COMS30127/COMSM2127 Computational Neuroscience

Lecture 6: Modelling neurons

Slides adapted from Dr. Cian O’Donnell

What we will cover today

- What is a model?
- What is the purpose of computational modelling?
- Levels of abstraction (spatial, temporal and conceptual)
- Compare models of single neurons.
- How should we choose the 'correct' model for the problem at hand?

What is a model?

- A model is simply a representation of something – often a simplified version of a real-world system.

- Models can be:
  - Physical (e.g. scale models of buildings)
  - Analogical (e.g. billiard-ball model of a gas)
  - Phenomenological (e.g. integrate-and-fire neuron)

- Models can be represented by:
  - A physical object
  - Words
  - Mathematical equations

- In experimental neuroscience we have animal ‘models’ that model human diseases

- Overview of the philosophy of models in science: https://plato.stanford.edu/entries/models-science/

What is a computational model?

- Fundamentally, a computational model is just a mathematical model that is programmed and then solved or simulated using a computer.
- Allows us to study the behaviour of complex, often non-linear systems using computer simulations
- Computational neuroscientists aim to explain how the brain represents and processes information in the form of electrical and chemical signalling
- There are many, many, many different types of neuronal models that range from simple models of individual neurons to huge networks comprising hundreds of detailed descriptions of neurons
- Processing power can be a limiting factor in what we can do

What is the purpose of a computational model?

“All models are wrong, but some are useful.”

— George Box

- Example: Through modelling the action potential waveform, Hodgkin and Huxley were able to predict the presence of ion channels and also the 3D-structure of them! It wasn’t perfect (wrong number of channel gates) but it completely revolutionised our understanding of neurons.

But not just neuroscience… google translate, brain-machine interfaces

What is the purpose of a computational model in neuroscience?

To gain an understanding of a system beyond what we could achieve via word models alone.

Computational models can be used to:

1. test if a set of concepts are mutually consistent. If not, why?
2. "link levels", i.e. to ask if a mechanism at one level of description can account for a phenomenon at another level.
3. simulate experiments that are technically difficult or impossible to do in the lab and direct future research
4. explore "what if?" scenarios that may never occur in the natural world.
5. validate a formal mathematical analysis.

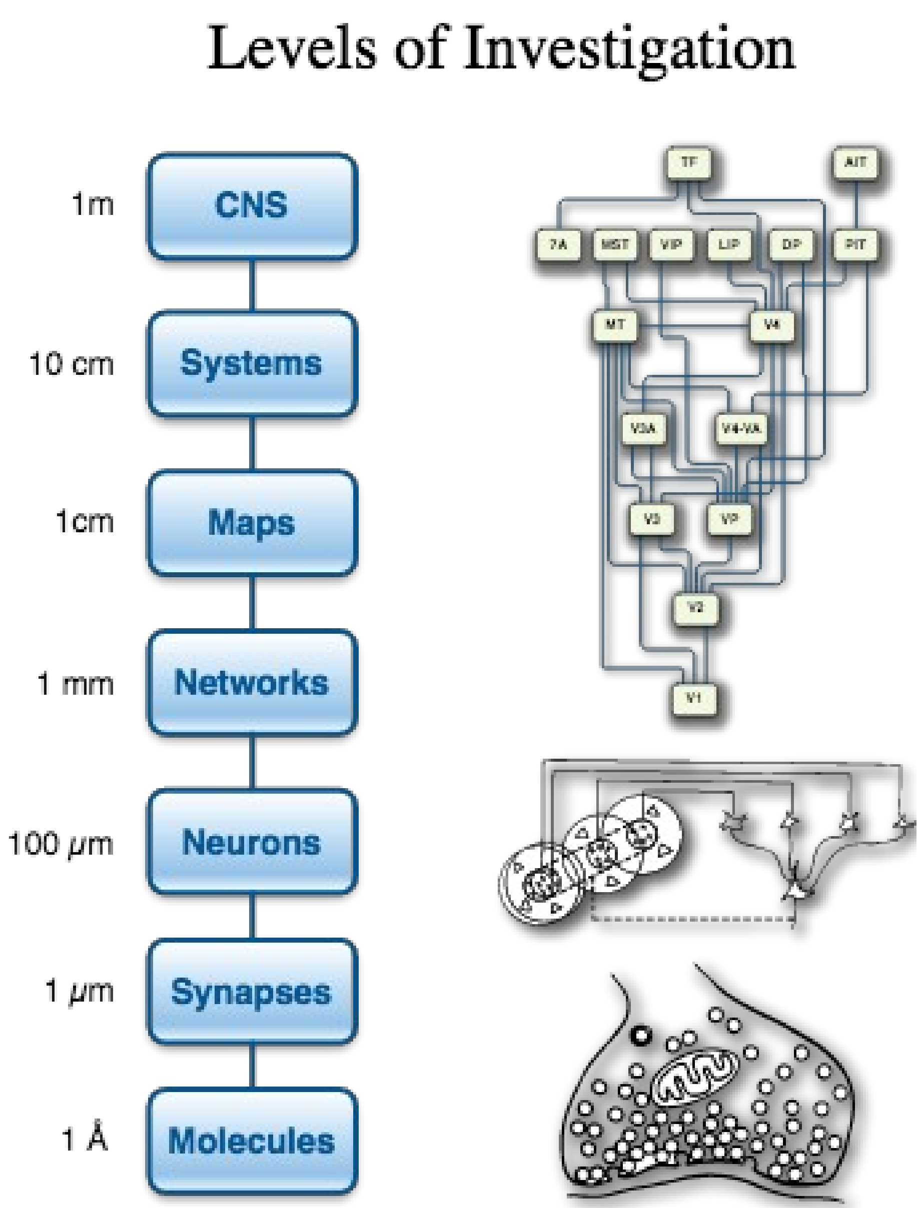
A few examples of computational models in neuroscience

Example usages of computational models in neuroscience:

- Hodgkin-Huxley model
  - can the action potential be explained by the voltage gating dynamics of sodium and potassium conductances?
- Simulating recurrent hippocampal neural networks with synaptic plasticity
  - Can synaptic plasticity mediate memory recall from partial cues?
- Simulating the biophysics of calcium signalling at a synapse
  - what happens during synaptic stimulation?
- Dynamic causal models
  - Connectivity between which brain regions are functionally affected in human disorders like depression or schizophrenia?

