Neuron simulation

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Outline

Introduction to Simulation in Science

- Simulation as a pivotal tool in scientific inquiry.
- It is important in decoding complex structures and phenomena.
- Allows for controlled manipulation of variables and in-depth analysis.

Challenges in Neuroscience

- The intricate structure of the brain poses significant challenges.
- Understanding neural processes requires advanced simulation techniques.
- Studies reveal vast diversity in neurons, with multiple morpho-electrical types.

Complexity of Neurons. Markram et al. (2015)

- 55 morphological profiles.
- 11 electrical types.
- 207 morpho-electrical types.
- Connectivity.

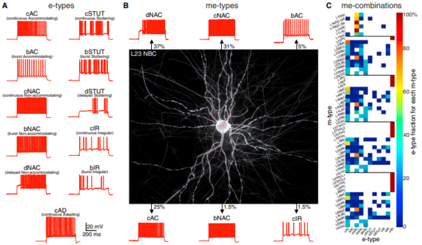

Figure 4. Table of Morpho-Electrical Neuron Types
(A) e-types. Diverse firing patterns in response to depolarizing step current injections in neocortical neurons. c, continuous; d, delayed; b, bursting. AC, accommodating; NAC, non-accommodating; STUT, stuttering, IR, irregular; AD, adapting.
(B) An exemplar neuron (L23NBC) with a diversity of e-types. Percentages indicate the relative frequency of e-type occurrence.
(C) Fractions of e-types (11 e-types) recorded experimentally in each of the 55 m-types, making up 207 me-types. Solid lines indicate layer boundaries. See Table 1 for relation of e-types to other classifications in the literature.

Figure: Morpho-Electrical types Markram et al. (2015)

Neuron Simulation Explained

- Action Potential is the most often used subject of neuron simulation.
- Simulating input-output relationships to study neuronal behavior.
- The synergy of simulation and experimental data to enhance understanding.

The Role of Neuron Simulation in Neuroscience

- Neuron simulation relies heavily on experimental neuroscience.
- Potential for simulations to predict and verify scientific hypotheses.
- Reproduce multiple experiments
- Integrated in modern neuroscience research.

Case Study - OpenWorm Project

- OpenWorm: Aiming to build the first digital life form.
- Simulates the *Caenorhabditis elegans*, a nematode with 302 neurons.
- Combines cellular-level simulation with behavioral outputs.
- Open source.

Figure: Open Worm simulation Szigeti et al. (2014)

Case Study - Blue Brain Project

- Blue Brain Project: A mission to digitally reconstruct the human brain.
- Part of the larger Human Brain Project in Europe.
- Uses supercomputers to simulate brain tissue and understand brain function.
- Simulated part of Neocortex Markram et al. (2015) and mouse brain.

The Impact of Simulation on Neuroscience

- Broadens the scope of research beyond physical experiments.
- Assists in the understanding of complex neural networks and brain functions.
- Provides a platform for education and training in neuroscientific principles.

The Hodgkin–Huxley Model

- Work on the model began in 1939, with key experiments conducted from 1946 to 1952 Hodgkin and Huxley (1952).
- Use of squid giant axon due to its size compatible with technology of the era.
- Introduction of the voltage-clamp technique for controlled experiments.

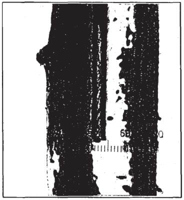

Figure: Electrod inside Giant Squid axon

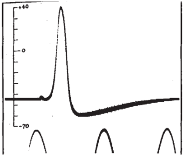

Figure: Recorded Action Potential

Hodgkin–Huxley Model: The Circuit and Ionic Currents

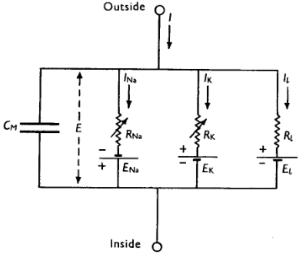

Figure: Electronic circuit representation of the Hodgkin-Huxley model

- Membrane as a capacitor with ionic channels as resistors.
- Formulation of equations to represent sodium and potassium ionic currents Hodgkin and Huxley (1952).
- Achieved the first simulated action potential.

Understanding the Hodgkin–Huxley Equations

- The total membrane current (I_m) is the sum of capacitive current, sodium (Na^+) current, potassium (K^+) current, and leakage current.

$$I_m = C\frac{dV}{dt} + g_{Na}(V,t)(V_m - E_{Na}) + g_K(V,t)(V_m - E_K) + g_L(V_m - E_l)$$

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m \quad \text{(Sodium activation)}$$
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h \quad \text{(Sodium deactivation)}$$
$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n \quad \text{(Potassium activation)}$$

- Parameters α and β represent the rate at which the ion channels open and close, varying with voltage.
- Fitting these equations to experimental data allowed Hodgkin and Huxley to simulate the first action potential.

