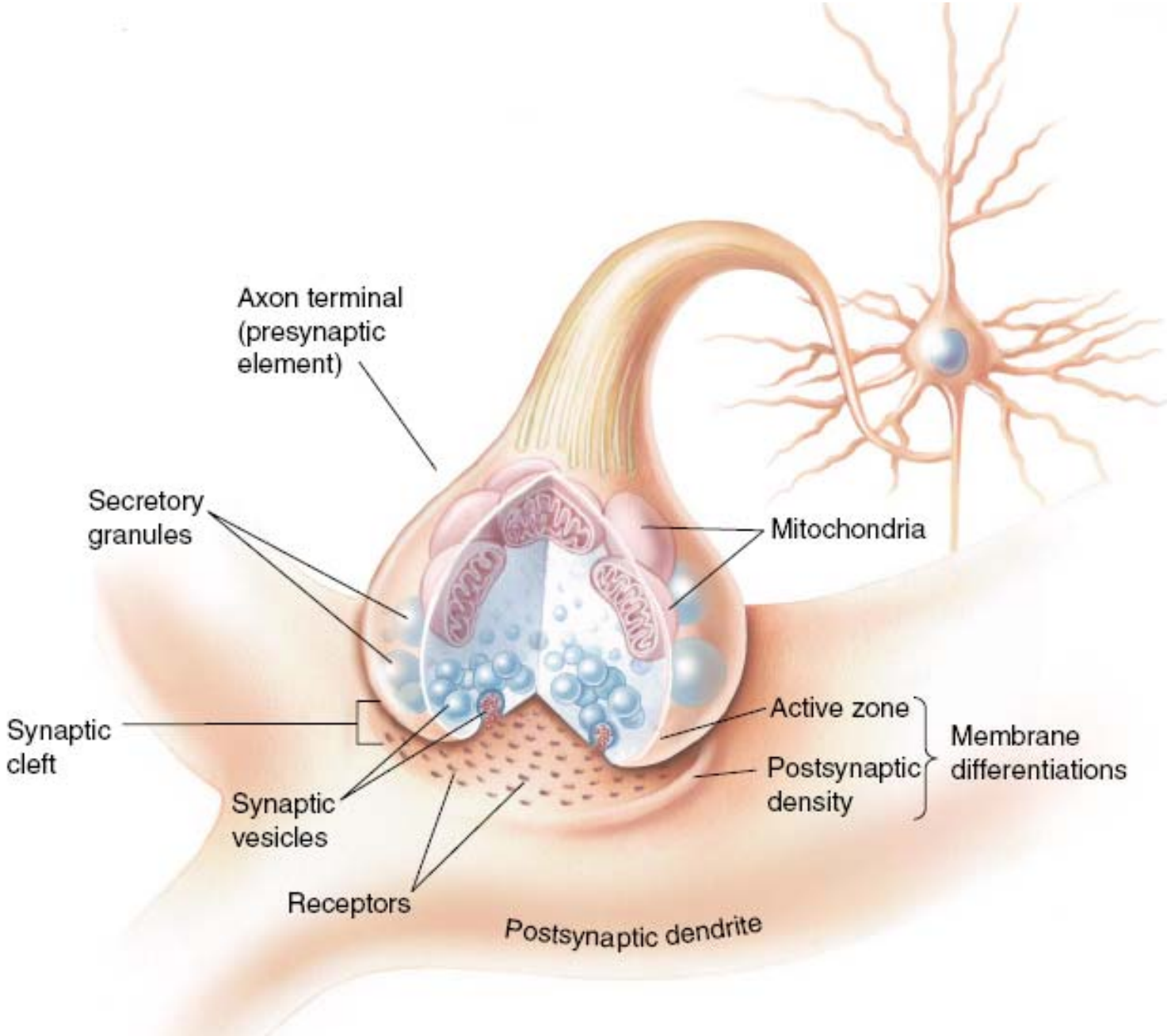
9.01 Introduction to Neuroscience
Fall 2007


Axon terminal
(presynaptic
element)
Secretory
granules
Mitochondria
Synaptic
cleft
Active zone
Postsynaptic
density
Membrane
differentiations
Synaptic
vesicles
Receptors
Postsynaptic dendrite

