Stochastic neuronal models

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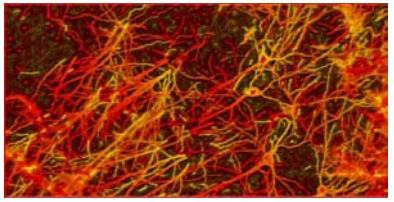

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Summary

- Basic Introduction to Neurosciences
  - Structure and function of the nervous system
  - Elements of Neuroanatomy
  - Neuronal signals
- Mathematical models for single units
  - Aims of models
    - First models
    - Hodgkin and Huxley type models
    - Stochastic models
  - Mathematical methods and related problems
- Models for assemblies of neurons
  - Aims of the models
    - Models of jump diffusion type
  - Mathematical methods and related problems
  - Alternative approaches and new researches topics

Basic in Neurosciences

- The brain
  - Macroscopic level
  - Microscopic level
- Ideal neuron
  - Ideal neuron
  - Measurement techniques
  - Neuron activity
  - Electrophysiological properties
  - Spike trains
- ….some numbers……..
- Stochastic phenomena in neurobiology
- Mathematical/computer sciences approaches
  - Macroscopic level
  - Microscopic level

The Brain: macroscopic level

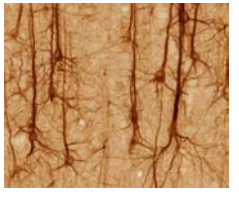
The **frontal lobes** are involved in motor function, problem solving, spontaneity, memory, language, initiation, judgement, impulse control, and social and sexual behavior.
The **parietal lobes** can be divided into two functional regions. One involves sensation and perception and the other is concerned with integrating sensory input, primarily with the visual system.
The **occipital lobes** are the center of our visual perception system.
The **cerebellum** is involved in the coordination of voluntary motor movement, balance and equilibrium and muscle tone.
The **temporal lobes** are involved in the primary organization of sensory input

Brain: macroscopic level

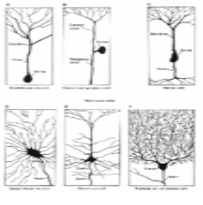
- New exciting discoveries about brain physiology appear in the scientific literature each year, often uncovering a relatively isolated aspect of brain dynamics or its relationships with pathological conditions.
- Large-scale knowledge of the nervous system is generally only casted in psychological terms, with little discussion of underlying mechanisms (and its mathematical description).
- Exciting goal: to explain all macroscopic phenomena - regardless of their nature on the basis of their underlying microscopic dynamics (as it is in physics)

Microscopic level

- Intricate network with triangular or circular cell bodies and long wire like expansion.
  - Elements: neurons (electrically excitable cells that process and transmit information) and glia cells (energy suppliers and structural stabilizers)
  - Signal is transmitted from a neuron to the next through synapses



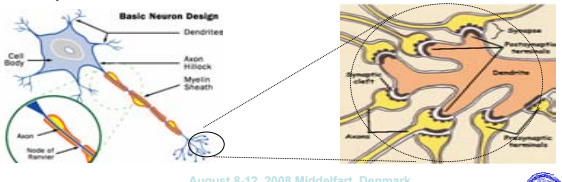
Ideal neuron



Three functionally distinct parts: dendrites, soma and axon

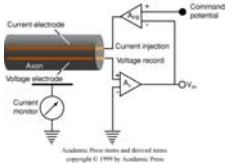
- dendrites: input device collecting signals
- soma: central processing unit (nonlinear)
- axon: output device

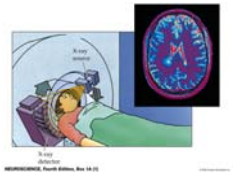
Junction between two neurons: synapses (presynaptic, postsynaptic): **chemical** neurotransmitter (receptors in postsynaptic membrane; electrical)



Measurement Techniques

- Single Neuron Electrical activity
  - Intracellular – typically in brain slices
    - Current Clamp – measures voltage
    - Voltage Clamp – measures current
    - Patch clamp – measure single channel activity
  - Extracellular – typically in vivo
    - Measures action potentials
    - One or more neurons at a time
- Intracellular molecules
- Local field potentials
  - Average electrical activity produced by collections of neurons
- Electroencephalograph (EEG)
  - Average electrical activity produced by entire brain
- Whole brain activity in three dimensions

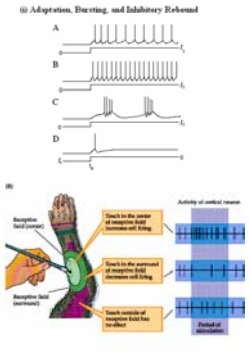




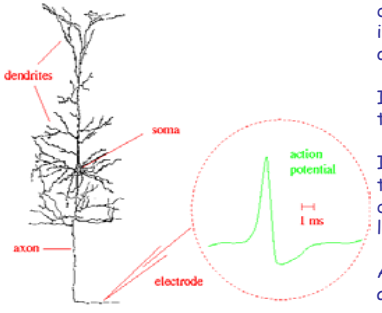
Neuron activity

Types of measurements of neuronal activity:

- Intracellular: $u(t)$ membrane potential. Difference between interior and surrounding. In absence of inputs spontaneously decays toward a resting value (~ -65 mV)
- Extracellular: Potential adjacent to neuron is compared with potential further away. Measure signal in response to behavior



Electrophysiological properties of single neurons



Intracellular measures show a difference of potential between inside and outside the cell membrane of about -70 mV

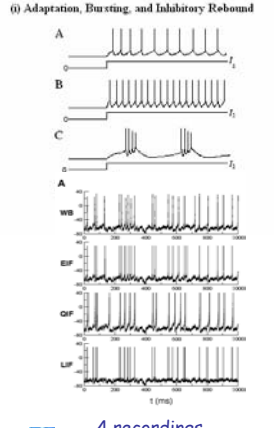
If the membrane potential is less than -70 mV the cell is inhibited

If the membrane potential is larger than -70 the cell is excited. When depolarization attains a sufficient level one observes an action potential.

Action potentials propagate along the axon

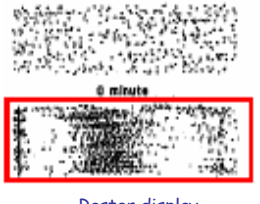
The action potentials is a short voltage pulse of 1-2ms of duration and amplitude of about 100 mV.
The action potentials of a specific neuron have a characteristic shape

Spike trains



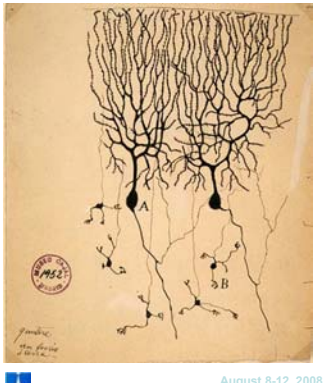
4 recordings

- Use of different scales disclose different properties.
- Using the raster displays one can observe spatio-temporal patterns
- Simultaneos recording show synchronization periods, delays,...



Raster display

Some numbers



1mm

10 000 neurons
3 km fibers

Number of neurons in our brain

> 10^{12} neurons

30 years old people: neurons start to progressevely expire and 10^5 neurons per day die after 70.
...but 10^6 is only the 0,0001%: .of the total!

10^3 morphologically different neurons

Other numbers

Mean number of synapses per neuron: **10^4**

The developing brain generates between **50 and 100 thousand** new cells per second from the fifth through twentieth weeks of gestation.

20-50 postsynaptic potentials, in short time, allow the starting of a spike

A presynaptic neuron can be connected with **104** postsynaptic neurons

Neurons in the cerebral cortex of the brain can have a wiring density of up to **4km per mm^3** by using incredibly thin axons as wires, with an **average diameter of 0.3 micrometers** (1 is one millionth of a meter).

Complexity or overcomplexity????

How to deal with such overwhelming complex system?

Is there any role for mathematicians in such context?

Stochastic phenomena in neurobiology

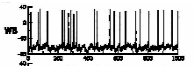
- Intrinsic noise sources:
  - Thermal noise (Johnson noise): the voltage across an electrical resistor *R* fluctuates at finite temperature: Source of minor imprtance.
    - The miniaturization economizes on space and energy but it increases the noise introduced by thermodynamic fluctuations in a neuron's voltage-gated ion channels
  - Number of ion open channels in a patch of neuronal membrane fluctuates
  - Neurotransmitters relased by synapses
- Extrinsic noise sources
  - Synaptic transmission failure
    - Network effect: networks of excitatory and inhibitory neurons with fixed random connectivity. High number of connectivities

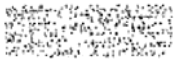
Mathematical/Computer Science Approaches

- Macroscopic level
  - **Observed features**: synchronization phenomena, spatio temporal pattern, specific areas activities
  - **Aim of models**: recover macroscopic behaviors and relate them with pathological (schizofrenia, epilepsy, tremor….) or health conditions
  - **Modeling approaches**:
    - brain as nonlinear system
    - Simulation of large networks through systems of differential equations
    - Computer simulated networks (object-oriented programs)

Mathematical/Computer Science Approaches

- Microscopic level: single neuron or small networks
  - Observed features:
    - intracellular recordings (observation from a single neuron): membrane potential evolution and spike activity
    - extracellular recordings (possible simultaneous recording from 1-100 neurons): measures of the electrical field; spike sorting activity reveals spike activities





  - Aim of the models: recover observed features, forecast responses to specific stimula
  - Modeling approaches (analytical, numerical and simulation methods):
    - Cable theory and related systems of equations (Hodgkin Huxley Models)
    - Threshold stochastic models (LIF models)

Mathematical models: historical hints

- Before 1952
- 1952 Hodgkin and Huxley model (Nobel laureate)
- Till Seventies: a golden period: many scientists cultivate the illusion to be proxime to "understand" the laws of the brain and the mind
- Till Eighties: main focus on single neuron activity models
- Ninties: a crisis period. Lack of mathematical results to support further improvements and slow entrance of computer science methods (simulations numerics). Single neuron models are used to understand specific features but a lack of mathematical instruments generate a sort of pessimism on attainability possible ambitious goals.
- ...new millenium: a new golden age? High speed computers and new techniques for simultaneous recording from groups of neurons open new challenges: mathematics methodologies are recognized an indispensable support for an interdisciplinary approach