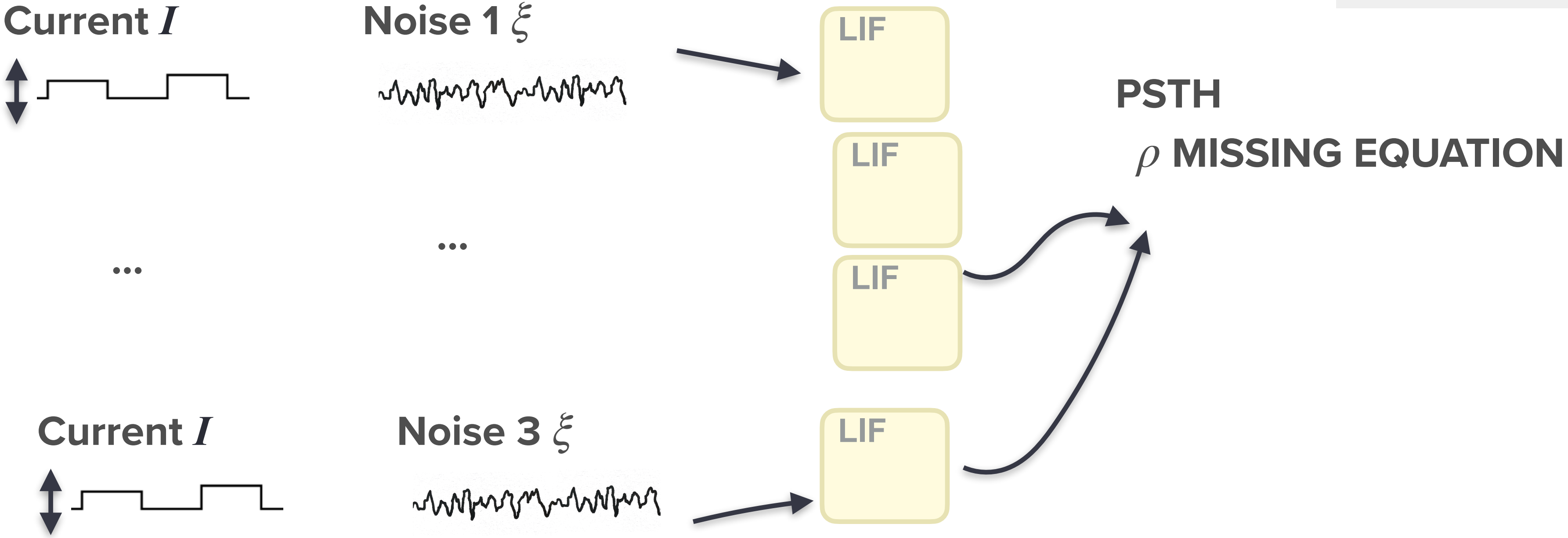
ρ



Missing:

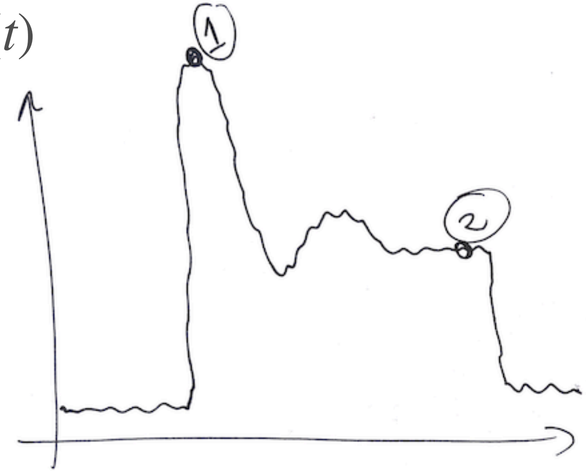
Formula

Ensemble Response

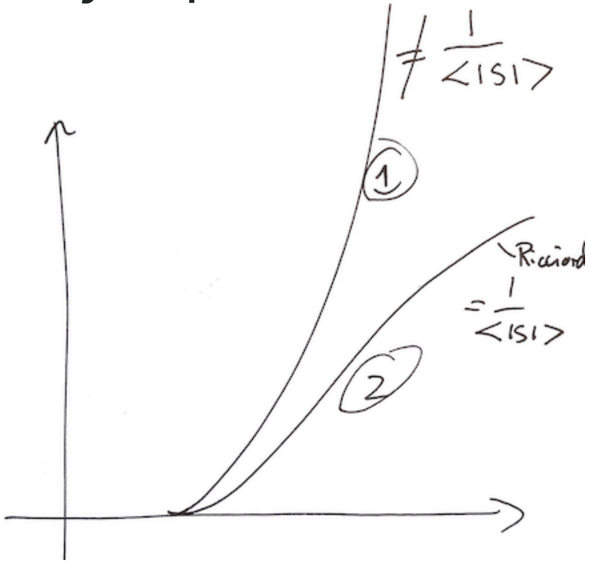


Leaky Integrate and Fire - Noisy Input

PSTH $\nu(t)$

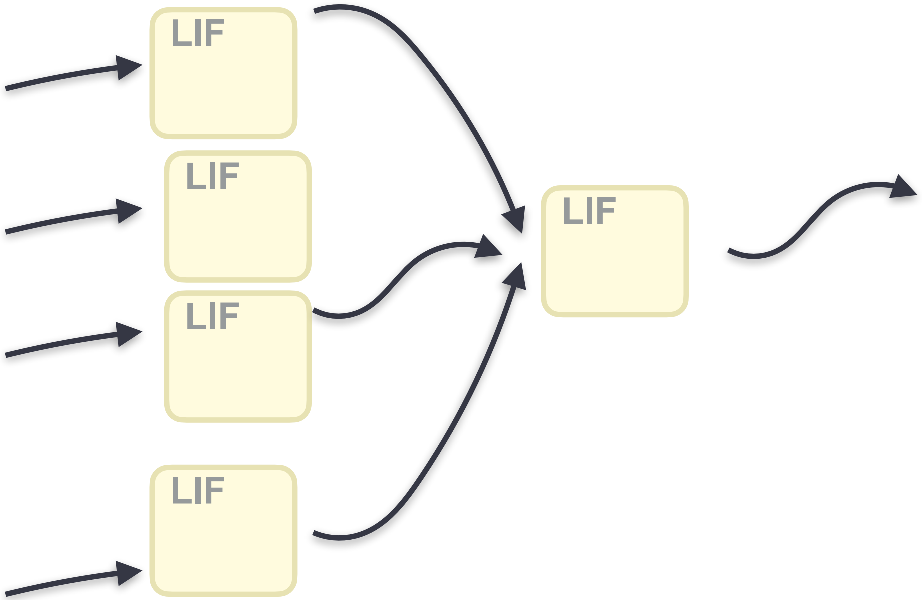


Time t



Current I

Transmission of Output Statistics



Transmission of Output Statistics

What comes next requires synapse models

Conclusion

Synaptic Transmission

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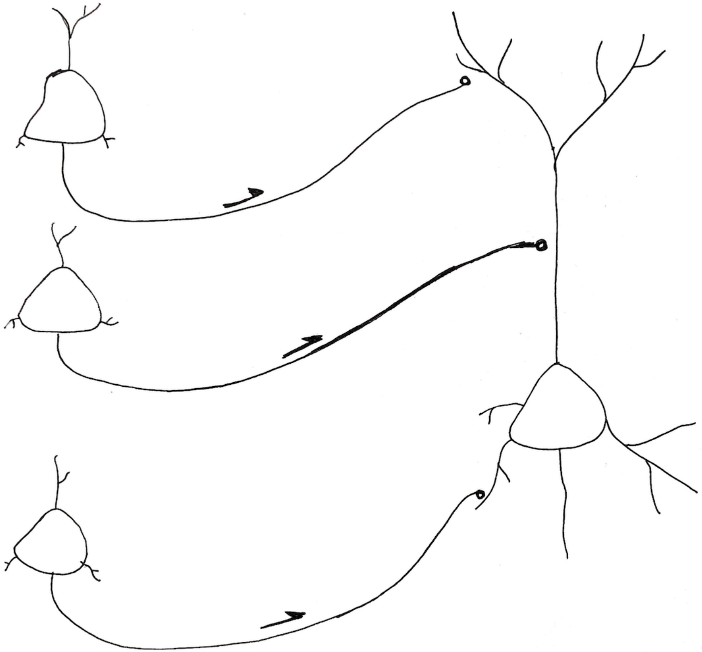
Transmission

How does a the firing of one given neuron affect the neuron connected to it?

