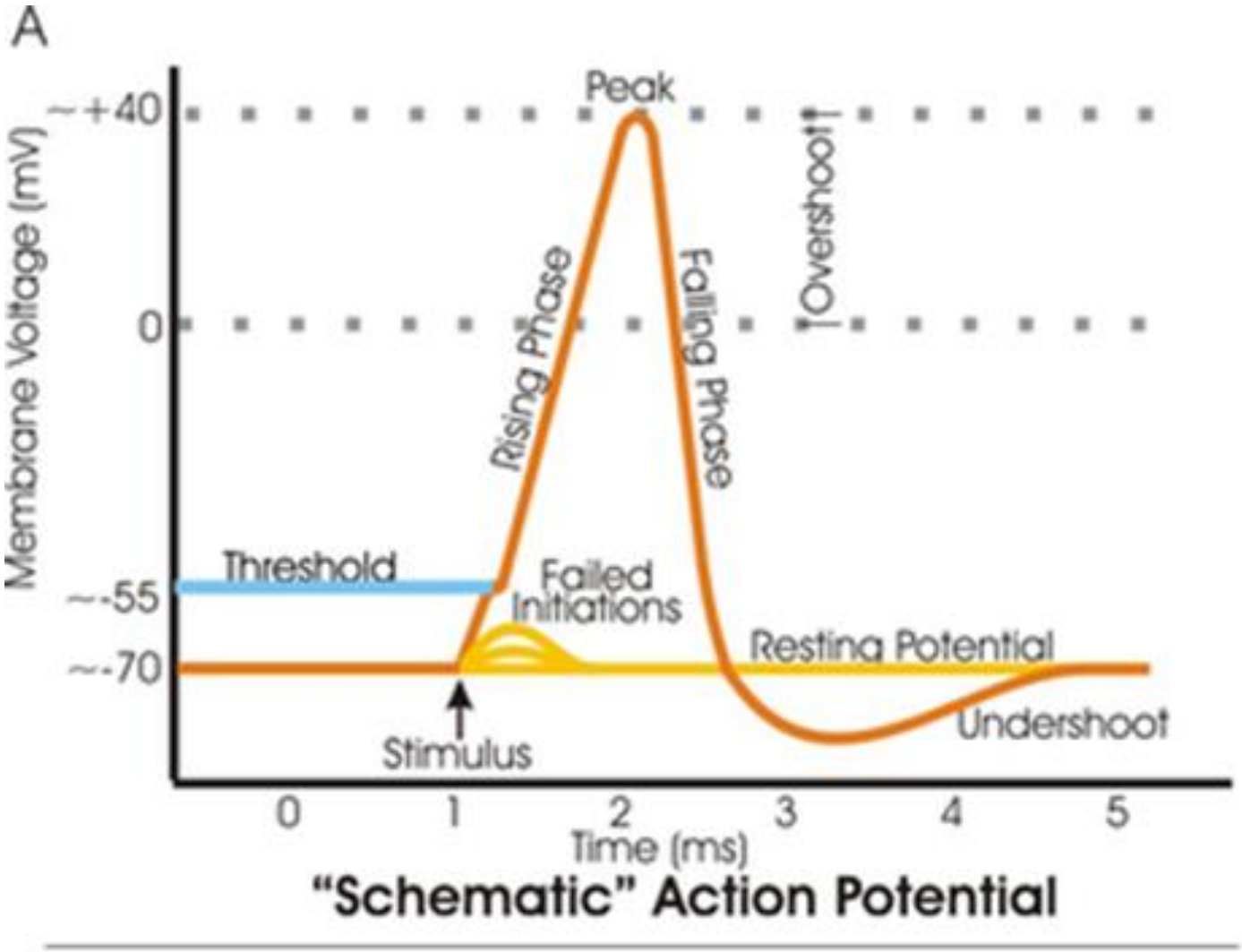
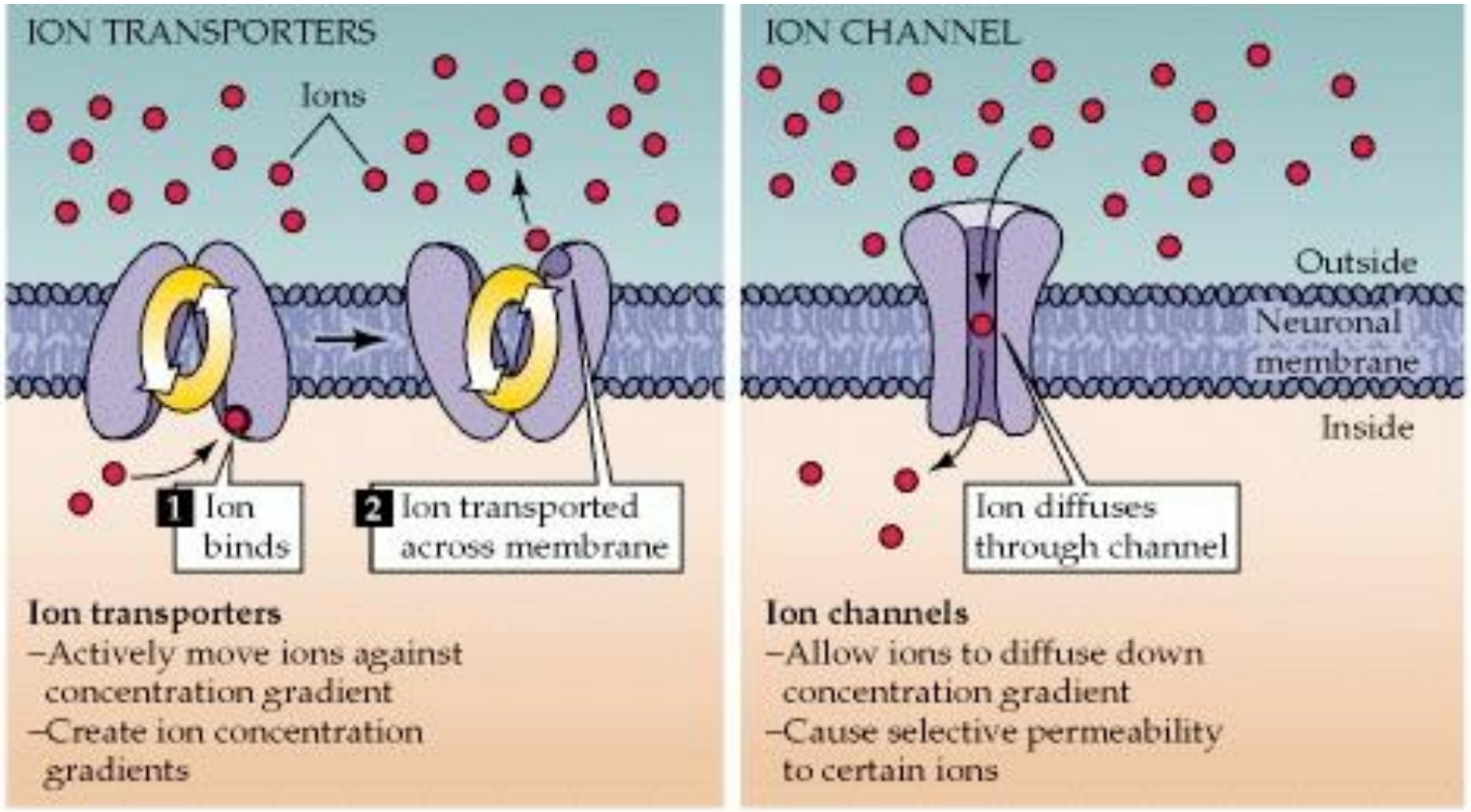
Brief Action Potential Review



