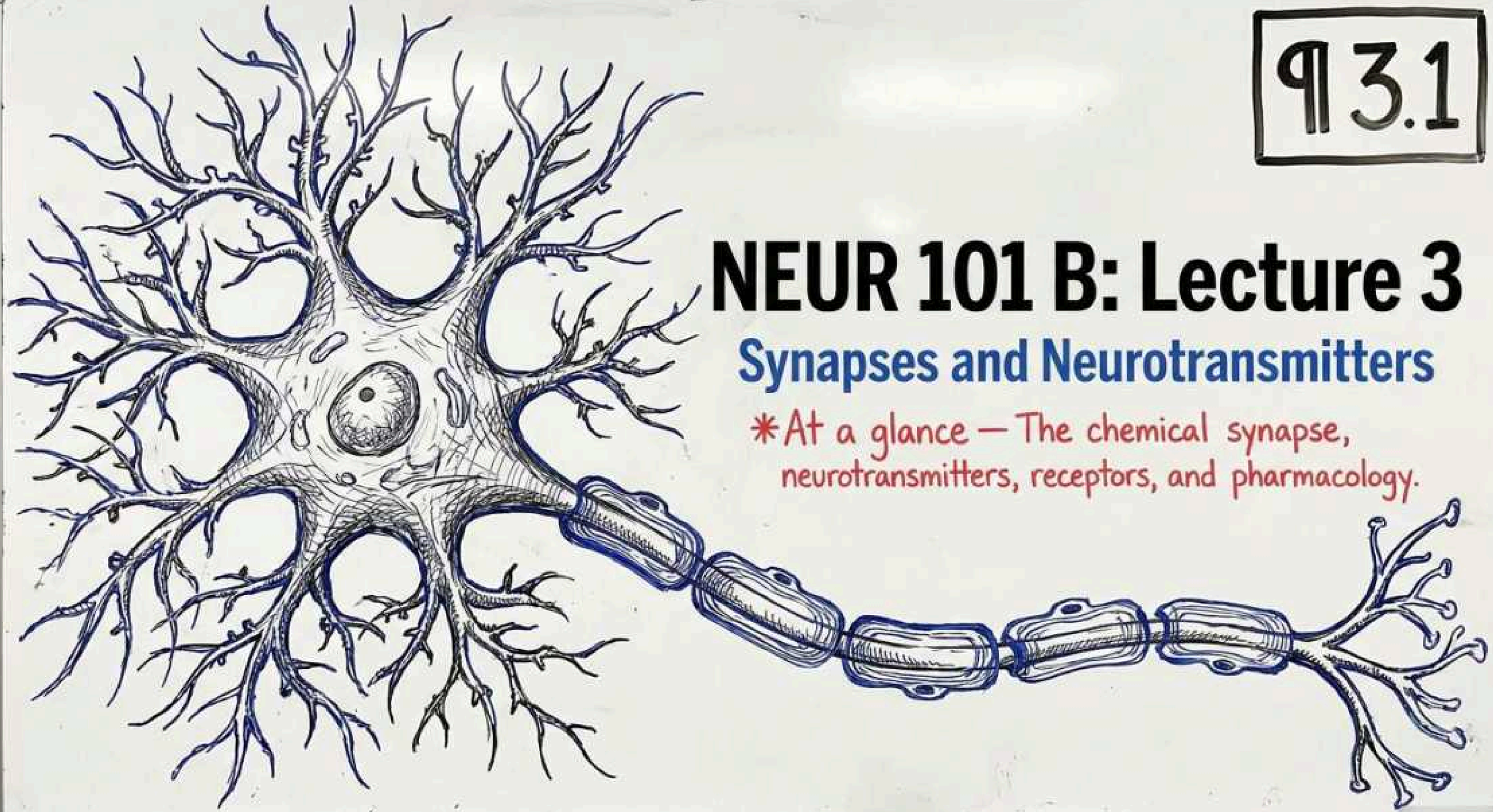
¶3.1

NEUR 101 B: Lecture 3

Synapses and Neurotransmitters

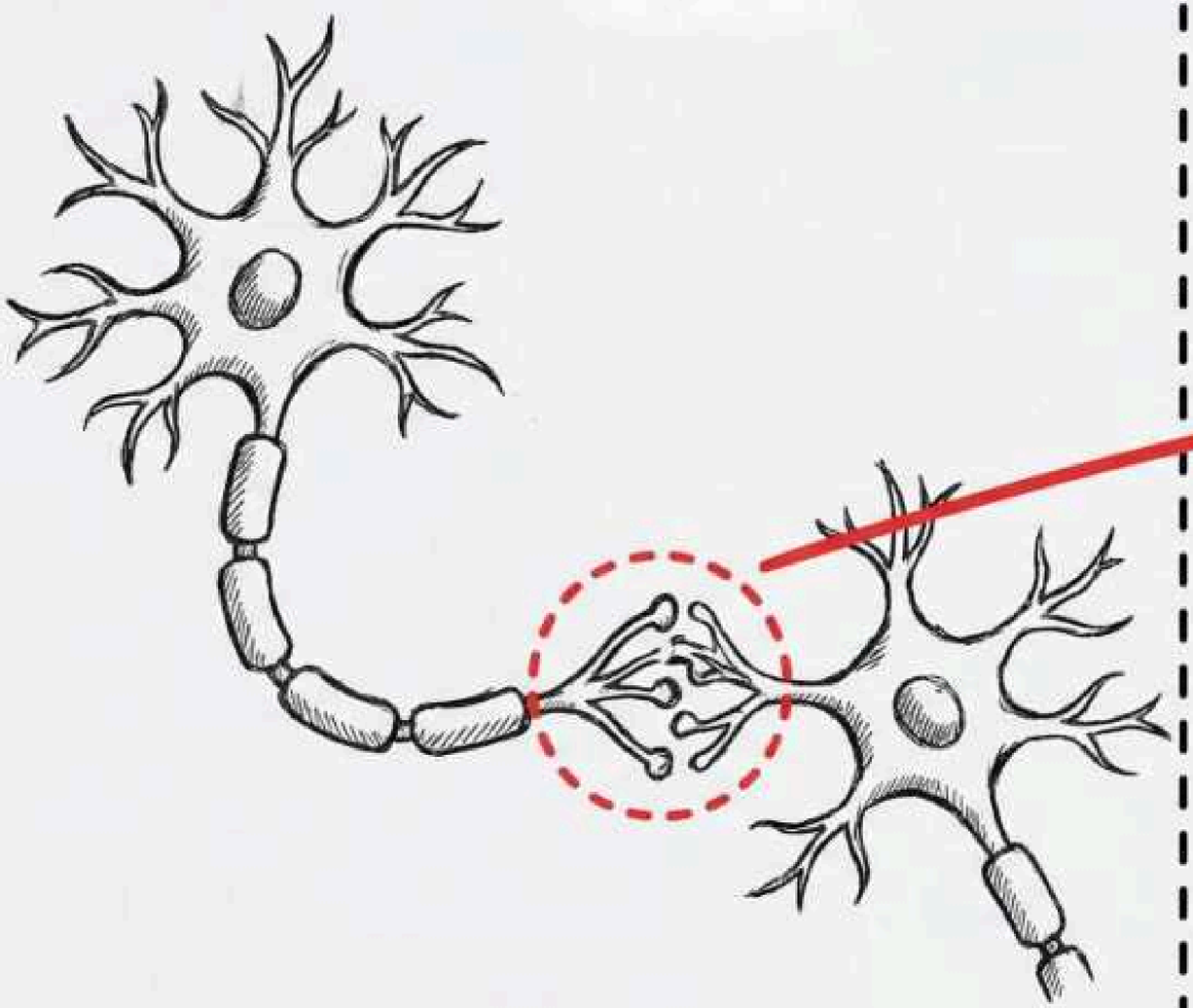
*At a glance — The chemical synapse, neurotransmitters, receptors, and pharmacology.