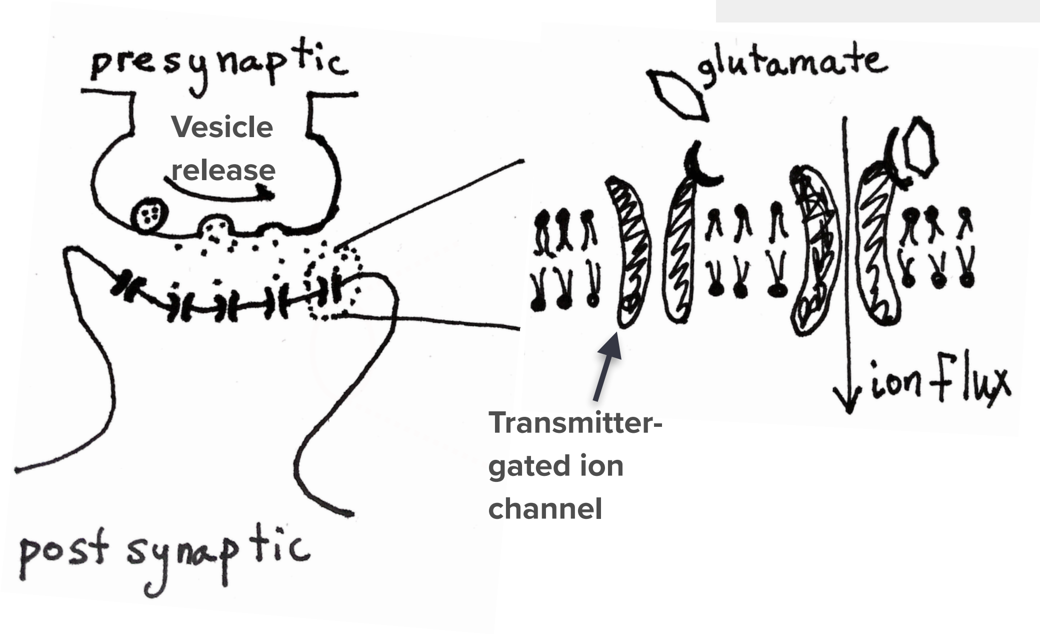
What statistical property is transmitted?



Synaptic Currents

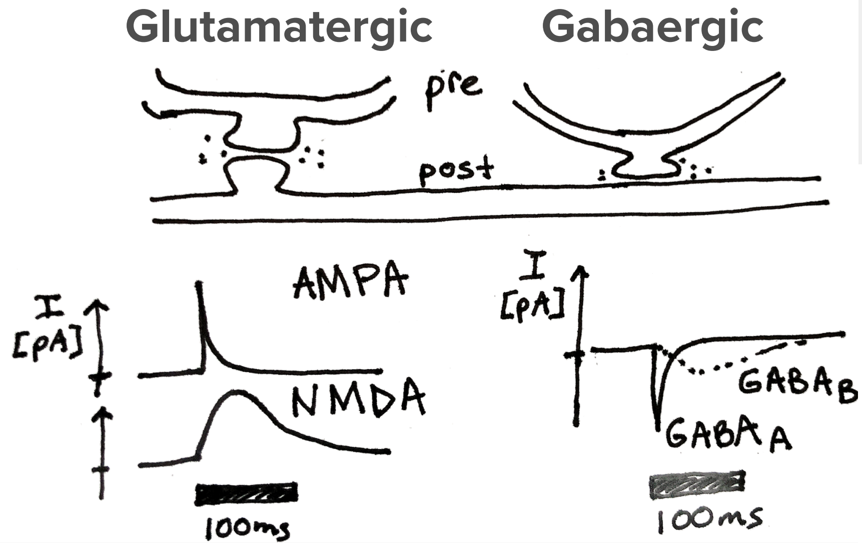
Pre-synaptic: Action potential arrives at the synapse and triggers transmitter release

Post-synaptic: transmitter binds to receptor and triggers changes in ionic conductance



Synaptic Currents

A presynaptic spike can cause both **fast** and **slow** post-synaptic currents **(PSCs)**



Glutamatergic synapses: release glutamate, causing excitatory PSCs (EPSCs).

Gabaergic synapses: release GABA, causing inhibitory PSCs (IPSCs)

Synaptic Currents

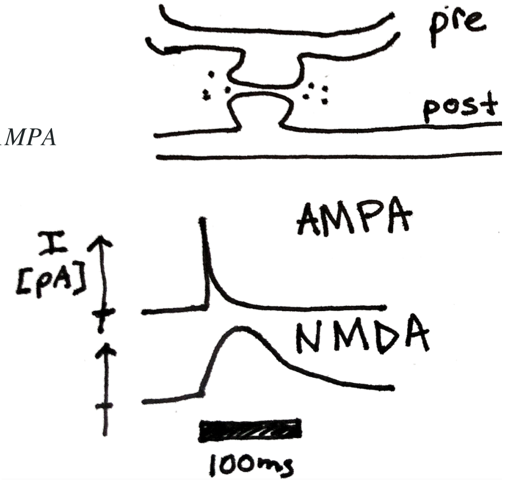
Currents are mediated by conductance changes:

$$I_{AMPA}(t) = g_{AMPA}(t)(V - E_E)$$

$$I_{NMDA}(t) = g_{NMDA}(V,t)(V - E_E)$$

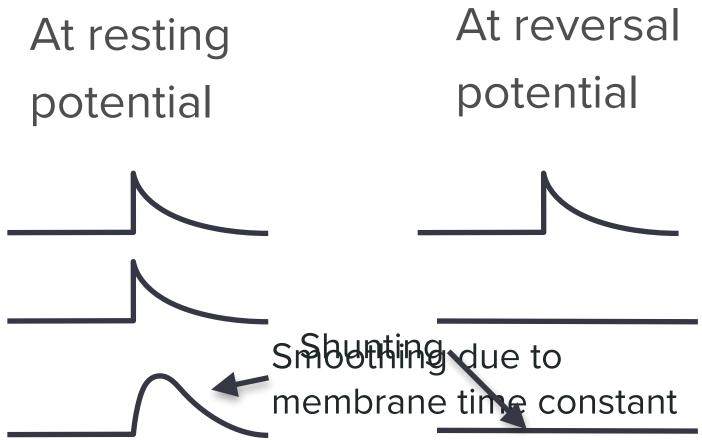
$$g_{AMPA} \sim \Theta(t - t_f)e^{-(t-t_f)/\tau_{AMPA}}$$