"Schematic" Action Potential

Neurons differentially conduct ions which gives rise to an electrical potential across the membrane. This membrane potential is caused by:

1. concentration gradients of ions
2. charge or voltage gradient



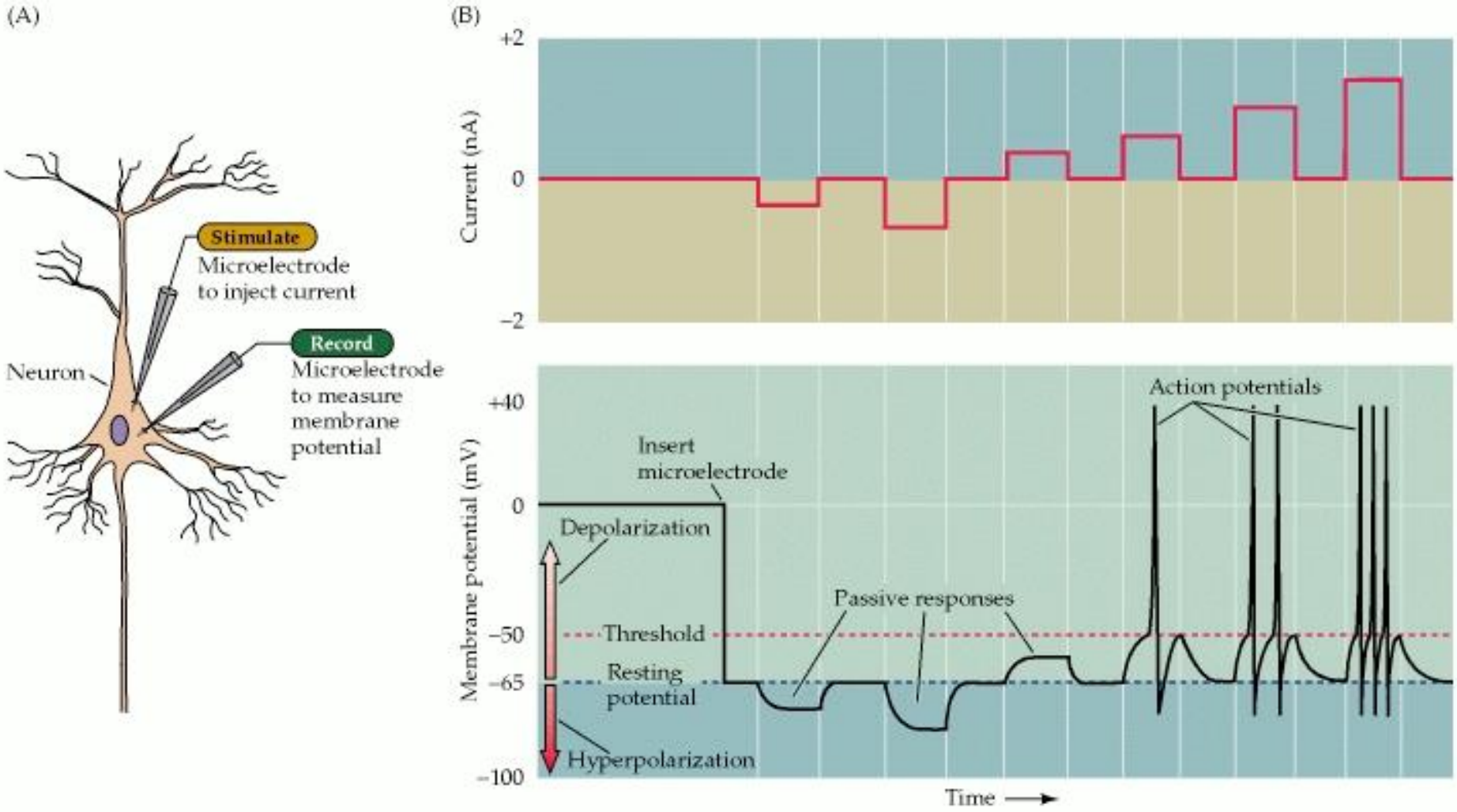
The "equilibrium potential" is defined as:

A. When there is no ion flow across the membrane
B. When the concentration gradient and electrical gradient are counterbalanced for a single ion
C. When the concentration of all ions are equal on both sides