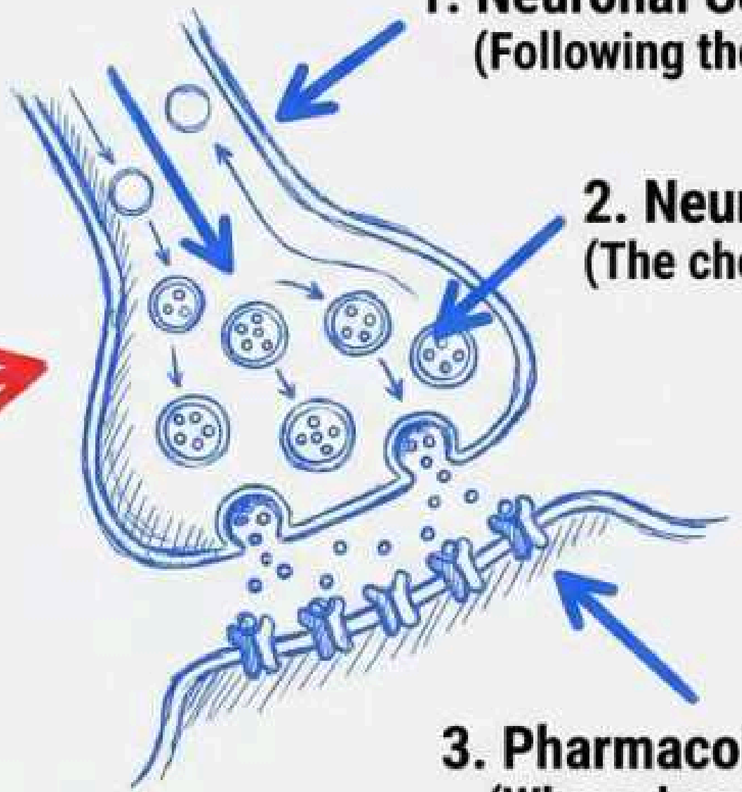


Gemini Notebook

The Computation Hub

¶ 3.2





1. Neuronal Communication
(Following the signal)

2. Neurotransmitters
(The chemical messengers)

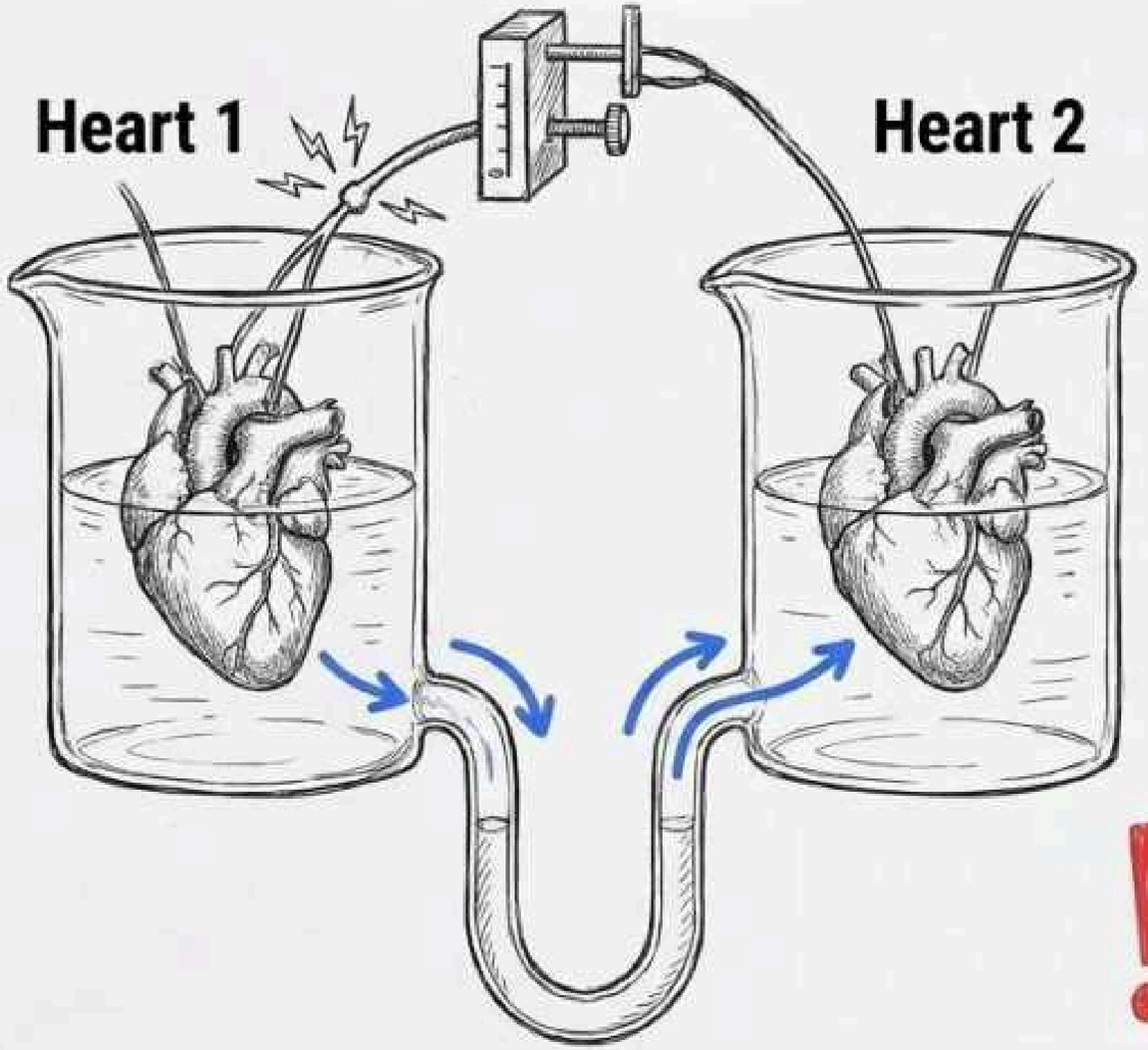
3. Pharmacology & Pathology
(Where drugs and diseases act)

The synapse is where the nervous system does most of its computing.

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Sparks vs. Chemicals (Otto Loewi, 1921)

