Simulation of Biological Neural Networks:
Neuron Models

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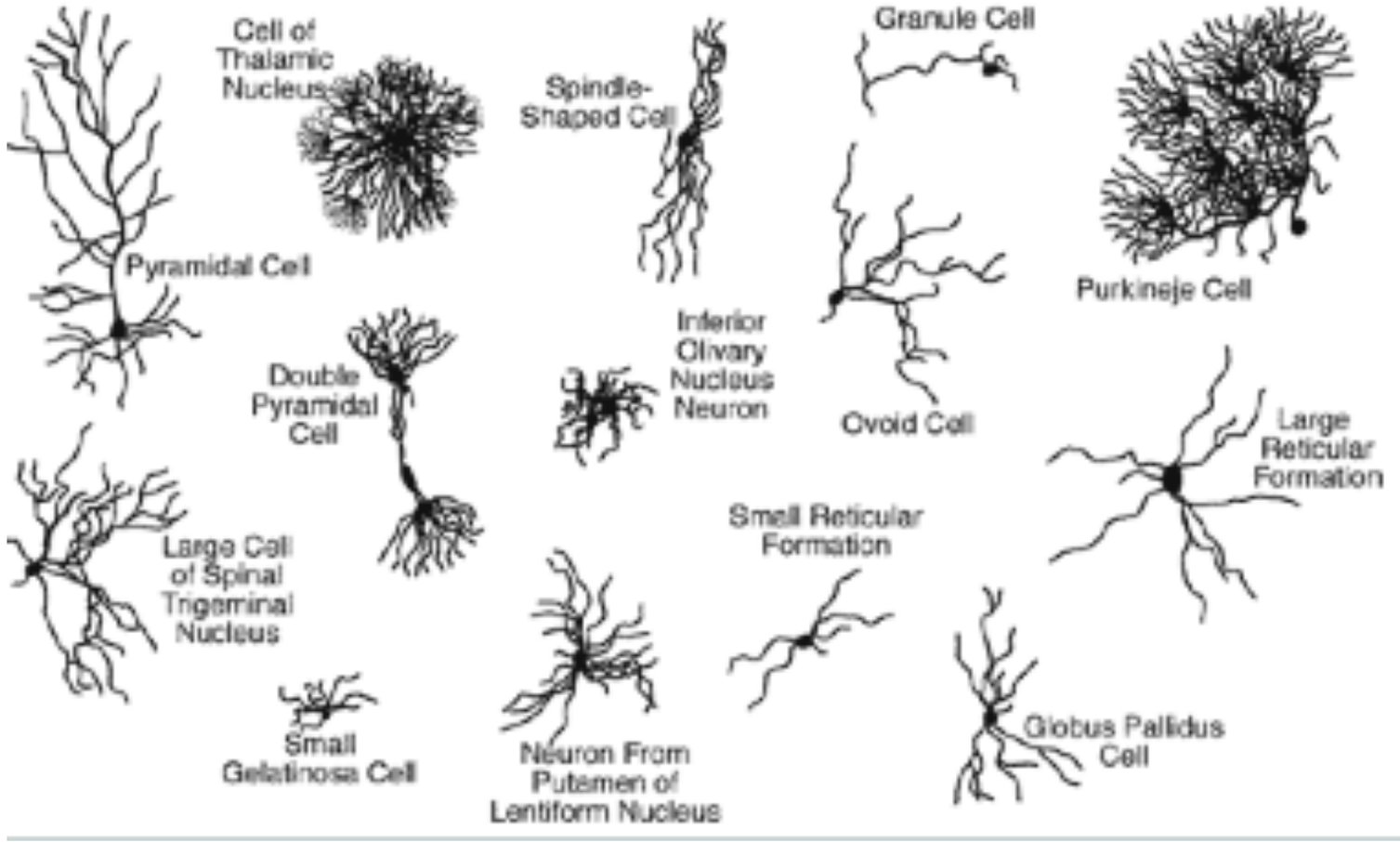
Overview

- Review of spatial structure and dynamics of a physiological neuron
- Modelling approaches: detail or abstraction?
- Representation of physiological neuron features in a point neuron model
- Advantages of the point neuron modelling approach
- Simulating a mathematical model
- Choosing a model