Levels of abstraction

Spatial

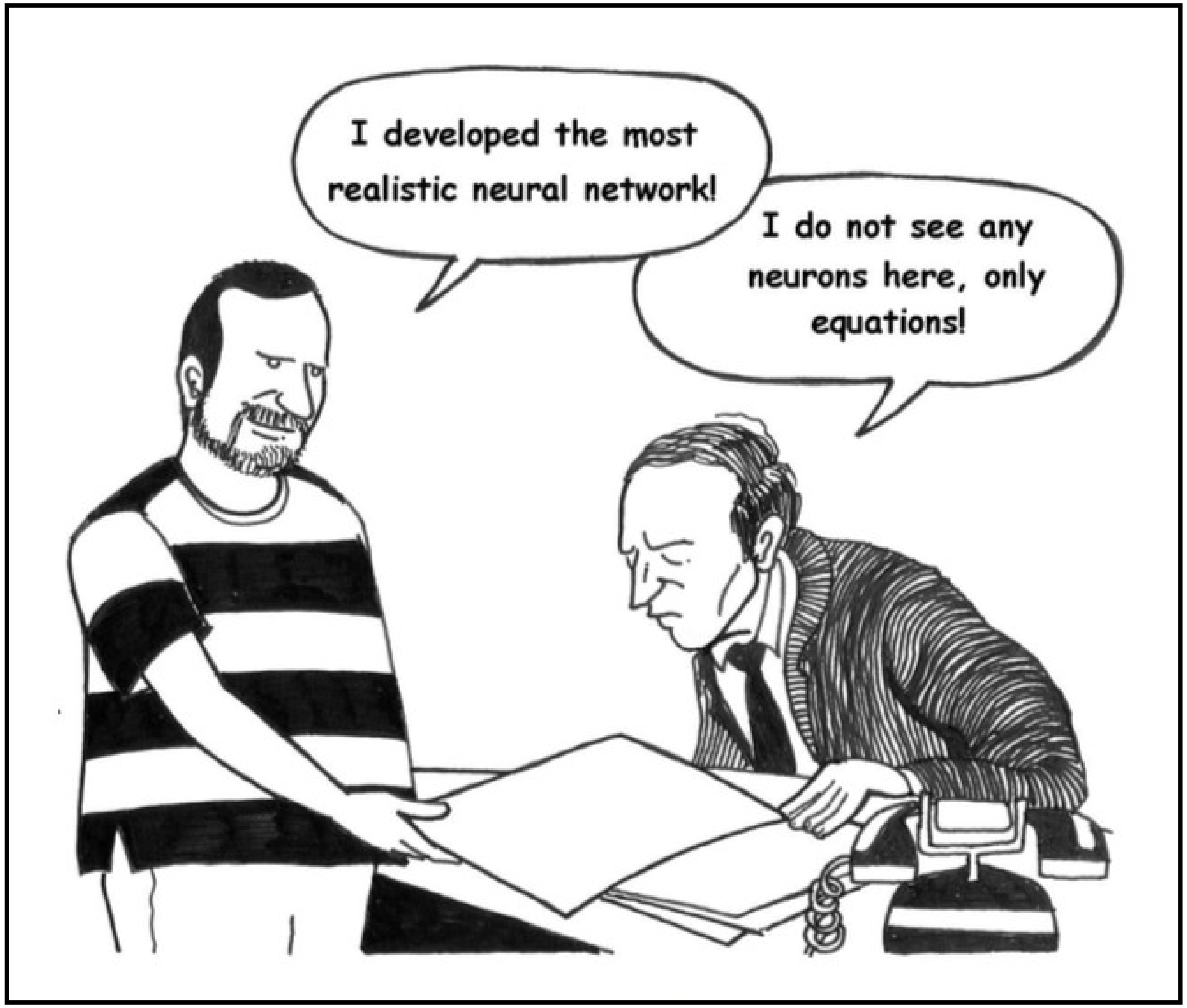


T. Sejnowski
http://cnl.salk.edu/

Temporal

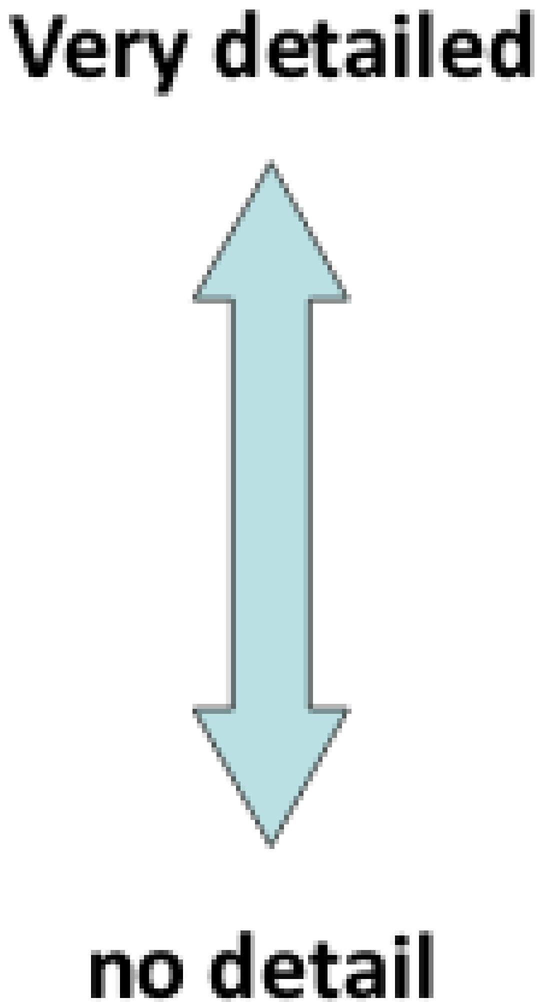
years	Memories
weeks	Brain development
hours	Gene expression
mins	Cellular signalling
s	Neural circuit dynamics
ms	Action potential

Models of single neurons



Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting. Izhikevich E.M. (2007)

Modelling the function of a single neuron: levels of description



Full compartmental HH models

Single compartment HH models

Leaky integrate-and-fire models

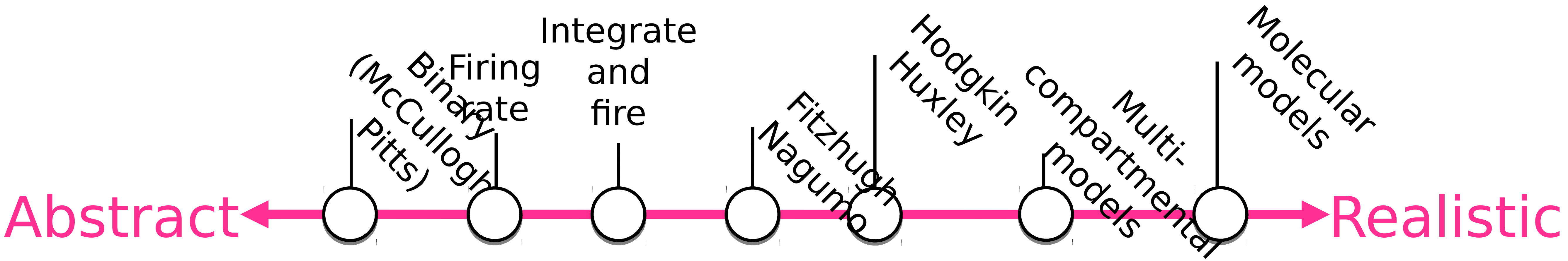
Integrate-and-fire models

Standard artificial neurons

Threshold logic (McCulloch-Pitts)

And this is keeping it simple: there are lots of them!