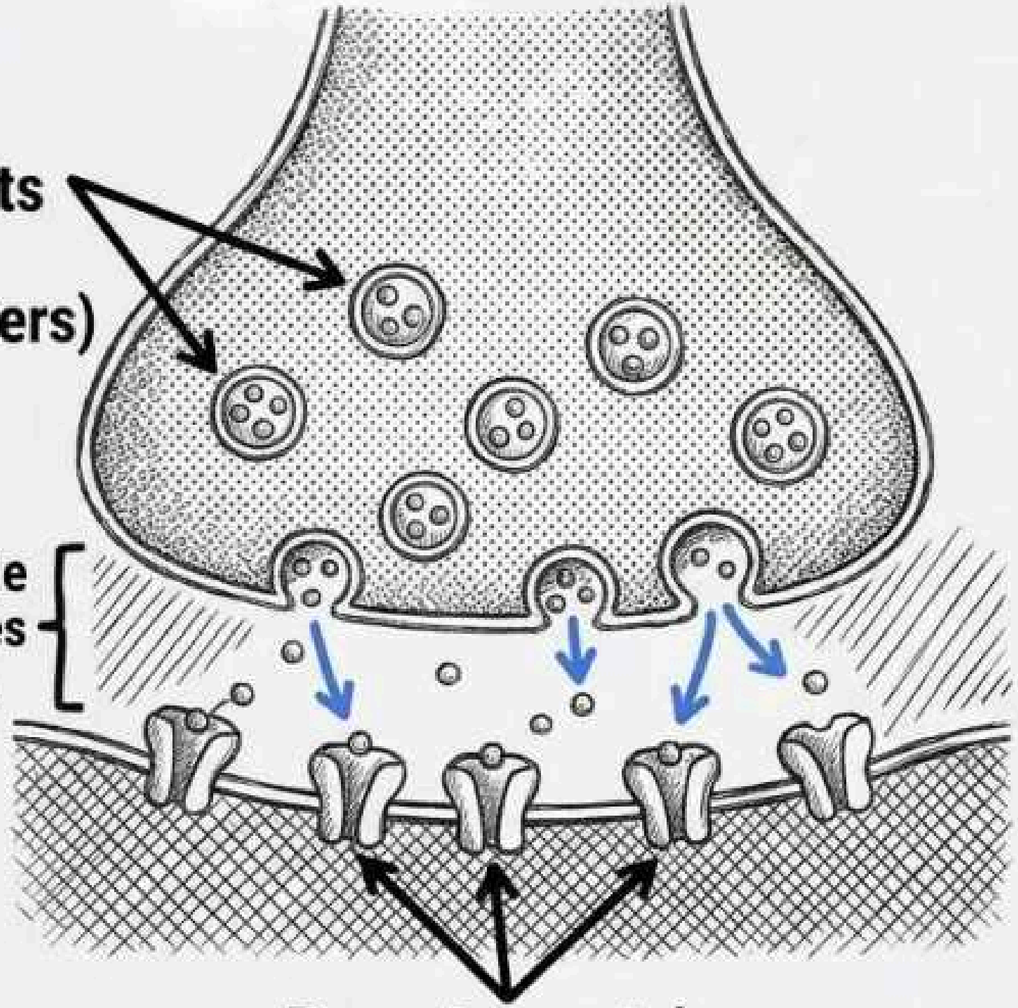
¶ 3.3



1. Stimulate nerve on Heart 1 (It slows down).
2. Surrounding fluid flows to Heart 2.
3. Heart 2 slows down without electrical stimulation.

! The message was chemical (Acetylcholine), not just electrical. A dream-inspired breakthrough!

Anatomy of a Chemical Synapse



Vesicles (small packets filled with neurotransmitters)

~20 nanometers wide (a few thousand times thinner than a hair).

Receptor proteins

Zone 1: Presynaptic Terminal (End of sending axon).

Zone 2: Synaptic Cleft (~20 nannometes wide).

Zone 3: Postsynaptic Membrane (Receiving cell).

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The Precision Sequence of Exocytosis

¶ 3.5

Step 1: Spike Arrives
→ Depolarizes the terminal.



Step 2: Calcium Influx
→ Voltage-gated Ca^{2+} channels open.

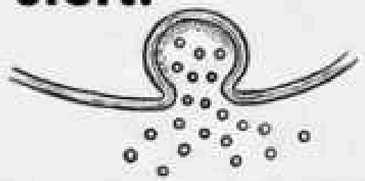




Step 3: Fusion
→ Calcium triggers vesicles to fuse with the membrane.



Step 4: Exocytosis
→ Contents spill into the cleft.

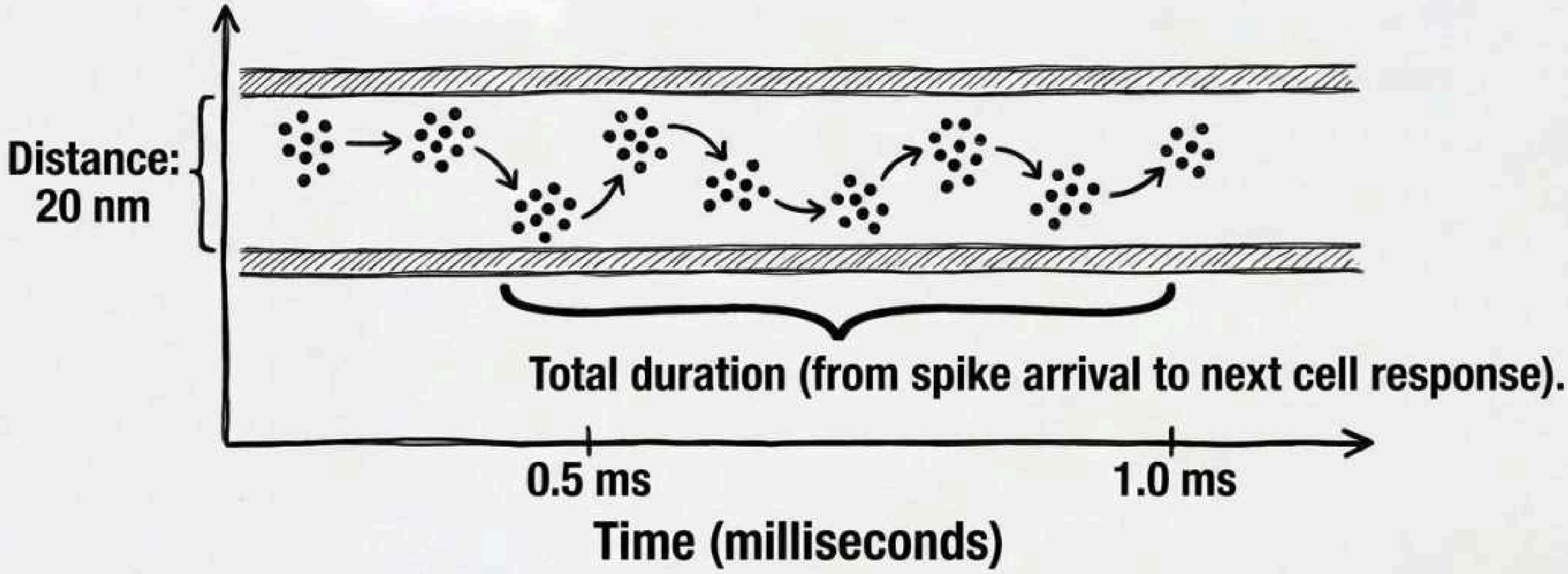


Electrical Signal → Chemical Signal

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¶ 3.6

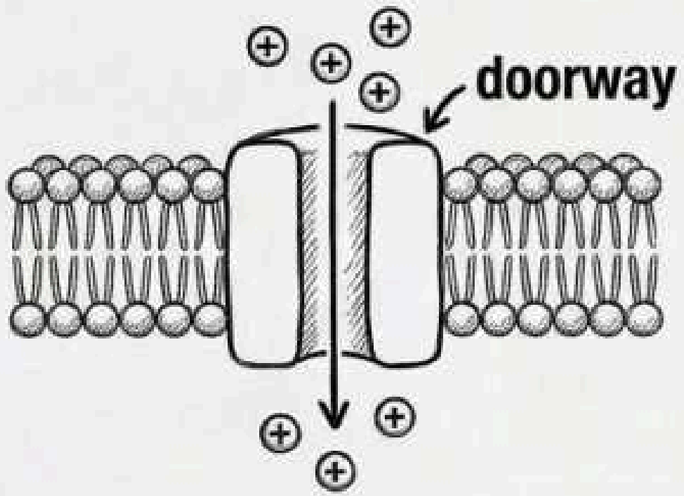
Diffusion & Synaptic Delay



Takeaway: This fractional millisecond delay at each synapse explains why even short reflex pathways take a measurable amount of time.

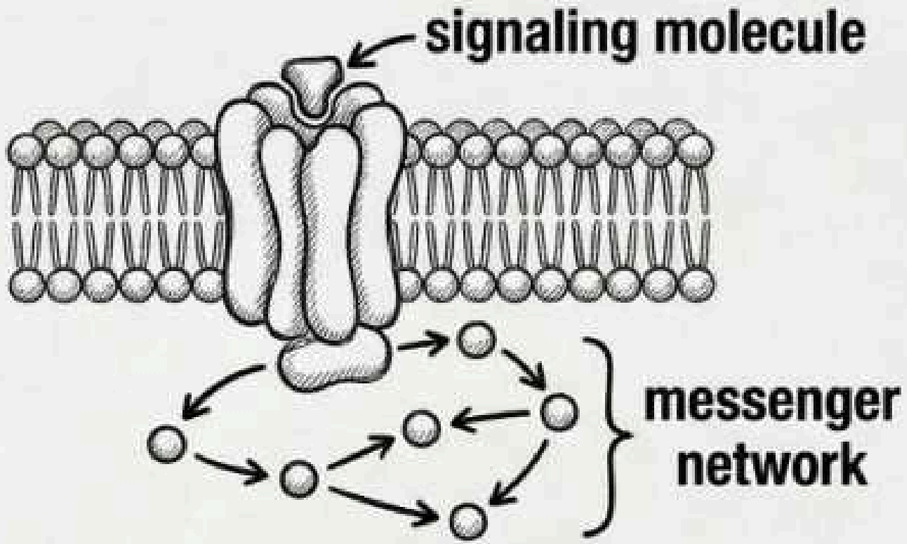
Two Main Receptor Types

Ionotropic



Mechanism: Directly acts as an ion channel.
Speed: Microseconds (Fast).
Duration: Brief.