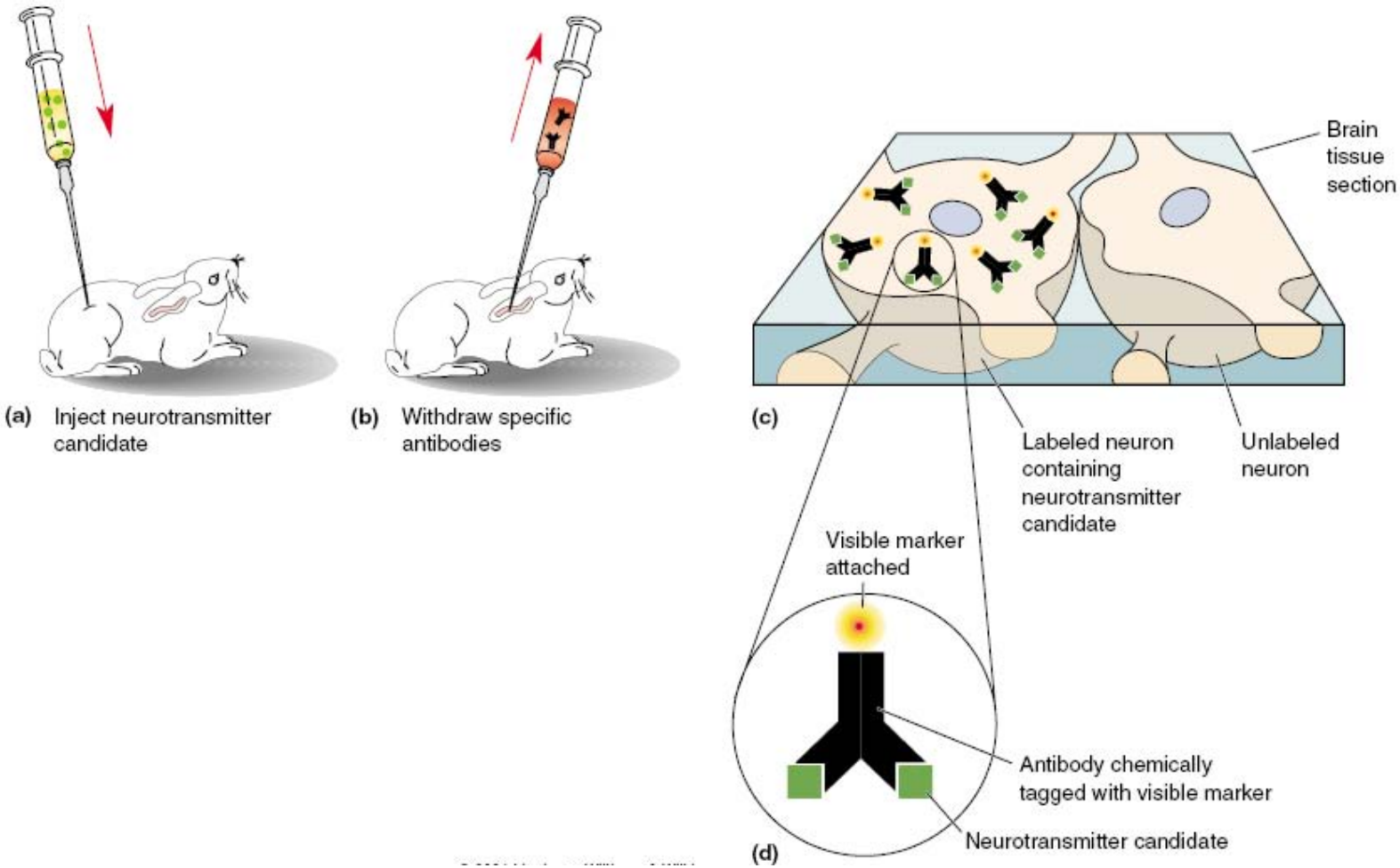
Criteria that define a neurotransmitter

1. The molecule must be synthesized and stored in the presynaptic neuron.

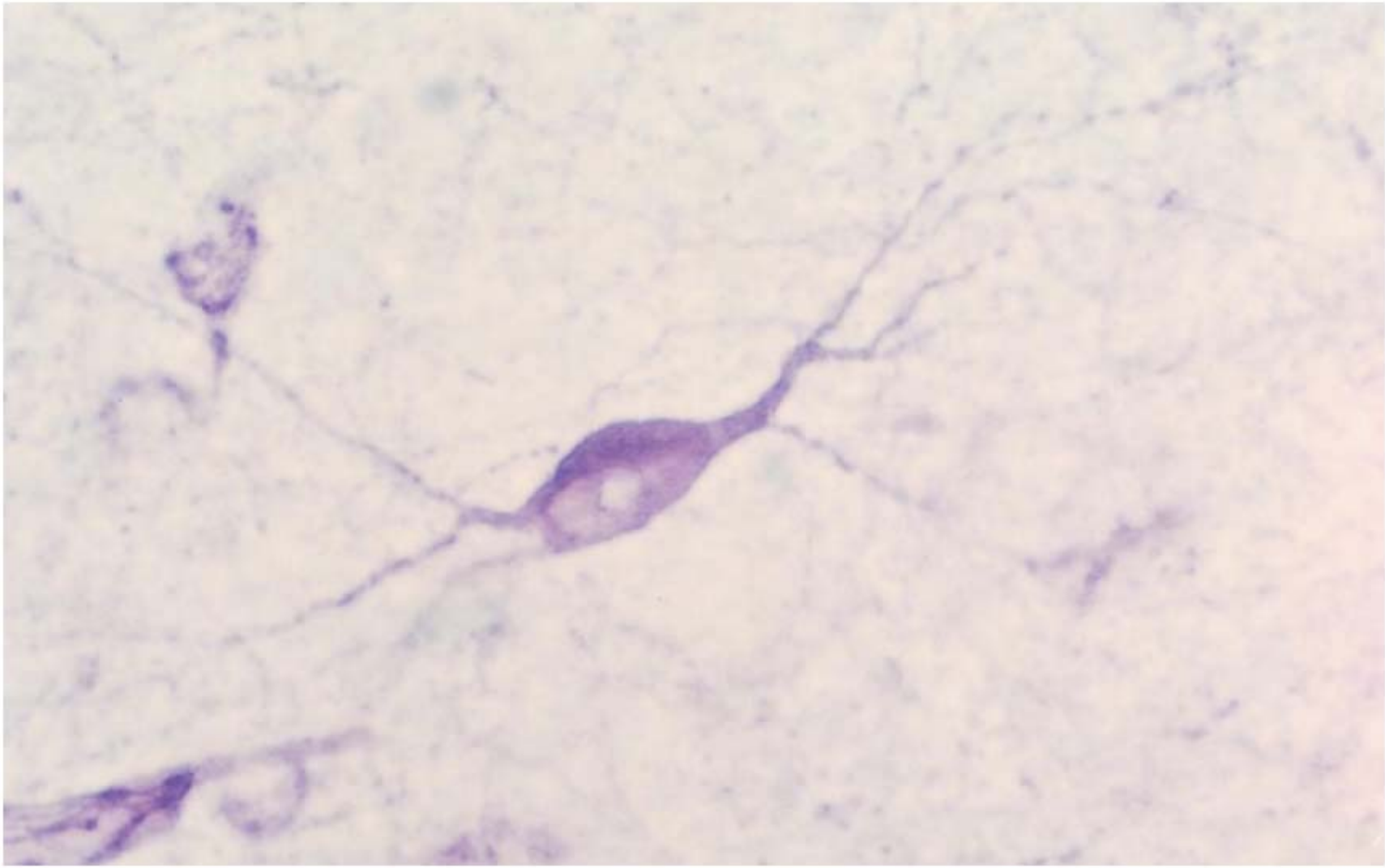
2. The molecule must be released by the presynaptic axon terminal upon stimulation

3. The molecule, when experimentally applied, must produce a response in the postsynaptic cell that mimics the response produced by the release of neurotransmitter from the presynaptic neuron

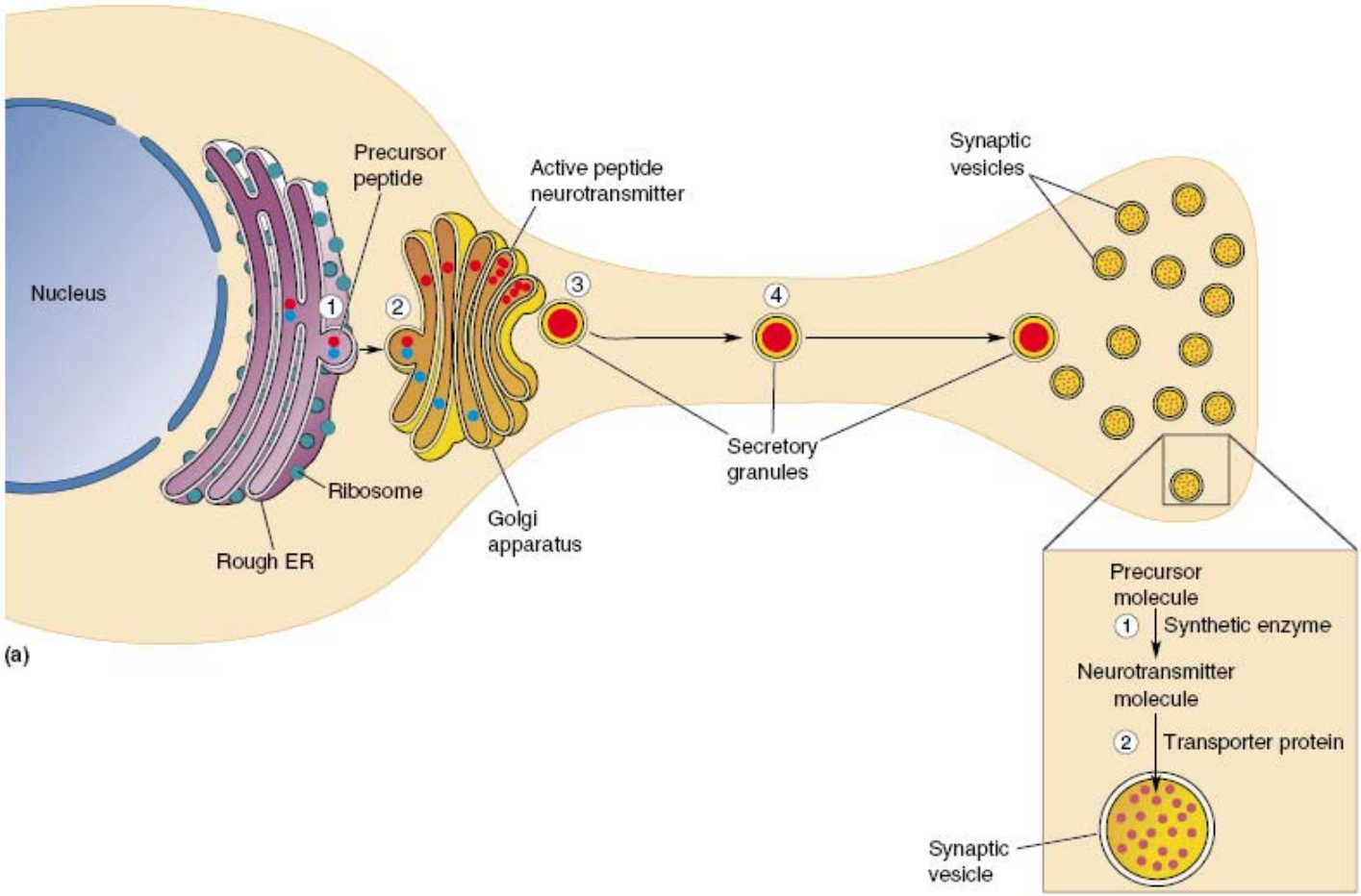
The generation of antibodies for immunocytochemistry



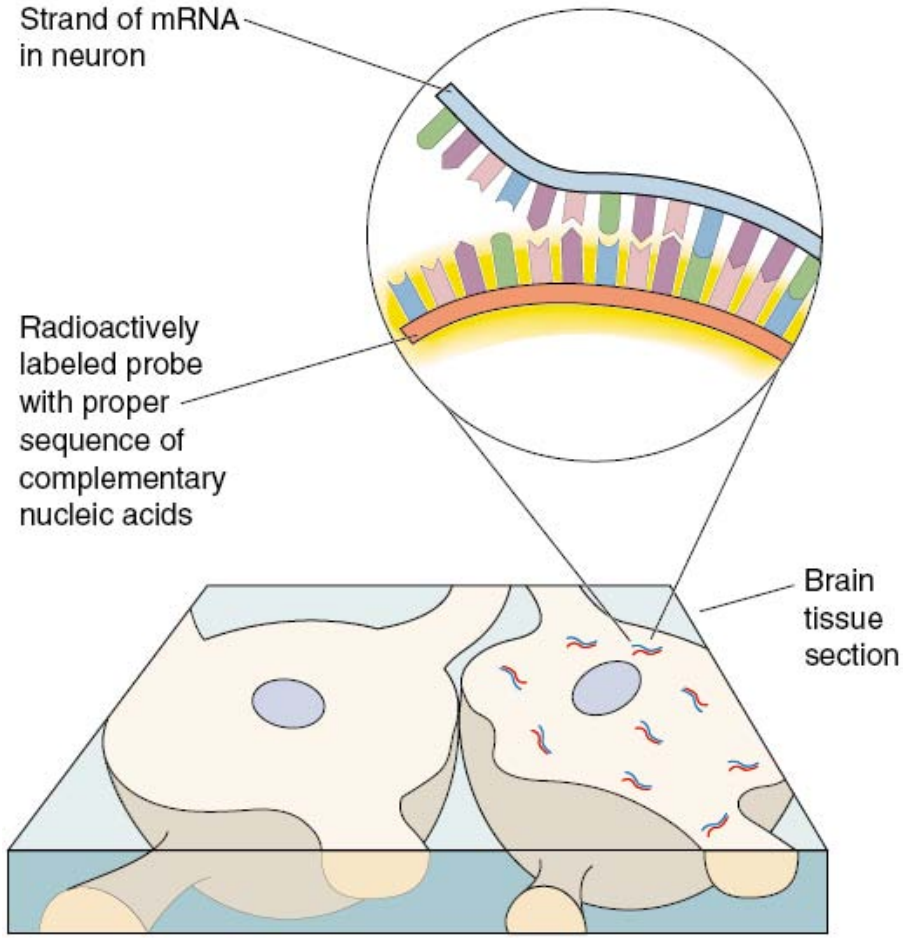
Immunohistochemistry for neurotransmitters