All others: g(t) is a bi-exponential function



Current vs Conductance vs Potential

$$I_{AMPA}(t) = g_{AMPA}(t)(V - E_E)$$



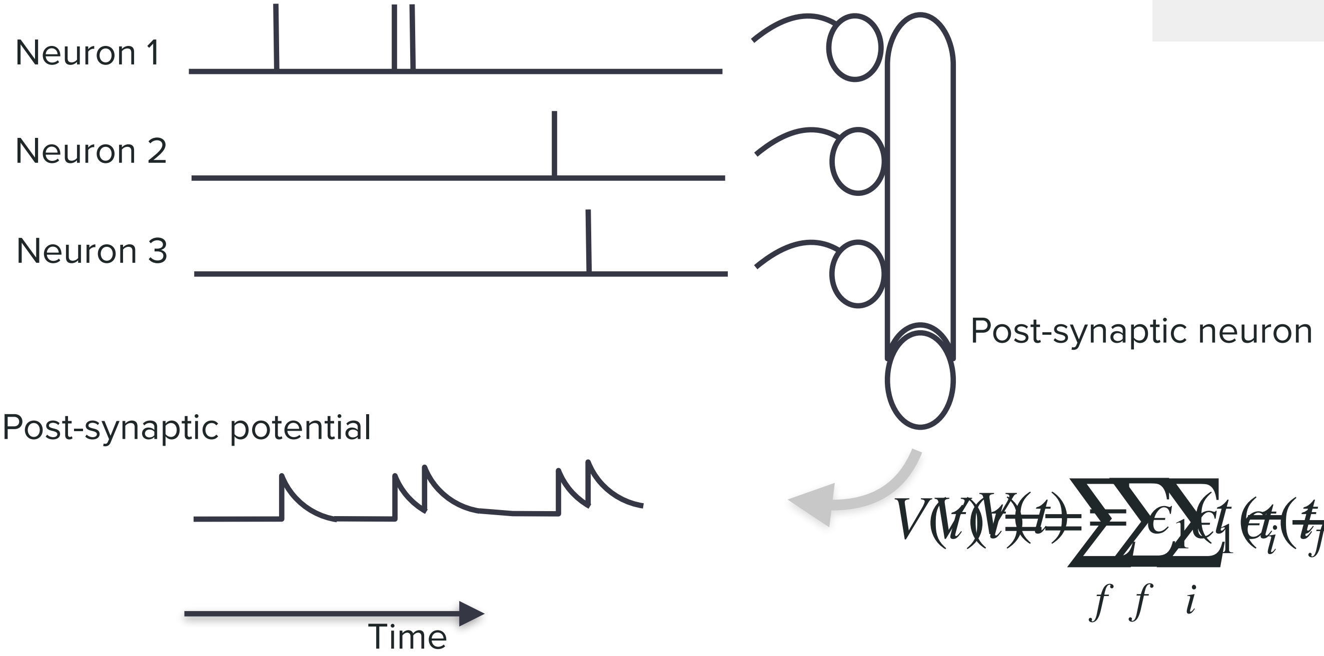
Excitatory post-synaptic **conductance** (EPS**C**)

Excitatory post-synaptic **current** (EPS**C**)

Excitatory post-synaptic **potential** (EPS**P**)

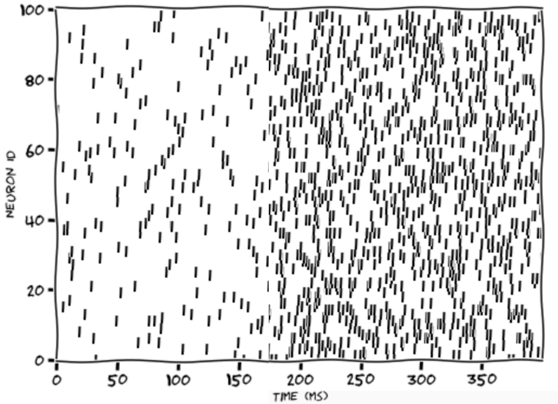
Because reversal potential is typically well above firing threshold: excitatory **conductance typically proportional to current** $I_{AMPA} \approx \alpha g_{AMPA}$

Synaptic bombardment



$$V(t) = \sum_f \sum_i \epsilon_i(t - t_f)$$

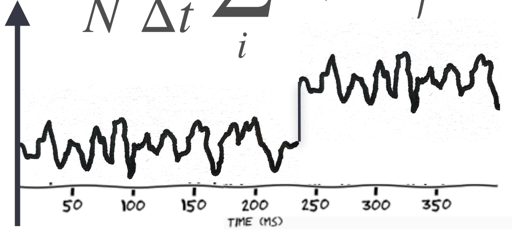
Ensemble Rate - Peri-Stimulus Time-Histogram



Raster plot: each line is neuron, each dot is a spike

PSTH

$$\nu(t) = \frac{1}{N}\frac{1}{\Delta t}\sum_i \epsilon(t - t_f^{(i)}, \Delta t)$$



PSTH: An average across columns of the raster plot

Ensemble Rate - Peri-Stimulus Time-Histogram

Ensemble rate

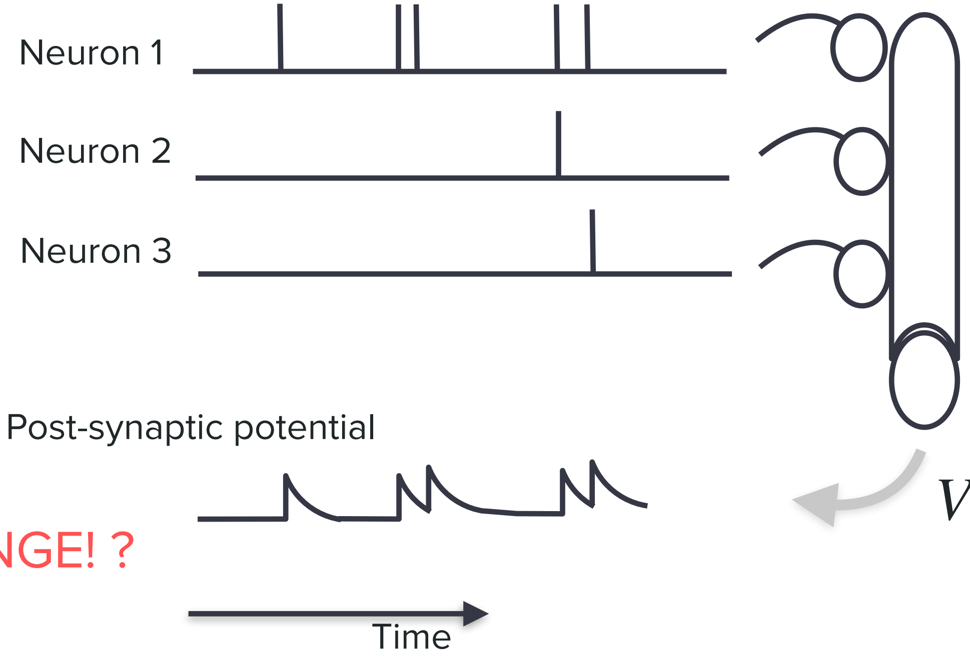
$$\nu(t) = \frac{1}{N}\frac{1}{\Delta t}\sum_i \epsilon(t - t_f^{(i)}, \Delta t)$$

Equivalent!

Synapses communicate the ensemble rate of the pre-synaptic population

$$V(t) = \sum_f \sum_i \epsilon_i(t - t_f)$$

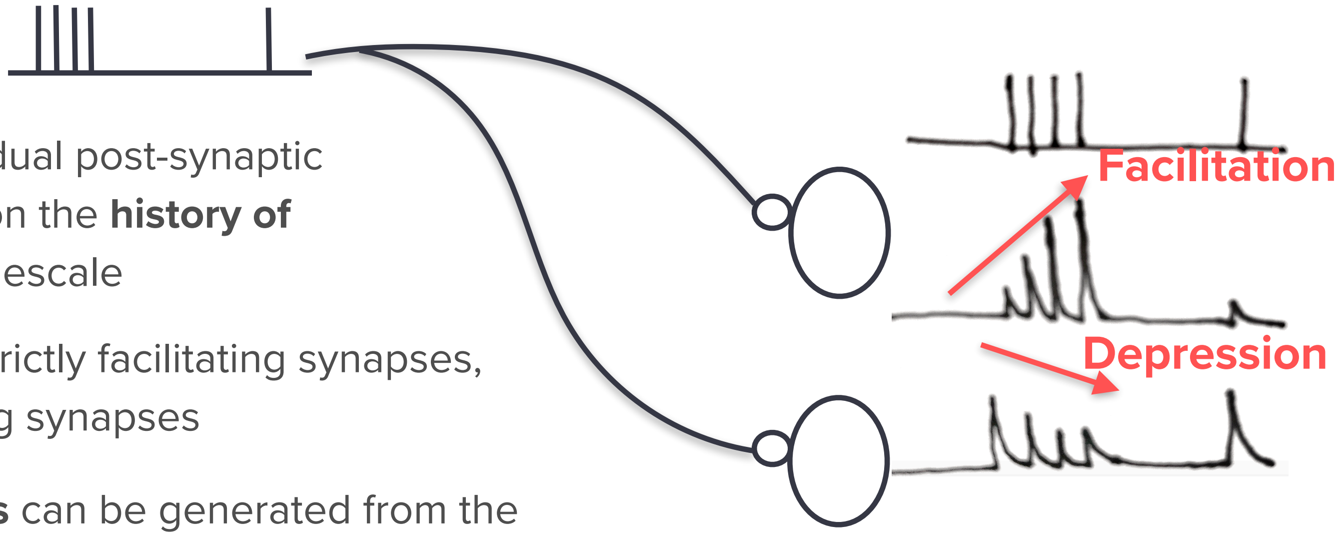
Can Spikes be Shuffled across Population?



$$V(t) = \sum_f \sum_i \epsilon_i(t - t_f)$$

NO CHANGE! ?