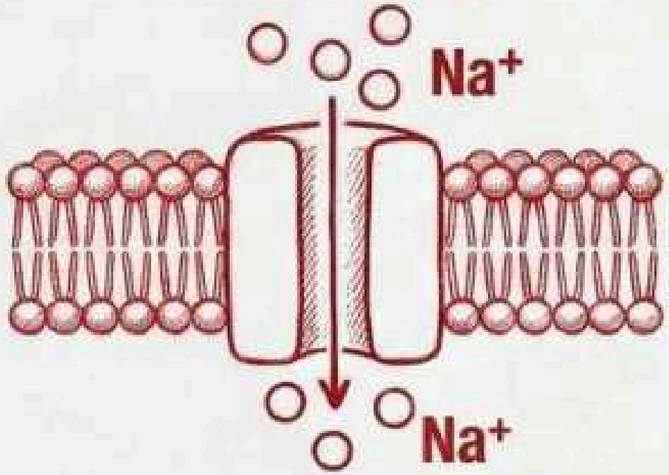
Metabotropic



Mechanism: Acts via internal chemical messengers.
Speed: Slower.
Duration: Longer.
Effect: Subtler cellular behavioral changes.

Excitation vs. Inhibition

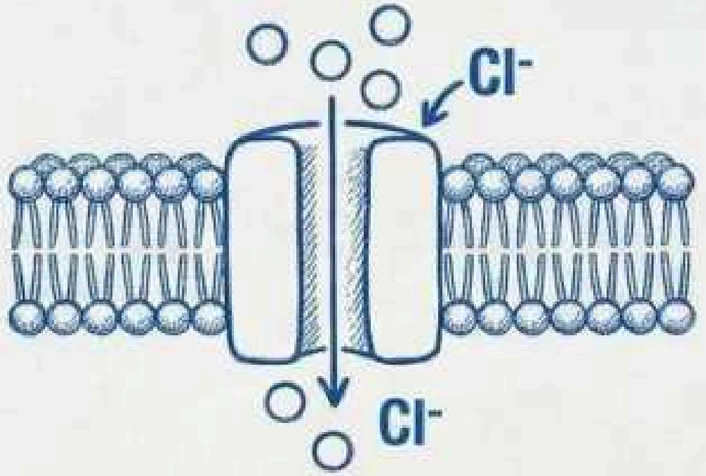
Glutamate



Main Excitatory Transmitter

Opens Na^+ channels → Depolarizes cell (pushes toward firing).

GABA



Main Inhibitory Transmitter

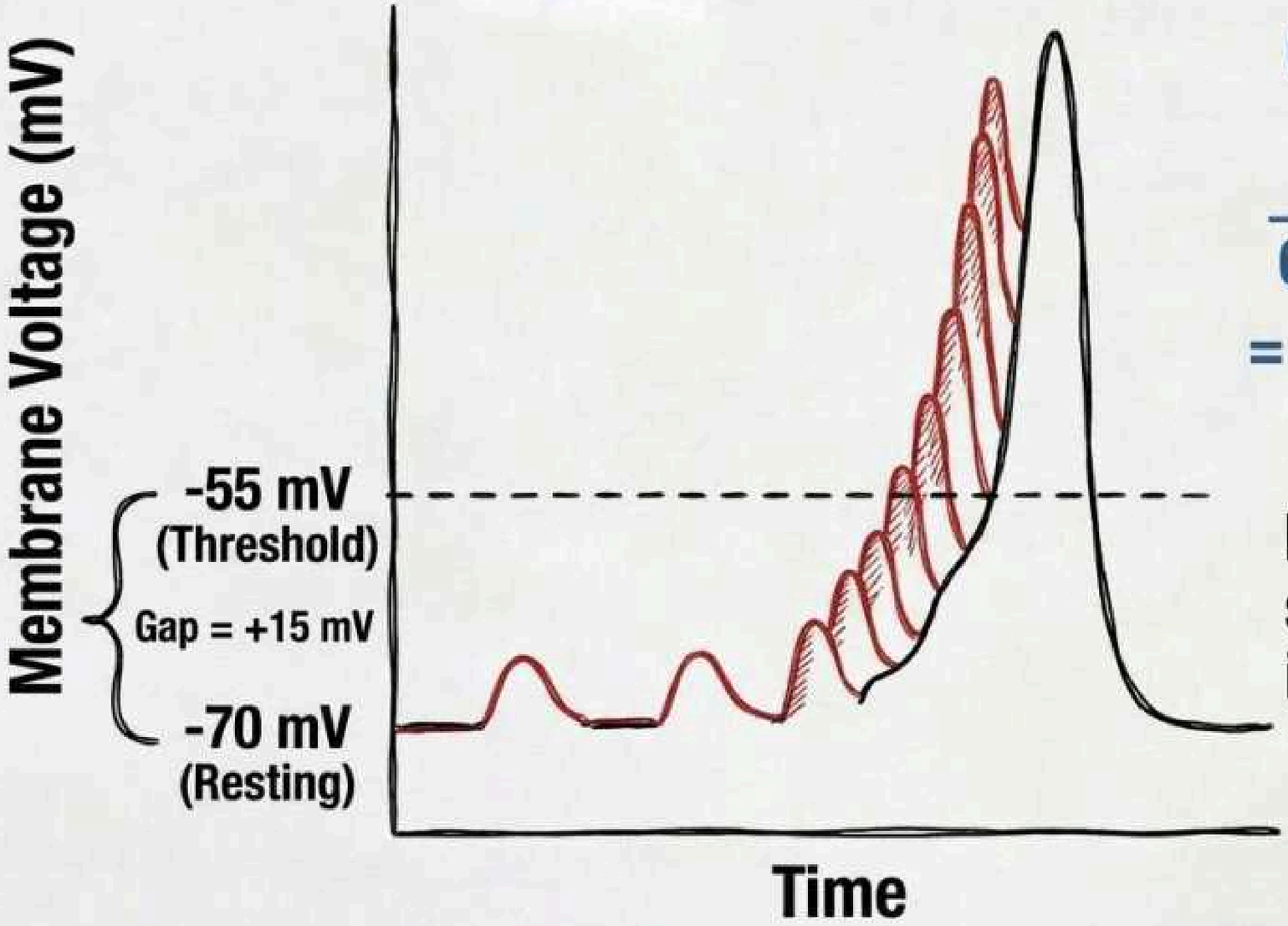
Opens Cl^- channels.

Math Focus: $E_{Cl} \approx -64$ mV. Because this equilibrium potential is below the firing threshold, opening Cl^- channels holds the cell back from firing.

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Neuronal Math (Summation)

¶ 3.9



One input ≈ +0.5 mV.