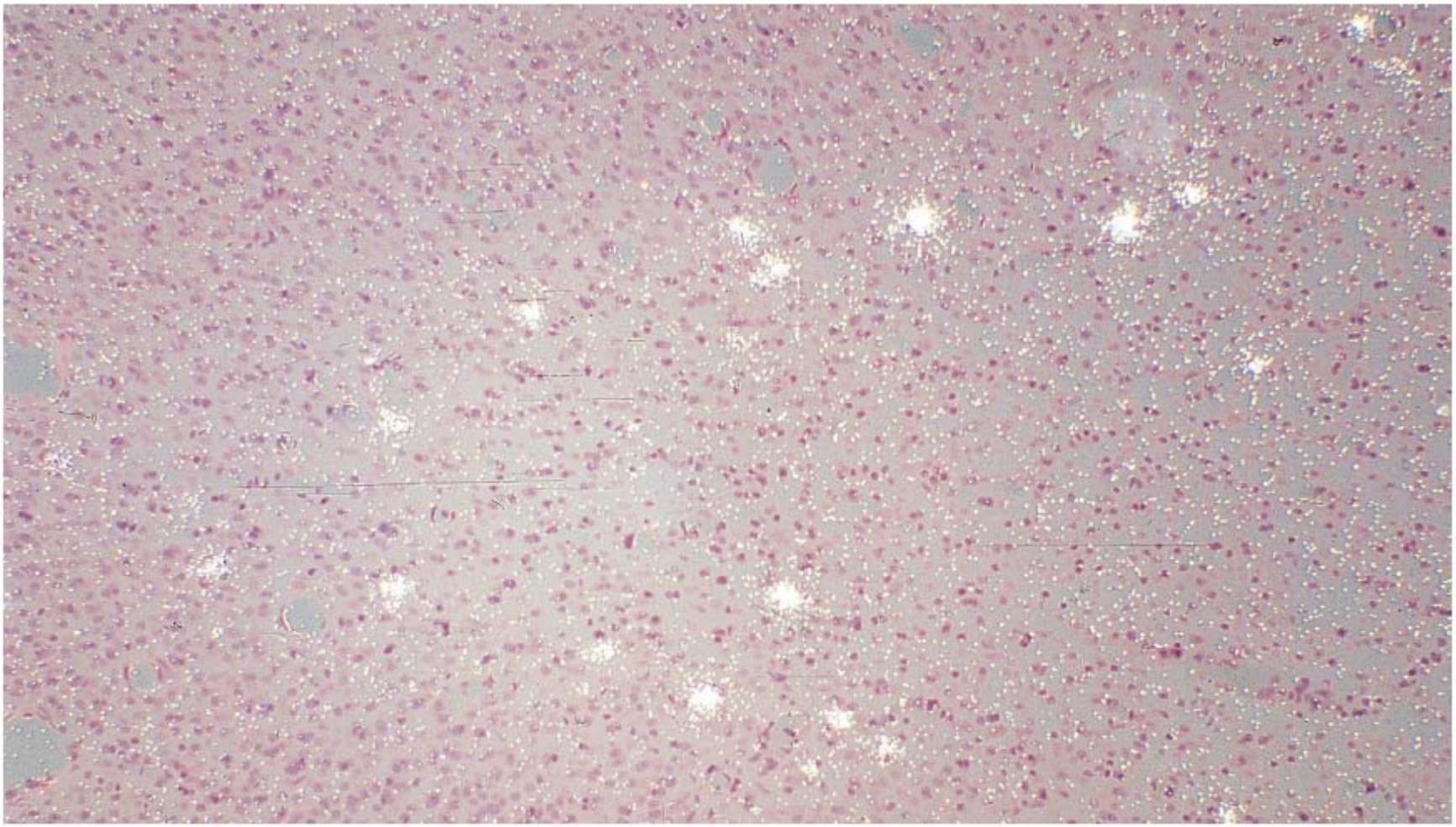
Synthesis of neurotransmitter



In situ mRNA hybridisation can be used to study the expression of genes

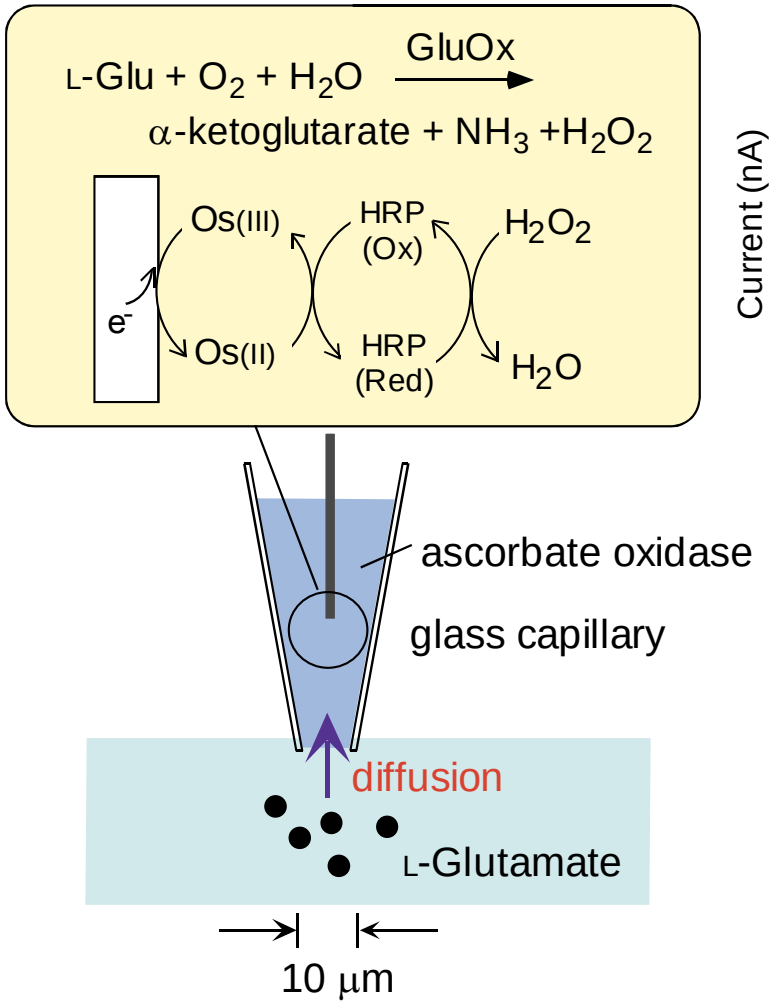


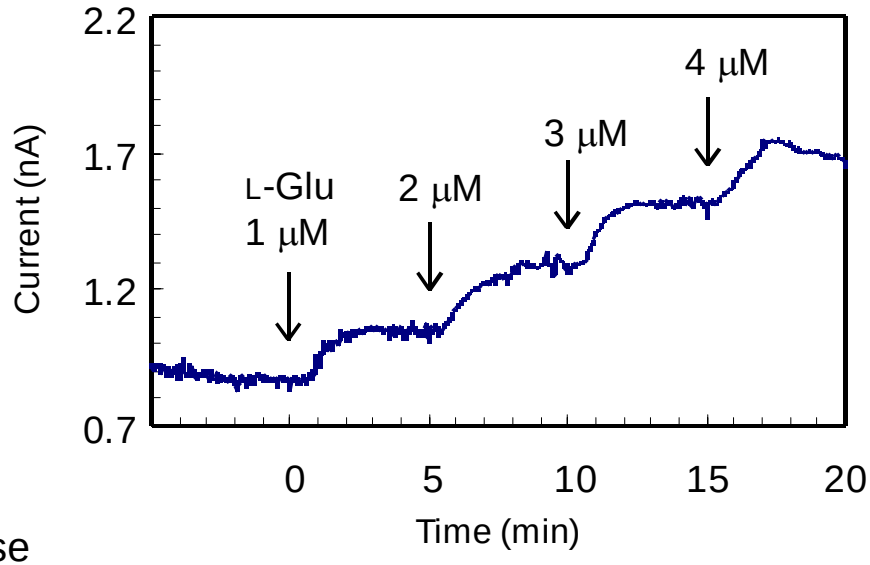
In situ hybridisation for a neuropeptide mRNA

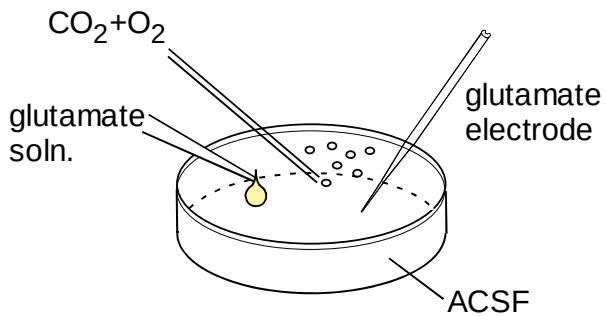


Radioactive ligands can be used to mark up receptors

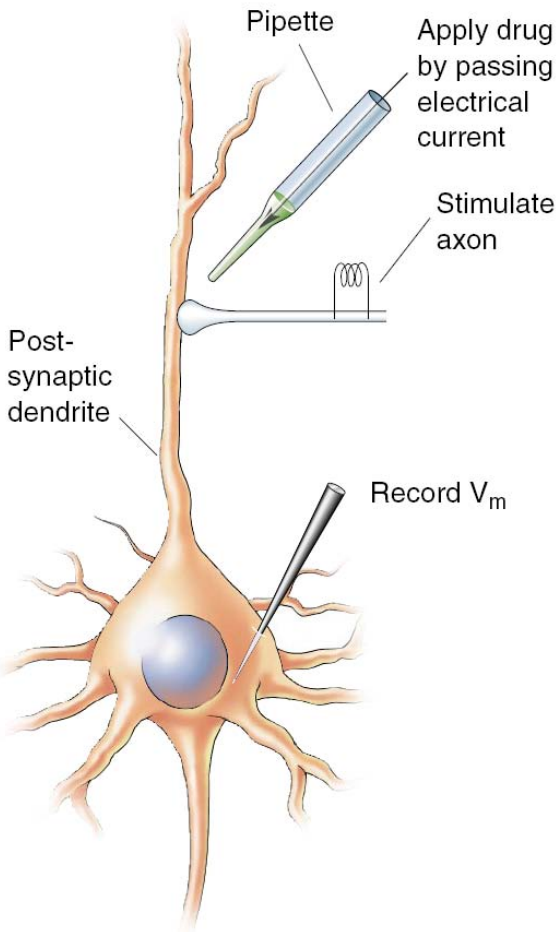
A novel glutamate-sensitive microelectrode

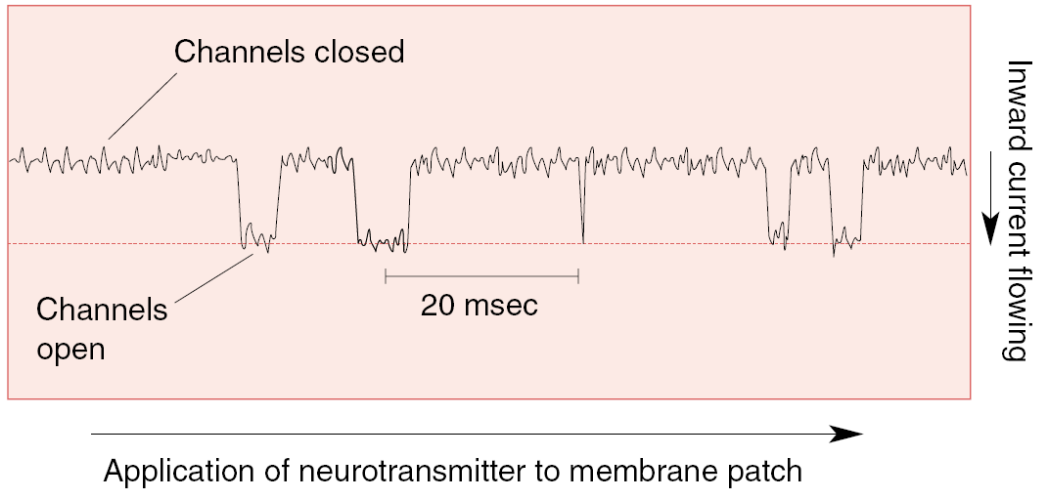






Microiontophoreisis to mimic neurotransmission





Summary of approaches to studying neurotransmitters

1. The molecule must be synthesized and stored in the presynaptic neuron (in situ hybridisation and immunohistochemistry).