Short-Term Dynamics



The **amplitude** of individual post-synaptic conductance depends on the **history of firing** on fast (0.1-5 s) timescale

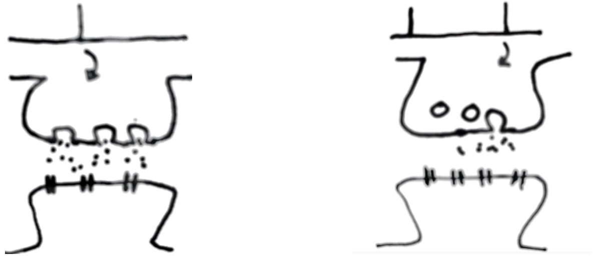
Some pathways make strictly facilitating synapses, others strictly depressing synapses

These **distinct dynamics** can be generated from the **same axon**

Distinct types of synapses

Facilitating: Firing causes increase in vesicle **release probability**

Depressing: Firing causes a decrease in **size of readily releasable pool**



Tsodyks Markram Model

PSC amplitude is conceived as a **multiplication** of two factors: uR

$$\frac{dR}{dt} = \frac{1-R}{\tau_R} \quad \text{if spike then } R \leftarrow uR$$

Depressing: Firing causes a decrease in R , which will recover to 1 on a time scale τ_R

$$\frac{du}{dt} = \frac{U-u}{\tau_u} \quad \text{if spike then } u \leftarrow f(1-u)$$

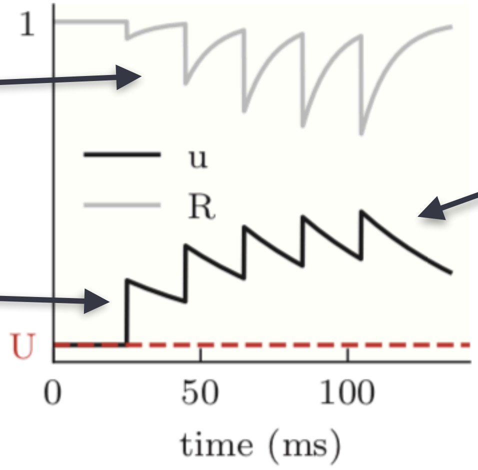
Facilitating: Firing causes increase in u controlled by by jump f and timescale τ_u , but ensuring it remains between 0 and 1

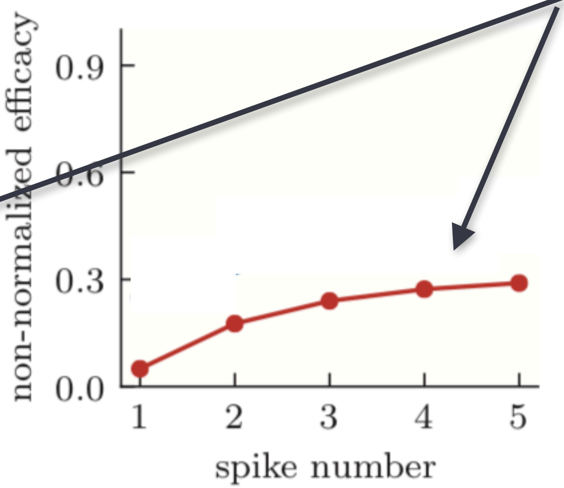
Tsodyks Markram Model

Example: fast τ_R , slower τ_u and high f leads to **facilitation**

jumps uR but decays fast

jumps $f(1-u)$

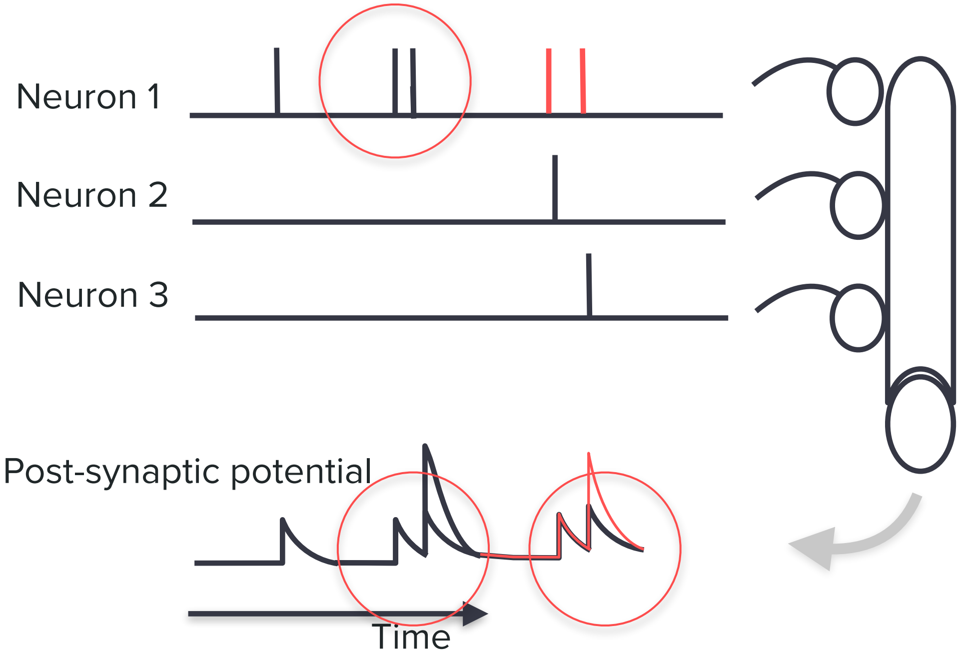




Saturation of jumps as u increases creates a saturation of facilitation

Figures: Rossbroich Trotter et al.. *BioRxiv* (2020)

Can Spikes be Shuffled across Population?

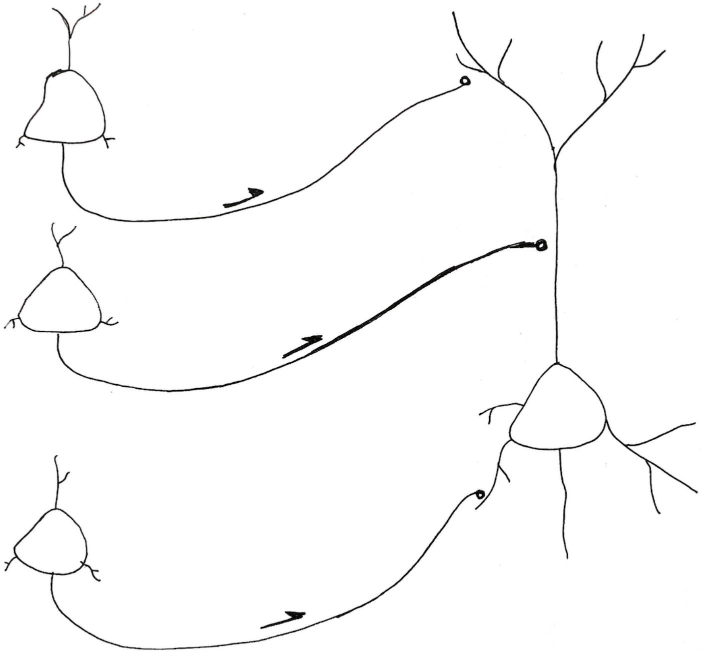


Not Equivalent!
Dynamic synapses do not communicate ensemble rate

Conclusion

Static synapse: cummunicate ensemble rate of pre-synaptic neurons

Dynamic synapse: introduce sensitivity to single-neuron interspike intervals



Further Information

Textbooks:
Gerstner, Kistler, Naud and Paninski, *Neuronal Dyanmics* (2014)
Koch, *Biophysics of Computation* (2004)
Dayan and Abbott, *Theoretical Neuroscience* (2001)