The physiological neuron: spatial structure

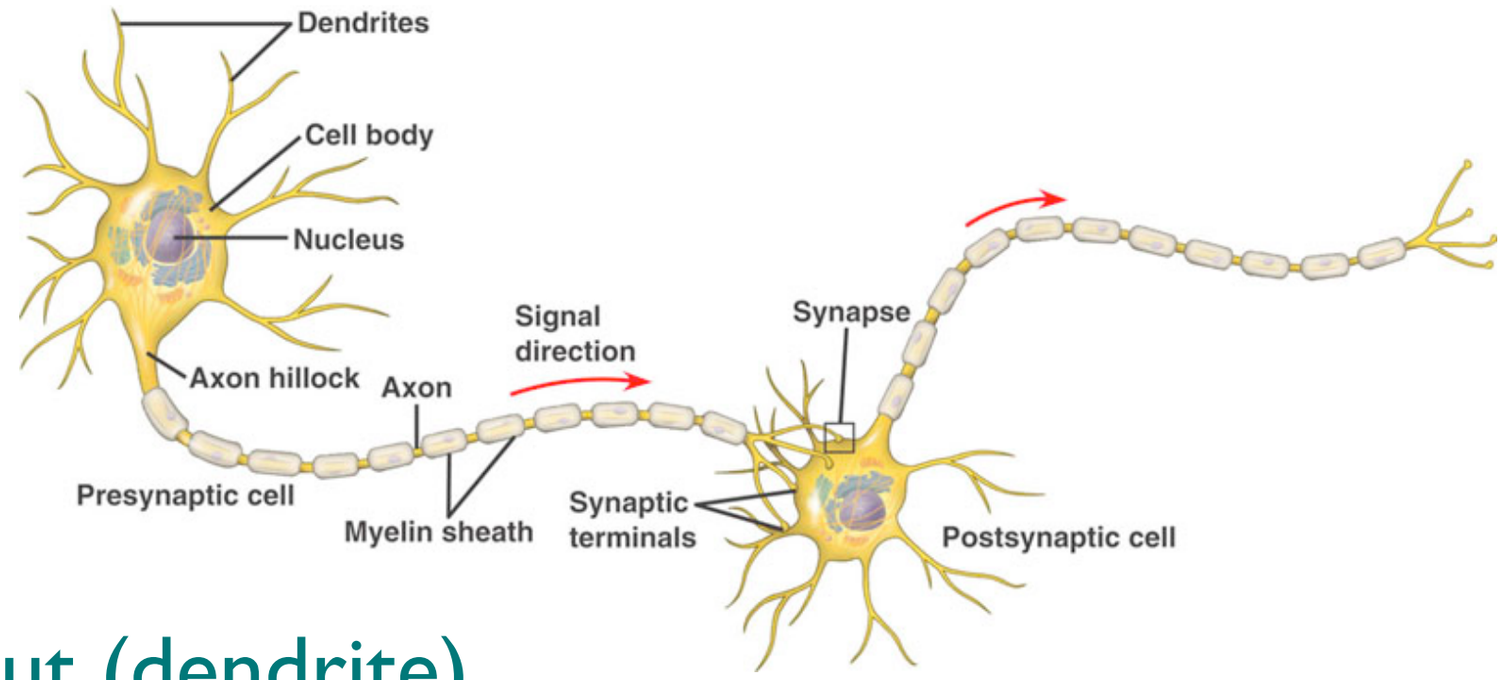
There are thousands of different neuron types with different structural features



based on drawings by Cajal (1852 -1934)

The physiological neuron: a "typical" cell

However, they all function in much the same way:

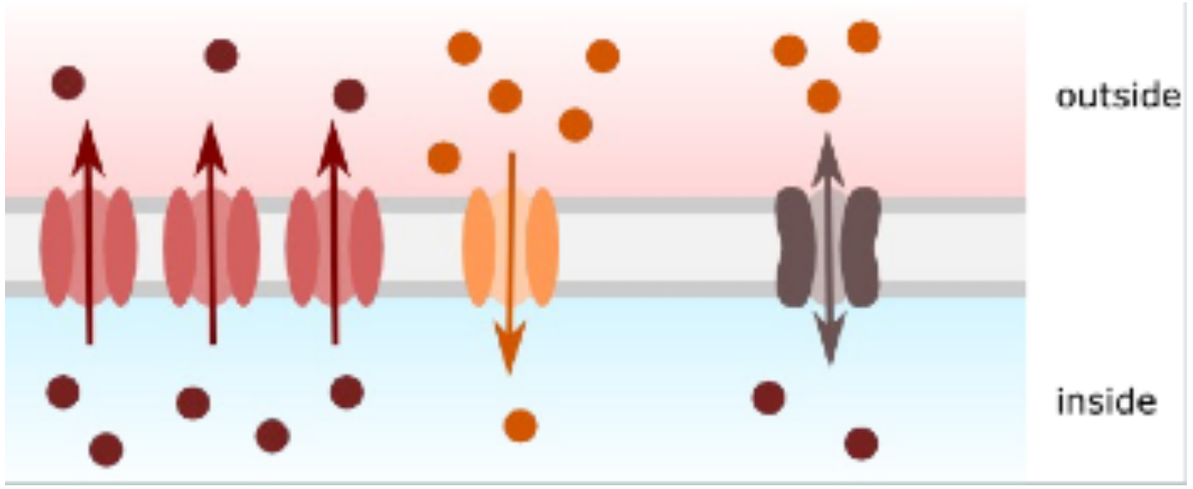


1. local input (dendrite)
2. integration (soma)
3. long range conducting (axon)
4. output (synapses)

The physiological neuron: resting potential

K^+/Na^+ pump pushes Na^+ out of the cell and K^+ into it

- This creates a concentration gradient
  - a 'force' which acts outwards on K^+



K^+ leaks out, dissipating the gradient

- This causes a net negative charge on the inside of the membrane
- electrical force now acts inwards on K^+