2. The molecule must be released by the presynaptic axon terminal upon stimulation (transmitter-sensitive electrodes).

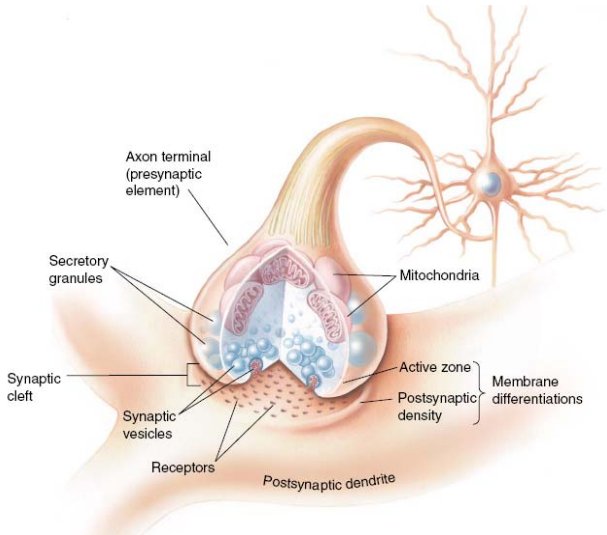
3. The molecule, when experimentally applied, must produce a response in the postsynaptic cell that mimics the response produced by the release of neurotransmitter from the presynaptic neuron (microiontophoreisis, pharmacological blockade or agonism).

Neurotransmitters

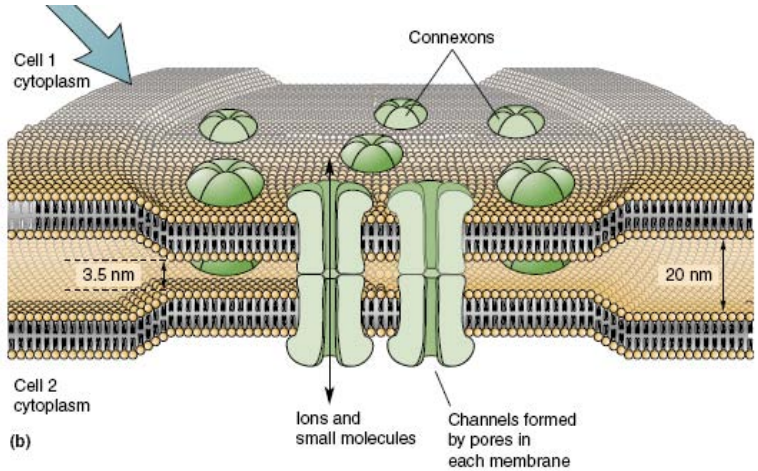
1. Amino acids – Glutamate, GABA, glycine.
2. Amines – Dopamine, norepinephrine, epinephrine, serotonin, acetylcholine.
3. Peptides – Substance P, NPY, somatostatin.
4. Other small molecules – ATP, NO, CO, endocannabinoids.

The war of soups and sparks in the brain

Pharmacologists (soups)

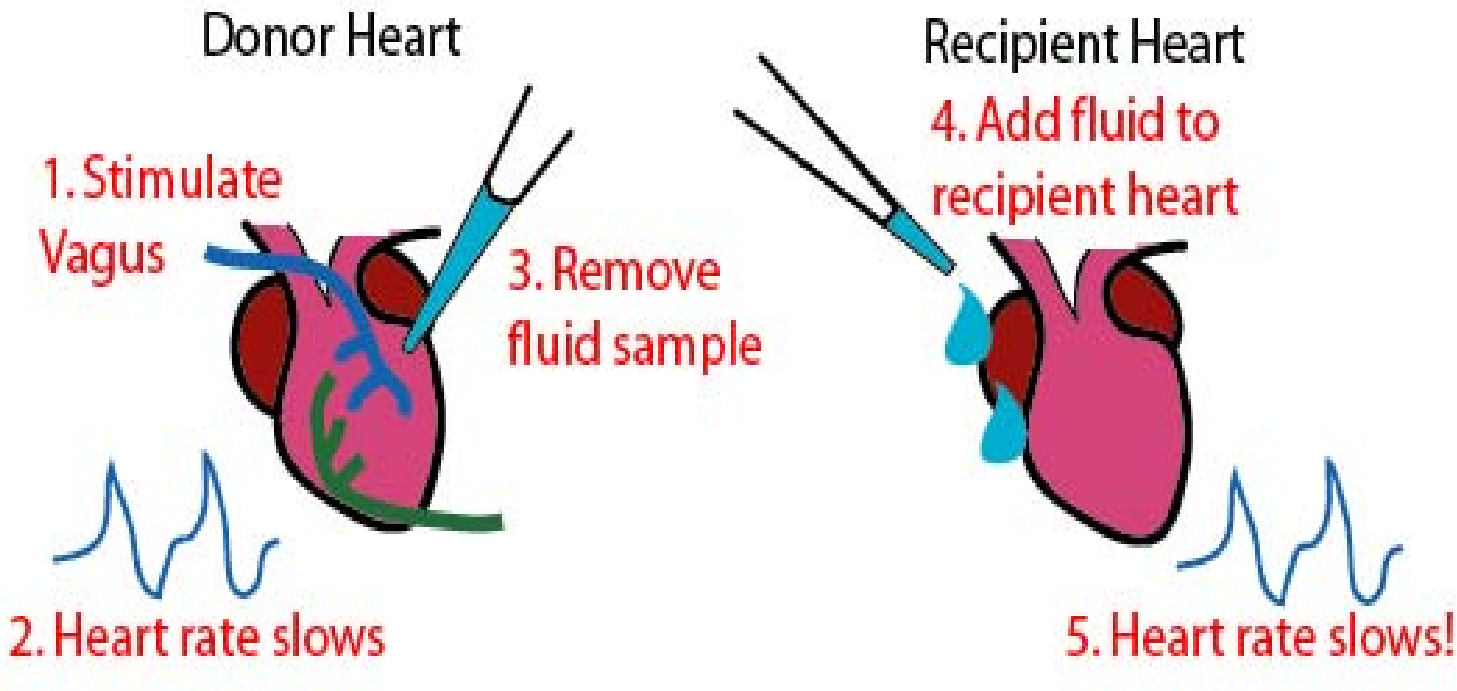


Electrophysiologists (sparks)



