The What and the Why of Neural Modeling

The moment-to-moment operation of the nervous system involves the generation, propagation and interaction of electrical and chemical signals that are distributed in space and time.

Empirically-based modeling is needed to test hypotheses about the mechanisms that govern these signals and how nervous system function emerges from these phenomena.

Topics

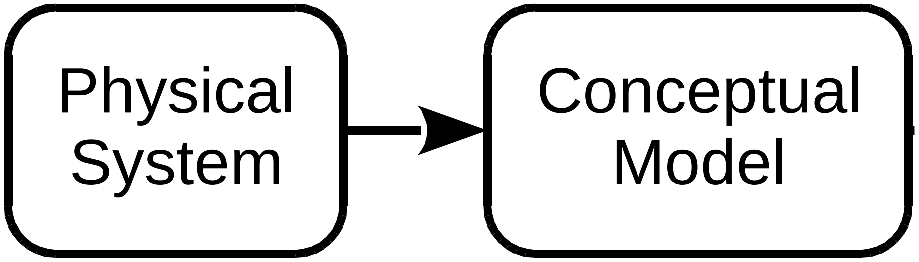
1. How to create and use models of neurons and networks of neurons
    - Specifying anatomical and biophysical properties
    - Controling, displaying, and analyzing models and simulation results
2. How NEURON works
3. How to add user-defined mechanisms

    Ion channels, synaptic mechanisms,
    chemical signals, artificial spiking neurons . . .

From Physical System to Computational Model

Physical
System

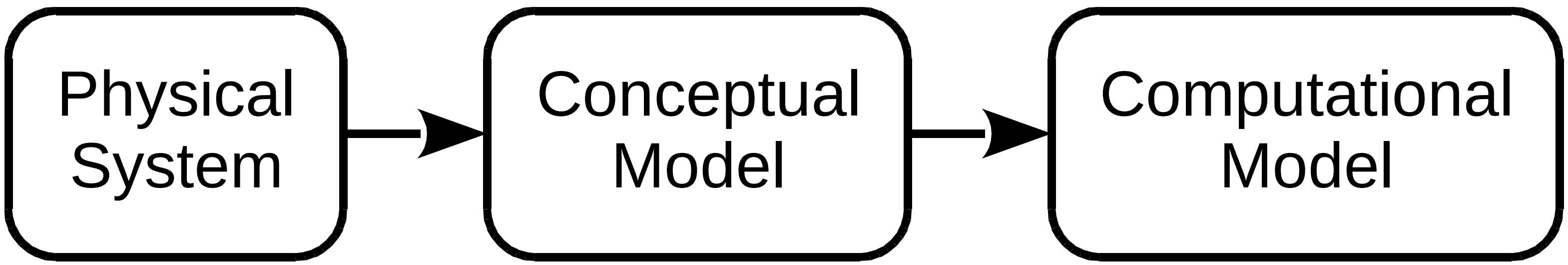
From Physical System to Computational Model



Conceptual model

a simplified representation of the physical system

From Physical System to Computational Model



Conceptual model

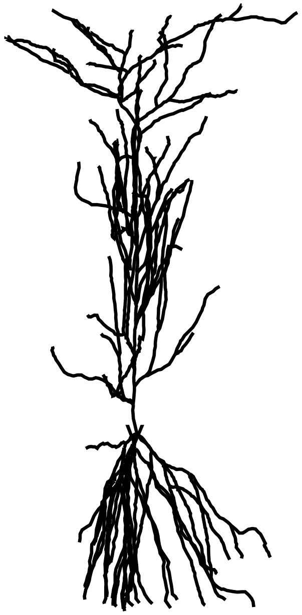
a simplified representation of the physical system

Computational model

an accurate representation of the conceptual model

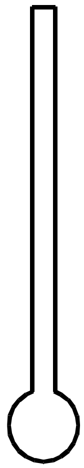
From Physical System to Computational Model

Physical system



Ca1 pyramidal cell

Conceptual model



ball and stick

Computational model

```
# python
soma = h.Section(name='soma')
dendrite = h.Section(name='dendrite')
dendrite.connect(soma(1))
```