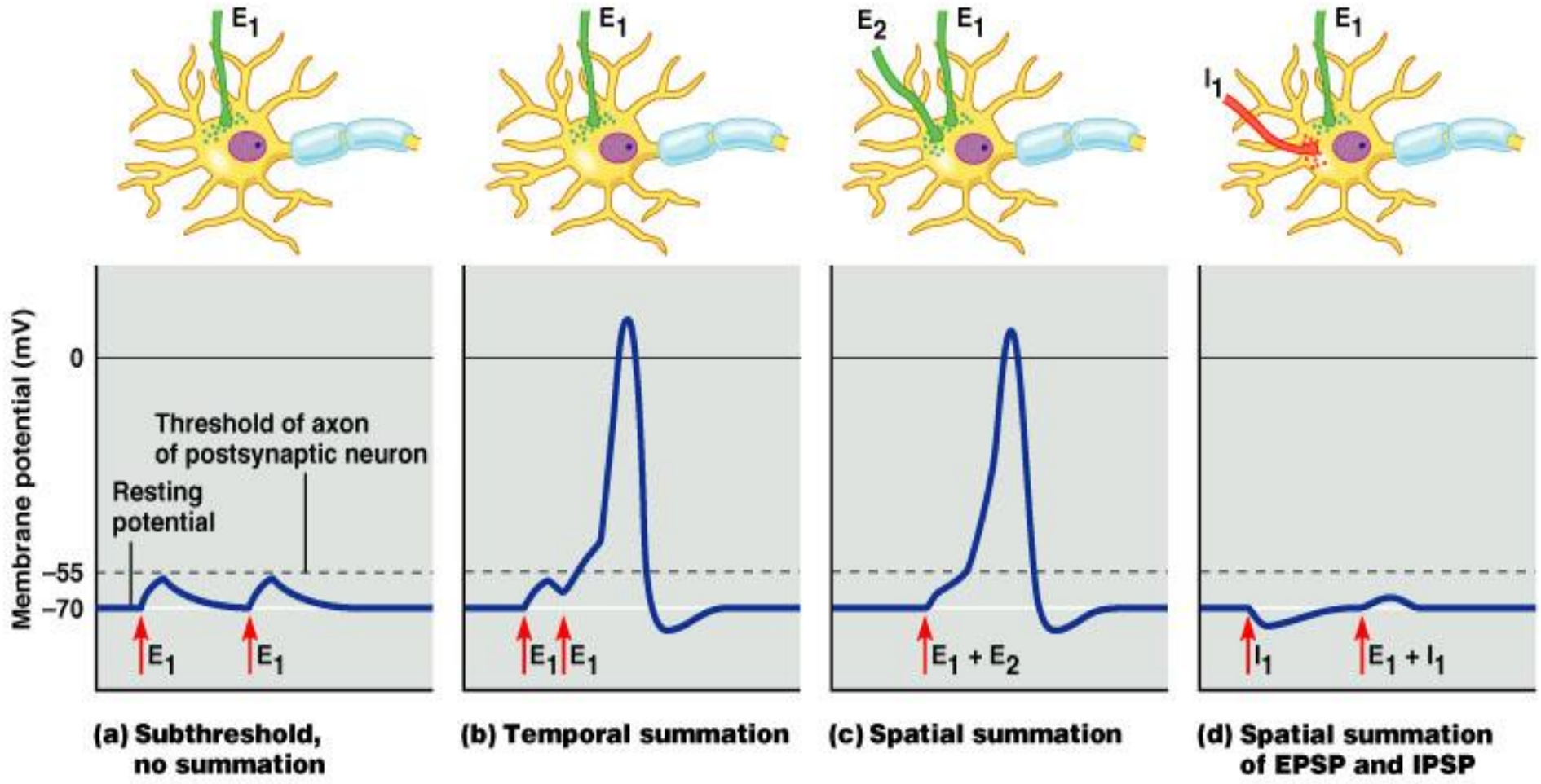
Na+ +60 mV
Cl- -70 mV

When nerve cells are at resting potential:

A. Ions are moving back and forth across the membrane
B. There is more Na+ on the inside, and more K+ on the outside
C. There is an overall more negative charge on the inside of the membrane with respect to the outside
D. Both A and C


(A)
Stimulate
Microelectrode
to inject current
Record
Microelectrode
to measure
membrane
potential
Neuron
(B)
+2
Current (nA)
0
−2
+40
Membrane potential (mV)
0
−50
−65
−100
Insert
microelectrode
Depolarization
Threshold
Resting
potential
Hyperpolarization
Passive responses
Action potentials
Time

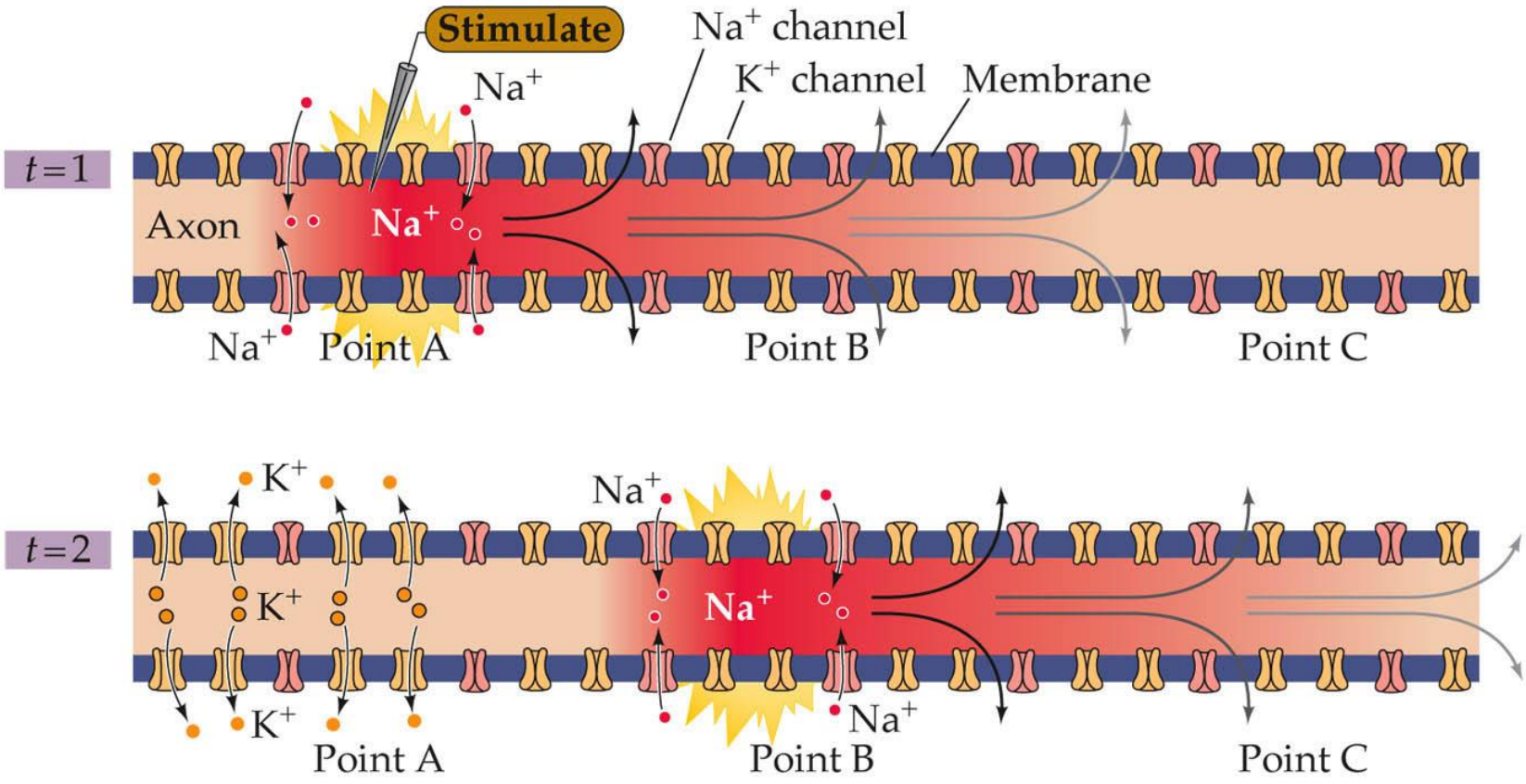
Summation


E1
E1
E2
E1
I1
E1
Membrane potential (mV)
0
–55
–70
Threshold of axon of postsynaptic neuron
Resting potential
E1
E1
E1
E1
E1 + E2
I1
E1 + I1
(a) Subthreshold, no summation
(b) Temporal summation
(c) Spatial summation
(d) Spatial summation of EPSP and IPSP