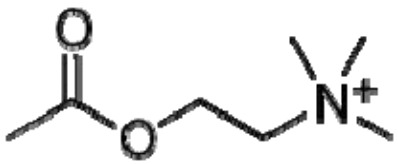
Vagusstoff

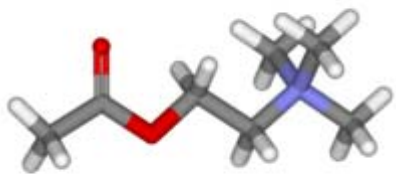
Otto Loewi

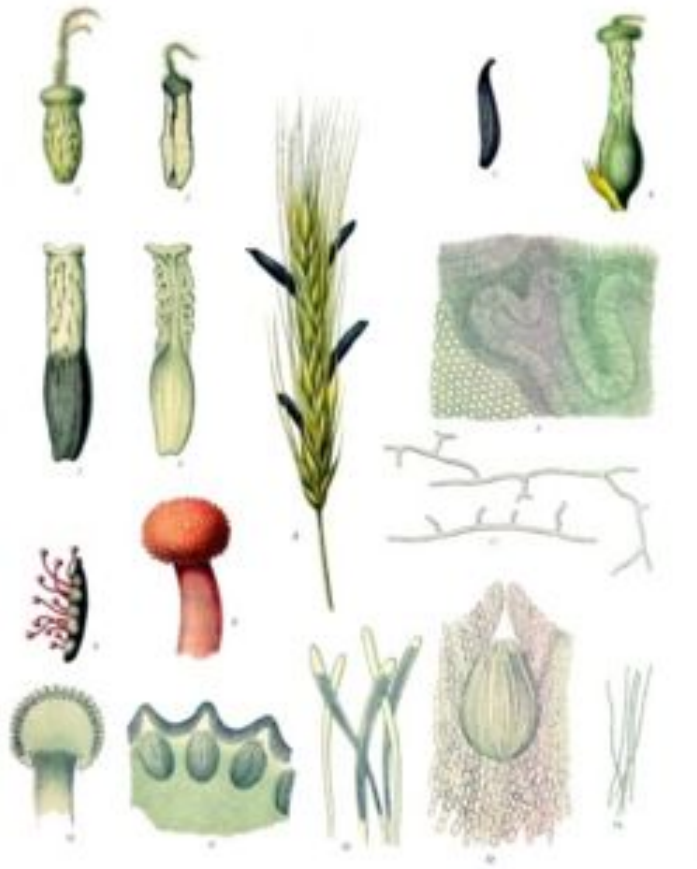


Acetylcholine

Henry Dale

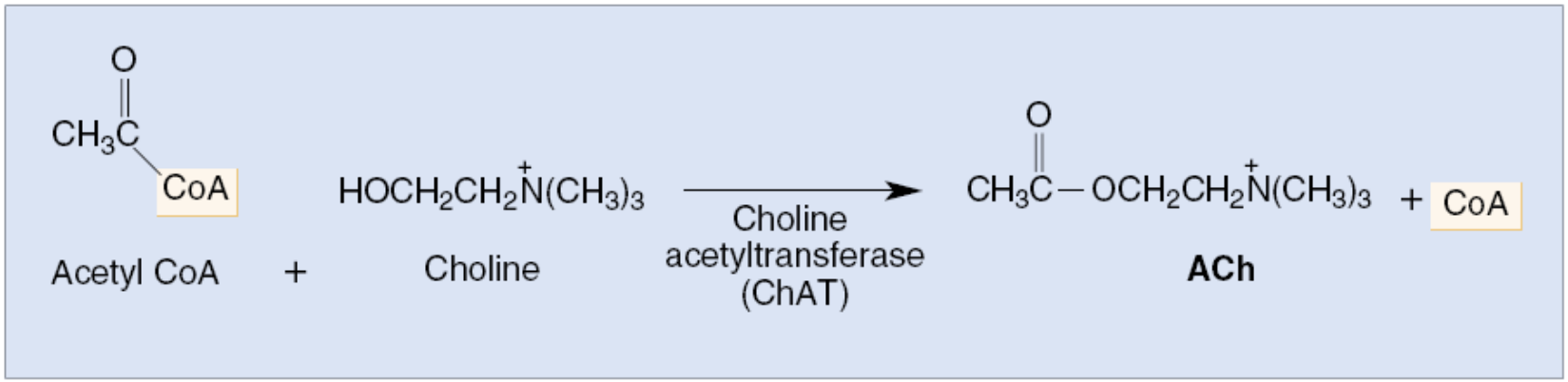




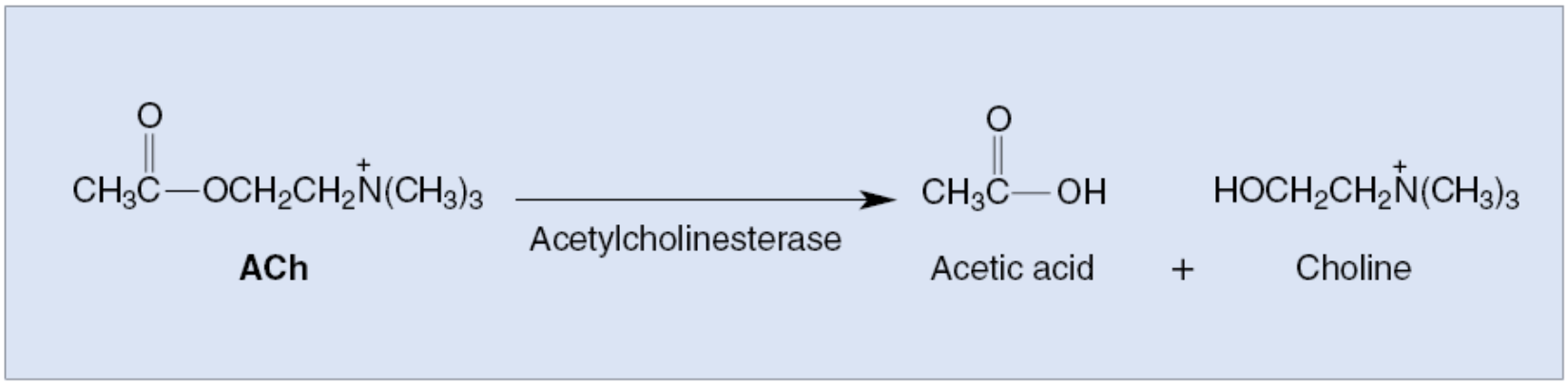


Ergot

Acetylcholine synthesis and degradation



(a)



(b)

Using pharmacology to study receptor function

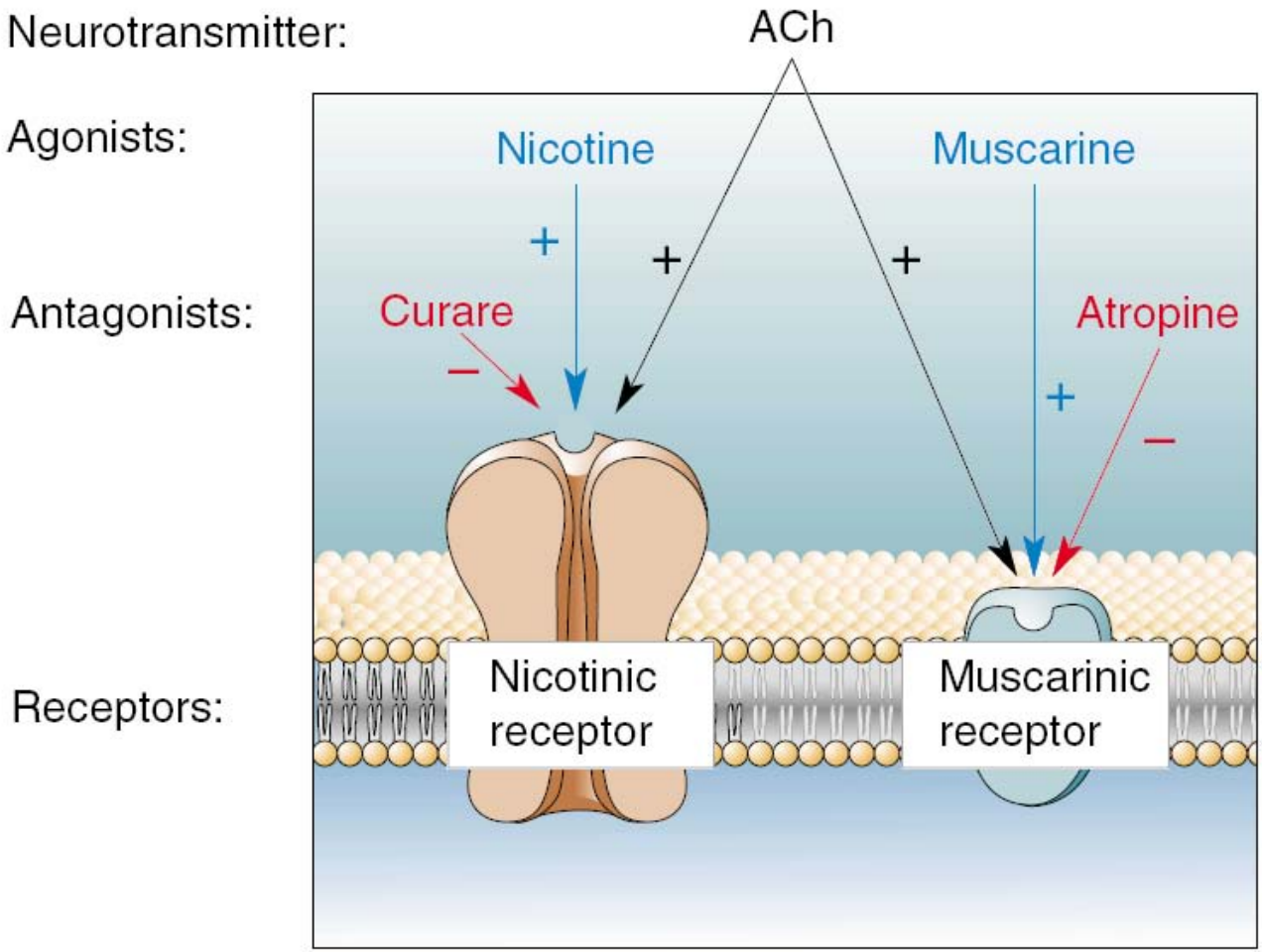
Nicotine

Fly agaric (Muscarine)