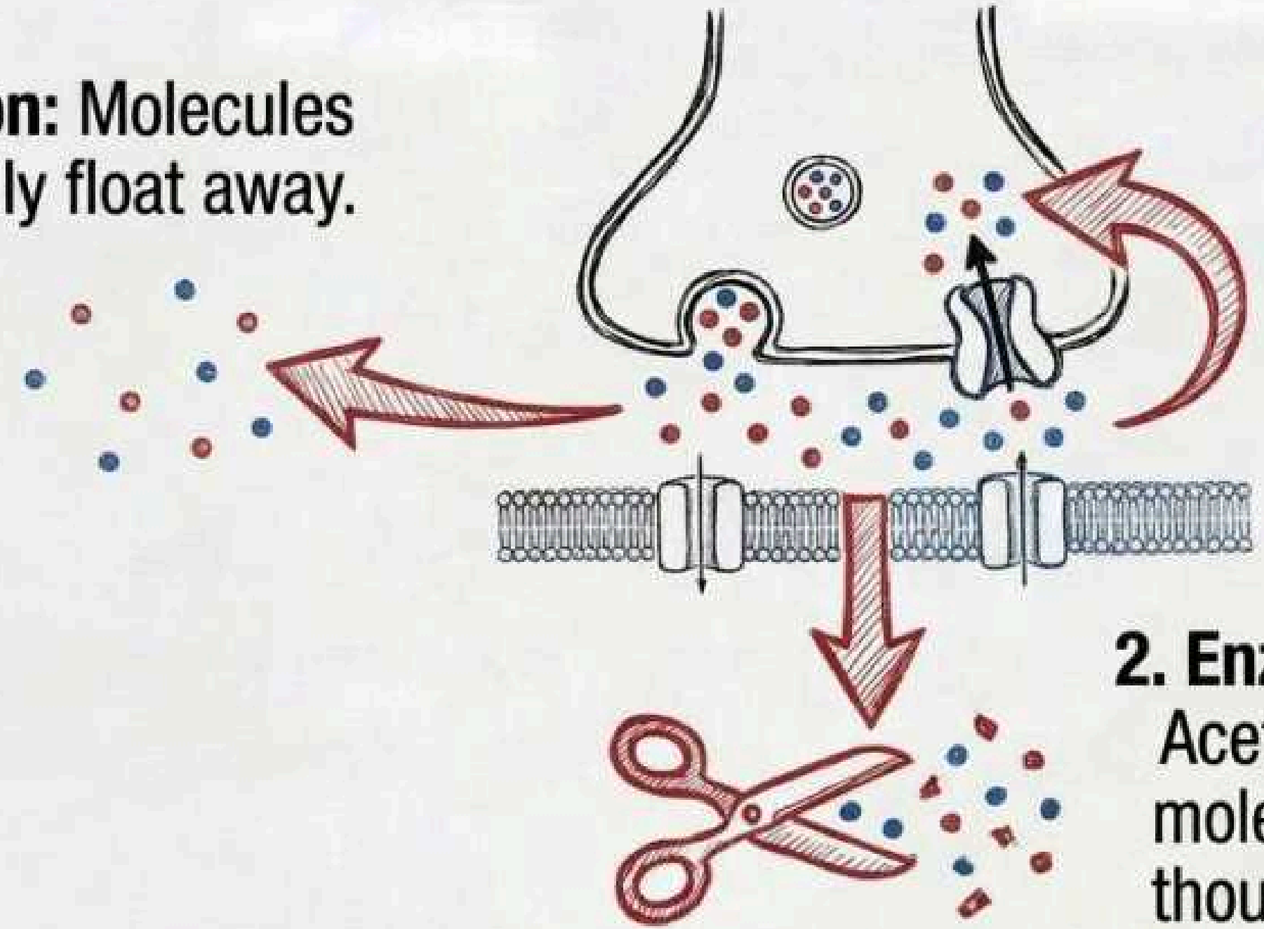
$$\frac{\text{15 mV gap}}{\text{0.5 mV per input}} =$$

= ~30 simultaneous inputs needed to fire.

Rules: Close in space/time sum together. Inhibitory inputs subtract.

Switching Off the Signal

1. **Diffusion:** Molecules physically float away.



3. **Reuptake:** Transporter proteins act as vacuums, pumping transmitters back into the presynaptic terminal.

2. **Enzymatic Degradation:** e.g., Acetylcholinesterase acts like molecular scissors, breaking down thousands of molecules/sec.

Without **termination**, messages blur into constant noise!

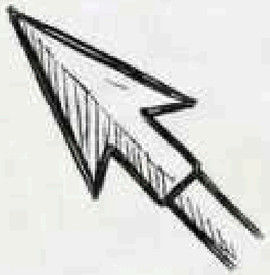
Gemini Notebook

Acetylcholine Pharmacology

¶ 3.11



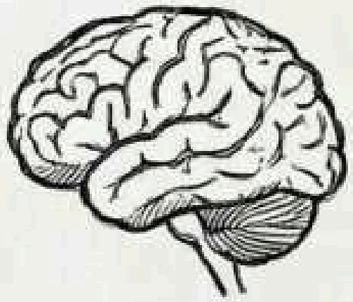
Botulinum Toxin:
Blocks ACh release
→ Paralysis.



Curare (Arrow tip poison):
Blocks muscle receptors
→ Paralysis.



Nerve Agents:
Block the clearing enzyme → Muscles overstimulated.



Alzheimer's Drugs:
Slow ACh breakdown
→ Modest symptomatic help.

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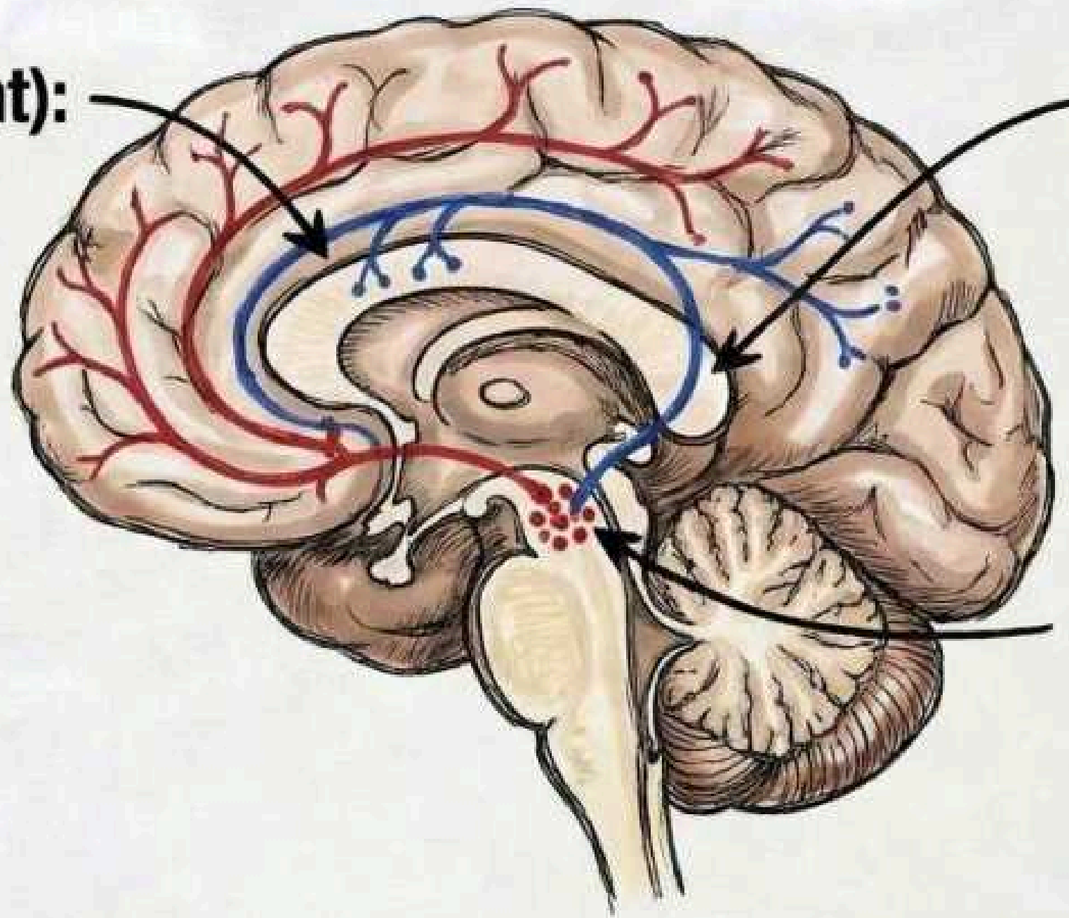
Dopamine — Movement & Motivation

¶ 3.12

Pathway 1 (Movement):
Midbrain to striatum.

Pathology:
Cell drath here
here = Parkinson's
(tremor/slowness).

Treatment: L-DOPA.



Pathway 2 (Reward):
Tied to motivation
and reward circuits.