Models of single neurons



Abstract models		Realistic models
Simple	vs	Detailed
Hard to relate to biology	vs	Contains stuff you could measure
Few parameters	vs	Lots of parameters
Fast simulation	vs	Slow simulation
Mathematical analysis	vs	Intractable
Generic	vs	Specific

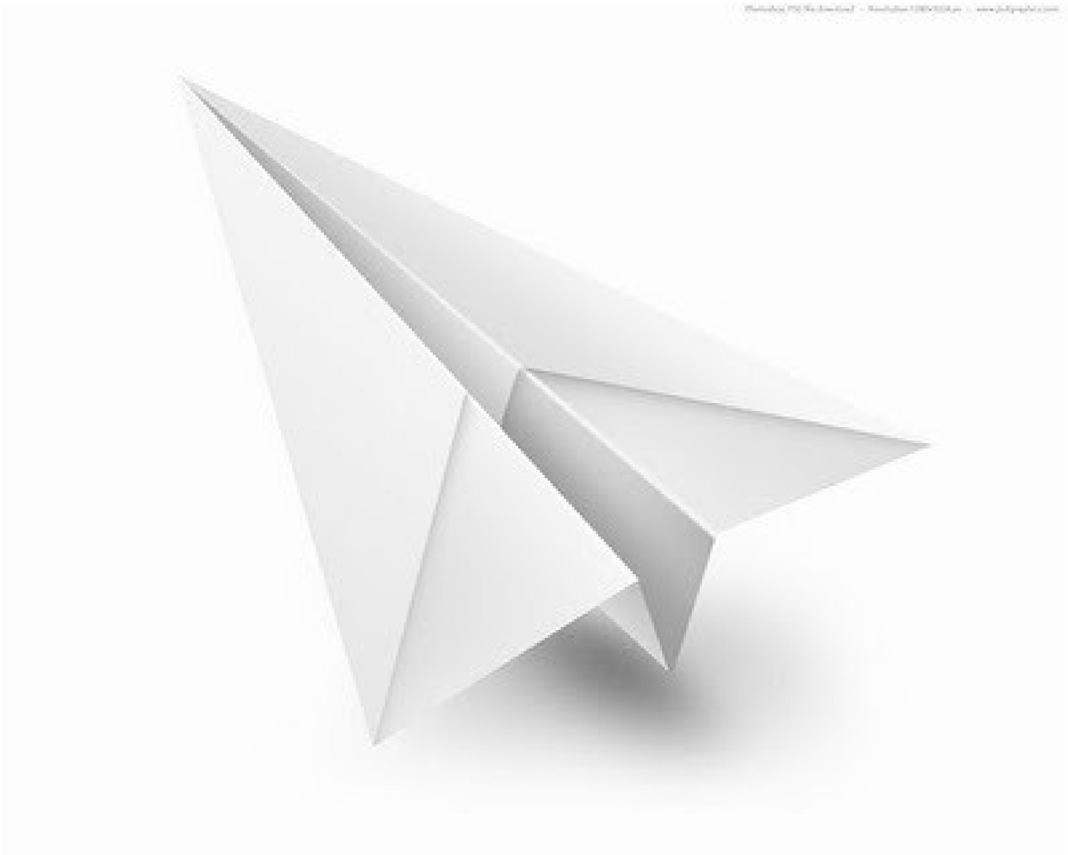
Which model is best for my problem?

Choose the form of the model that best matches the granularity (the scale and/or level of detail) in the data and/or your scientific question.

- "A model should be as simple as possible, but no simpler"
  — Albert Einstein

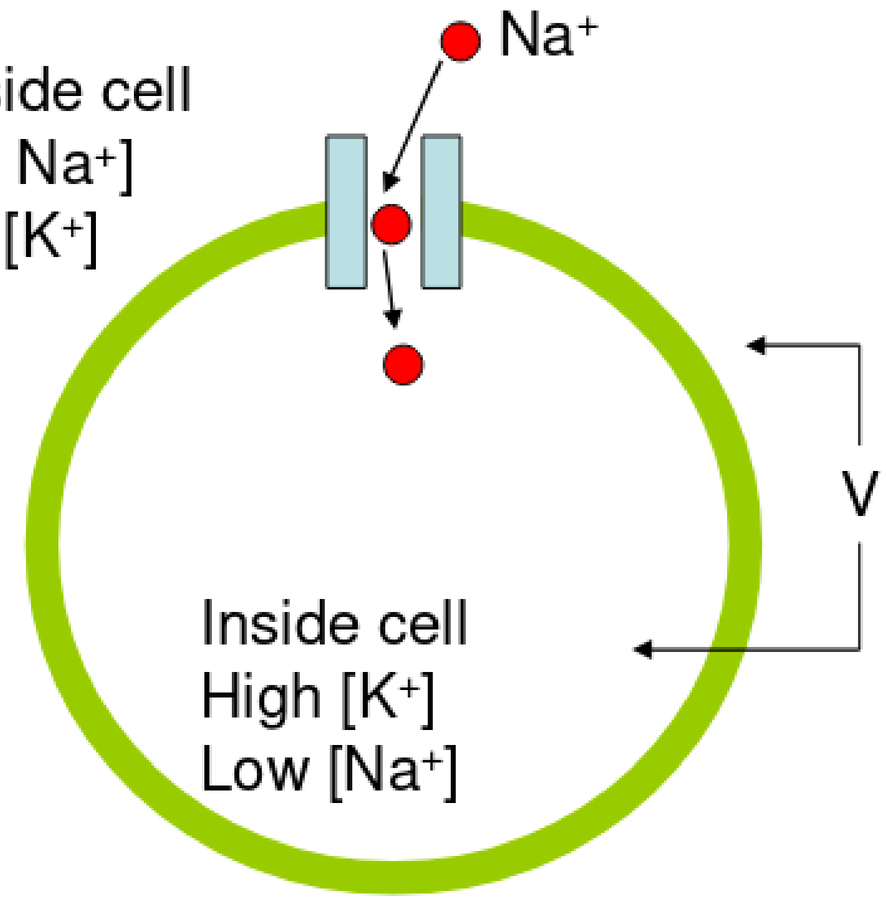
- Often this choice is dictated by:
  - the data you have to constrain the model
  - the phenomenon you wish to explain
  - the computational resources you have available
  - how much maths/programming you know
  - ~~what someone else did previously~~