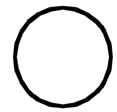
```
// hoc
create soma, dendrite
connect dendrite(0), soma(1)
```

source code

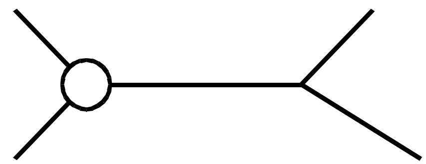
Hierarchies of Complexity

Structure

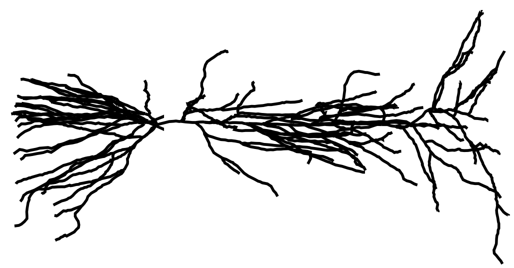
Single compartment



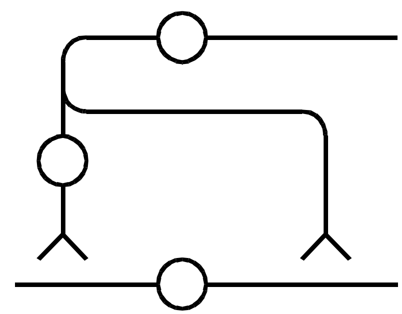
Stylized



Anatomically detailed



Network



Hierarchies of Complexity

Mechanism

Passive and Active currents
- HH-style
- kinetic scheme

Synaptic transmission
- continuous
- spike-triggered

Gap junctions

Extracellular fields, Linear circuits

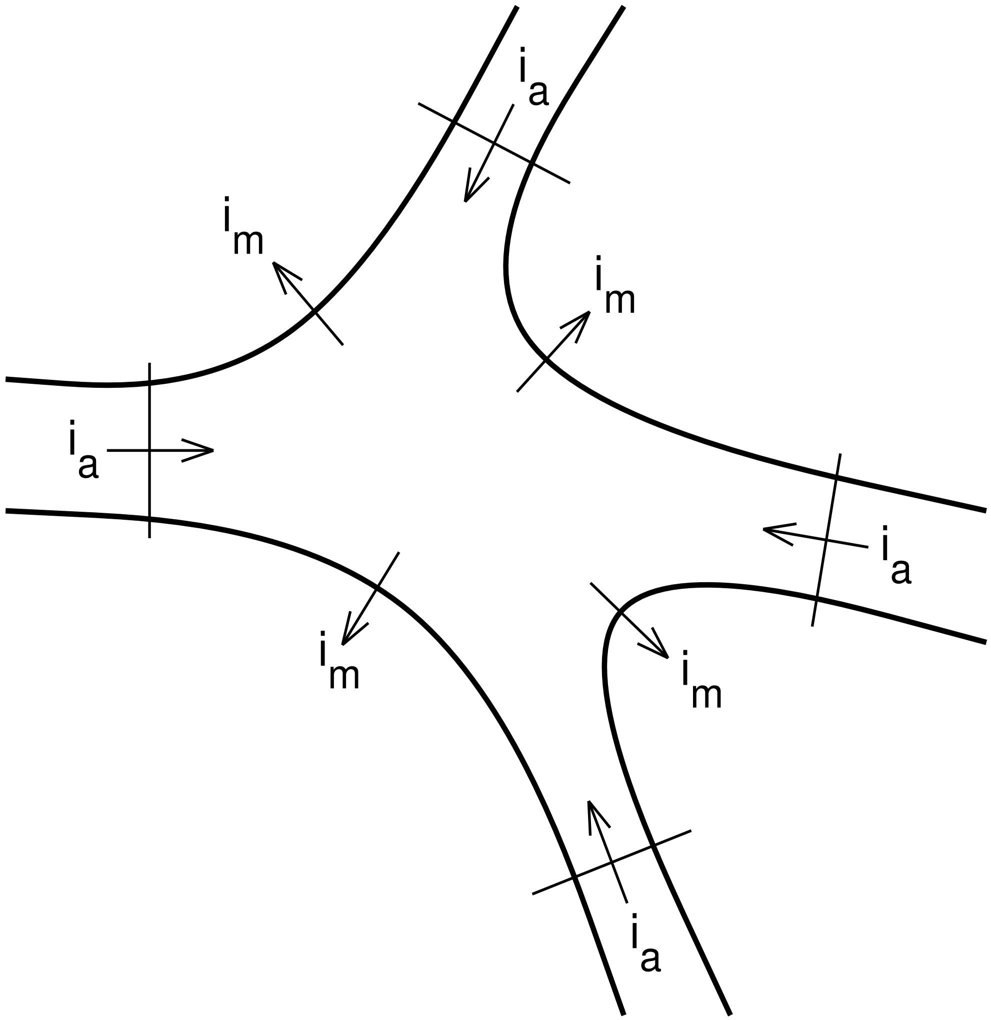
Diffusion, buffers, transport & exchange