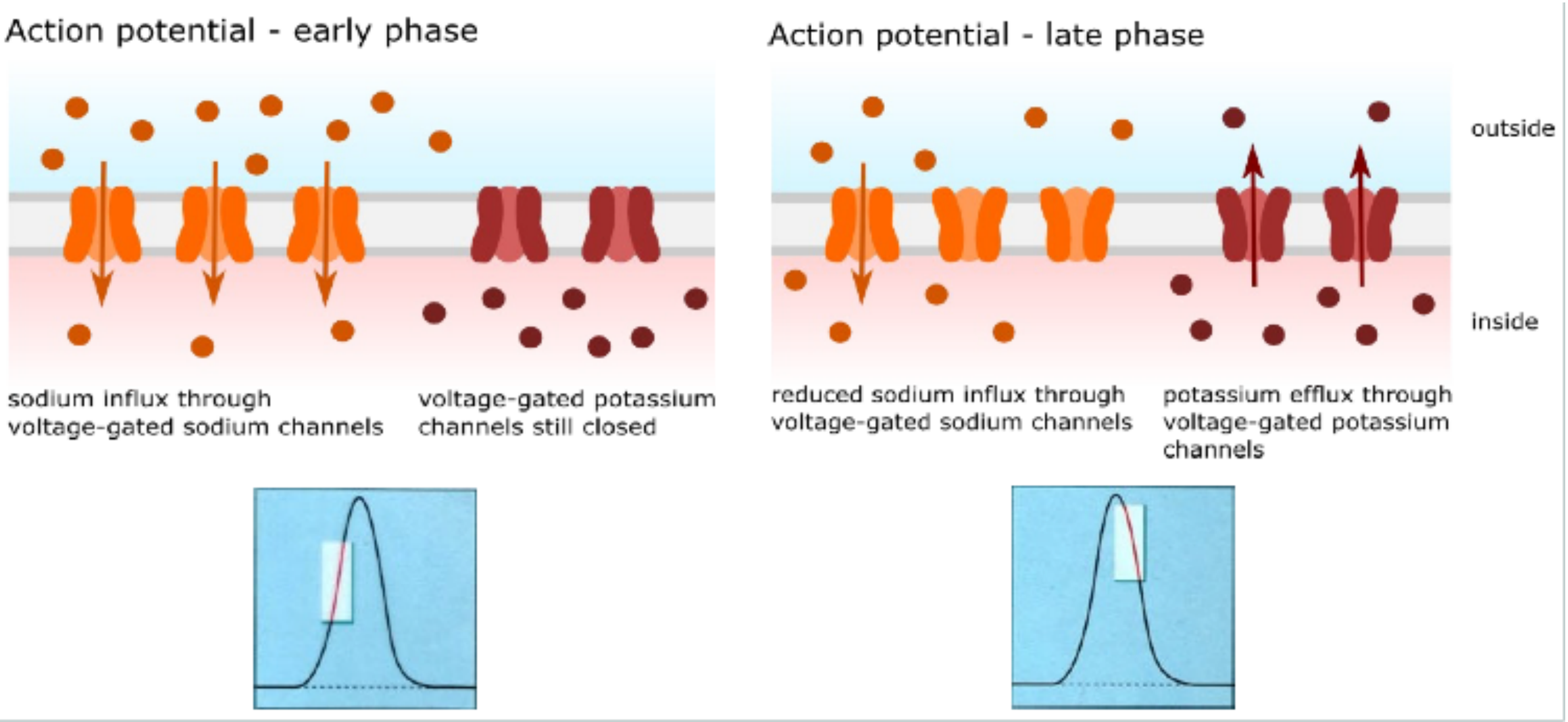
Equilibrium reached when diffusion and electrical forces balanced: the Nernst Potential

$$E_{eq,K^+} = \frac{RT}{F} \ln \frac{[K^+]_o}{[K^+]_i}$$

Resting potential is the weighted average of the equilibrium potentials for each ion

$$E_m = \frac{P_{K^+}}{P_{tot}} E_{eq,K^+} + \frac{P_{Na^+}}{P_{tot}} E_{eq,Na^+} + \frac{P_{Cl^-}}{P_{tot}} E_{eq,Cl^-}$$

The physiological neuron: action potential



Essential features of neurons

- Connectivity / morphology
- Internal dynamics that integrate inputs
- Generation of action potentials

Modelling neurons

If we want to investigate the behaviour of neurons outside of the electrophysiology lab, we need a model that captures these essential features

There are two main approaches:

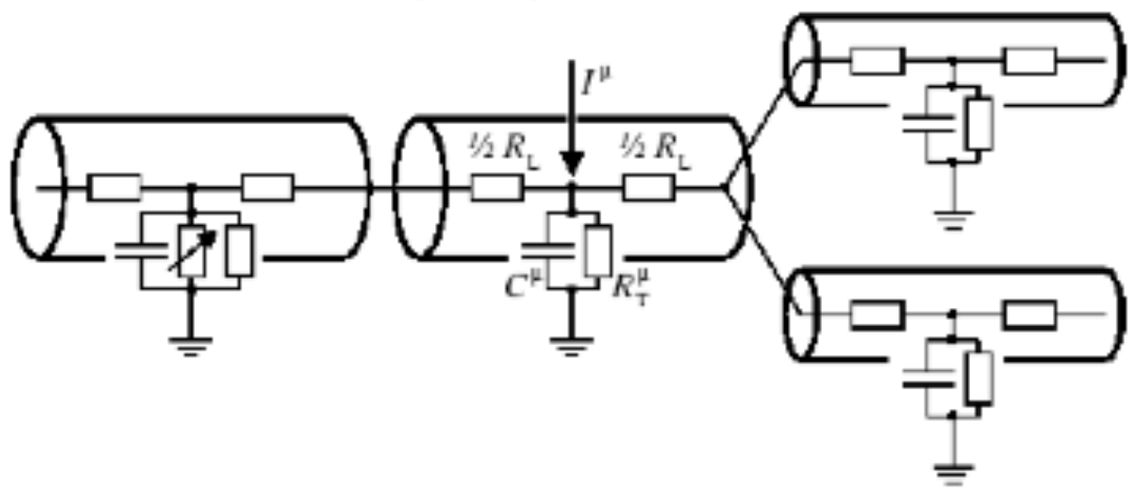
- Detailed (biophysical) neuron models
- Reduced (abstract) neuron models

Here we focus on the latter approach, specifically on point neuron models.

Detailed neuron models

de Schutter & Bower (1994)

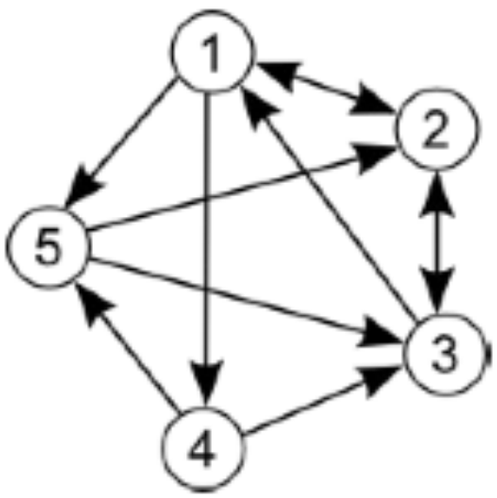
Gerstner & Kistler (2001)



- reconstruct neuron morphology from images
- decompose into many compartments
- define properties of each compartment
- simulate using e.g. NEURON or GENESIS

Point neuron models: spatial structure

Morphology of the real neuron is reduced to a directed graph

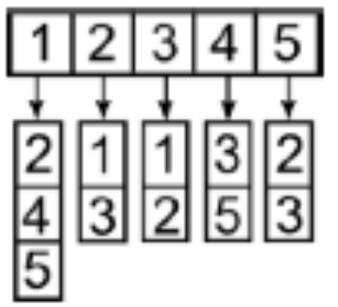


directed graph

from →
to ↓

$$\begin{pmatrix} 0 & 1 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 1 & 1 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 \end{pmatrix}$$

connectivity matrix



adjacency list

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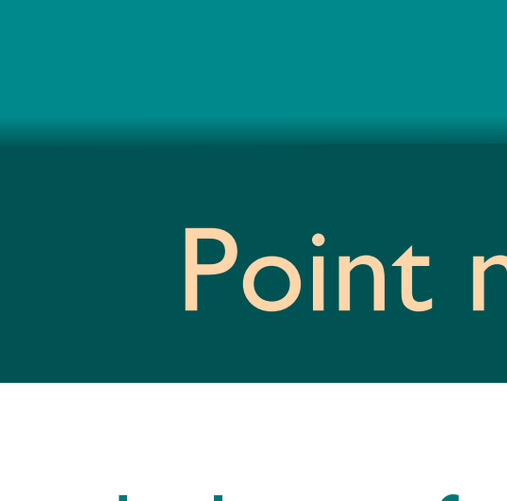

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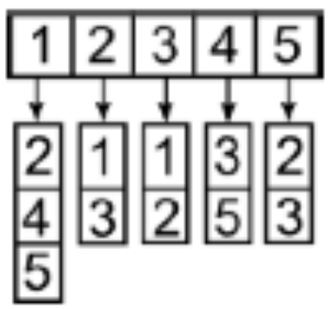

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w_{ij}

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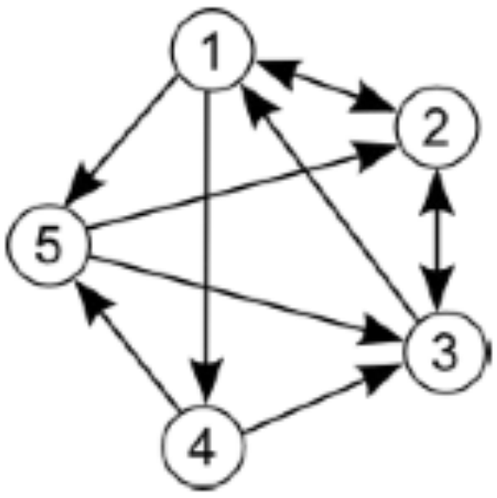