Details vs realism

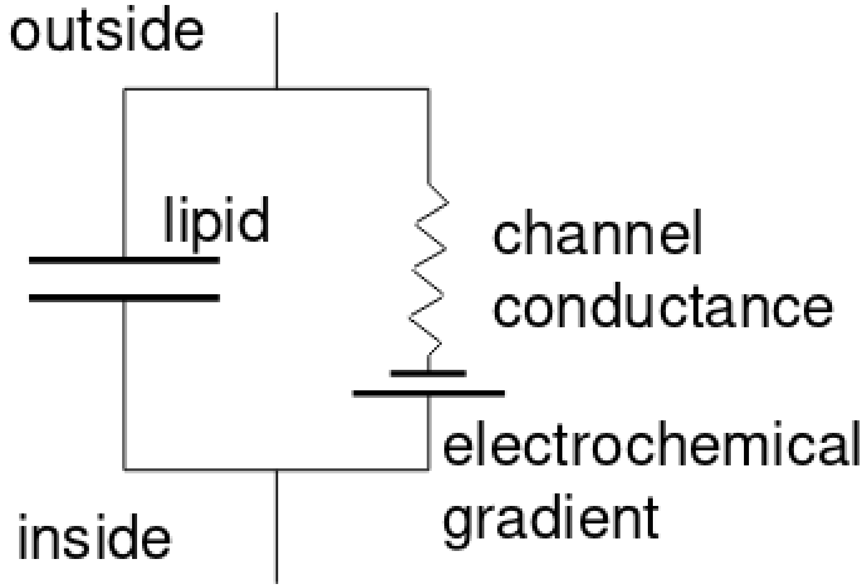


c.f. Brette, PLoS Comput Biol, 2015

Neurons code information as transmembrane voltage changes



[K+] gradient sets resting potential of -70mV



A neuron can be likened to an electrical circuit:

Ohm's law: V = IR

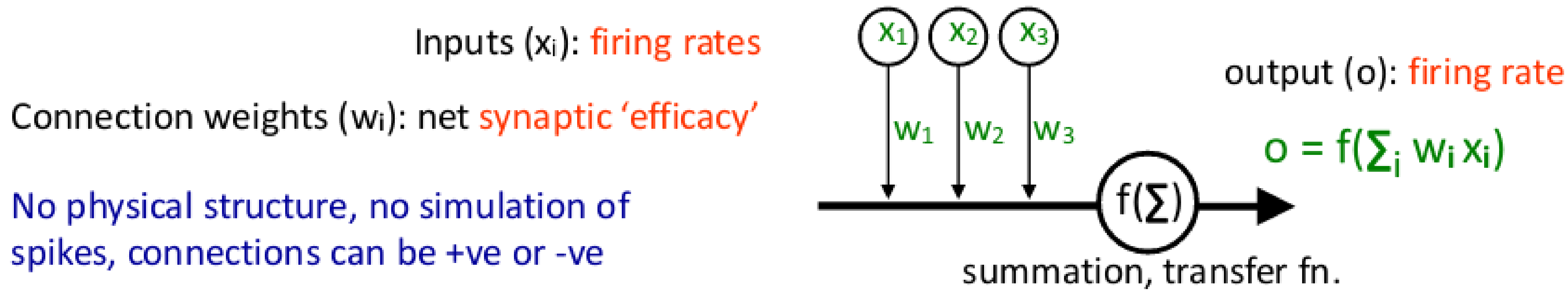
Capacitor = phospholipid bilayer
Battery = electrochemical gradient
across the cell membrane
Resistor = membrane channels

Computational models of neurons capture the dynamics of the membrane voltages to a greater or lesser extent

...

A whistle-stop tour of single neuron models

Standard Artificial Neuron



X_1, X_2 and X_3 are three inputs coded as firing rates from three different neurons.

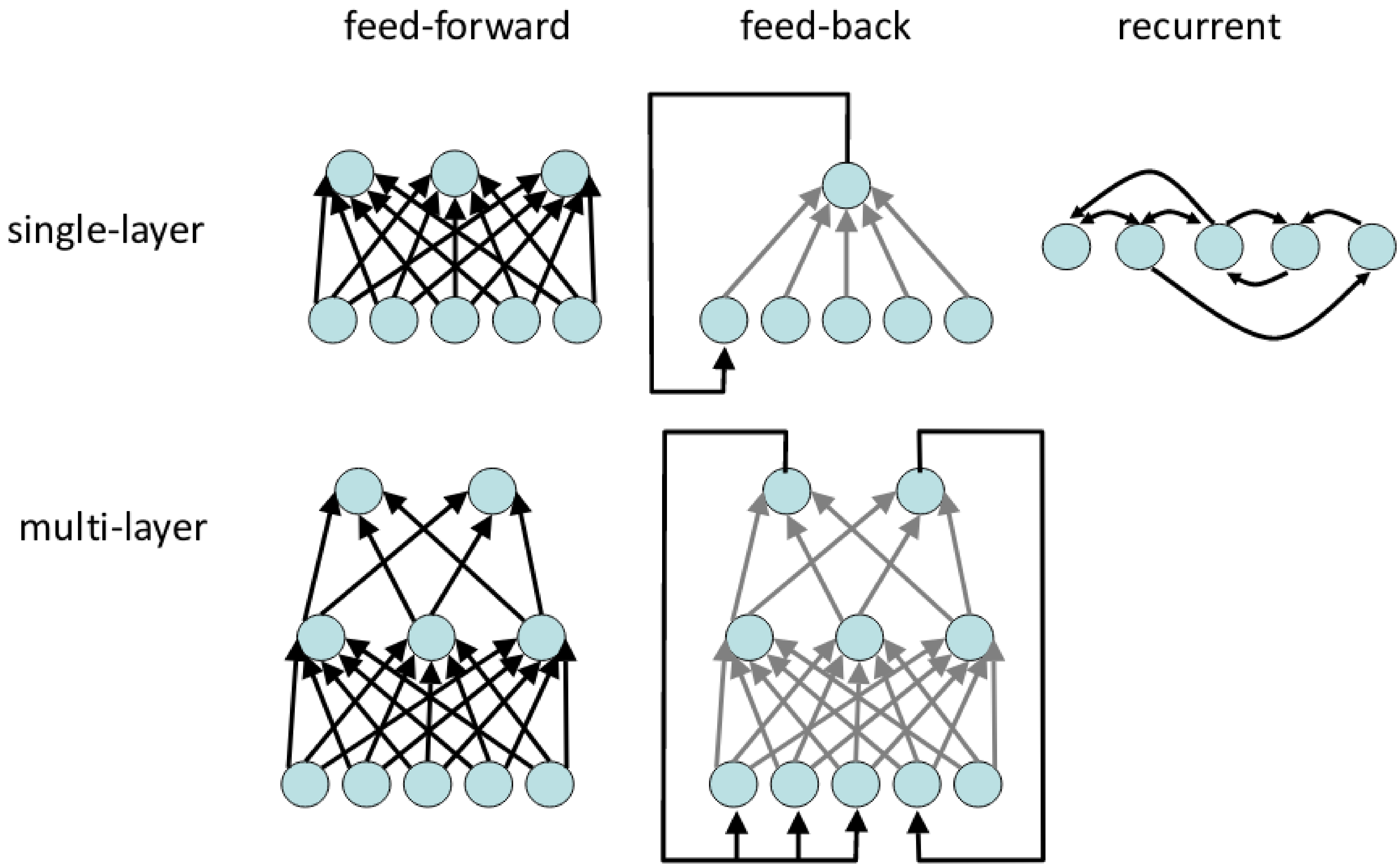
W_1, W_2 and W_3 represent the strength of the connection from each of the inputs X to the neuron we are simulating.