Simulated Curves

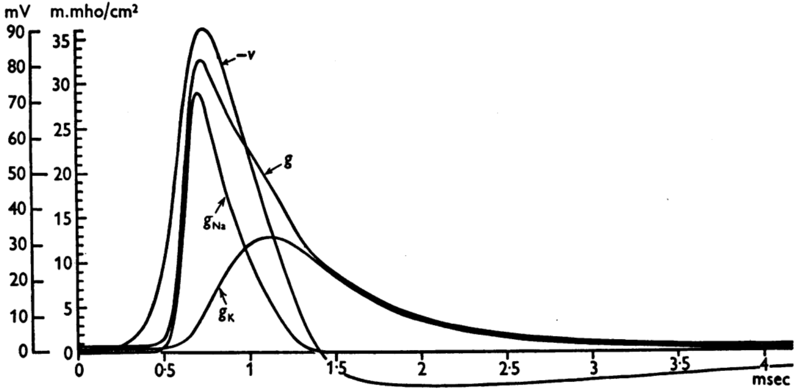

Figure: Numerical solutions of Hodgkin-Huxley equations Hodgkin and Huxley (1952)

Post Hodgkin–Huxley Advances

- Discovery of new ion channels and incorporation into the model for enhanced accuracy Hille (1992).
- Development of new models considering different cell types Nandi et al. (2022).
- The FitzHugh-Nagumo model as a simplified representation FitzHugh (1961) Nagumo et al. (1962).
- Multicompartment models using computing advancements Rall (1959) Rall (1962) Rall and Shepherd (1968).

Early Computational Neuron Simulation

- Introduction of GENESIS and NEURON simulators Wilson and Bower (1989), Hines (1993).
- NEURON's evolution from HOC to Python integration Hines (2009).

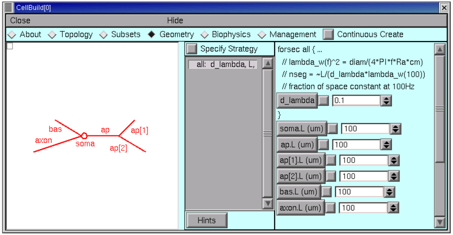

Figure: NEURON Cell builder

Advancements in Simulation Performance

- The development of NCS for parallel simulations.
- Emergence of SPLIT simulators designed for large neuron networks Hammarlund and Örjan Ekeberg (1998).
- The need for user-friendly interfaces leads to the creation of Nest Gewaltig and Diesmann (2007).

Table 1 Comparison of features of the different simulators

Question	NEURON	GENESIS	NEST	NCS	CSIM	XPP	SPLIT	Mvaspike
HH	B.I.	B.I.	YES	B.I.	B.I.	YES	B.I.	POSS
LIF	B.I.	POSS	YES	B.I.	B.I.	YES	POSS**	B.I.
Izhikevich IF	YES	B.I.	YES	NO	B.I.	YES	POSS**	POSS**
Cable eqs	B.I.	B.I.	NO	NO	NO	YES	B.I.	NO
ST plasticity	YES	B.I.	YES	B.I.	B.I.	YES	B.I.	YES
LT Plasticity	YES	YES	YES	B.I.	B.I.	YES	NO**	YES
Event-based	B.I.	NO	YES	NO	NO	YES	NO	YES
Exact	B.I.	–	YES	–	–	NO	–	YES
Clock-based	B.I.	B.I.	YES	B.I.	YES	YES	YES	POSS**
Interpolated	B.I.	NO	YES	NO	NO	YES	B.I.	POSS
G synapses	B.I.	B.I.	YES	B.I.	B.I.	YES	B.I.	POSS**
Parallel	B.I.	YES	B.I.	B.I.	NO**	NO	B.I.	NO**
Graphics	B.I.	B.I.	NO(*)	NO(*)	NO(*)	YES	NO	NO
Simple analysis	B.I.	B.I.	YES	NO(*)	NO(*)	YES	NO	NO
Complx analysis	B.I.	YES	NO(*)	NO(*)	NO(*)	YES	NO	NO
Development	YES	YES	YES	YES	YES	YES	YES	YES
How many p.	3	2–3	4	2–3	2	1	2	1
Support	YES	YES	YES	YES	YES	YES	YES	YES
Type	e,p,c	e	e	e	e	e	e	e
User forum	YES	YES	YES	NO	NO	YES	YES	NO
Publ list	YES	YES	YES	YES	YES	NO	NO	NO
Codes	YES	YES	YES	YES	YES	YES	NO	NO
Online manual	YES	YES	YES	YES	YES	YES	YES	YES
Book	YES	YES	NO	NO	NO	YES	NO	NO
XML import	NO**	POSS	NO**	NO**	NO	YES	NO	NO**
XML export	B.I.	NO**	NO**	NO**	NO	NO	NO	NO**
Web site	YES	YES	YES	YES	YES	YES	YES	YES
LINUX	YES	YES	YES	YES	YES	YES	YES	YES
Windows	YES	YES	YES	YES	YES	YES	NO	NO
Mac-Os	YES	YES	YES	NO	NO	YES	NO	NO
Interface	B.I.	B.I.	POSS	B.I	YES	POSS	POSS	POSS
Save option	B.I.	YES	NO**	B.I.	NO	NO	NO	NO