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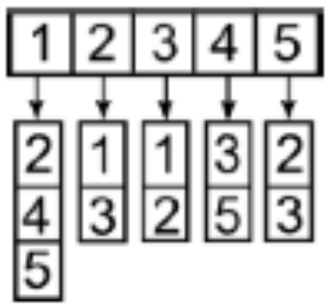


adjacency list

$w_{ij}\,(t)$

Point neuron models: dynamics

- One isopotential compartment
- Reduction of dynamics to a few differential equations
- Some examples:

Integrate-and-fire (Lapicque, 1907)

$$C\frac{dU}{dt} = I$$

Hodgkin-Huxley (1952)

$$C\frac{dU}{dt} = -\sum_i I_i(t,U)$$

FitzHugh-Nagumo (1962)

$$\begin{aligned} \frac{dU}{dt} &= U - U^3 - w + I \\ \tau\frac{dw}{dt} &= U - a - bw \end{aligned}$$

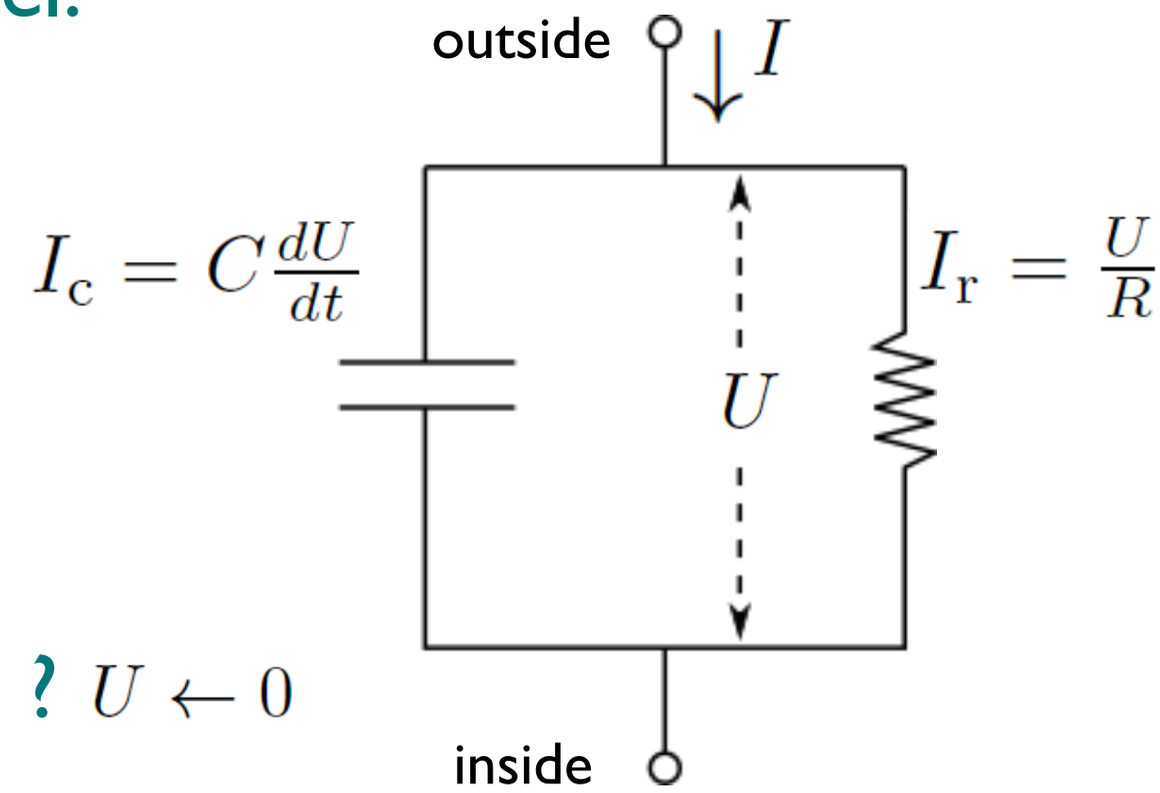
Point neuron models: dynamics

The leaky integrate-and-fire model:

- Kirchhoff's current law:

$$C\frac{dU}{dt} + \frac{U}{R} = I$$

$$C\frac{dU}{dt} = -\frac{U}{R} + I$$



- Threshold behaviour: $U > \Theta \;\; ? \;\; U \leftarrow 0$
- Additional simplifications:
  - linear subthreshold integration
  - time invariant parameters

Comparison of detailed and point neuron models

Detailed neuron models:

- have physical extent
- give a good approximation of the electrical properties of a physiological neuron
- can be made arbitrarily complex

Point neuron models:

- have no physical extent
- represent the dynamics in an extremely reduced fashion
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Why would anyone want to use a point neuron model?

Why use point neuron models?