The 'net input' to our neuron is: $h = \sum_i w_i x_i = w_1 x_1 + w_2 x_2 + w_3 x_3$

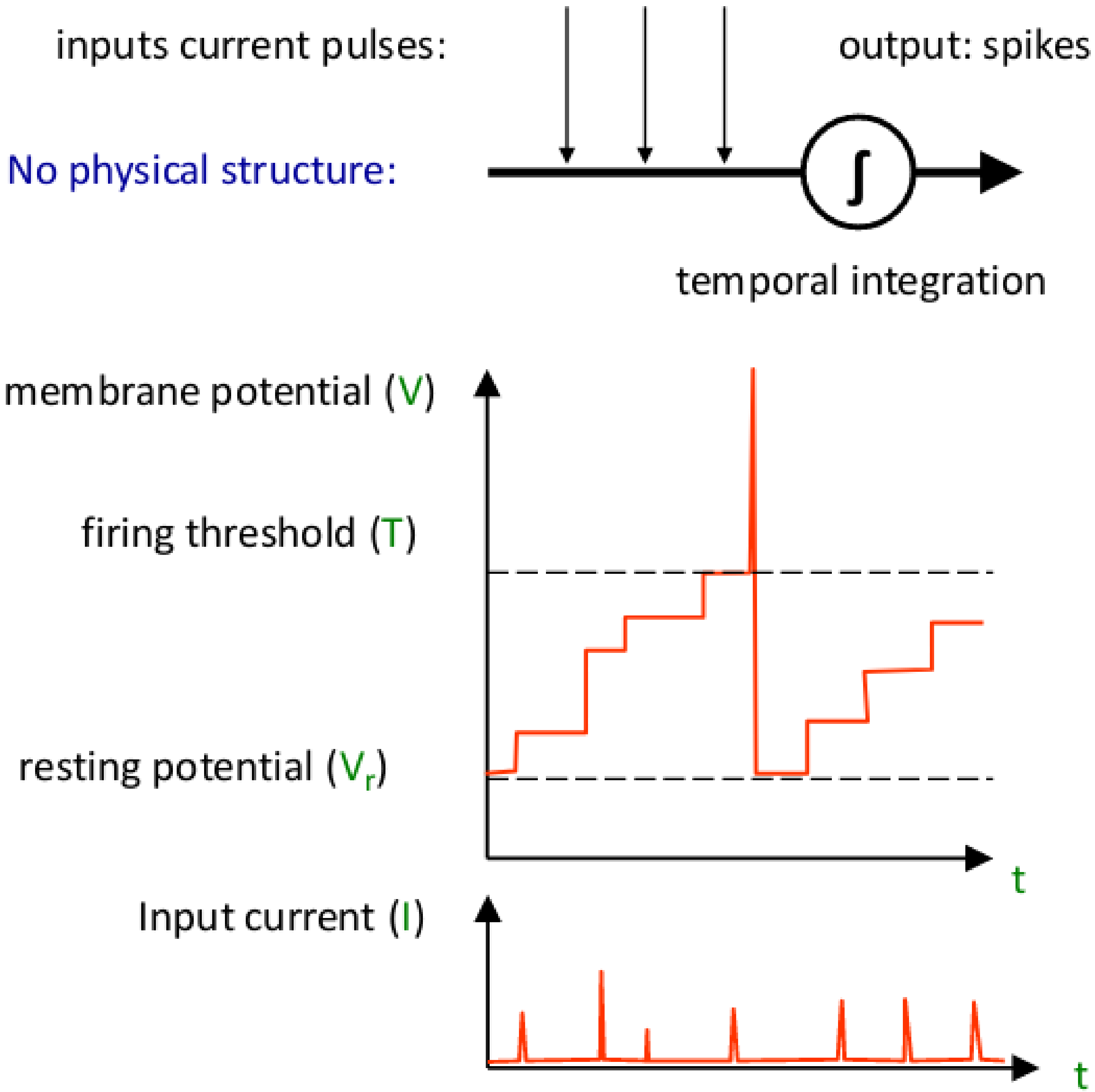
This is the 'weighted sum' of input activation.

The output from these simulated neurons is just a firing rate value. We don't know V_m