Figure: Simulators comparison Brette et al. (2007)

Modern Computational Tools and Neuromorphic Hardware

- Introduction of the user-friendly and efficient Brian2 simulator Stimberg et al. (2019).
- Development of neuromorphic hardware: SpiNNaker and BrainScaleS Furber et al. (2014), Müller et al. (2023).
- These systems emulate neural architectures for direct hardware simulation.

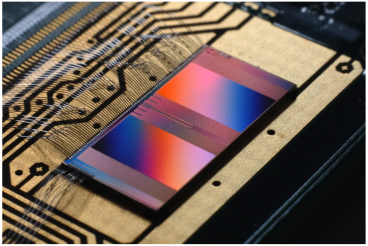

Figure: BrainScales-2 Müller et al. (2023)

Databases for Model Sharing and Reproducibility

- ModelDB and NeuroDB for sharing computational models McDougal et al. (2016), Zeighami and Shahabi (2021).
- NeuroMorpho.org for neuron morphology data sharing Ascoli et al. (2007).
- Enhancing reproducibility and collaborative research.

Introduction to PyNN

- PyNN: A simulator-independent framework Davison (2008).
- Allows model description once and execution on various platforms.
- Supports NEURON, NEST, Brian 2, and some neuromorphic hardware.

Creating a Simple Neuron Model with PyNN

- PyNN abstracts away simulator-specific APIs.
- A single PyNN script can run on multiple simulators.

```python
import pyNN.neuron as sim
sim.setup(timestep=0.01, min_delay=1.0)
hh_neuron = sim.Population(1, sim.HH_cond_exp())
current_source = sim.DCSource(amplitude=0.5, start=20.0,
    stop=80.0)
hh_neuron.inject(current_source)
hh_neuron.record('v')
sim.run(100.0)
data = hh_neuron.get_data().segments[0].analogsignals[0]
```

Listing 1: PyNN example

Visualization of Simulation Results

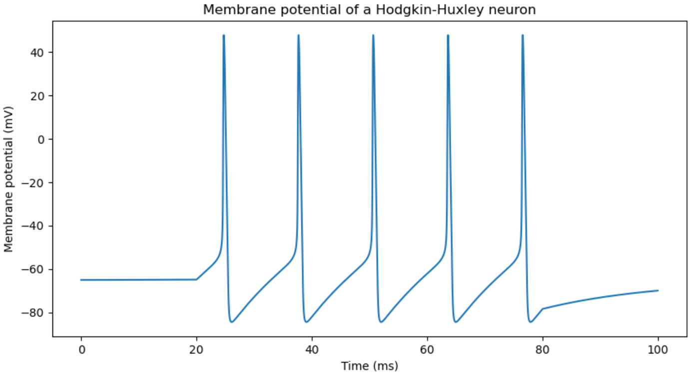

Figure: Simulation result using PyNN

Running Simulations on Different Simulators

- PyNN allows consistent simulation across different platforms.
- NEURON and Brian2 simulations compared.
- Challenges encountered with Nest integration.
- Focus on execution time and memory usage.

Comparison and Results

Table: Comparison of Neuron Simulators running with PyNN

Simulator	Time	Memory Usage
NEURON	0:00.73	104,728 KB
Brian2	0:03.29	164,108 KB

Table: Comparison of Neuron Simulators natively

Simulator	Time	Memory Usage
NEURON	0:00.76	66,156 KB
Brian2	0:06.48	246,076 KB

- NEURON shows better performance and efficiency.
- Challenges in running Nest led to its exclusion from the comparison.
- Source code available at GitHub repository.

Impact of Computational Power on Simulations

- Increased computational power has allowed for more complex simulations.
- Entire organisms and regions like the neocortex are now within our modeling capabilities Szigeti et al. (2014), Markram et al. (2015).
- Initiatives such as the Blue Brain Project and Human Brain Project highlight the significance of simulation software in neuroscience research.

Evolution of Simulation Software

- The landscape of simulation tools is diverse, targeting different aspects of usability and complexity.
- Recent efforts like PyNN aim to standardize model creation with a simulator-independent API.
- This approach facilitates the writing of code once to run across multiple platforms.

Comparative Usability and Complexity

- While some simulators like Brain2 may present usability challenges, the advantage in complexity is not always clear.
- Simulators like NEURON, despite their maturity, offer an ease of use that rivals newer, unified APIs like PyNN.
- The selection of a simulator often depends on the specific needs and goals of the research at hand.

End

Thank you!

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