- Much less initial investment
- Analysis
- Network simulation
- Not as bad an approximation as one might think

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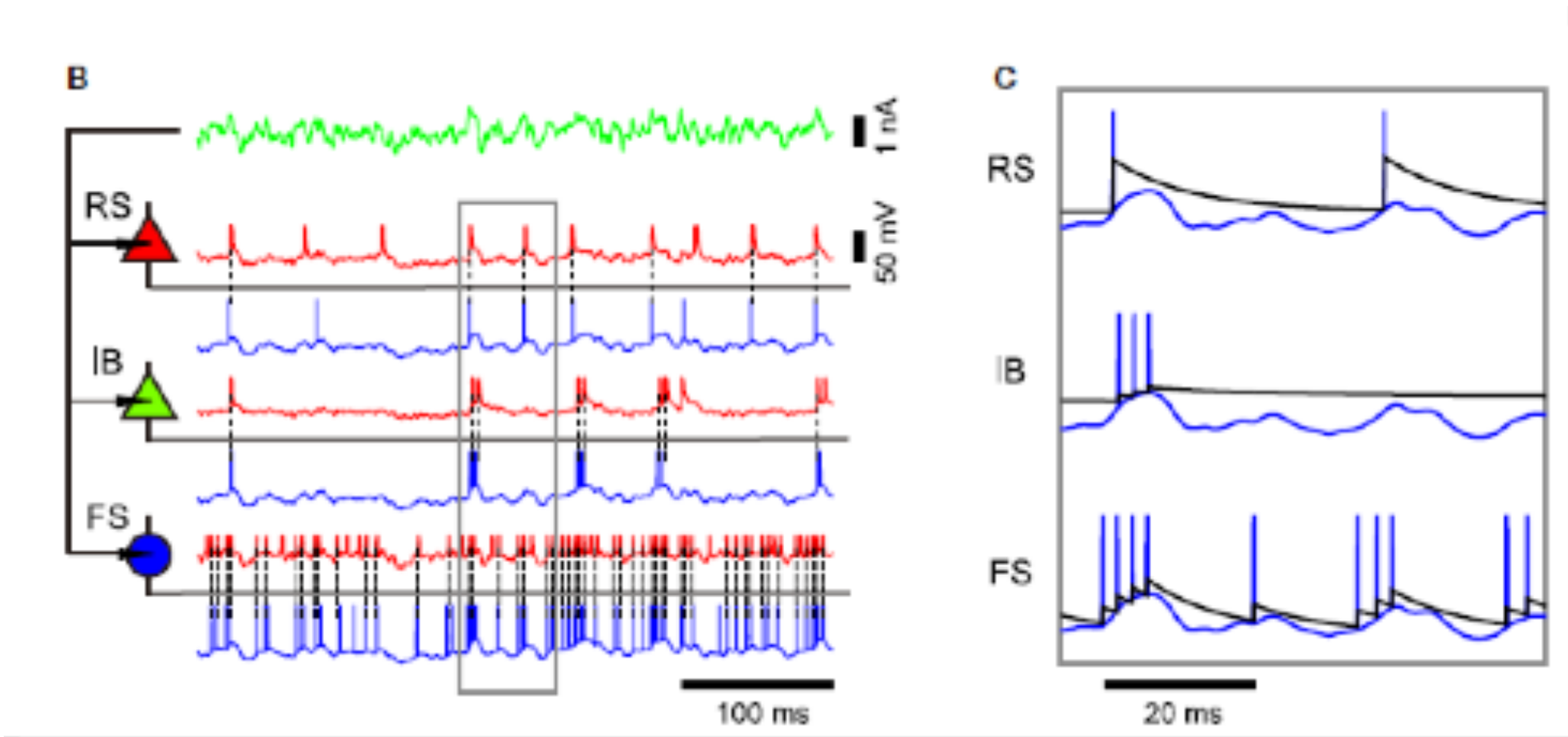
Point neurons: not as bad as all that

Point neurons can exhibit a wide range of dynamics:



Kobayashi et al. (2009);
see also Izhikevich (2004)

Point neurons: not as bad as all that

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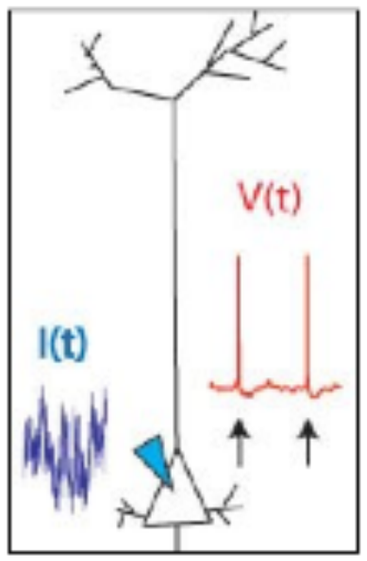
- DIADEM
- Spike Time Prediction
  - 2009
    - Challenge A
      - Submissions
    - Challenge B
    - Challenge C
    - Challenge D
  - 2007
  - 2008

CHALLENGE A

Predict the spike timing of a regular spiking L5 pyramidal cell responding to in-vivo-like current injection.

Experimental Methods

The experiments were performed by Thomas Berger and Richard Naud in the laboratory of Henry Markram at the EPFL. A 14-day-old Wistar rat was decapitated and its brain was quickly transferred to a slicing chamber filled with iced artificial cerebrospinal fluid (ACSF). 300 mm thick slices of the primary somatosensory neocortex were prepared using a HR2 vibratome (Sigmann Elektronik, Heidelberg, Germany). Slices were incubated at 36°C for 45 min and left at room temperature until recording. The ACSF contained (in mM): 125 NaCl, 2.5 KCl, 25 D-glucose, 25 $NaHCO_3$, 1.25 NaH_2PO_4, 2 $CaCl_2$, and 1 $MgCl_2$.