These neurons can be connected into artificial neural networks



Integrate and Fire

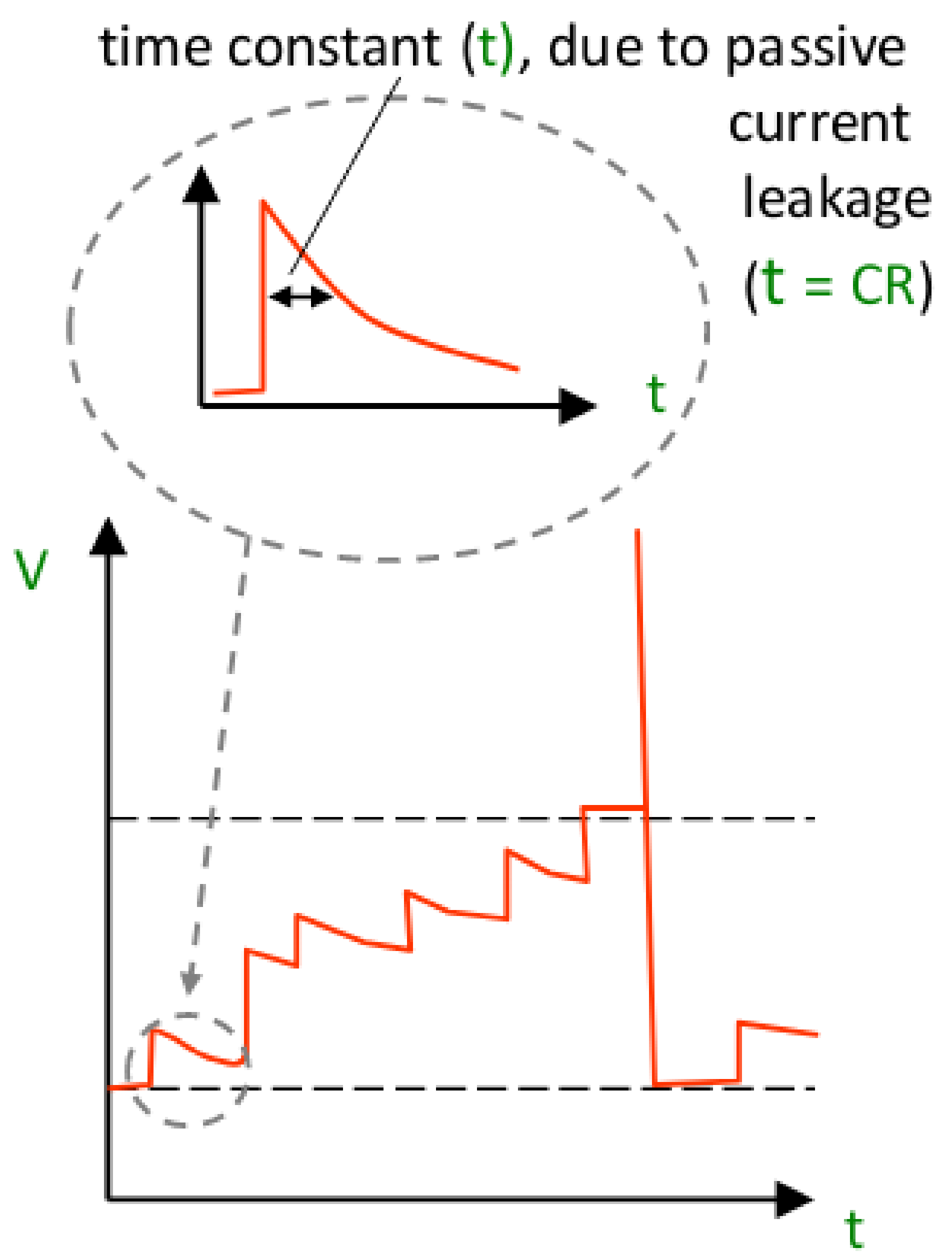


Inputs get integrated in time and summate. If the membrane potential increases above a threshold value, the neuron fires a spike.

$C = q/V$, $CV = q$, $C\,dV/dt = I$; $C\,dV/dt = (V_r - V)/R + I$,

$V = IR$, $I = V/R$; with spike if $V = T$

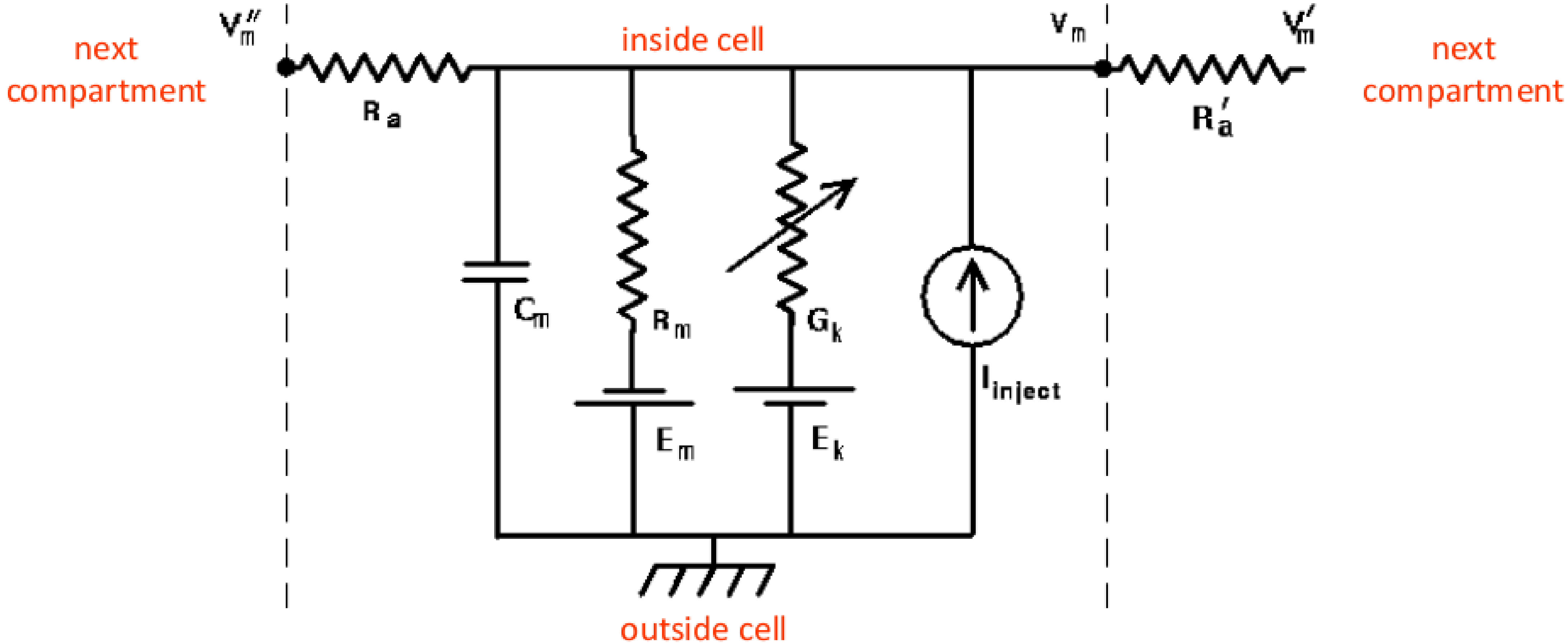
Leaky Integrate and Fire



Leaky integrate and fire neuron models include a membrane time constant that models the leakage of current from the inside of the cell to the outside of the cell over time.

Leakage of the current means that it takes longer for the cell to reach threshold.
Inputs must also arrive closer in time in order to summate and make the cell reach threshold.

Compartmental neuron models



V_m: membrane potential inside the compartment (relative to "ground" outside cell).

C_m: membrane capacitance - charged or discharged as ions flow in or out of the compartment (changing V_m) from adjacent compartments (V_m' and V_m'', axial resistances R_a and R_a') or through the membrane.

R_m: leakage resistance & equilibrium potential E_m represent passive channels (rate and direction of current flow depends on size V_m versus E_m).

G_k: variable conductances (1/resistance) specific to particular ions. Each has its own equilibrium potential E_k and may vary with V_m (**active** channels).