Artificial spiking cells ("integrate & fire")

Fundamental Concepts

Signals	What moves	Driving force	What is conserved
Electrical	charge carriers	voltage gradient	charge
Chemical	solute	concentration gradient	mass

Conservation of Charge



$$c_m \frac{dV_m}{dt} + i_{ion} = \sum i_a$$

The Model Equations

$$c_j \frac{dv_j}{dt} + i_{ion_j} = \sum_k \frac{v_k - v_j}{r_{jk}}$$

v_j membrane potential in compartment j

i_{ion_j} net transmembrane ionic current in compartment j

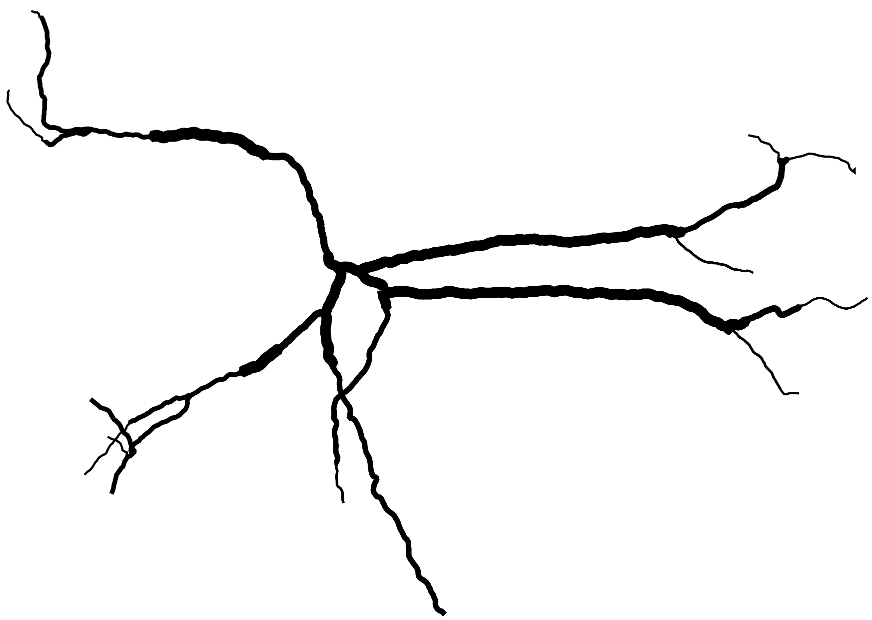
c_j membrane capacitance of compartment j