Somatic recordings were performed at 33-35°C with a Axopatch 200B amplifier (Molecular Devices, Union City, CA) in the current clamp mode. Voltage traces were filtered with a 2.4 kHz Bessel filter. The amplifier was connected to a ITC-18 acquisition board (Instrutech Co, Port Washington, NY), which was in turn connected to a PC or Macintosh running a custom written routine under IgorPro (Wavemetrics, Portland, OR). Patch pipettes were pulled with a Flamming/Brown micropipette puller P-97 (Sutter Instruments Co, Novato, CA) and had an initial resistance of < 4MΩ. Pipettes were filled with intracellular solution (ICS) containing (in mM): 110 potassium gluconate, 10 KCl, 4 ATP-Mg, 10 Na-Phosphocreatine, 0.3 Na-GTP,10 Hepes, 30 Mannitol, and 8 Biocytin. Chemicals were provided by SIGMA or MERCK. The liquid junction potential between the ACSF and the ICS was around 12 mV and not corrected for.

The current-clamp stimulus has two parts. The first part is 17.5 seconds of various stimulus waveforms frequently used to calibrate neuron models. It consists of a series of four step current with a duration of 2 seconds and an inter-step rest time of two seconds (one hyperpolarizing and 3 depolarizing steps). The steps are followed by an injection of white noise of two seconds. The white noise injection can be used to remove the artefact

Point neurons: not as bad as all that

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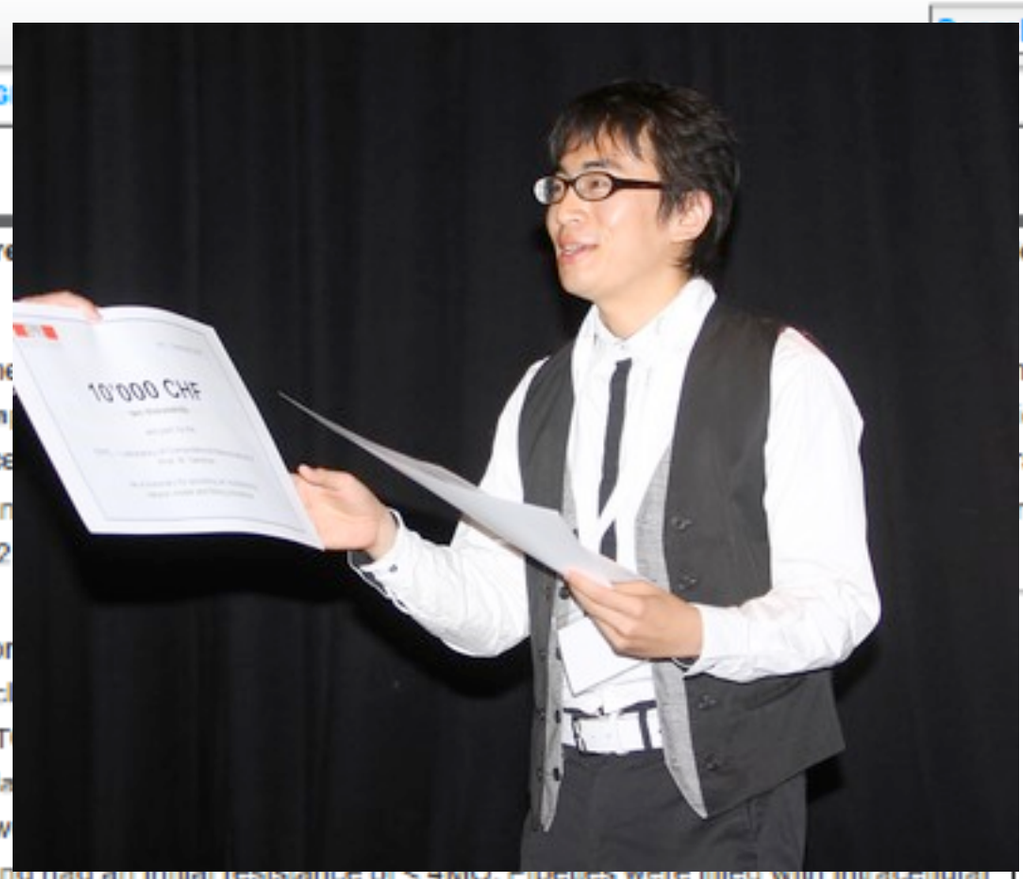

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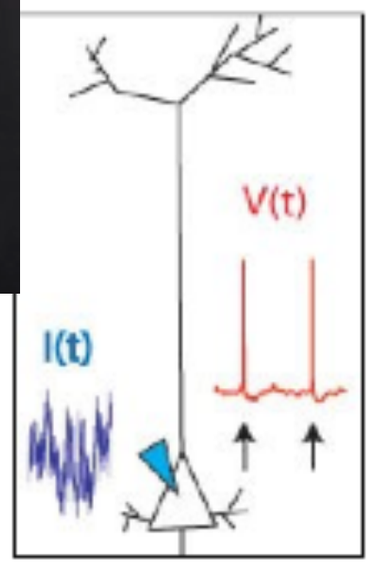