Compartment Models

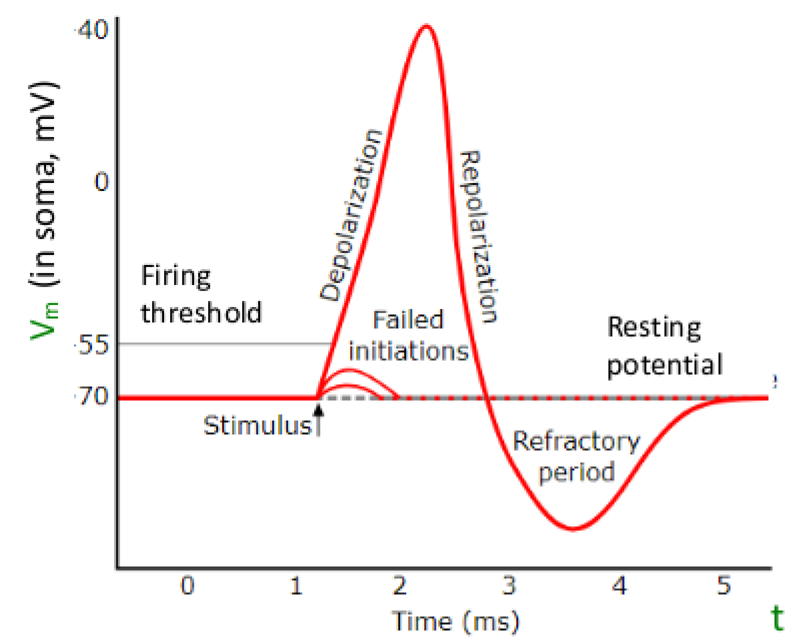
Compartment models are biophysical neuron models and simulate the membrane potential of the neuron.

The output can therefore be a voltage trace and we can model the action potential.

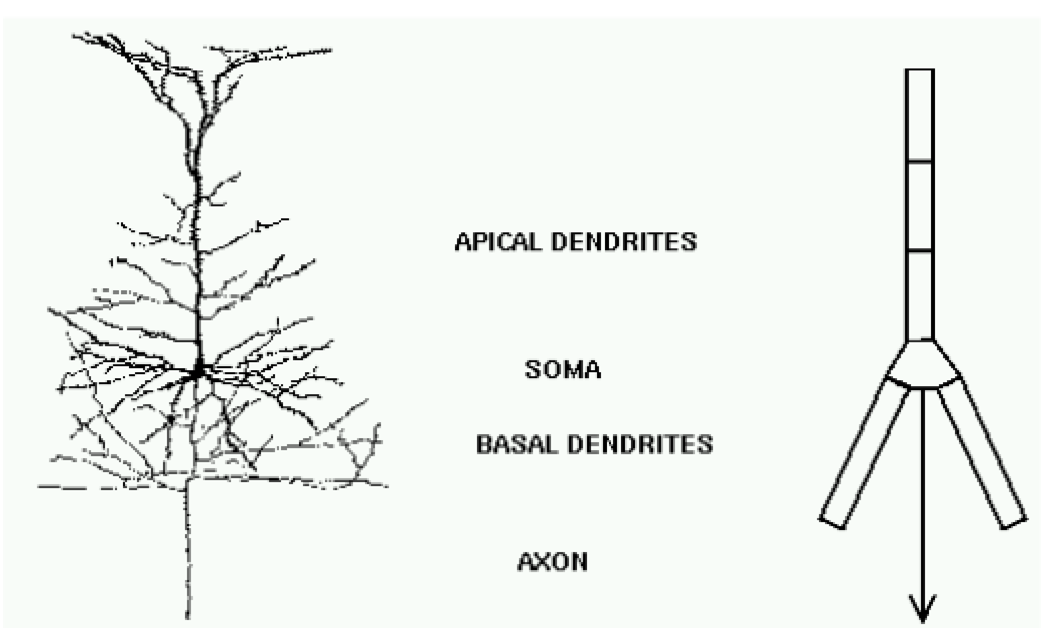
Of course from this information we can also then calculate firing frequency, variability etc.

We can choose the number of different compartments to include in the model:

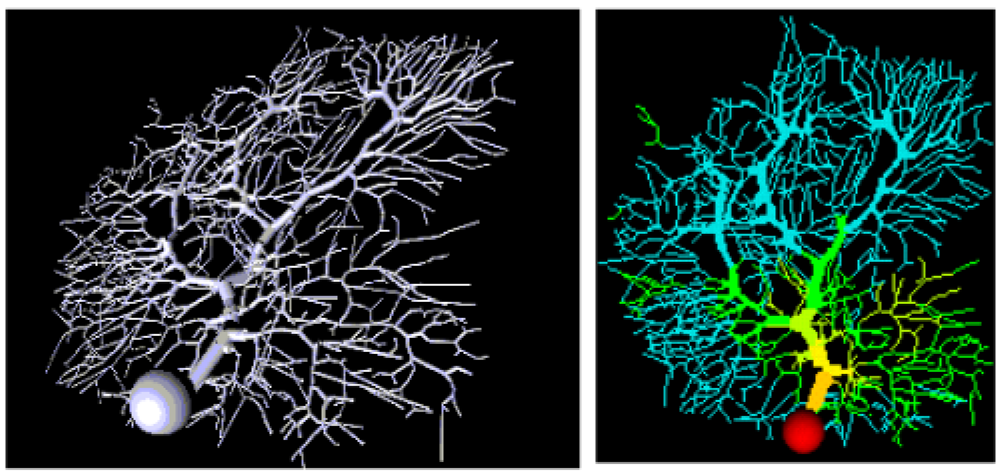
action potential ('spike')