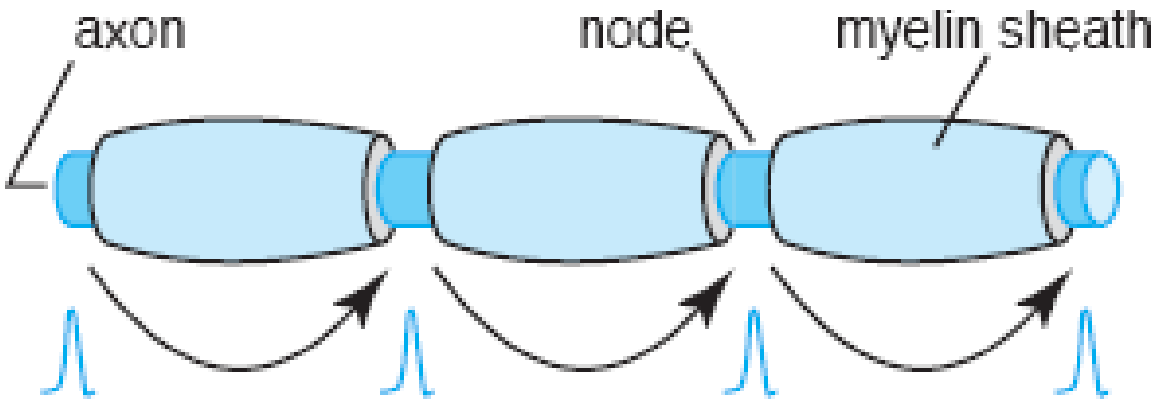
When neurons are "active", we mean those cells are sending or receiving action potentials and if one region of the brain is more active than another regions then

A. The action potentials are larger
B. The action potentials are longer
C. The action potentials are more frequent
D. The actions potentials release different neurotransmitters

Propagation down the axon



Myelination: insulation



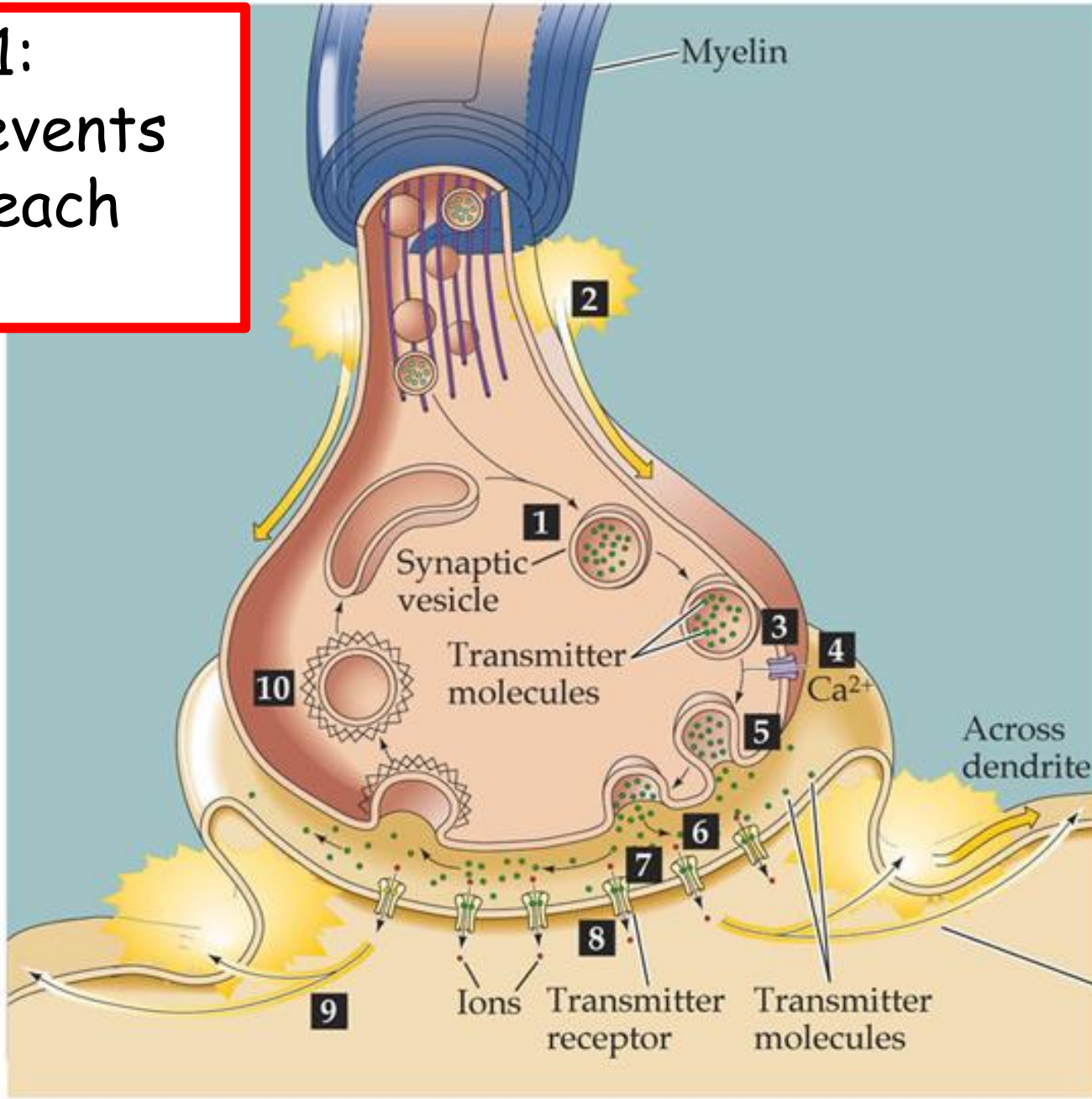
Myelination decreases the internal resistance to passive current flow (under the myelin sheath, no ions can leak out)

This allows the action potential to "hop" from node to node

Myelination speeds up conduction from ~10 meters/sec to ~150 meters/sec!

Loss of myelination has severe consequences: e.g. multiple sclerosis

Team Workshop 1:
What molecular events are occurring at each numbered step?



Methods to study exocytosis

Membrane capacity (Cm)

Cm = Qm/V (Q is the charge across the membrane) specific capacitance is mainly determined by the thickness and dielectric constant of the phospholipid bilayer. Therefore, the increase in plasma *membrane area* due to exocytosis is *proportional to* the increase in Cm.