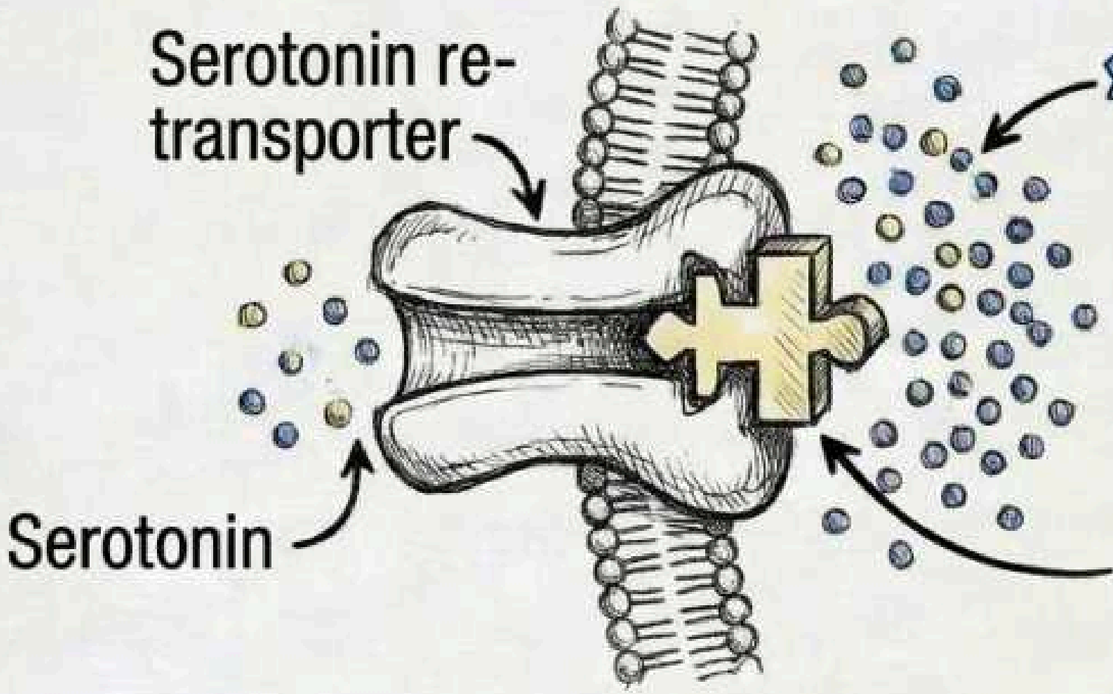
Origin: Small cluster
of neurons with
widespread reach.

Key Principle: A drug targeting one transmitter alters multiple brain functions simultaneously.

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Serotonin & Mood

Made in brainstem. Shapes mood, sleep, appetite.



Mechanism of SSRIs: Block the transporter, forcing serotonin to linger longer in the cleft.

The Mystery: SSRIs act in hours, but full benefits take weeks to appear. Suggests complex downstream changes, not just instant receptor action.

Familiar Substances at the Synapse

¶ 3.14

Caffeine:
Blocks receptors for adenosine (the molecule that builds up to make us sleepy).





Alcohol & Benzos:
Strengthen GABA's inhibition -> Calms the brain.



Opioids/Morphine:
Mimic the body's natural endorphins -> Reduce pain.



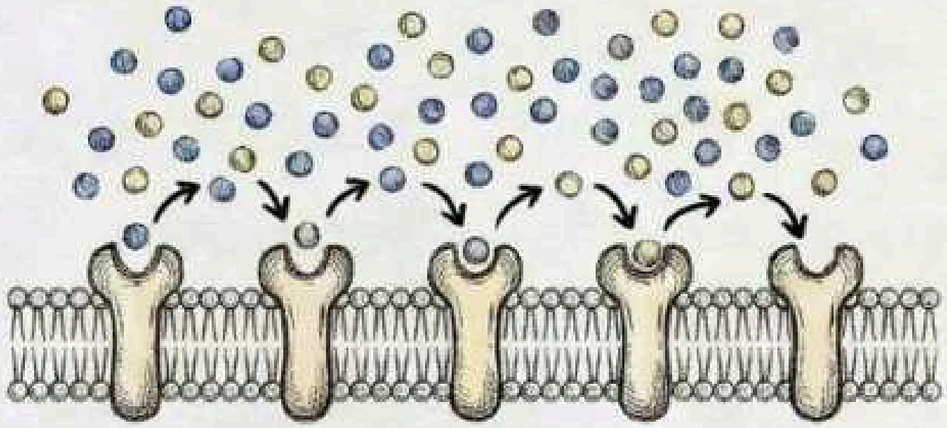
Nicotine:
Mimics acetylcholine at a specific class of receptors.

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Addiction, Tolerance, and Dependence

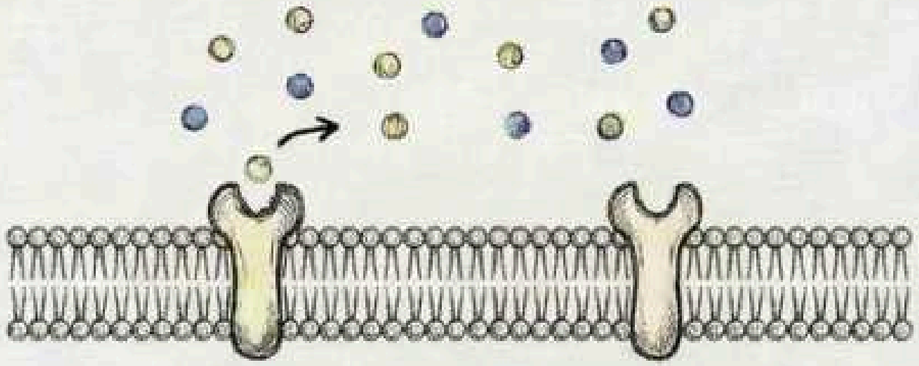
Hijacking Reward: Cocaine blocks dopamine transporters; Amphetamines promote massive dopamine release.

Before



Receiving neuron

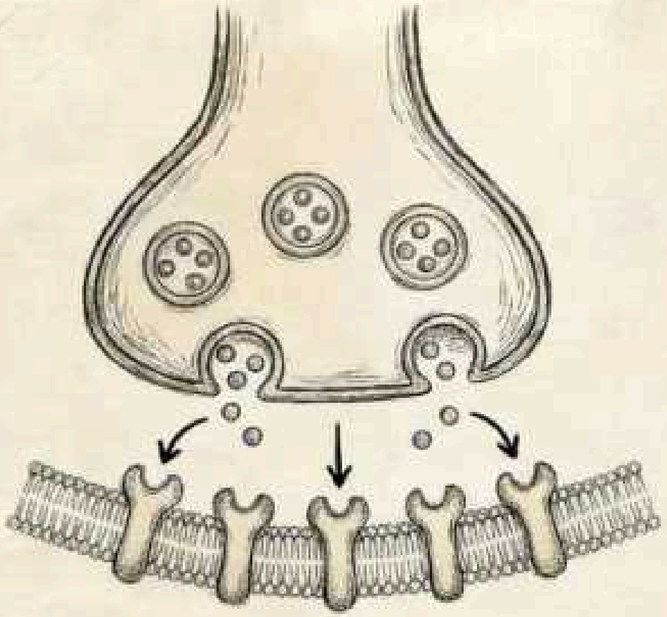
After (The Adaptation)



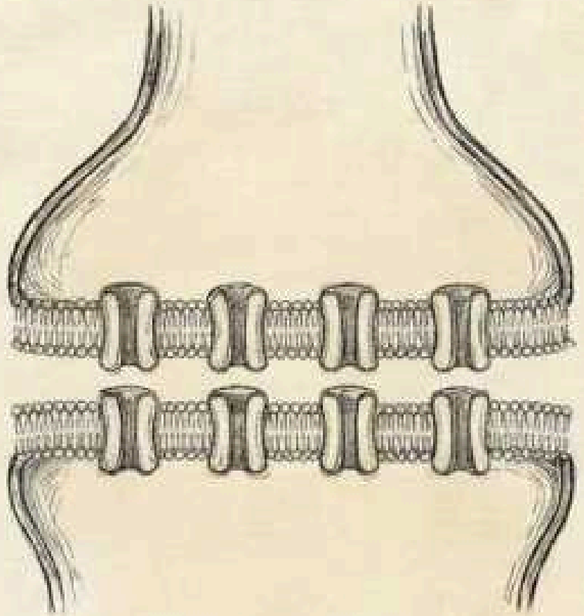
Receiving neuron

The Result (Tolerance): The brain adapts to the extra signal by reducing the number of receptors. Over time, the same dose has a smaller effect.