Short-term dynamics
Tsodyks and Markram *PNAS* (1997)
Markram and Tsodyks *PNAS* (1998)
Hennig *Frontiers in Computational Neuroscience* (2013)
Naud and Sprekeler *PNAS* (2018)
Rossbroich, Trotter et al. *BioRxiv* (2020)

Spike Timing and Plasticity

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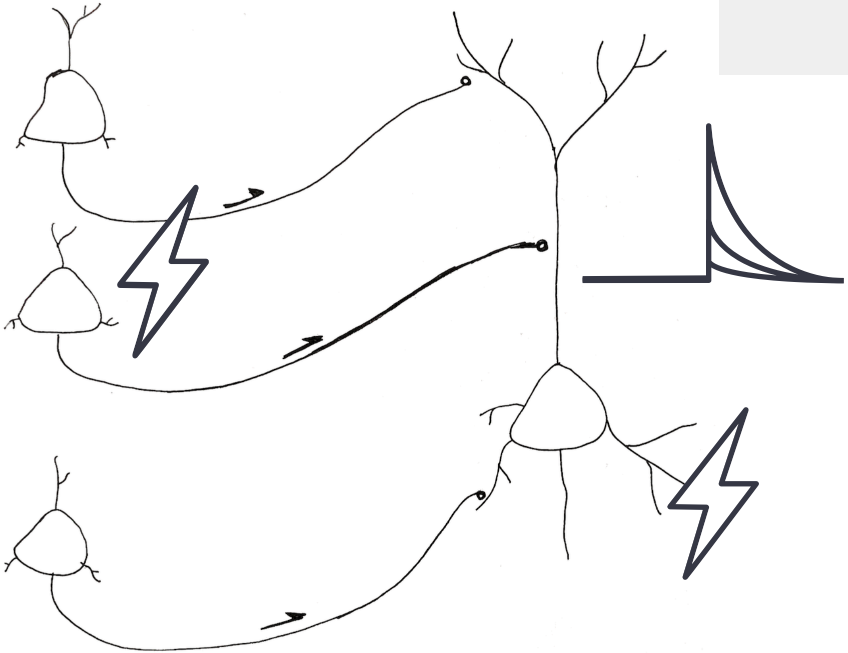
neuromatch academy

Plasticity

The **connection strength** of a synapse is **plastic**, **malleable**. It is is sculpted by patterns of activity.

Synaptic plasticity if often loosely described by ‘what fires together wires together’, but does this mean that ‘what spikes together wires together’?

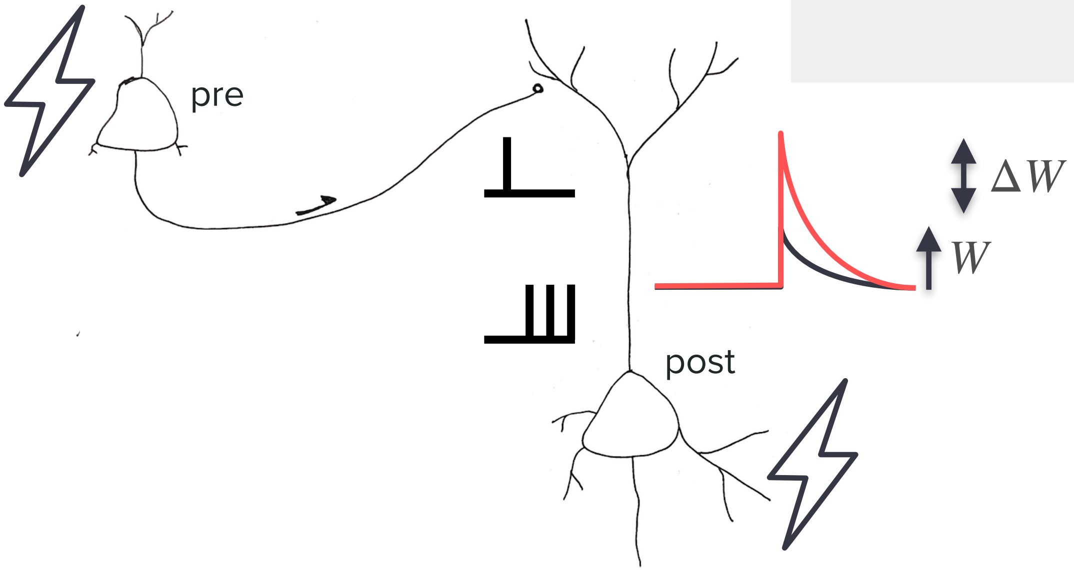


Synaptic Weights

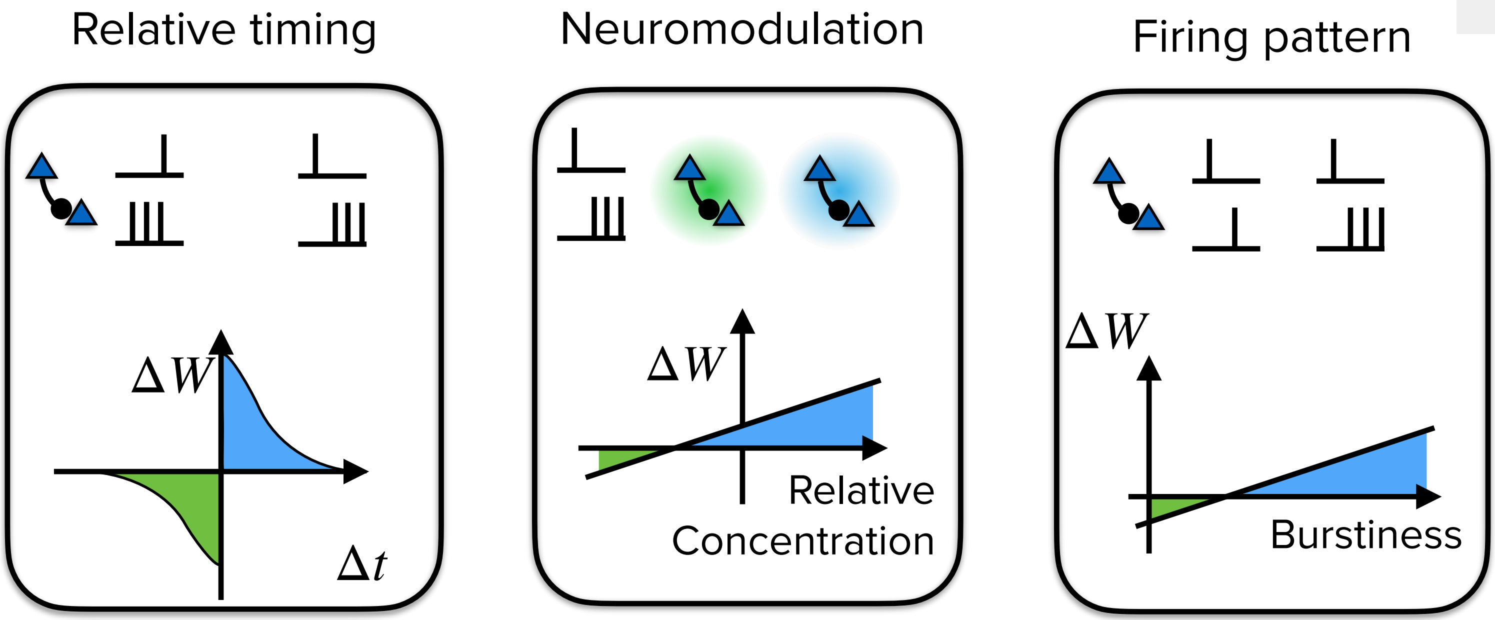
The **connection strength**, W, is the amplitude of the PSC.