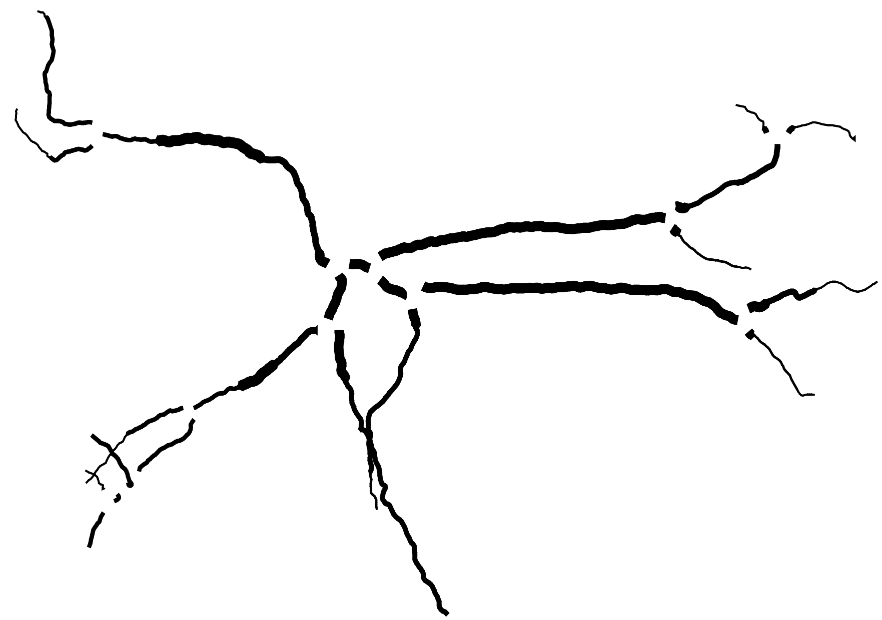
r_{jk} axial resistance between the centers of
compartment j
and
adjacent compartment k

Separating Anatomy and Biophysics from Purely Numerical Issues

section

a continuous length of unbranched cable





Anatomical data from A.I. Gulyás

Mathematical description of a section

What we want:

$$c_j \frac{dv_j}{dt} + i_{ion_j} = \sum_k \frac{v_k - v_j}{r_{jk}}$$

What a new section gives us:

$$c_j \frac{dv_j}{dt} = \sum_k \frac{v_k - v_j}{r_{jk}}$$

i.e. membrane capacitance and axial resistance,
but no ionic current.

How can we add ion channels, pumps, reactions . . . ?

Adding mechanisms to sections

Density mechanisms
- distributed channels
- ion accumulation

Point processes
- electrodes, synapses

Described by
- differential equations
- kinetic schemes
- algebraic equations

Constructed with
- NMODL
- Channel Builder
- (*rxd discussed later*)

hoc

```
create soma, dend

connect dend(0), soma(1)

soma {
  L = 50 // [um] length
  diam = 50 // [um] diameter
  nseg = 1
  insert hh // HH mechanism
}

dend {
  L = 200
  diam = 2
  nseg = 3
  insert pas // passive channels
  e_pas = -65
}
```

Python

```
from neuron import h

soma = h.Section(name='soma')
dend = h.Section(name='dend')

dend.connect(soma(1))

soma.L = 50 # [um] length
soma.diam = 50
soma.nseg = 1
soma.insert('hh')

dend.L = 200
dend.diam = 2
dend.nseg = 3
dend.insert('pas')
dend.e_pas = -65
```