Patch clamp

micropipet has tight seal to allow low noise, high sensitivity, electric measurement.

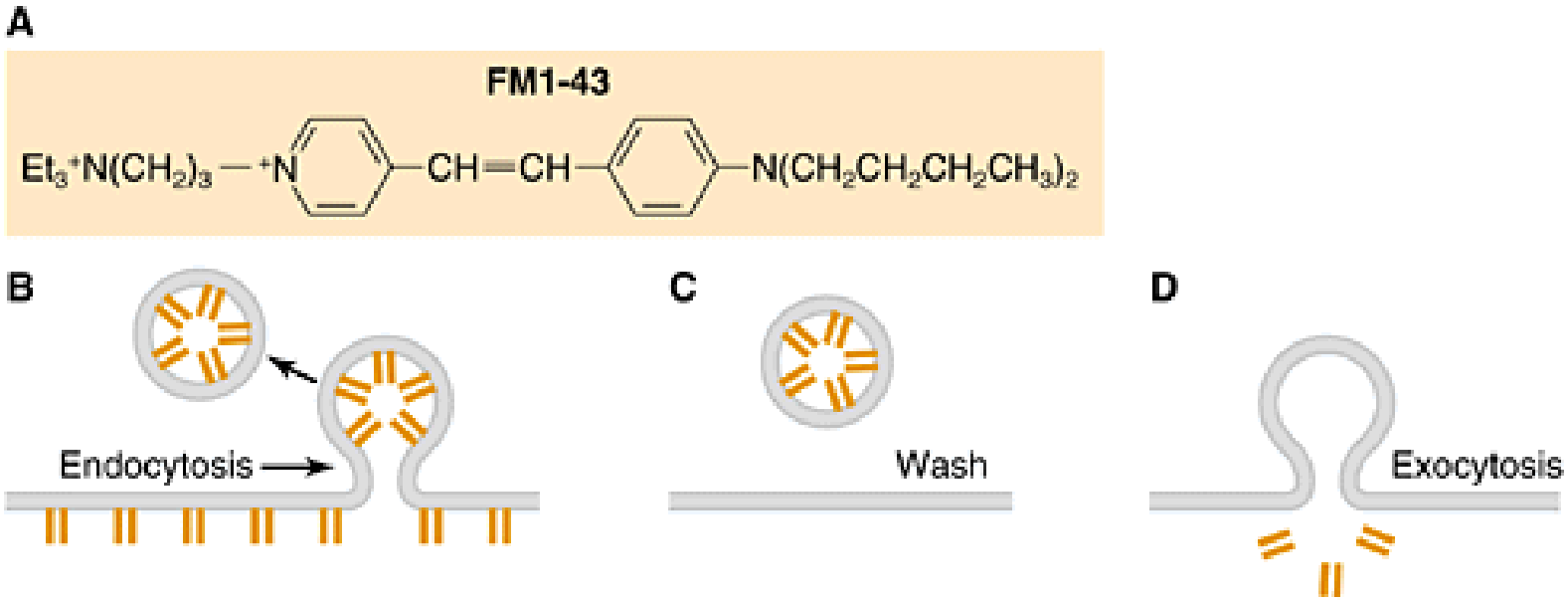
Amperometry

Measurement of released neurotransmitter through oxidative electrochemistry

Fluorescence

FM-dye unloading, synaptoPhluorin

Optogenetics

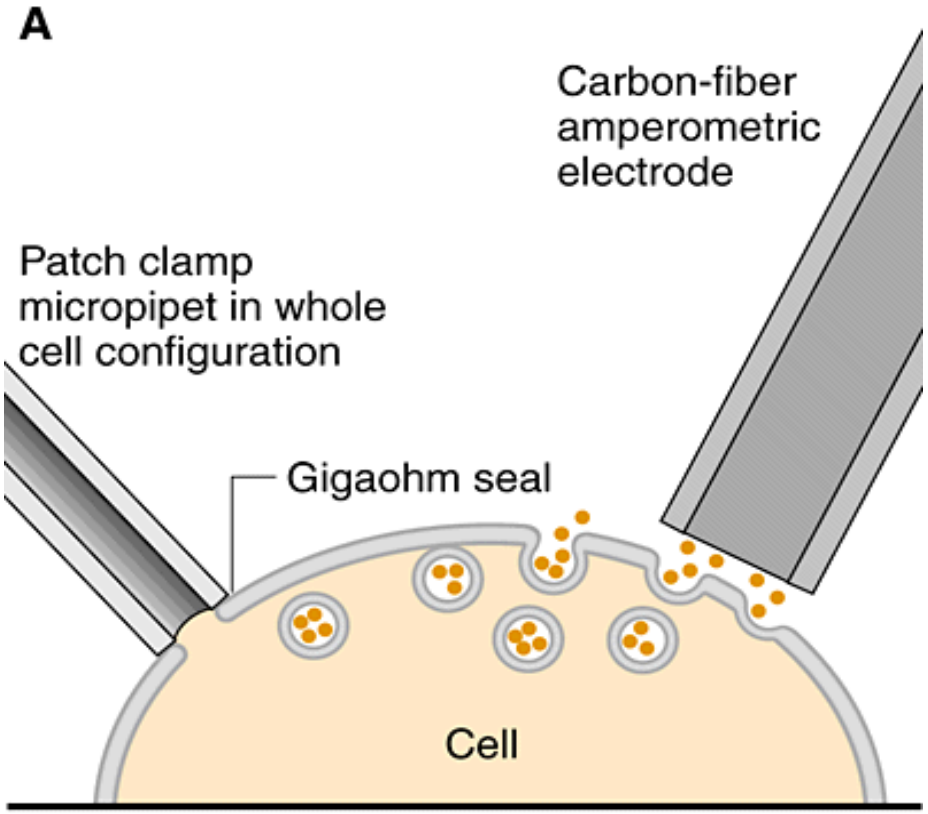


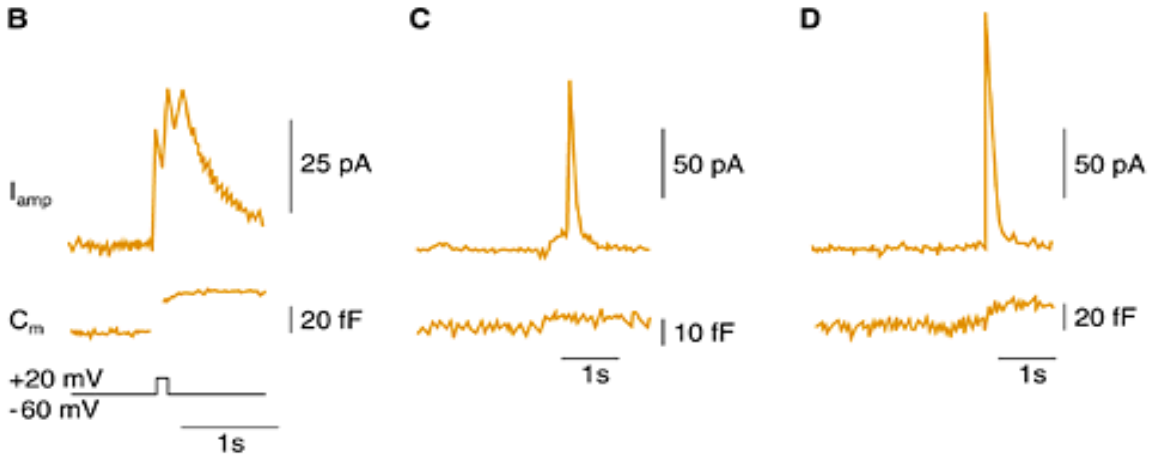
The use of fluorescent dye FM1-43 to label the membrane and visualize *endocytosis and exocytosis* at the NMJ:

1. Complete cycle of exocytosis and endocytosis app. 1 min

2. A single impulse releases 0.1% of the recycling pool.