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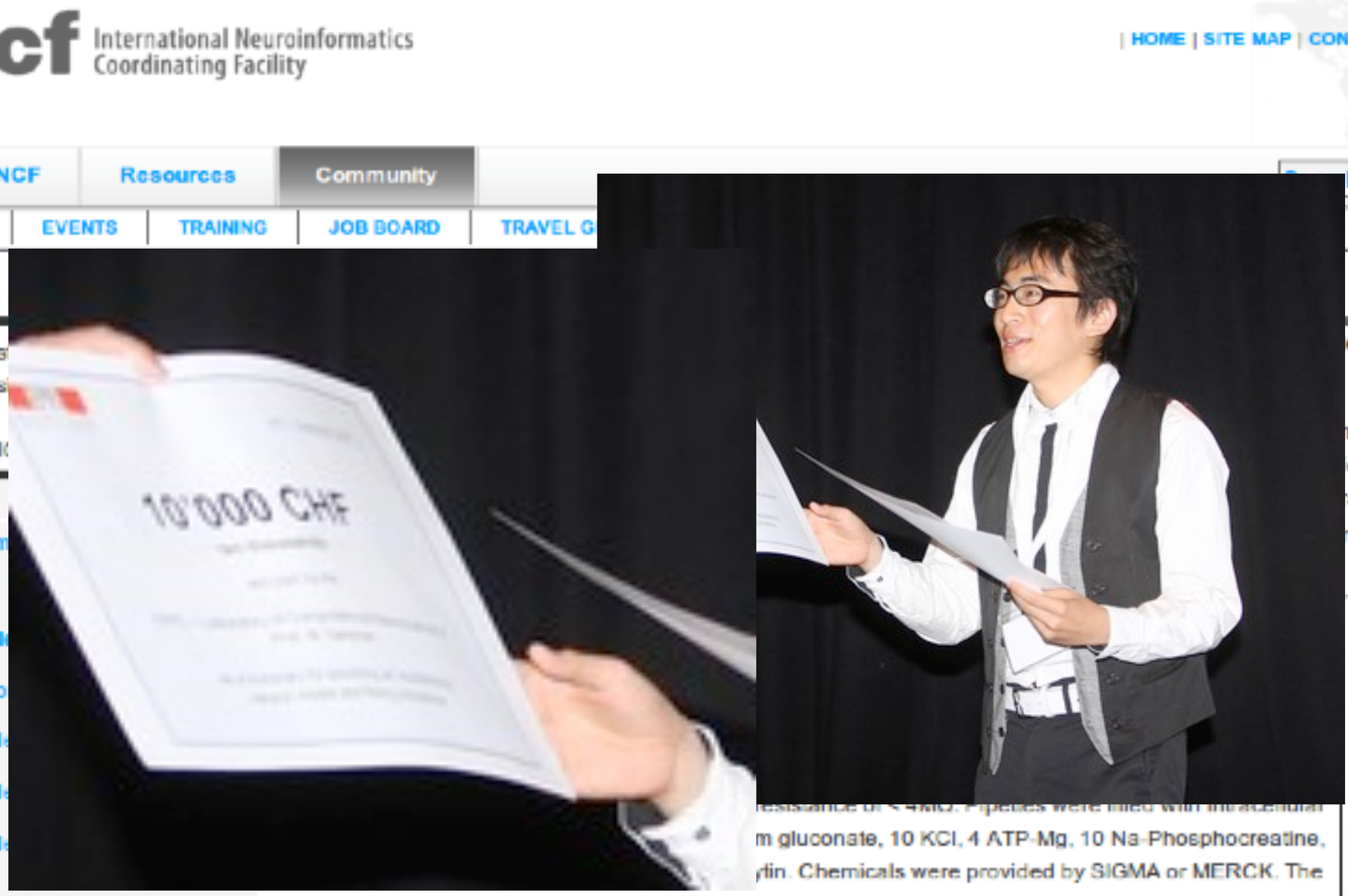

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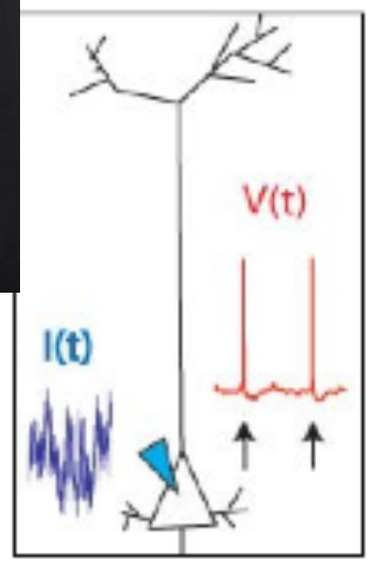

Point neurons: not as bad as all that

- Point neurons won all challenges in all years, despite behaviourally relevant incentives
- The MAT2 model (Kobayashi et al., 2009) only has one dynamic variable more than the standard leaky I&F model
- The arbitrary complexity of biophysical neuron models makes them a parameter fitting nightmare
- Save complexity for when you really need it