Long-Term Potentiation (LTP): plasticity-inducing protocol, causing the connection strength to increase $\Delta W > 0$.

Long-Term Depression (LTD): The connection strength is decreased $\Delta W < 0$.

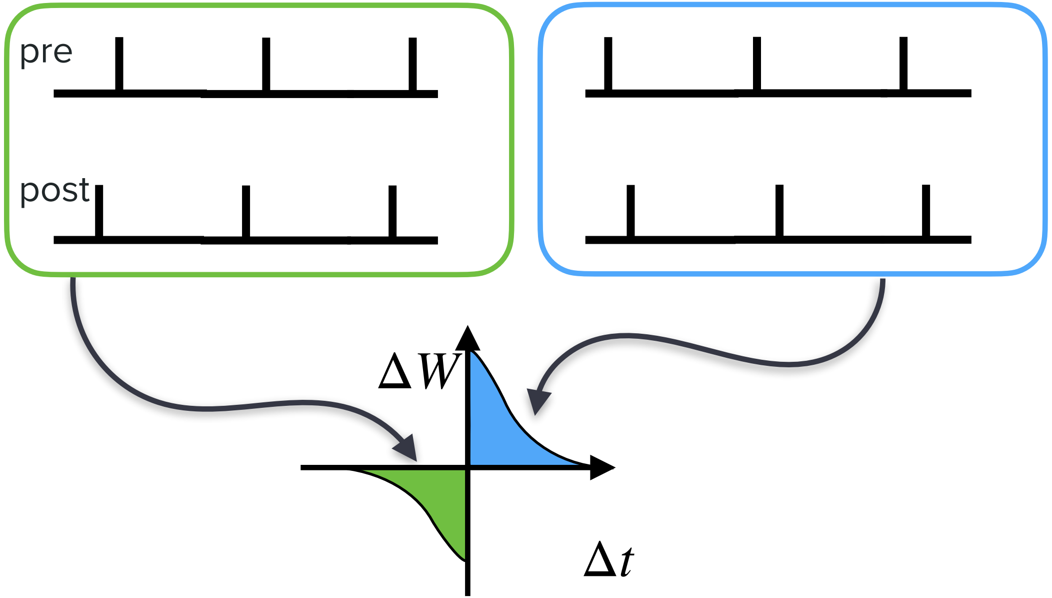


Plasticity Factors

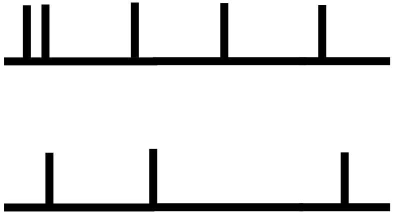


Modelling Spike-Timing-Dependent Plasticity

Experimental Data



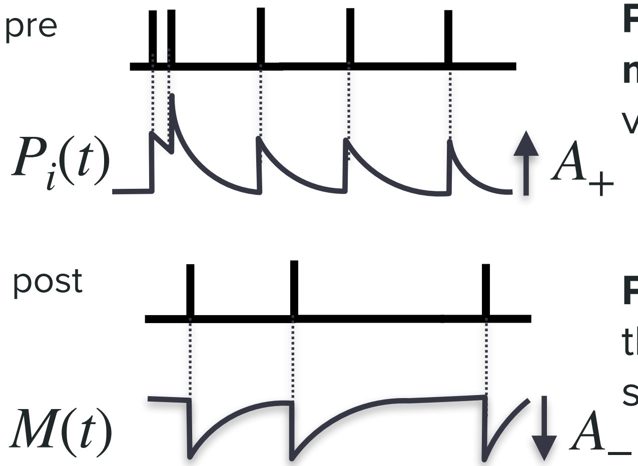
In-vivo like spike trains



How should W evolve?
Nearest neighbour?
Triplets? How?

Modelling Spike-Timing-Dependent Plasticity

Pre- and post-synaptic traces

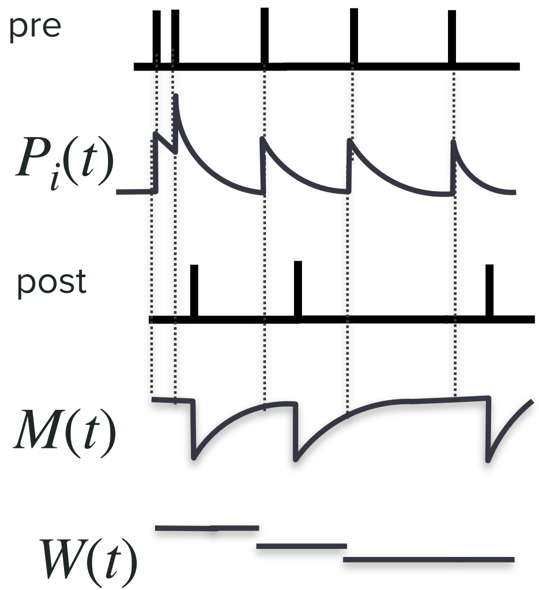


Pre-synaptic trace is thought to be the **activation of a metabotropic receptor**, or a pathway triggered by spike voltage: triggered by pre-synaptic spike and evanescent

Post-synaptic trace is thought to be the voltage **trace from the back-propagating action potential** to the location of the synapse: triggered by post-synaptic spike and evanescent

Modelling Spike-Timing-Dependent Plasticity

Pre- and post-synaptic traces

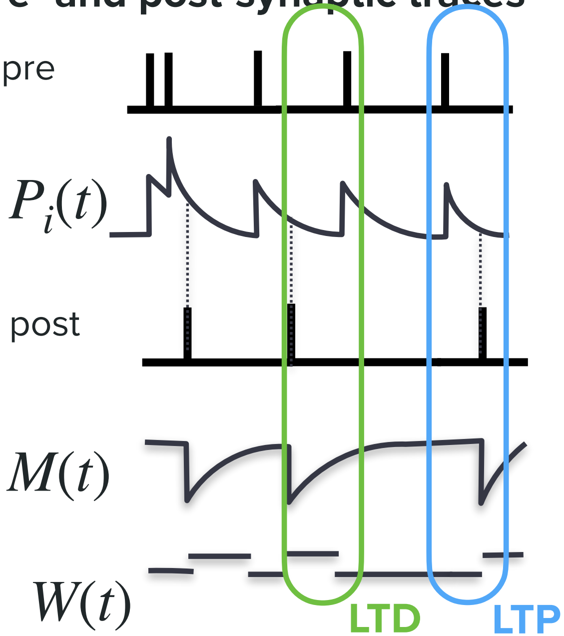


At each **pre-synaptic spike**, change weight according **post-synaptic trace**

$$\Delta W(t_{pre}) = M(t_{pre})W(t_{pre})$$

Modelling Spike-Timing-Dependent Plasticity

Pre- and post-synaptic traces



At each **pre-synaptic spike**, change weight according **post-synaptic trace**

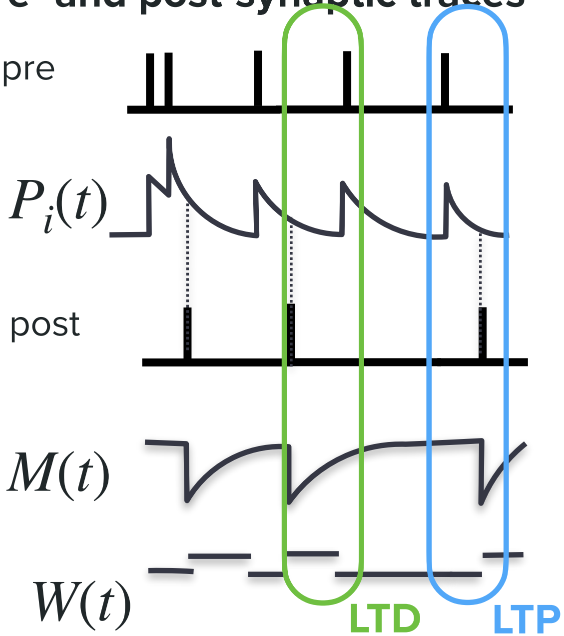
$$\Delta W(t_{pre}) = M(t_{pre})W(t_{pre})$$