Range Variables

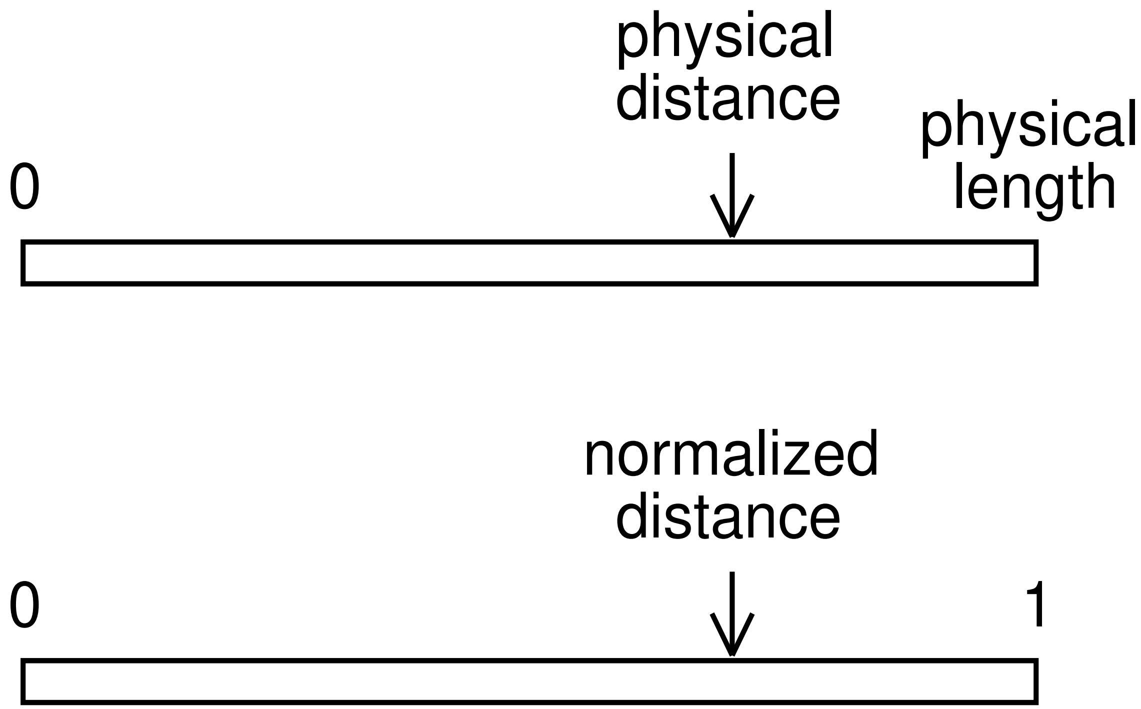
Name	Meaning	Units
`diam`	diameter	[µm]
`cm`	specific membrane capacitance	[µf/cm^2]
`g_pas (hoc)` `pas.g (Py)`	specific conductance of the pas mechanism	[siemens/cm^2]
`v`	membrane potential	[mV]

range

normalized position along the length of a section

$0 \leq \text{range} \leq 1$

any variable name can be used for range, e.g. x



nseg

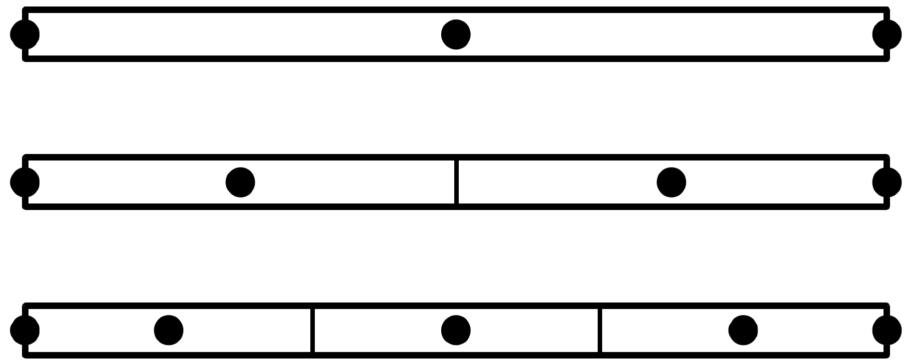
the number of points in a section at which v is calculated

