Theoretical neuroscience:

Single neuron dynamics and computation

STAT 42510 - CPNS 35510

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Practical details

First course in a 3-course series:

- **Single neuron dynamics and computation (Fall, STAT 42510 - CPNS 35510)**
  Instructor: Nicolas Brunel

- **Network dynamics and computation (Winter, STAT 42520 - CPNS 35520)**
  Instructor: Nicolas Brunel

- **Statistics and information theory (Spring, STAT 42600 - CPNS 35600)**
  Instructor: Stephanie Palmer
Practical details

• Problem sets will be issued every Tuesday from Week 2 to Week 9 (total of 8), and due the next Tuesday in class.

• A take-home final will be issued on December 3, and due on December 17 in my office (Eckhart 106)

• Grades: Problem sets will account for 50% of the grade; The take-home final for the remaining 50%.
Introduction

- What is theoretical neuroscience?
- Theoretical tools
- Brief history
- Overview of the brain, experimental tools, spatial scales, temporal scales
- Outline of the course
What is theoretical neuroscience?

(a.k.a. computational neuroscience;
includes neuromathematics; neurophysics; neurostatistics; neuroinformatics)

Using quantitative tools (from mathematics/statistics/computer science/physics) to advance our understanding of how brains work.
Questions in theoretical neuroscience

**What?** Describe in a mathematically compact form a set of experimental observations.

**How?** Understand how a neural system produces a given behavior.

**Why?** Understand why a neural system performs the way it does, using e.g. tools from information theory.
Classification of problems

- **Dynamics**: Neural systems are dynamical systems.
- **Coding**: Neural systems are information processing systems.
- **Learning and memory**: Neural systems are information storage devices.
- **Computing**: Neural systems are computing devices.
- **Motor control**: Neural systems organize and execute actions.
Methods in theoretical neuroscience

- Numerical simulations
  - Write your own code (e.g. in C, C++)
  - Use available software
    * Dedicated software for single neuron models: Neuron, Genesis
    * Dedicated software for network simulations: NEST
    * Matlab
    * Brian
Methods

• Analytical methods
  – Networks: Graph theory, linear algebra. Large $N$ limit: tools of statistical physics
  – Noise: ubiquitous at all levels of the nervous system. Statistics, probability theory, stochastic processes.
  – Coding: Information theory
A few historical landmarks

Before mid-1980s: a few isolated pioneers

- 1907: Louis Lapicque (leaky integrate-and-fire neuron)
- 1940s: Warren McCulloch, Walter Pitts (binary neurons, neural networks)
- 1940s: Donald Hebb (neuronal assemblies, synaptic plasticity)
- 1940s-50s: Alan Hodgkin, Andrew Huxley (model for AP generation)
- 1950s: Wilfrid Rall (cable theory)
- 1950s: Frank Rosenblatt (perceptron)
- 1960s: Horace Barlow (coding in sensory systems)
- 1960s-70s: David Marr (systems-level models of cerebellum/neocortex/hippocampus)
- 1970s: Hugh Wilson, Jack Cowan, Shun-Ishi Amari (‘rate models’)
- 1980s: John Hopfield, Daniel Amit, Hanoch Gutfreund, Haim Sompolinsky (associative memory models)
A few historical landmarks

From the 1990s: establishment of a field

- First annual computational neuroscience conference in 1992 (now two main conferences/year, CNS and Cosyne, each around 500 participants per year)

- Many specialized journals created from the beginning of the 1990s (Neural Computation; Network; Journal of Computational Neuroscience; Frontiers in Computational Neuroscience; etc)

- Annual computational neuroscience summerschools since mid-1990s (Woodshole, ACCN in Europe, Okinawa, CSHL China)

- Birth of major Computational Neuroscience centers in the US (1990s, Sloan-Swartz), Israel (HU, 1990s) and Europe (Gatsby Unit, Bernstein Centers, 2000s)

- Now widely accepted as an integral part of neuroscience (theory papers routinely published in major neuroscience journals)
The human brain: a network of $10^{11}$ neurons connected by $10^{15}$ synapses
## Other brains: how many neurons and synapses?