Model cell with small no. of compartments

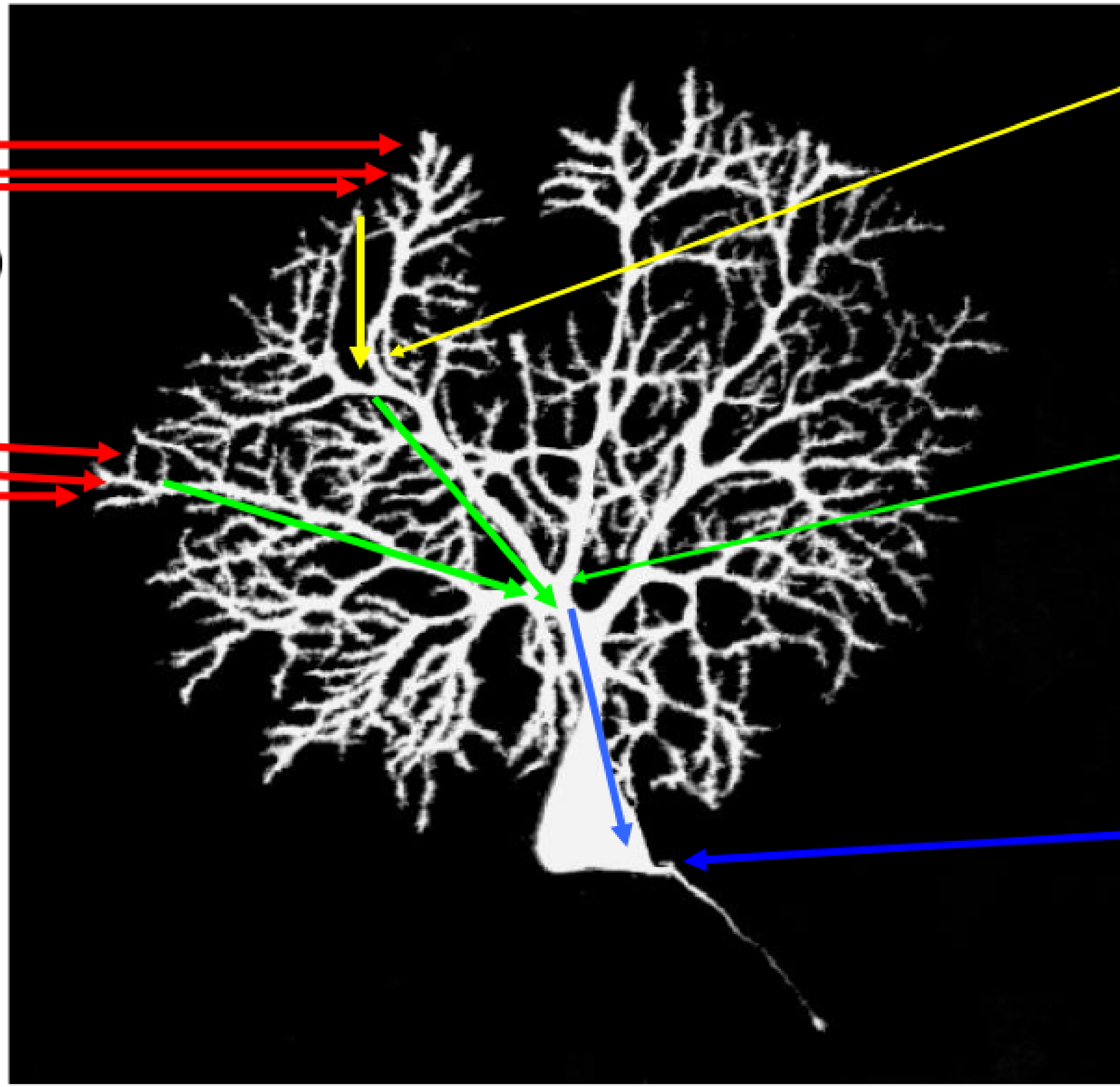


or large no. of compartments..



Computer simulation of Purkinje cell, color ~ membrane potential.

Spread of signals through the dendritic tree



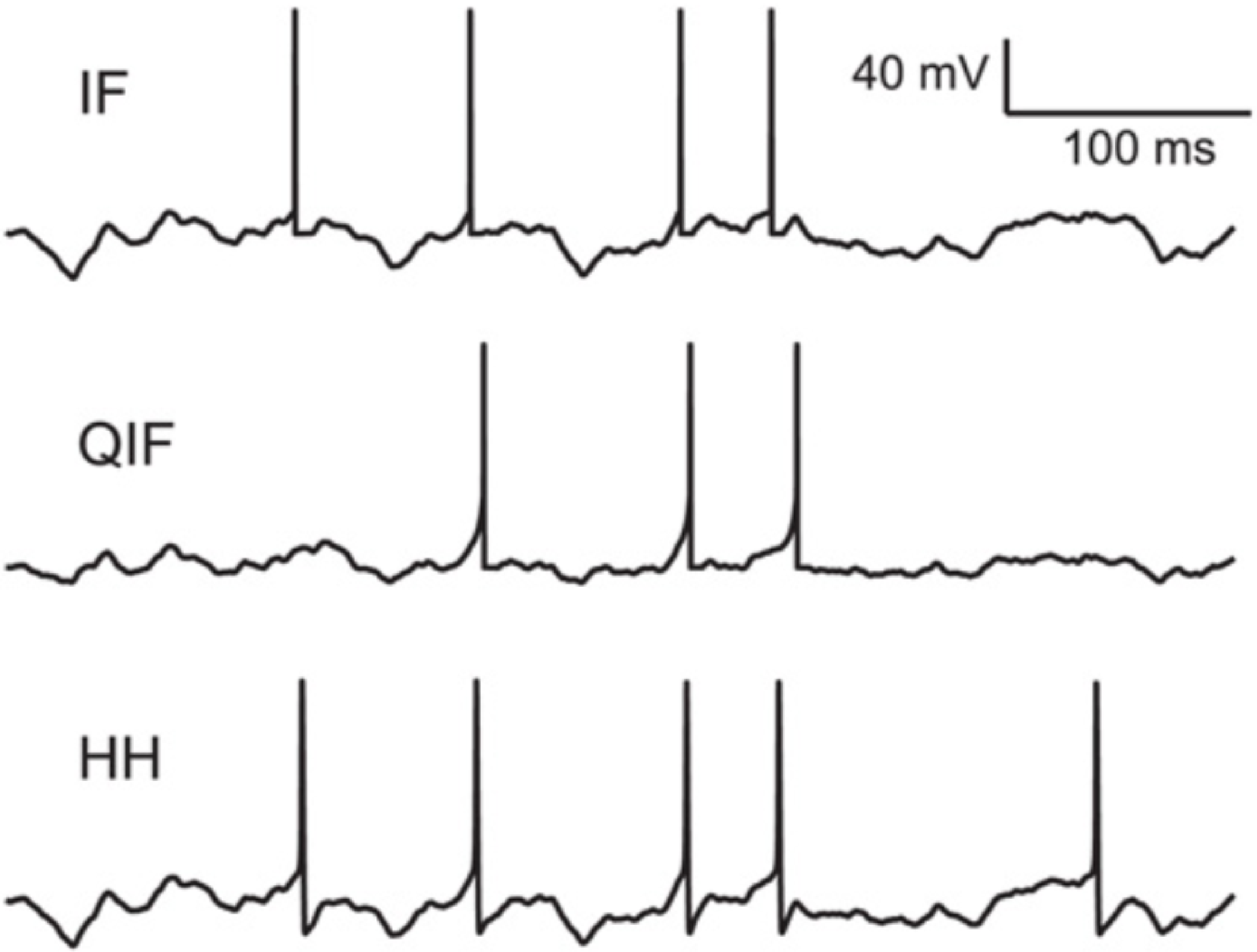
There are lots of separate opportunities for information processing in the dendritic tree

Outputs from compartmental models

Integrate-and-fire

Leaky integrate-and-fire

Hodgkin and Huxley



Voltage from three different model neurons in response to the same identical input current.

Brette, PLoS Comput Biol, 2015

Next Tuesday

- McCollough-Pitts neurons
- Classic binary neuron models that can do surprisingly powerful computations.
- Some nice pre-reading on Pitts: http://nautil.us/issue/21/information/the-man-who-tried-to-redeem-the-world-with-logic