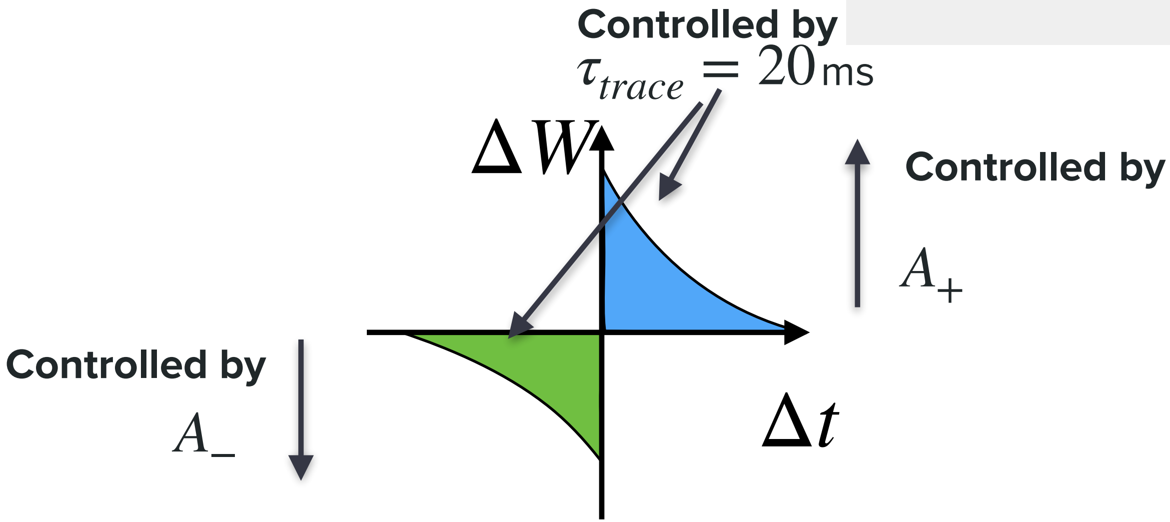
At each **post-synaptic spike**, change weight according **post-synaptic trace**

$$\Delta W(t_{post}) = P_i(t_{post})W(t_{post})$$

Modelling Spike-Timing-Dependent Plasticity

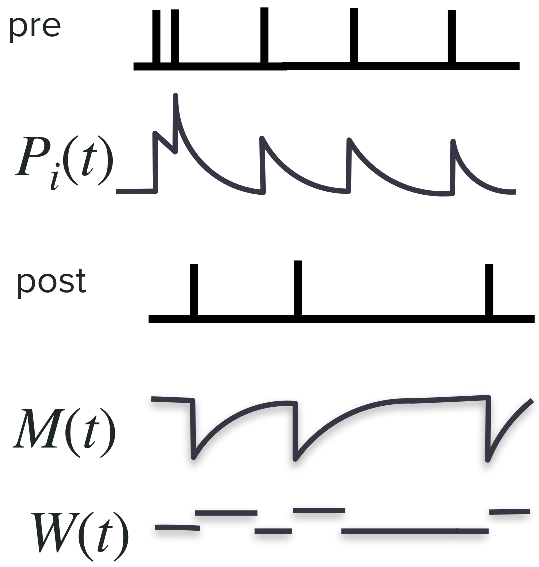
Pre- and post-synaptic traces





Modelling Spike-Timing-Dependent Plasticity

Synaptic bounds



At each pre-synaptic spike, change weight according post-synaptic trace **or up to upper bound**

$$\Delta W(t_{pre}) = min(M(t_{pre})W(t_{pre}),1)$$

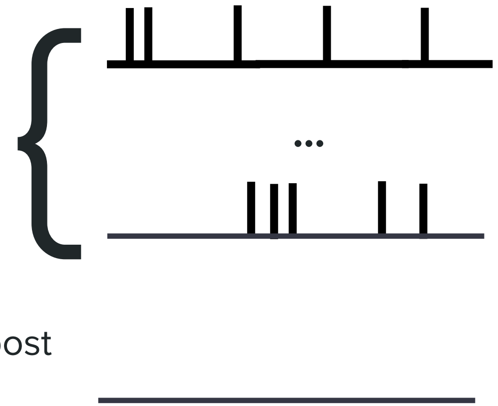
At each post-synaptic spike, change weight according post-synaptic trace or down to zero

$$\Delta W(t_{post}) = max(P_i(t_{post})W(t_{post}),0)$$

Exploring Spike-Timing-Dependent Plasticity

Start simulation with weak connections and **silent post** synaptic neuron

pre

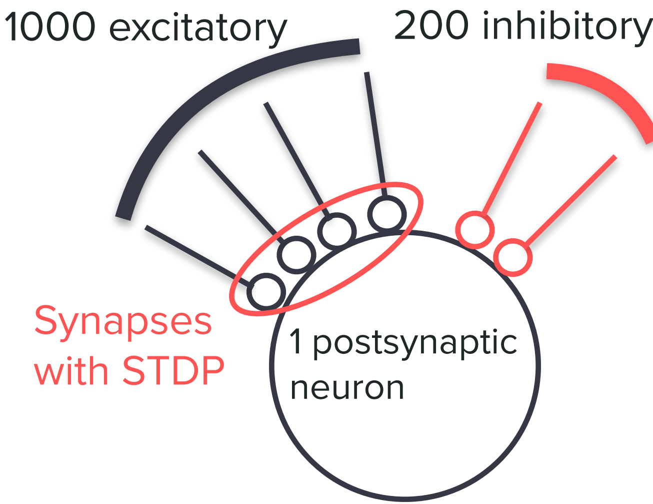


post

No pre-post Coincidence

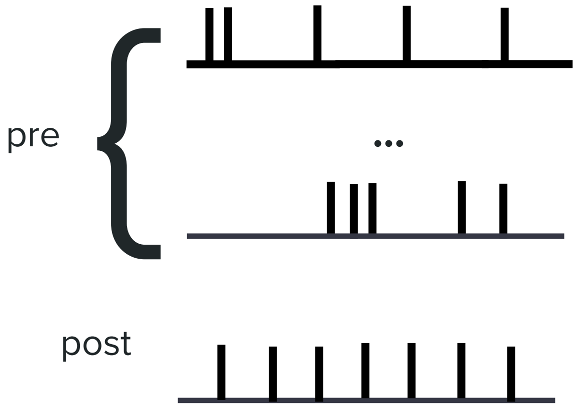
No plasticity

Neuron remains silent



Exploring Spike-Timing-Dependent Plasticity

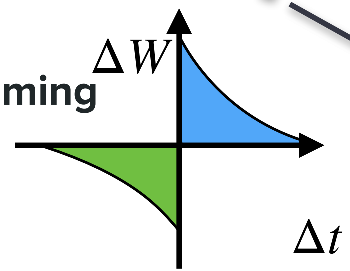
Start simulation with stronger connections and **active** post synaptic neuron