3. Endocytosis follows ~20 sec. after exocytosis.



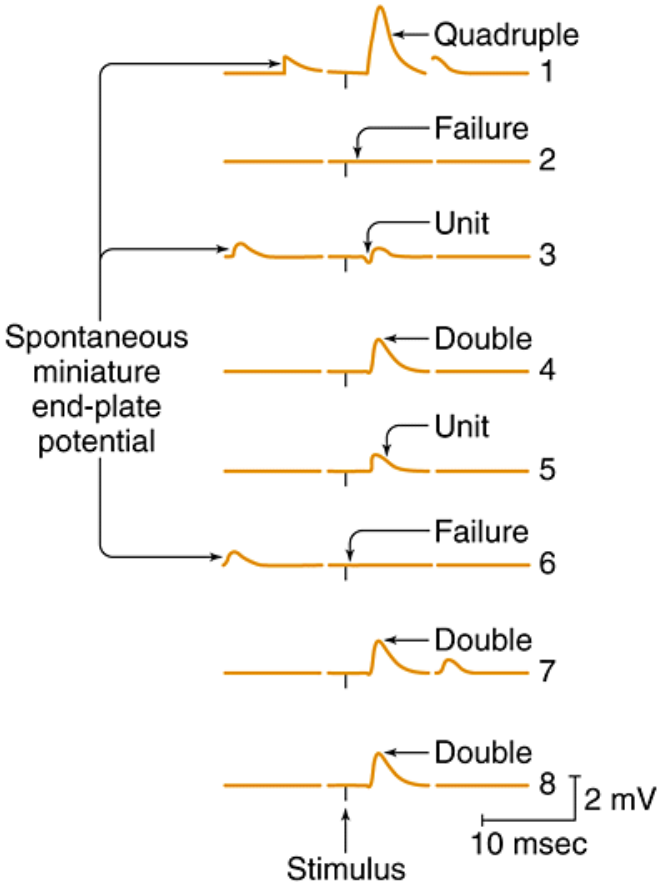


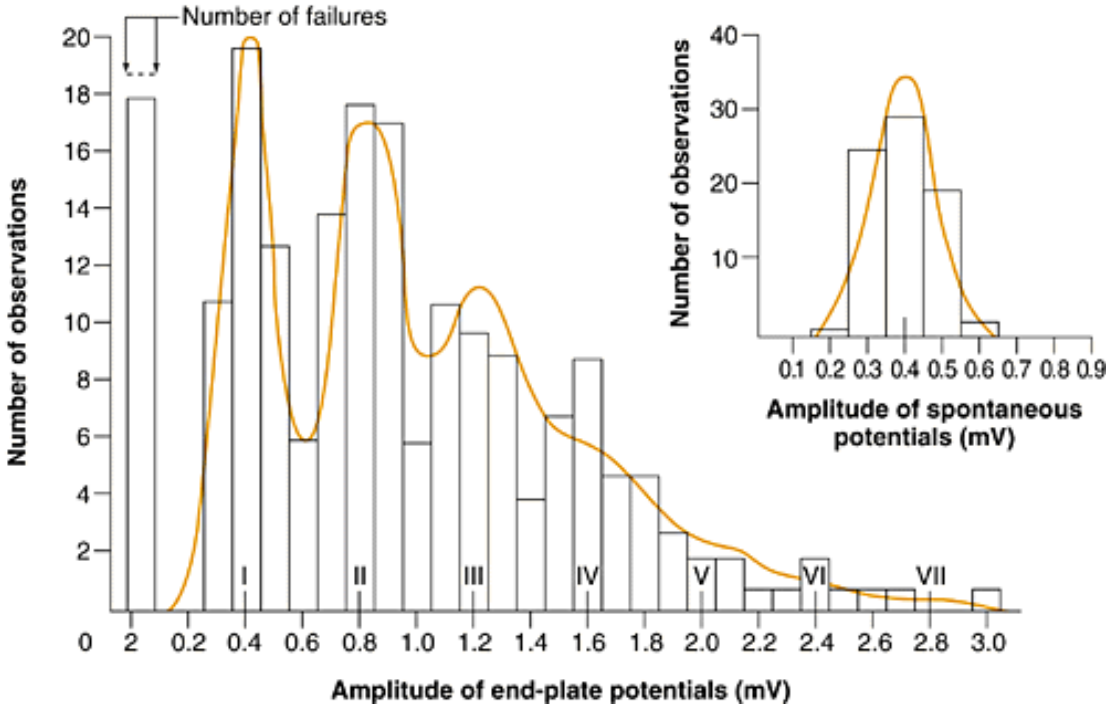
Electrochemical:
amperometric

Electrophysiological:
capacity

Quantum release : mechanism of release as *Exocytosis*

1. **Fatt and Katz (1952) observed motor neuron stimulation results in spontaneous potentials of approximately 1 mV at the motor end plate (miniature end-plate potentials [MEPPs]).**
2. **Measurement of quantum release: amplitude fixed; but number variated.**


Quadruple
1
Failure
2
Unit
3
Spontaneous miniature end-plate potential
Double
4
Unit
5
Failure
6
Double
7
Double
8
2 mV
10 msec
Stimulus