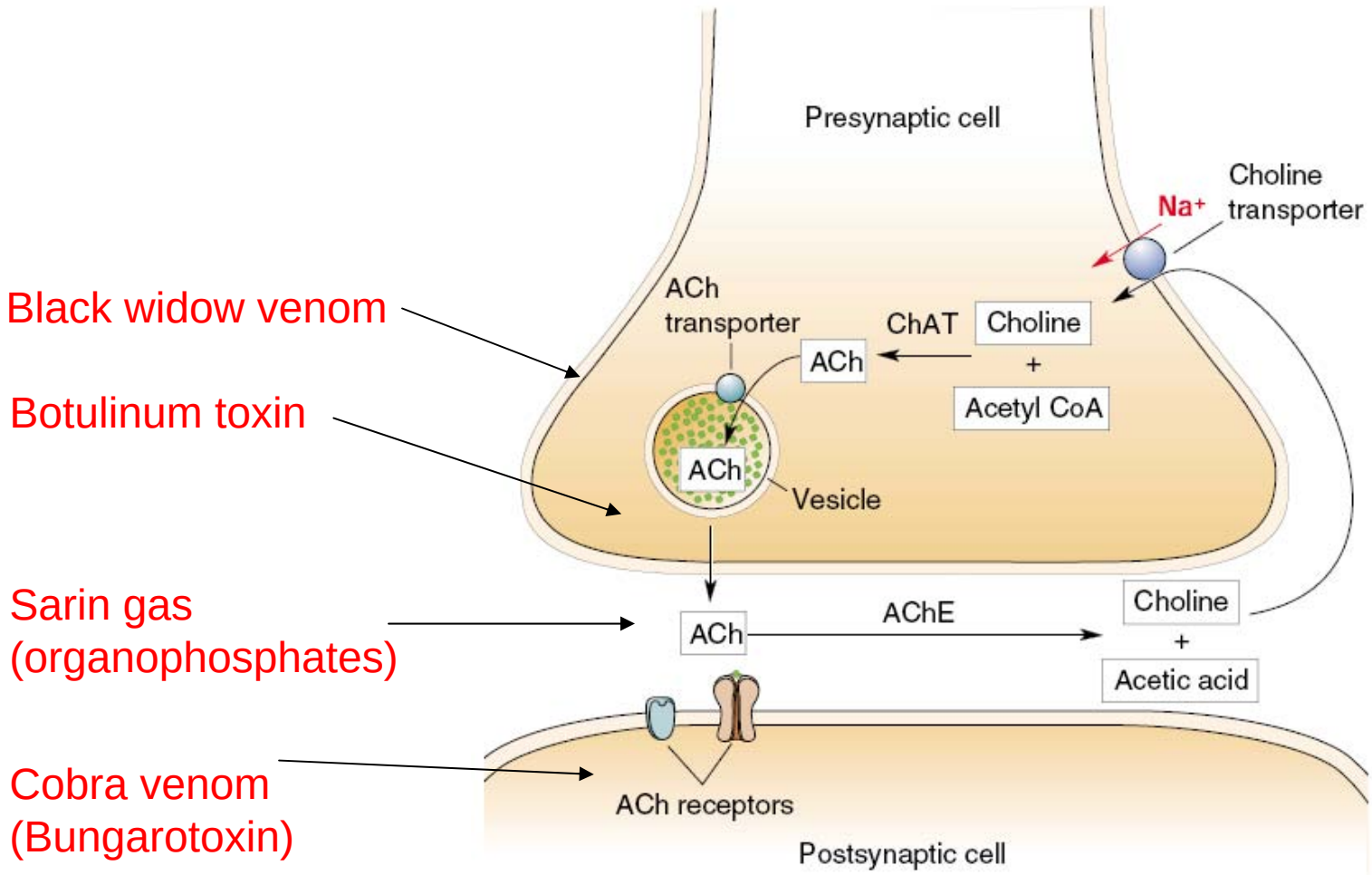
Curare

Belladonna (Atropine)

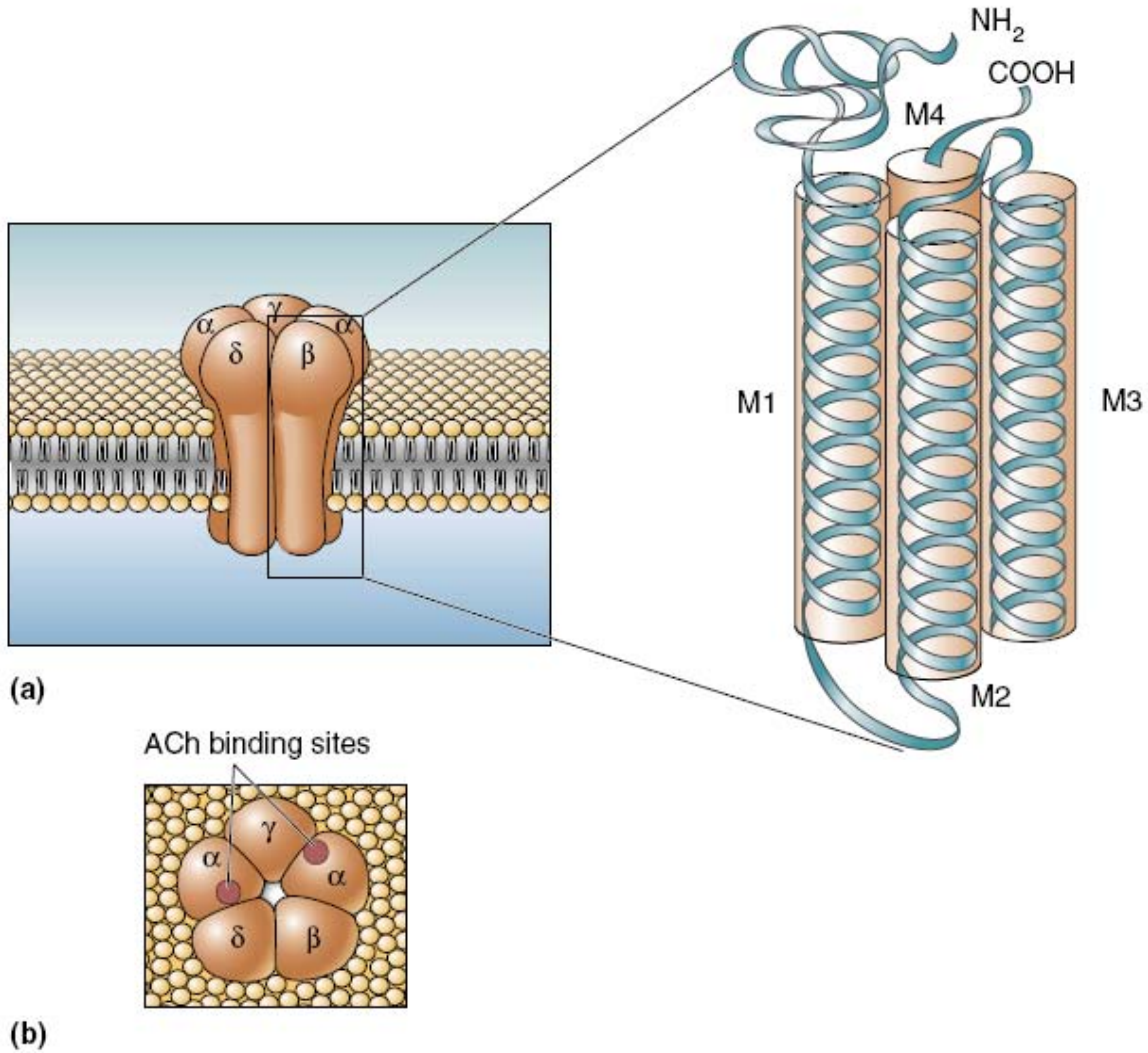
The neuropharmacology of cholinergic transmission



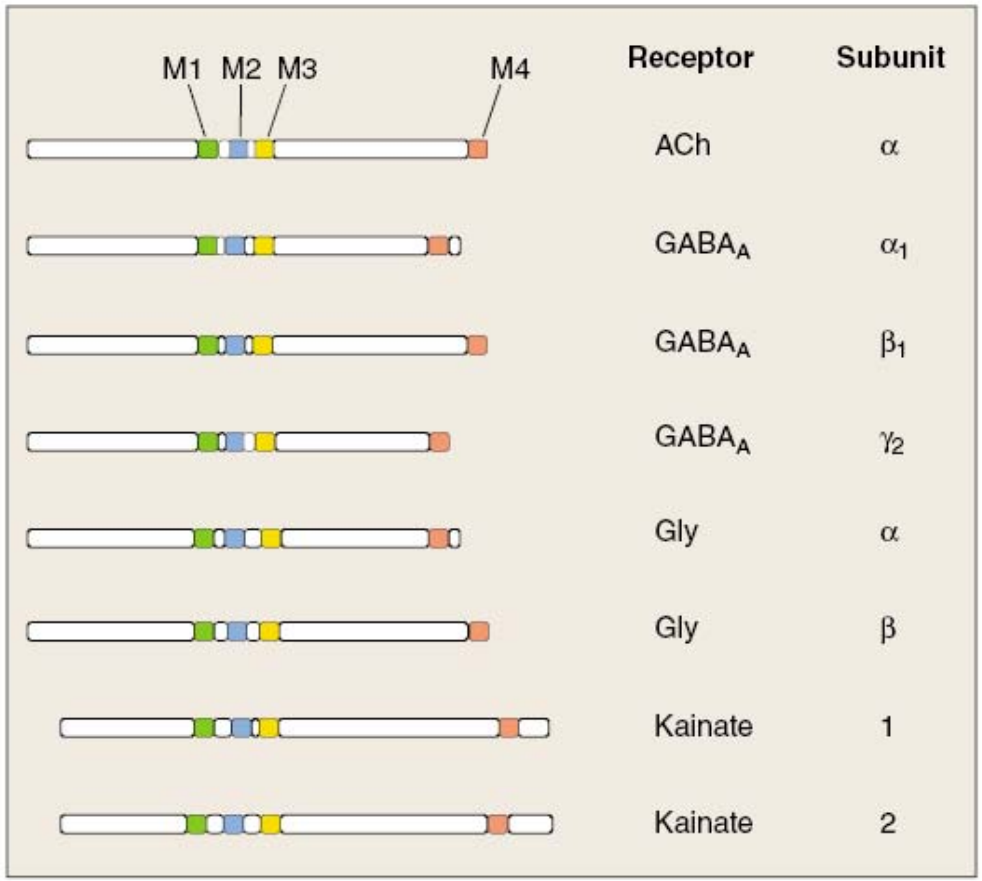
The life cycle of acetylcholine



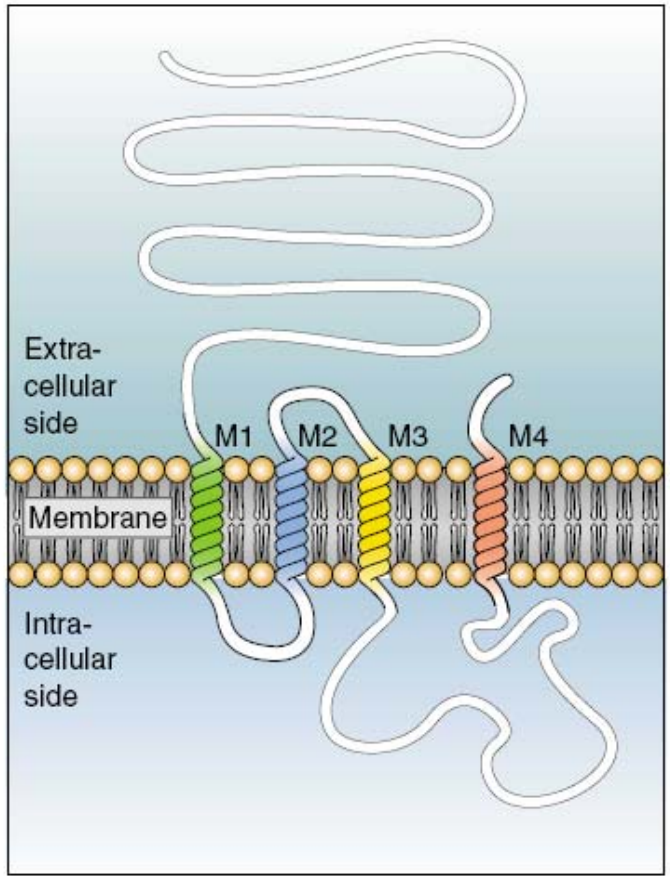
The subunit arrangement of the nicotinic acetylcholine receptor



