L03. ROOTS of NEUROETHOLOGY IN CELLULAR NEUROBIOLOGY

Announcements

1) Course website: http://courses.cit.cornell.edu/bionb4240/index.htm
Google Chrome?

2) Writing Assignments
W1

3) Discussion section
Wednesday 9:05 AM, this room.

Outline

L03. Roots in Cellular Neurobiology
1. Krogh's Principle
2. Neuron doctrine
3. Neuron as connector, integrator, rectifier, transducer, logical device, memory storage, circuit.

KROGH'S PRINCIPLE

“For a large number of problems [in biology] there will be some animal of choice, or a few, on which it can be most conveniently studied.”

The Discovery of the Giant Squid Axon
(Description of the giant axon of squid, Loligo)

Young thought the these curious structures were blood vessels, but he was able to show that upon stimulation with electrical currents they caused the mantle to contract, so he realized they were nerve fibers.

After the Discovery of Squid Axon

- ability to record intracellular voltage
- first voltage clamp (2 electrodes inside: I, V)
- ability to perfuse (replace) intracellular ions,
- development of quantitative description of action potentials
- ability to record from both pre- and post-synaptic neurons at giant synapse

“...The squid axon did more for axonology than any other single advance in technique during the previous 40 years.”

Alan Hodgkin (1973) see quote by R. Keynes (2005)

Nerve nets in hydra and jellyfish (Cnidaria)

- Neuronal doctrine
Santiago Ramon y Cajal

used Golgi method
provided evidence for Neuron doctrine
first evidence of multitude of cell types, neural circuits

Kitten cerebellum
Basket endings convincing proof of separate cells.
- basket cell surrounds cell body but does not connect to purkinje cell.
Axons may cross, but not connect.
Each element autonomous (a cell).

Calaj’s Neuron Doctrine

- The nervous system is composed of cells: glial cells and neurons.
- Neurons are morphological units.
- Neurons make intimate contacts (contiguous but not continuous).
- Cell bodies and dendrites are conductors, just like axons.
- Dynamic polarization
- When there are axon collaterals, they act together.
- Axons arise in development by neurite outgrowth

Electron Microscopy Clinches The Neuron Doctrine

First EM: Germany, 1930’s.
Fixation of tissues (Palade and Porter, 1950’s)
Palay, Palade, DeRobertis:
Neurons with distinct membranes at synapses (extra-cellular space in synaptic cleft) (1954-6).

ANALYSIS LEVEL

molecular
whole animal

cellular
subcellular
circuits
Neuron as a Wire

Neuron Shape: long axon makes long distance, highly specific contact possible.

Neuron electrical properties:
- signals travel within a neuron (insulation)
- travel at high speed (propagation)
- use electric signals (=action potentials)

Branching: permit elaborate connections
- divergence
- convergence

Axon bundles make up nerves

Dorsal Roots (sensory)
- gray matter
- white matter
-Filaments of dorsal root

Ventral roots (motor)
- gray matter
- white matter
-Filaments of ventral root

Sensory ganglion (cell bodies)

Spinal nerve
-Internal root

Spinal cord

Neuron Shape

Axon serves as information conduit.
- long distances
- efficiently packaged

Consider a scale model of motor neuron (soma = 100 microns; axon = 1 m)
(ratio = 1:10,000)

Dye filled axons

Nerve Cells Communicate with Targets Using Electric Signals

1) Resting neurons are electrically polarized.
   - resting potential

2) Action potentials: transient events caused by opening of ion channels in membrane. Propagates down axon.

3) Slow potentials: originate in sensory receptors, and at synapses. Local, do not propagate.
Nerve cell at rest has a voltage across its membrane = resting potential

Action Potentials

The Action Potential (spike):
- Transient (1 millisecond duration)
- “de-polarization”
- peak voltage = +55 mV inside (mainly due to influx of Na+ ions)
- All or None (threshold)
- propagates along axon

Some Ion Channels in Nerve Membranes are Voltage-Dependent

- Ion selective AND Voltage dependent (opening controlled by voltage)

The Sodium Channel

Potassium Channels

Structure worked out in 1998 (Doyle et al. – Roderick MacKinnon lab)
How the action potential propagates

Propagation Velocity

- Measuring velocity with two electrodes
- velocity = distance / time
- myelinated nerve: 10 to 100 m/sec

Neuron as Rectifiers

SYNAPSES

Excitatory influx of cations (+ charge) cause membrane depolarization

Neuron as a Transducer

Crayfish Stretch Receptor

Neural code for stretch intensity is the frequency of nerve impulses
Pharmacological blockers can sort out the various ion channels responsible for the receptor potential, adaptation, and spikes.

Adaptation

Membrane channels MSC mechanosensitive Na – sodium K – potassium Cl - chloride

Pharmachological blockers can sort out the various ion channels responsible for the receptor potential, adaptation, and spikes.

Summation

Synapses: synaptic potentials sum on the post-synaptic cell, providing for:

-- spatial summation:
-- temporal summation:
-- subtraction:

Fine Tuning the Neuron as Integrator (summing network)

Excitatory synapse generates a depolarizing potential.

Membrane voltage decreases exponentially with distance.

Rise time increases with distance.

Consider a synapse on a dendrite.

Neuron as Connector

Some neurons serve to relay signals from one cell to another. Signal is relayed from input to the output.
Neuron Logic

AND logic
Output spike only if 1 + 2 are active at same time.

OR logic
Output spike if either 1 or 2 are active

NOT logic
Output spike if 1 OR 2, but NOT 3

Neuron Memory

Synapses retain a memory of recent events.

Depression: recent activity leads to decrease in response.

Facilitation: recent activity leads to increase.

Pre-synaptic inhibition.

Pre-synaptic facilitation.

Changing the Strength of a Synapse

- Fatigue
  - depletion of synaptic transmitter
- Habituation
  - decrease in amount of transmitter released, but not due to fatigue
- Sensitization
  - increase in amount of transmitter released

Changing the Strength of Synapses

- Pre-synaptic excitation
  - a synapse on a synapse (primes synapse to be stronger).

- Hebbian Learning
  - NMDA receptor for glutamate: synapse is made stronger if activated when cell already depolarized

Neural Circuits and Behavior

Tracing circuitry of neural connections leads to understanding of how behavior is influenced by neuronal action.

Perception correlates with characteristics of neural circuit.
Neuronal Activity is both Necessary and Sufficient

A) Correlation between behavior and activity of a particular neuron (LGI)

B) Sufficient: artificial stimulation of the neuron causes both a spike, and the behavior.

C) Necessary: if the neuron spike is blocked, the natural behavior is blocked, even though stimulus is OK.

Complex Behavior, Complex Circuits

Stomatogastric Ganglion of Lobster.

A restricted neural network (30 cells).

Controls muscles of gastric mill and the pylorus (movements involved in grinding of food and of digestion).

The PYLORIC muscles and patterns of contraction.

References