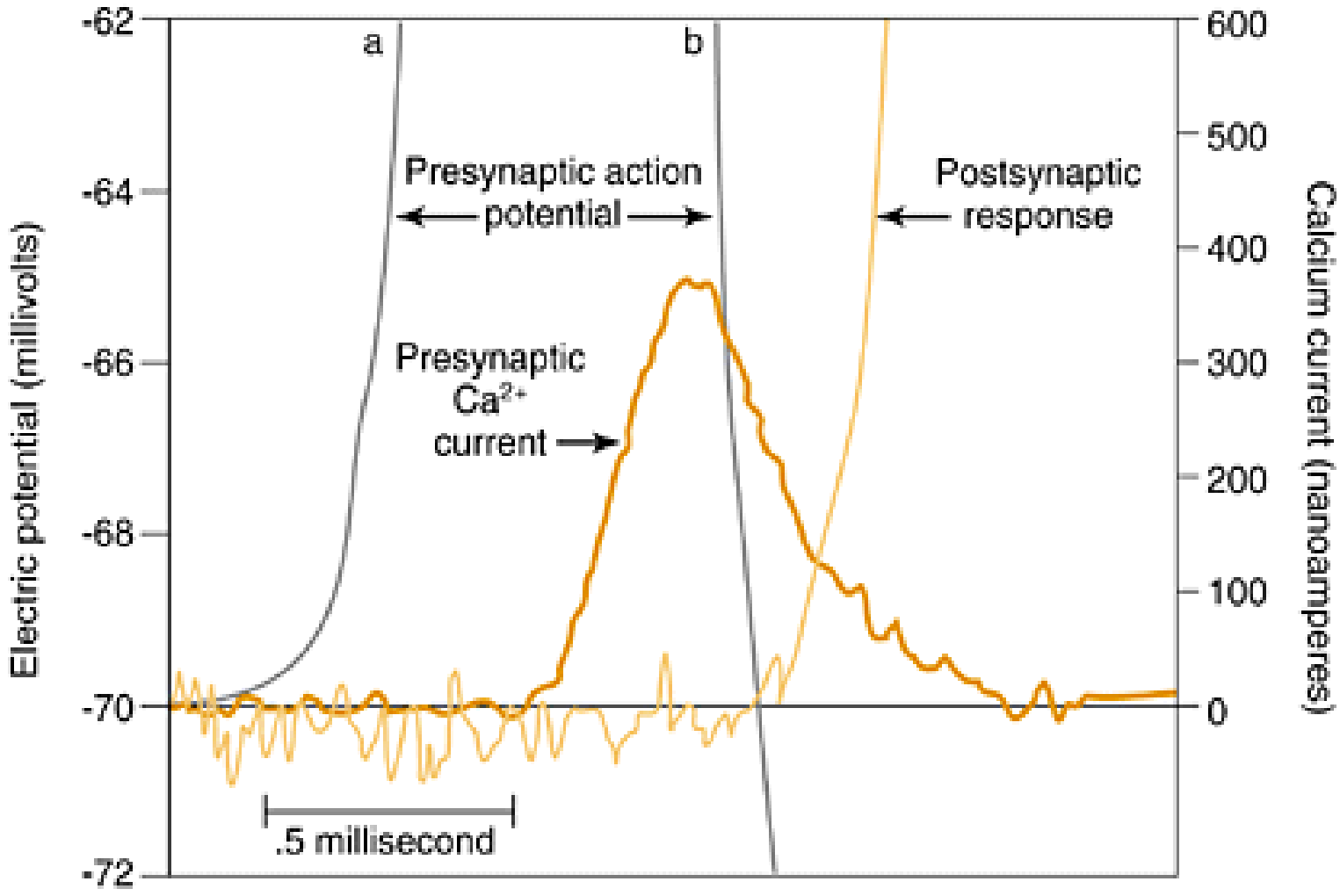

Number of failures
Number of observations
Amplitude of end-plate potentials (mV)
I
II
III
IV
V
VI
VII
Number of observations
Amplitude of spontaneous potentials (mV)

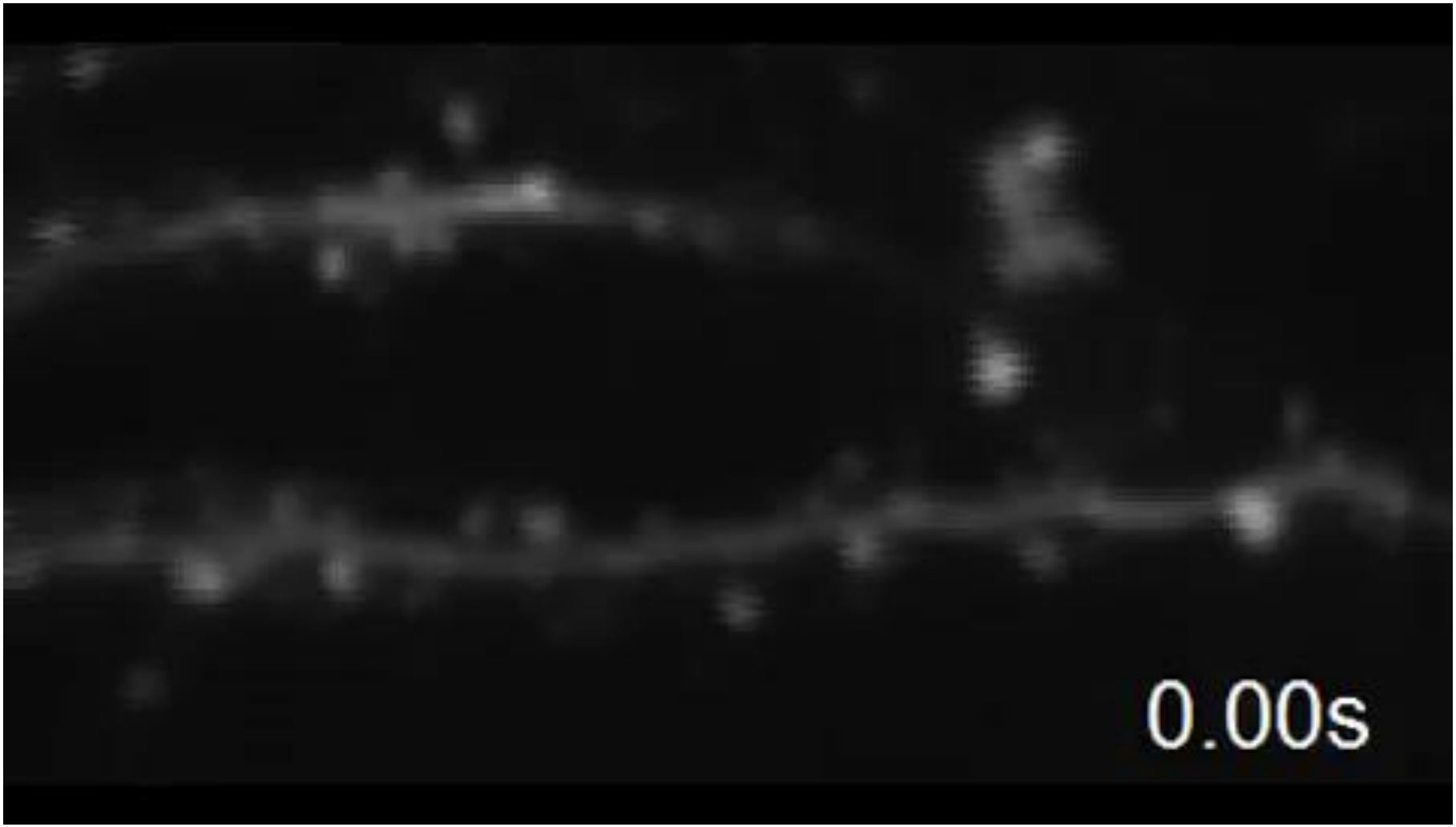
Calcium is necessary for transmission at the NMJ and other synapses