Similarities of structure for different neurotransmitter-gated ion channels



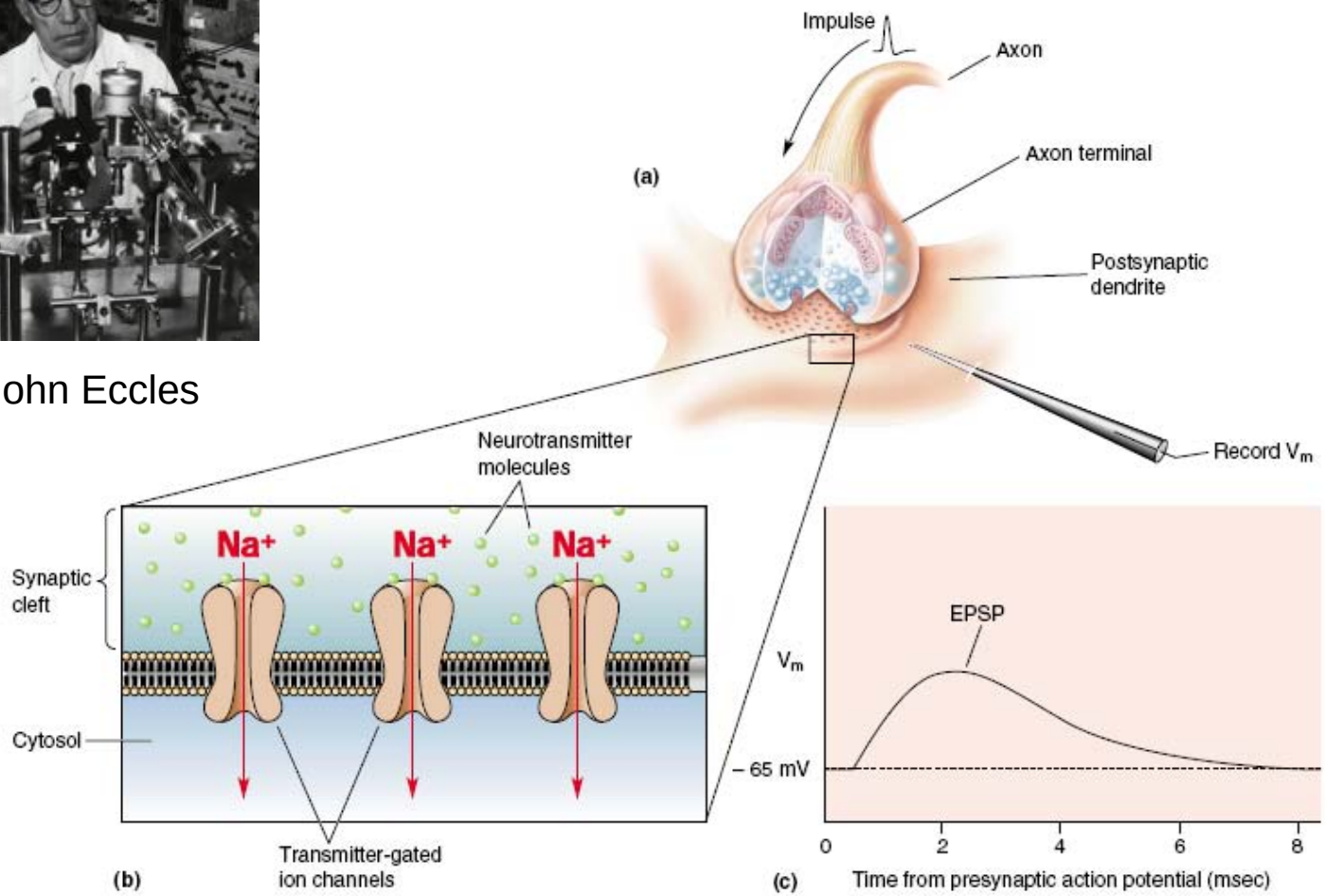
(a)



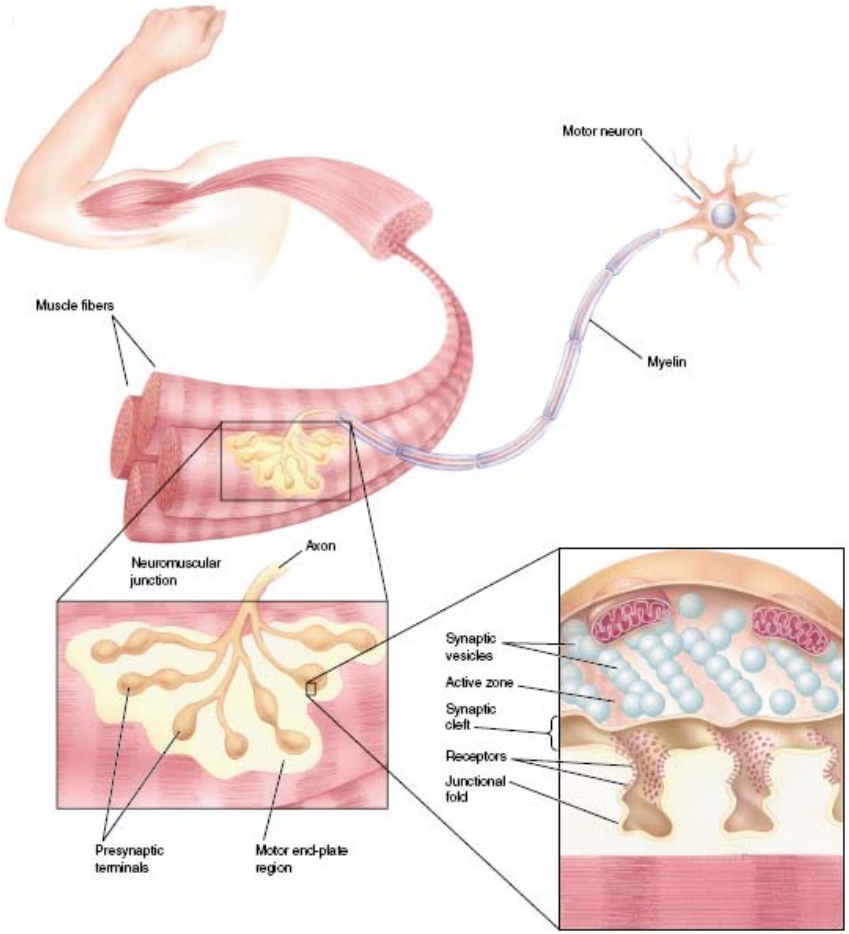
(b)