<table>
<thead>
<tr>
<th>Animal</th>
<th>Neurons</th>
<th>Synapses</th>
</tr>
</thead>
<tbody>
<tr>
<td>C Elegans</td>
<td>302</td>
<td>5,000</td>
</tr>
<tr>
<td>Fruit fly</td>
<td>$10^5$</td>
<td>$10^7$</td>
</tr>
<tr>
<td>Honey bee</td>
<td>$10^6$</td>
<td>$10^9$</td>
</tr>
<tr>
<td>Mouse</td>
<td>$10^8$</td>
<td>$10^{11}$</td>
</tr>
<tr>
<td>Cat</td>
<td>$10^9$</td>
<td>$10^{12-13}$</td>
</tr>
<tr>
<td>Human</td>
<td>$10^{11}$</td>
<td>$10^{15}$</td>
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</tbody>
</table>
## Spatial scales of the brain

<table>
<thead>
<tr>
<th>Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>~10cm</td>
<td>Whole brain</td>
</tr>
<tr>
<td>~1cm</td>
<td>Brain structure/cortical areas</td>
</tr>
<tr>
<td>100μm- 1mm</td>
<td>Local network/‘column’/‘module’</td>
</tr>
<tr>
<td>10μm- 1mm</td>
<td>Neuron</td>
</tr>
<tr>
<td>100nm- 1μm</td>
<td>Sub-cellular compartments</td>
</tr>
<tr>
<td>~10nm</td>
<td>Channel, receptor, intracellular protein</td>
</tr>
</tbody>
</table>
Experimental tools
The whole brain level

- Experimental tools (in vivo, non invasive): fMRI, EEG, MEG, PET, psychophysics, (invasive) neuroanatomy, etc..
- Brains are interconnected networks of structures/areas
The area level

- Experimental tools (in vivo, invasive): optical imaging (VSD), intrinsic imaging, electrophysiology, neuroanatomy
• Areas are interconnected networks of local networks
The local network level

- Experimental tools (in vivo, invasive): calcium imaging, electrophysiology; (in vitro) calcium imaging, electrophysiology, electron microscopy
Local networks in cerebral cortex

- Size $\sim$ cubic mm
- Total number of cells $\sim$ 100,000
- Types of cells:
  - pyramidal cells - excitatory (80%)
  - interneurons - inhibitory (20%)
- Total number of synapses $\sim 10^9$
  (10,000 per neuron)
- Cells connect potentially to all other cell types ($E \rightarrow E$, $E \rightarrow I$, $I \rightarrow E$, $I \rightarrow I$)
- Connection probability $\sim 10\%$
The neuron level

- Experimental tools (in vivo, invasive): calcium imaging, electrophysiology; (in vitro) calcium imaging, electrophysiology, electron microscopy
• Neuron = complex tree-like structures with many compartments (e.g. dendritic spines)
The subcellular compartment level

- Experimental tools: high resolution imaging, electron microscopy
- Dendritic spines contain a huge diversity of molecules (in particular protein kinases and phosphatases) whose interactions define complex networks.
The molecular level

- Experimental tools: (in vitro) patch-clamp recording, tools of molecular neurobiology

1. Patch-clamping setup: A fire-polished micropipette with a diameter of about 1 μm is carefully placed against a cell, such as the neuron shown here.

2. Membrane patch isolation: Gentle suction is applied to form a tight seal between the pipette and the plasma membrane. Typically only one or a few channels will be in the membrane within the pipette.

3. The flow of ions is recorded while the membrane is subjected to a depolarizing step in voltage, yielding traces of individual Na⁺ currents during channel opening. Two separate traces are shown.
## The many temporal scales of the brain

<table>
<thead>
<tr>
<th>Days-Years</th>
<th>Long-term memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seconds-Minutes</td>
<td>Short-term (working) memory</td>
</tr>
<tr>
<td>100ms - 1s</td>
<td>Behavioral time scales/Reaction times</td>
</tr>
<tr>
<td>$\sim 10$ms</td>
<td>Single neuron/synaptic time scales</td>
</tr>
<tr>
<td>$\sim 1$ms</td>
<td>Action potential duration; local propagation delays</td>
</tr>
<tr>
<td>$\ll 1$ms</td>
<td>Channel opening/closing</td>
</tr>
</tbody>
</table>
Experimental tools for observing the brain
Submillisecond

- Molecular time scales (channel opening/closing; diffusion of neurotransmitter in synaptic cleft; etc)
Millisecond

- Width of action potentials; axonal delays in local networks
Tens of ms

- Synaptic decay time constants; membrane time constant of neurons; axonal delays for long-range connections
Hundreds of ms