by integrating the discretized cable equation

nseg=1

nseg=2

nseg=3



nseg

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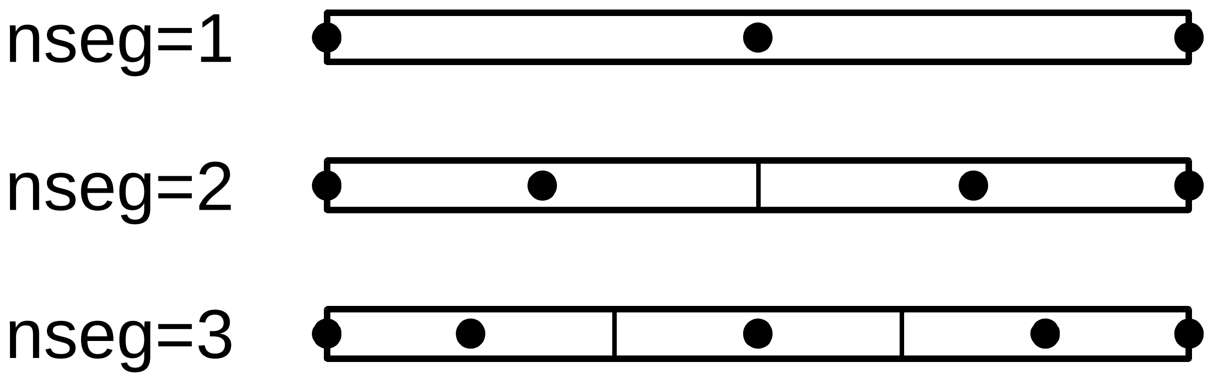
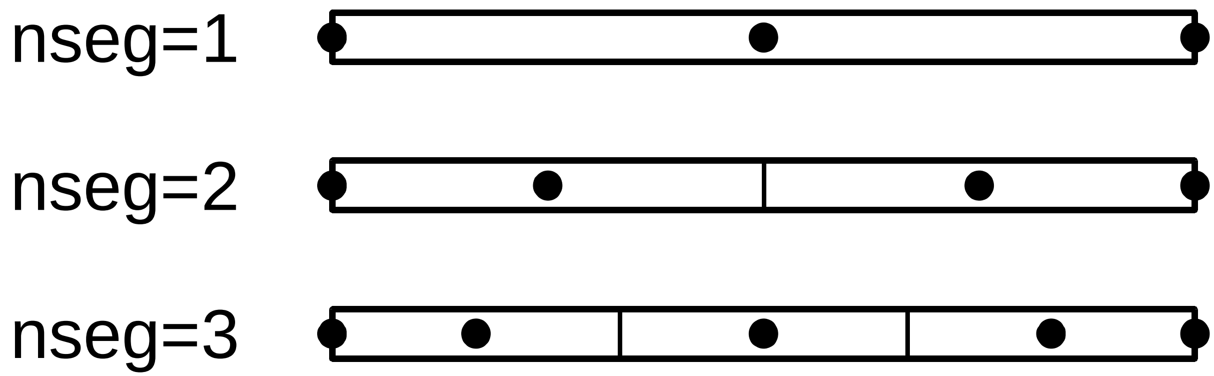


Example: `axon.nseg = 3`

nseg

the number of points in a section at which v is calculated
by integrating the discretized cable equation



Example: `axon.nseg = 3`

To test spatial resolution

```
for sec in h.allsec():
    sec.nseg *= 3
```

and repeat the simulation

hoc: `forall nseg *= 3`

Syntax:

`secname``(`*`range`*`).`*`rangevar`*

Translation: "in *secname*
at the location specified by *range*
access the value of *rangevar*"

Examples:

```
dend(0.5).v # v at middle of dend
            # hoc: dend.v(0.5)
            # shortcut: dend.v

# at each point in dend where v is calculated
#   print range, distance from 0 end, and v
for seg in dend.allseg():
  print(seg.x, seg.x*dend.L, dend(seg.x).v)
```

(less typing:

```
  print(seg.x, seg.x*dend.L, seg.v)
```

)

Category	Variable	Units
Time	`t`	[ms]
Distance	`diam, L`	[µm]
Voltage	`v`	[mV]
Current		
specific	`i`	[mA/cm^2] (density)
absolute		[nA] (point process)
Capacitance		
specific	`cm`	[µf/cm^2]
absolute		[nf] (point process)
Conductance		
specific	`g`	[S/cm^2] (density)
absolute		[µS] (point process)
Cytoplasmic resistivity	`Ra`	[Ω cm]
Resistance	`SEClamp.rs`	[10^6 Ω]
Concentration	`cai`, `nao`, etc.	[mM]