The Electrical Synapse



Chemical Synapse (Gap)



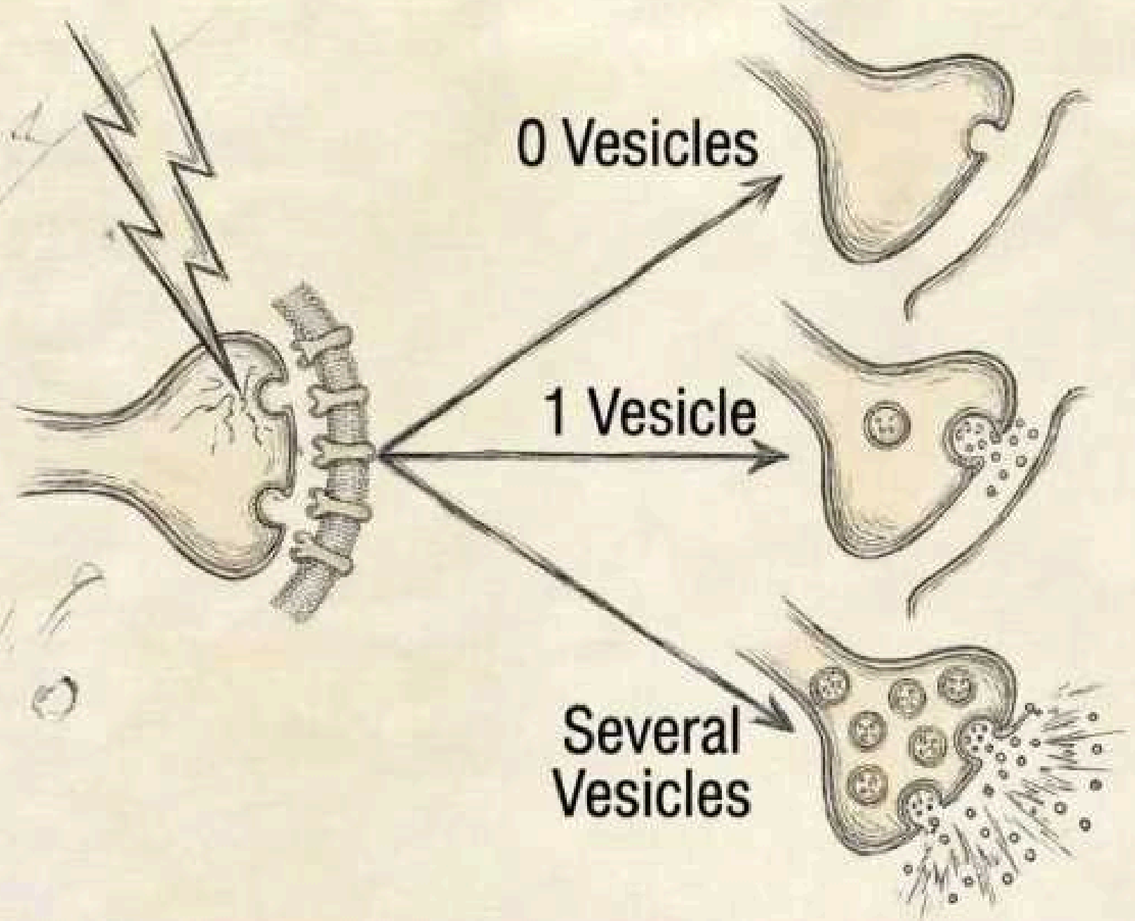
Electrical Synapse

- **Mechanism:** Gap junctions directly connect cells. Current flows straight through.
- **Traits:** Near-zero delay, bidirectional flow.
- **Function:** Synchronizes groups of neurons (e.g., reflex circuits, rhythmic networks, heart muscle cells).

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Synaptic Unreliability (By Design)

¶ 3.17



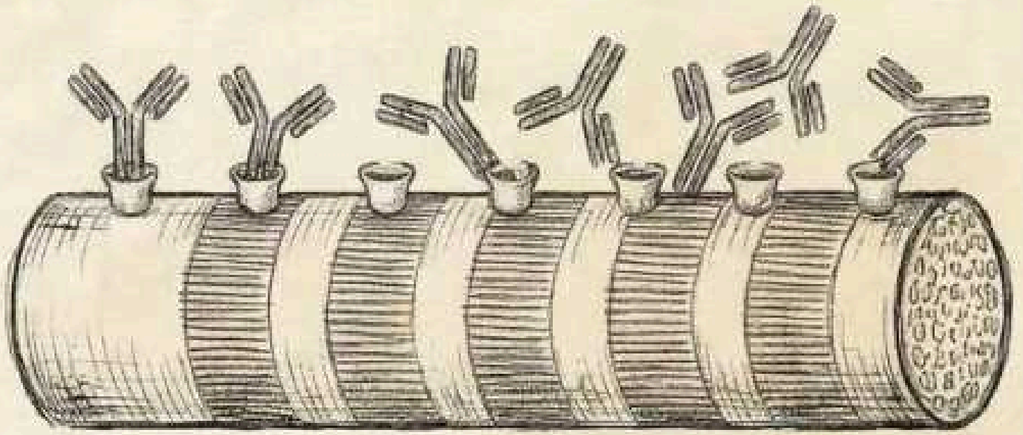
- **The Math:** A vesicle holds thousands of molecules. Yet, at many central synapses, the chance an arriving spike releases anything is well **under one half** ($P(\text{release}) < 0.5$).
- **The Solution:** Reliability emerges from network consensus (many synapses working together).

The changeable strength of each synapse is the fundamental basis of learning.

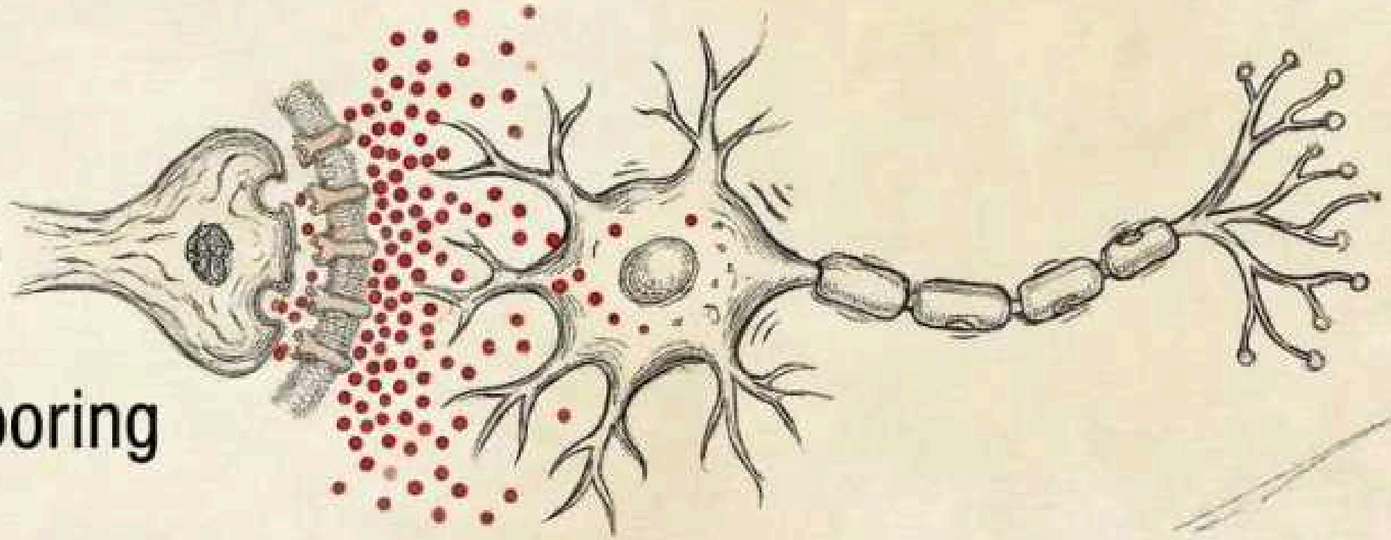
Disease at the Synapse

Note: Understanding synapses leads directly to treatments!