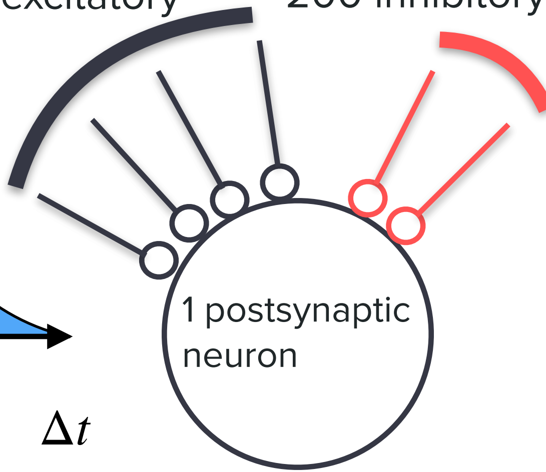


Regular firing

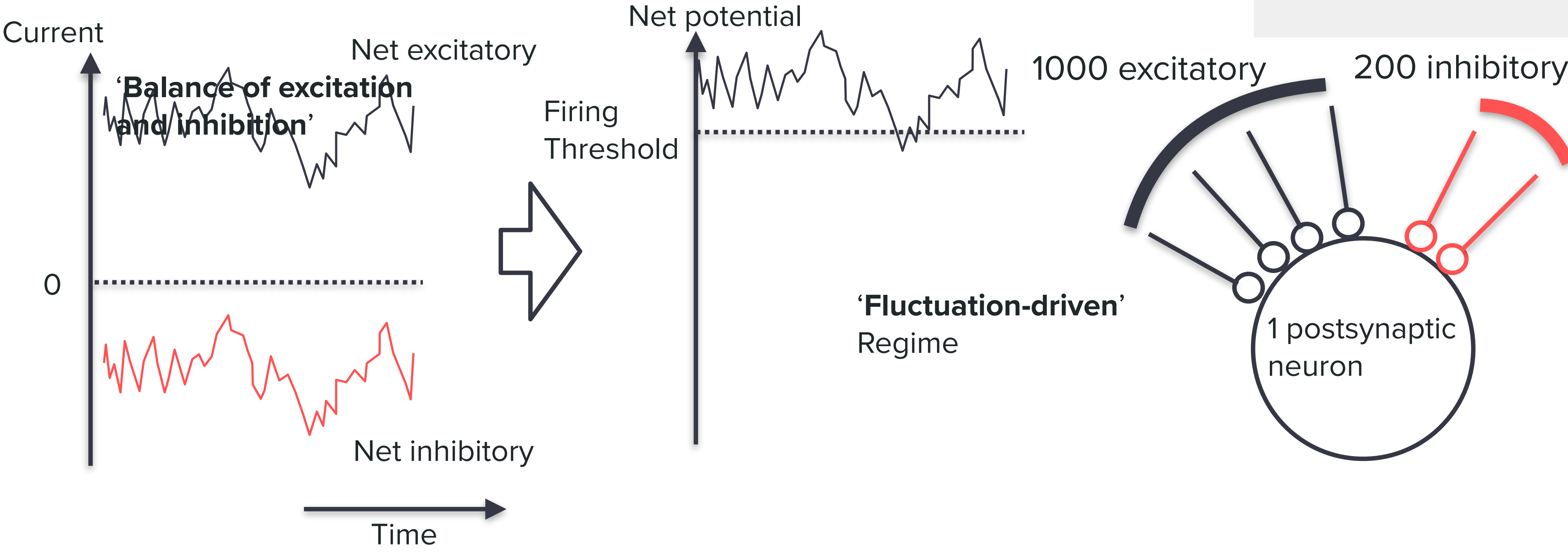
Random pre-post timing

Net depression if $A_{-} > A_{+}$



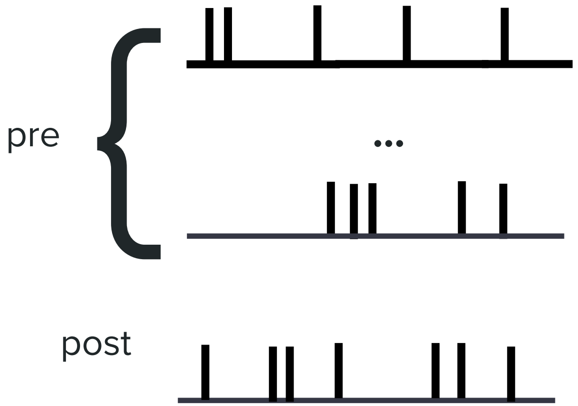


Exploring Spike-Timing-Dependent Plasticity



Exploring Spike-Timing-Dependent Plasticity

Start simulation with stronger connections and **active** post synaptic neuron

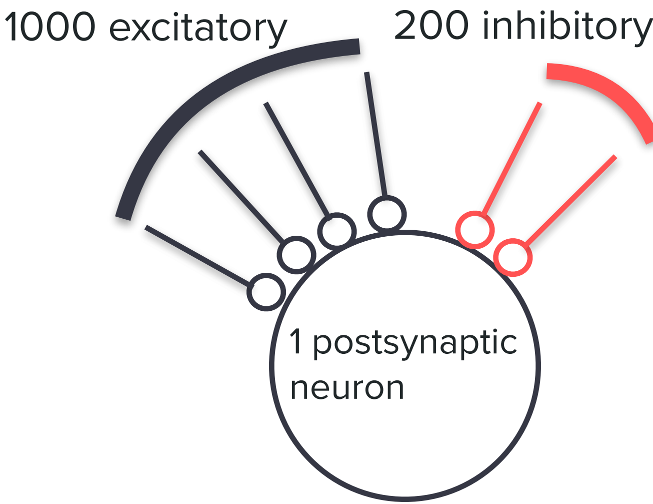


Regular firing

Random pre-post timing

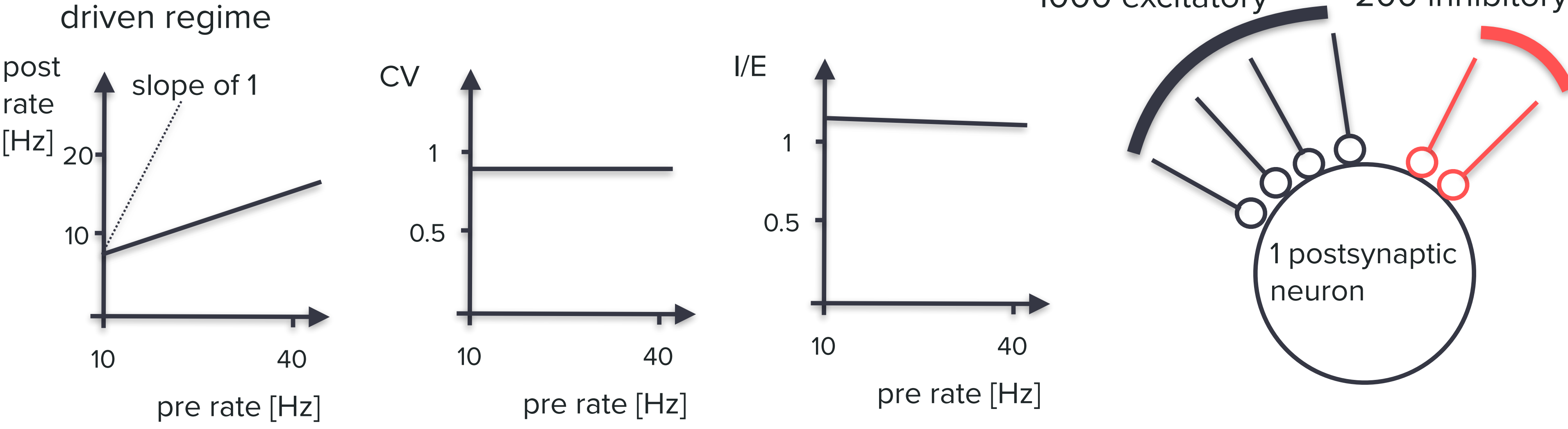
Net depression

Irregular firing



Exploring Spike-Timing-Dependent Plasticity

STDP can **stabilize net excitation** at the fluctuation-driven regime



Redrawn from : Song, Miller and Abbott *Nature Neuroscience* (2000)

Further Information

Textbooks:
Gerstner, Kistler, Naud and Paninski, *Neuronal Dynamics* (2014)
Dayan and Abbott, *Theoretical Neuroscience* (2001)

Spike-Timing Dependent Plasticity (STDP)
Gerstner et al. *Nature* (1996)
Kempter et al. *Phys Rev E* (1999)
Song, Miller and Abbott *Nature Neuroscience* (2000)
Song and Abbott *Neuron* (2001)
Vogels et al. *Science* (2011)

Neuromodulation and Firing Patterns
Izhikevich *Celrebral Cortex* (2007)
Payeur et al. *BioRxiv* (2020)
Pawlak et al. *Front. Synap. Neurosci.* (2010)