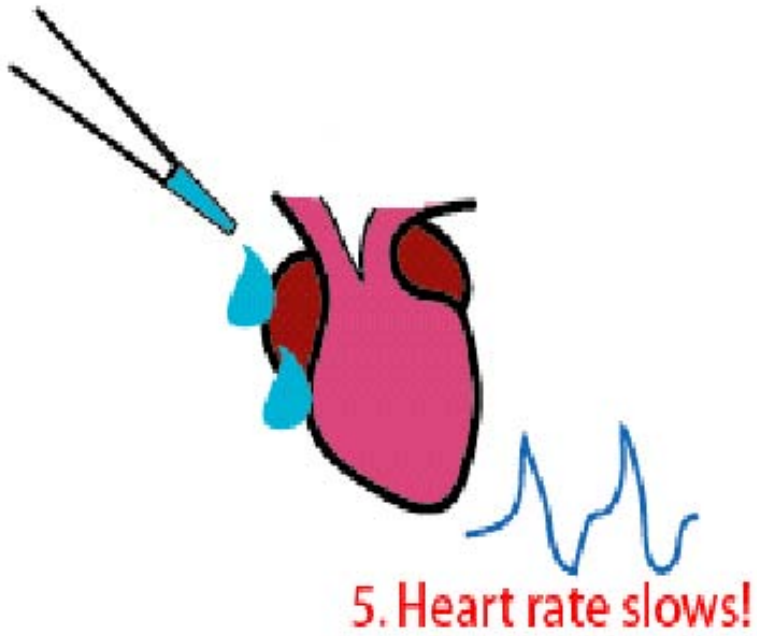
The generation of an EPSP

John Eccles

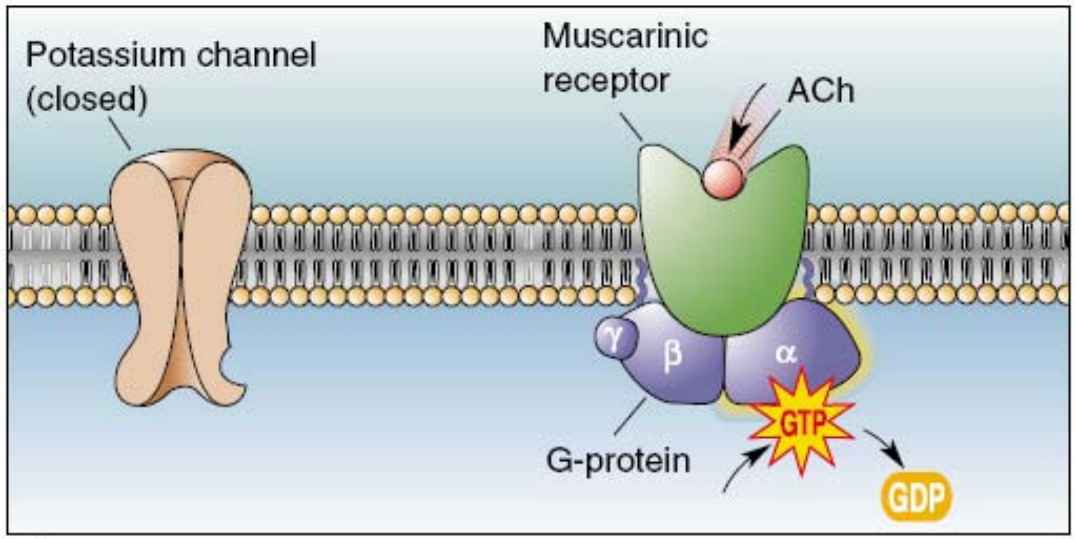


Opposing effects of acetylcholine

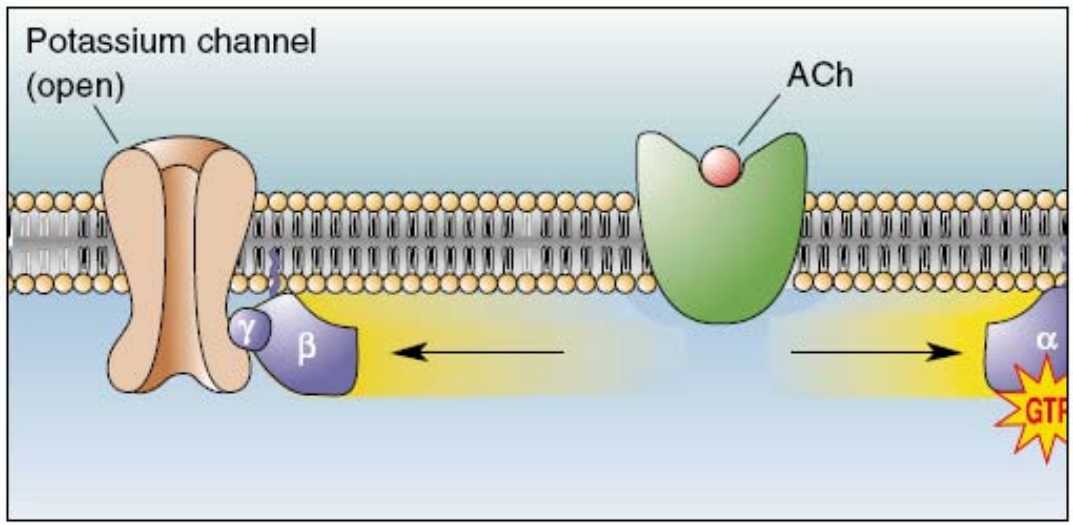




Muscarinic receptors



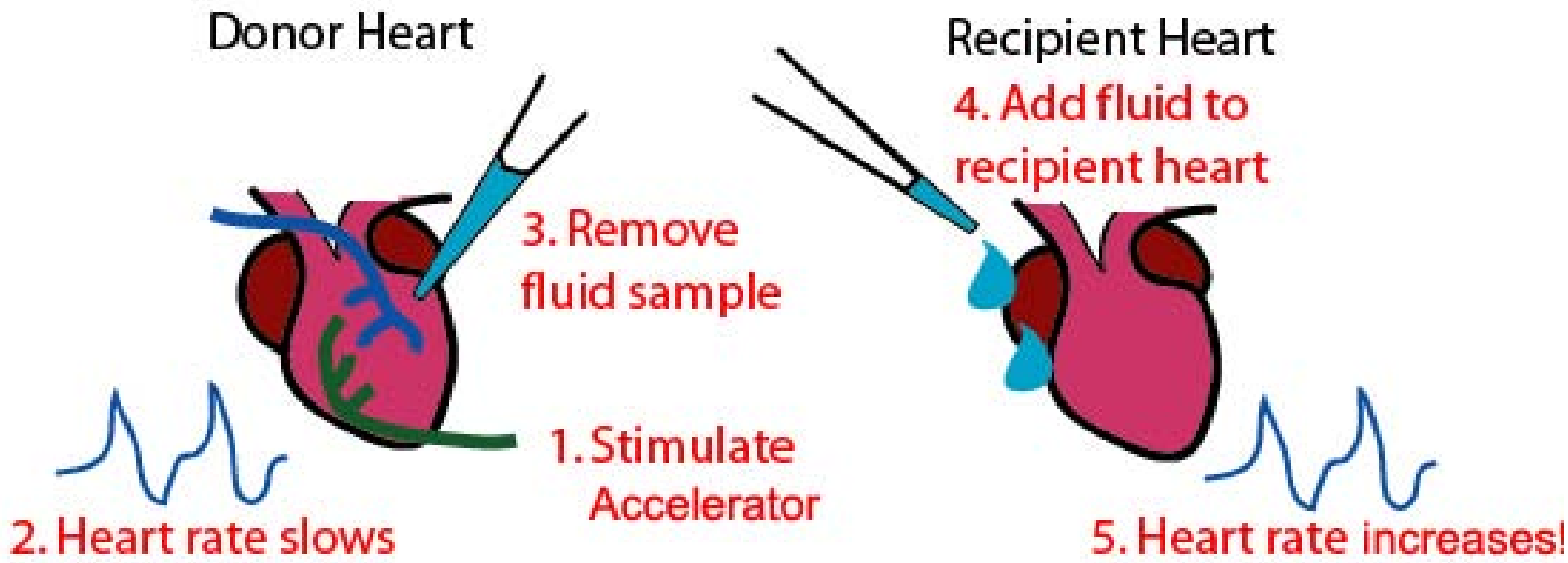
(a)



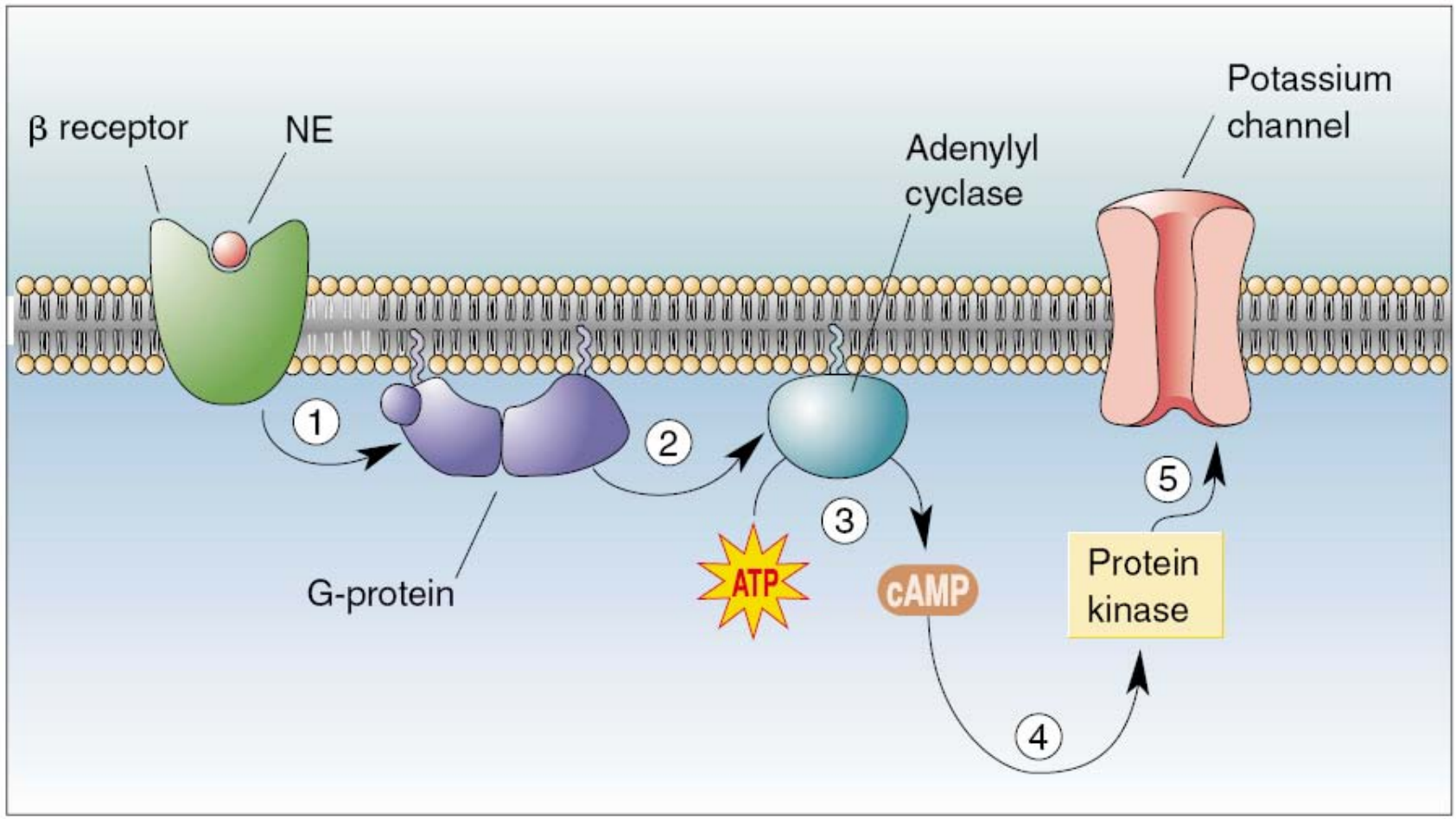
Acceleranstoff or Sympathin

Otto Loewi

Walter Bradford Cannon



Beta-adrenergic receptors – opposing action to muscarinic receptors



Summary of the discovery of chemical transmission

1. In the war of the ‘soups’ and the ‘sparks’ the soups came out on top – although it took a long time to accept that chemical transmission played a major role in the brain itself

2. They did so by studying the autonomic nervous system – finding that the parasympathetic effector transmitter was acetylcholine and the sympathetic effector transmitter was norepinephrine

3. These transmitters have opposing effects at the same sites – one speeds heart rate up, the other slows it down etc.