Myasthenia Gravis:
The immune system attacks acetylcholine receptors –> Signals fail, muscles weaken.



Stroke & Excitotoxicity:
Injured cells dump massive amounts of glutamate –> Overexcites and kills neighboring cells.

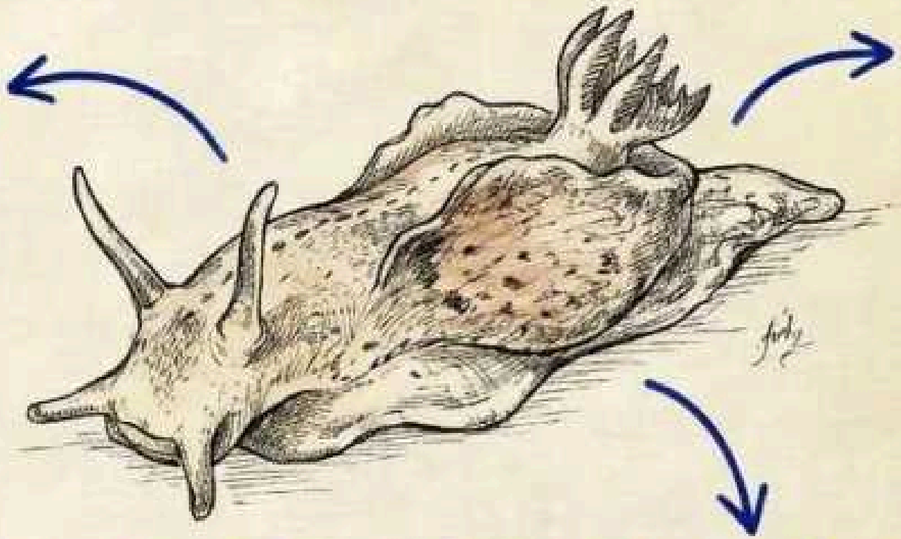


Gemini Notebook

Why Use Chemistry?

If electrical is faster, why use chemical synapses at all?

1. They can **Amplify** a weak signal.



2. They can **Invert** signals (turning excitation into inhibition).

3. They possess **Plasticity** (can be strengthened or weakened with experience).

Eric Kandel's 2000 Nobel Prize proved learning in sea slugs physically changes their synapses.

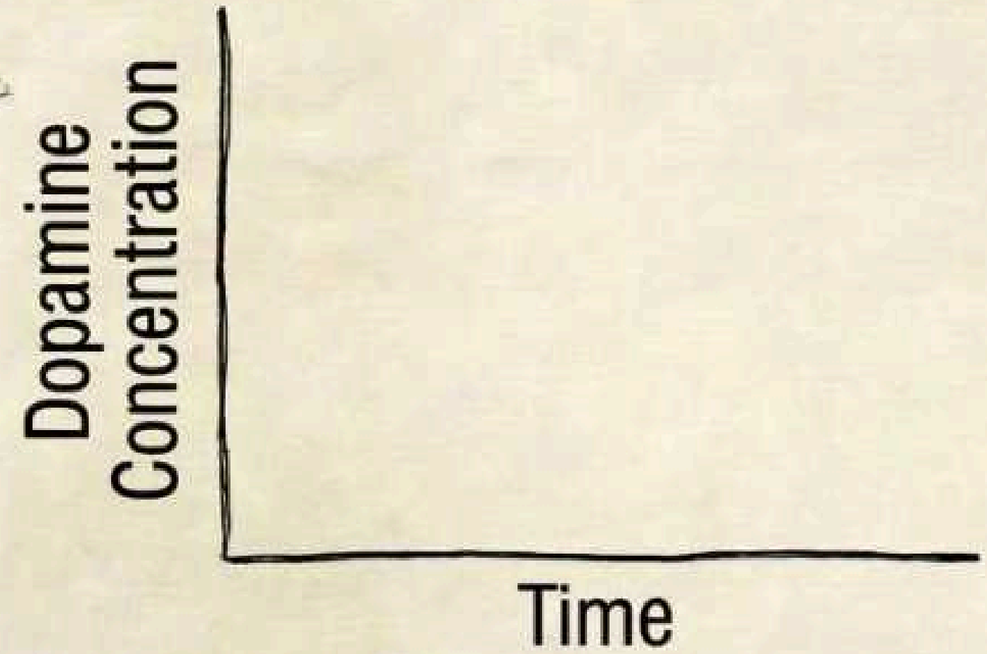
¶ 3.20

Lecture Question — Apply Your Knowledge

Scenario: A drug blocks the transporter that removes dopamine from the cleft. The amount of dopamine released per spike does not change.

Question 1: Predict what happens to the concentration of dopamine in the cleft after a spike.

Question 2: Explain why the receiving cell receives a stronger or longer signal.

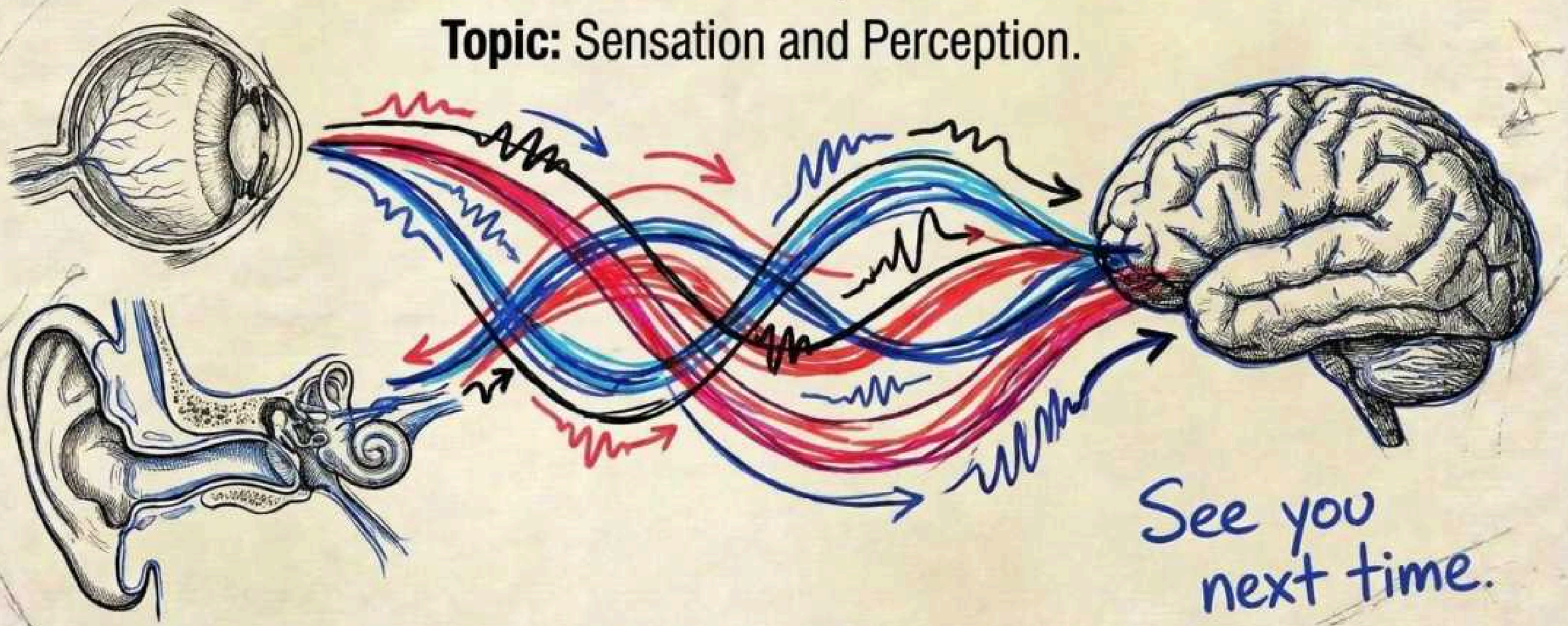


¶ 3.21

Looking Ahead to Lecture 4

The Next Question: How does the brain turn raw signals from our senses into a cohesive experience of the world?

Topic: Sensation and Perception.



See you next time.