1. In most cases in the CNS and PNS, chemical transmission does not occur unless Ca^{2+} is present.
2. EPPs could not be elicited if the calcium pulse immediately followed the depolarization; but should be beforehand (pulse as short as 1 msec preceded the depolarization).
3. Extracellular calcium: 2 mM vs. intracellular 0.1 μM; the requirement to activate calcium channels: 50-100 μM.
4. Origin of calcium could be *extracellular* (thru voltage-dependent Ca^{2+} channel) or *intracellular*: GPCR-coupled PI-PLC activation release IP_3, thus Ca^{2+} release from ER.

Pre-synaptic event and time scale

1. The time between calcium influx and exocytosis at the terminal is very short (0.5 -1.0 msec at NMJ; 200 μsec at squid axon; 60 μsec in CNS neuron)
2. In such short time (due to docking and fusion of synaptic vesicle), synaptic vesicle cannot move significantly (calcium diffuses only 850 Å)
3. The supply of synaptic vesicles in the terminal is limited. ***Rapid recycling from the synaptic membrane with plasma membrane via clathrin mediated endocytosis is essential*** (endocytosis occurs away from active zones).


-62
-64
-66
-68
-70
-72
Electric potential (millivolts)
a
b
Presynaptic action potential
Postsynaptic response
Presynaptic Ca^{2+} current
.5 millisecond
600
500
400
300
200
100
0
Calcium current (nanoamperes)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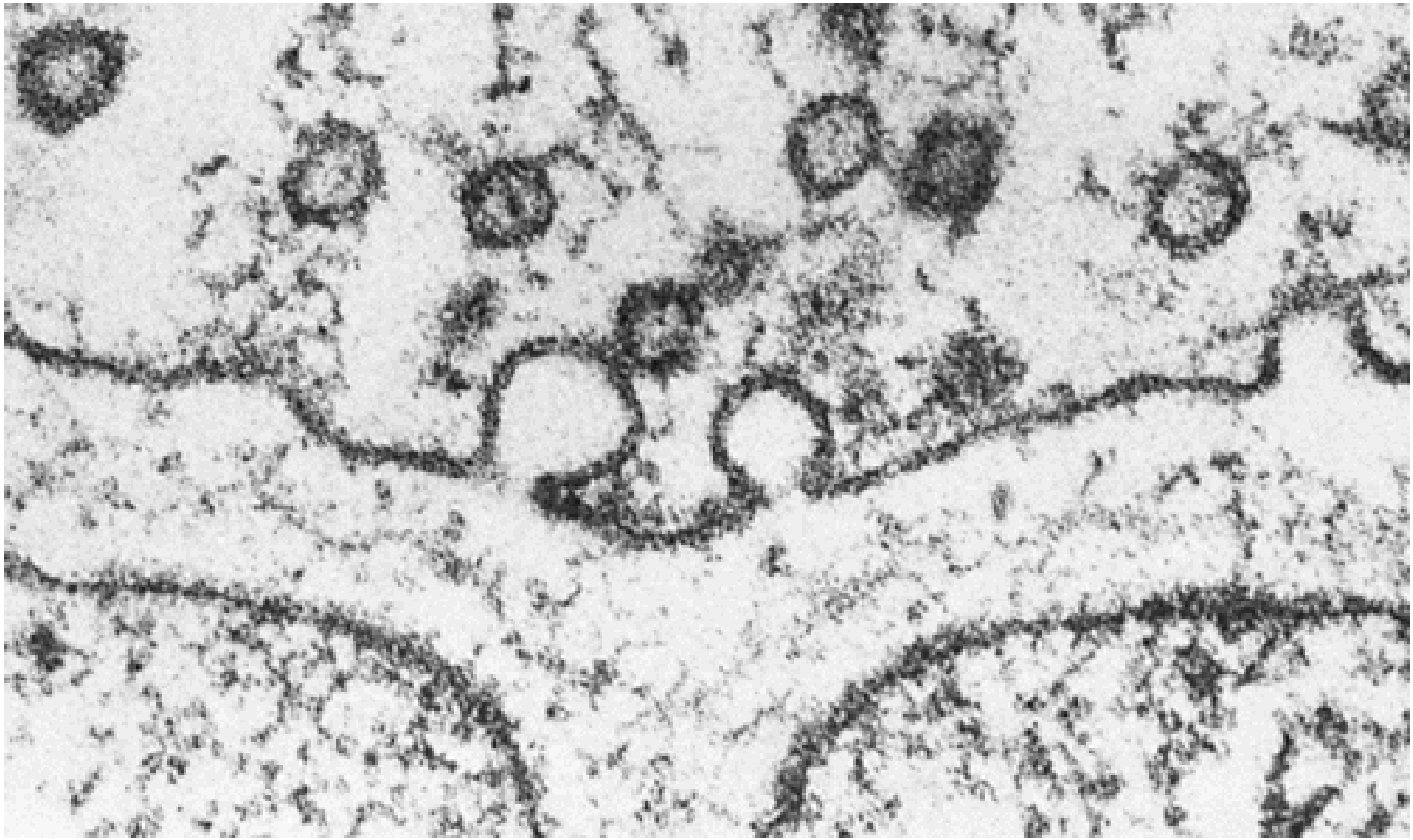

Team Workshop 2: Draw the expected endplate potential curve for this picture

Fast synaptic transmission vs. peptide/protein release at the nerve terminals

1. Fast transmission: catecholamines, amino acid transmitters; can be synthesized within the n. terminals (***synaptic vesicle***) or transported rapidly across the membrane (***uptake carrier***).
2. In contrast, peptide/protein are inserted in the ***secretory granules***, then transport down to n. terminals (no carrier)
3. Peptidergic granules are far less numberous than vesicles involved in fast exocytosis and are not generally localized at active zone (maybe function to maintain the long-lasting effect on postsynaptic neuron)

Team Workshop 3:
Discuss what moleculae mechanisms could be responsible for LTP?