- Behavioral time scales (e.g. motor response to a stimulus)
Seconds-minutes

- Short-term memory
- Working memory
Days-years

- Long-term memory
<table>
<thead>
<tr>
<th>Week 1</th>
<th>Oct 1</th>
<th>Introduction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oct 3</td>
<td>Biophysics, Hodgkin-Huxley (HH) model</td>
</tr>
<tr>
<td>Week 2</td>
<td>Oct 8</td>
<td>2D models for spike generation</td>
</tr>
<tr>
<td></td>
<td>Oct 10</td>
<td>Ionic channels and firing behaviors</td>
</tr>
<tr>
<td>Week 3</td>
<td>Oct 15</td>
<td>From HH to leaky integrate-and-fire (LIF) neurons</td>
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<tr>
<td></td>
<td>Oct 17</td>
<td>Stochastic dynamics of neurons</td>
</tr>
<tr>
<td>Week 4</td>
<td>Oct 22</td>
<td>From LIF to ‘firing rate’ and binary neurons</td>
</tr>
<tr>
<td></td>
<td>Oct 24</td>
<td>Axons</td>
</tr>
<tr>
<td>Week 5</td>
<td>Oct 29</td>
<td>Dendrites</td>
</tr>
<tr>
<td></td>
<td>Oct 31</td>
<td>Synapses</td>
</tr>
<tr>
<td>Week 6</td>
<td>Nov 5</td>
<td>Plasticity</td>
</tr>
<tr>
<td></td>
<td>Nov 7</td>
<td>Coding I: basic concepts</td>
</tr>
<tr>
<td>Week 7</td>
<td>Nov 12</td>
<td>Coding II: information maximization</td>
</tr>
<tr>
<td></td>
<td>Nov 14</td>
<td>Decoding</td>
</tr>
<tr>
<td>Week 8</td>
<td>Nov 19</td>
<td>Unsupervised learning</td>
</tr>
<tr>
<td></td>
<td>Nov 21</td>
<td>Supervised learning</td>
</tr>
<tr>
<td>Week 9</td>
<td>Nov 26</td>
<td>Reinforcement learning</td>
</tr>
<tr>
<td></td>
<td>Nov 28</td>
<td>THANKSGIVING (no class)</td>
</tr>
<tr>
<td>Week 10</td>
<td>Dec 3</td>
<td>Computing I</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>~1-10nm</td>
<td>Molecules (channels, receptors, etc)</td>
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Single neuron models

- **Hodgkin-Huxley neuron**
  
  \[
  C \frac{dV}{dt} = -I_L(V) - \sum_a I_a(V, m_a, h_a) + I_{syn}(t)
  \]

  - \( I_L(V) = g_L(V - V_L) \)
  - \( I_a(V, m_a, h_a) = g_a(V - V_a) m_a^x h_a^y \)
  - \( \tau_{m_a}(V) \frac{dm_a}{dt} = -m_a + m_a^\infty(V) \)
  - \( \tau_{h_a}(V) \frac{dh_a}{dt} = -h_a + h_a^\infty(V) \)

- **Integrate-and-fire neuron**
  
  \[
  C \frac{dV}{dt} = -g_L(V - V_L) + I_{syn}(t)
  \]

  Fixed threshold \( V_t \), reset \( V_r \), refractory period;

- **How do single neurons work?**

- **What are the mechanisms of action potential generation?**

- **How do neurons transform synaptic inputs into a train of action potentials?**
Single synapses

- ‘Conductance-based’

\[ I_{i,syn}(t) = \sum_{a=E,I} (V - V_a) \sum_{j,k} g_{a,i,j} s_a(t - t_j^k) \]

\[ \tau_a \frac{\dot{s}_a}{s_a} = \ldots \]

- ‘Current-based’

\[ I_{i,syn}(t) = \sum_{a=E,I} \sum_{j,k} J_{a,i,j} s_a(t - t_j^k) \]

Popular choices of \( s \)
- Delayed difference of exponential;
- Delayed delta function

- How do synapses work?
- What are the mechanisms for synaptic plasticity on short time scales?
Synaptic plasticity

Synaptic efficacy can be modified in various ways:

- Spike timing
  (STDP experiments)

- Firing rate
  (BCM, Sjostrom et al, etc)

- Post-synaptic $V$
  (pairing, etc)

- Can we capture this experimental data using simplified ‘plasticity rules’?

- What are the mechanisms of induction of synaptic plasticity?
Learning in a single neuron: the perceptron

- \( N \) synapses/inputs;
- sums linearly its inputs;
- emits a spike if inputs > \( \theta \sim 10 \) mV (threshold)
- has to learn a set of \( p \equiv \alpha N \) input/output associations
- by appropriate choice of its synaptic weights \( w_i \geq 0 \).
- in a robust way (as measured by \( \kappa \));
- can be achieved using simple learning algorithms

- How much information can a single neuron/a population of neurons store?
- What kind of learning algorithms/rules allow to reach optimal storage?
Useful books

- Ermentrout and Terman, “Mathematical Foundations of Neuroscience” (Springer, 2010)