SYNAPTIC TRANSMISSION

Information transfer at a synapse

Plays role in all the operations of the nervous system

Concept: 1897
Charles Sherrington
“synapse”

Two types of synapses:
Chemical
Electrical

1921
Otto Loewi
“Vagusstoff”

1951
Bernard Katz
John Eccles

1959
Furshpan & Potter
Two general classes of synapses:

- **Electrical**: Direct transfer of ionic current
- **Chemical**: Neural transmission involving neurotransmitters
ELECTRICAL SYNAPSE – direct and passive current flow

Gap junction
- Formed by 6 connexins
- Electrically coupled
  - Ions flow directly from one cytoplasm to the next

Ionic current flows through the connexon channels

Note: Channels are called connexons - larger than ion channel.
Gap junction channels bridge the cytoplasm of the two cells – There is electrical continuity between the two cells.

- Ions and small molecules can pass in both directions through these channels.
- 6 connexin subunits = 1 connexon
- 2 connexons = 1 gap junction channel
- Many gap junction channels = 1 gap junction synapse
6 connexins in

\[ \text{2 connexons} = \text{1 GAP Junction} \]
An AP generated in cell-1 causes a small amount of ionic current to flow through gap junction channels into a cell-2, inducing a PSP.

- Very fast transmission
- Postsynaptic potentials (PSPs)
- Synaptic integration:
  - Several PSPs occurring simultaneously to excite a neuron (i.e. causes AP)
Important points:
1. Almost instantaneous
2. Ions + other molecules
   + 2nd messengers + metabolites
   → Coordinate signaling
3. Ionic current
   - Passively
4. Bidirectional information
5. Transfer subthreshold potentials
**GENERAL PURPOSE OF ELECTRICAL SYNAPSES**

1. **Synchronization:** brainstem neurons that regulate breathing are electrically coupled.

2. **Hormone release:** in hypothalamus hormone-secreting neurons fire action potentials at about the same time, facilitating a burst of hormone into the circulation.

3. **Intracellular signaling:** gap junction pores allow ATP and second messengers to diffuse (neurons and glia.)
Electrically coupled motor neurons firing together can produce synchronous behaviors.
Very interesting, the frog’s heartbeat slows down when the vagus nerve is stimulated...
Stimulate vagus nerve

solution transferred

start stimulation

contraction force

Time (s)

contraction force

Time (s)
What is the neurotransmitter cycle of use?

What triggers neurotransmitter secretion?

How do synaptic vesicles fuse and release their contents?
How is a postsynaptic potential evoked?

What are the two major classes of receptors?

What determines if the postsynaptic action of a particular neurotransmitter is excitatory or inhibitory?
CNS synapses are distinguished by which part of the neuron is postsynaptic.
Gray's Type I
Excitatory

Gray's Type II
Inhibitory

Asymmetrical membrane differentiations
Symmetrical membrane differentiations

Structural differences predict functional differences.
Pre-synaptic

Axon terminal bouton

Vesicles with XMTR transported from soma to terminal

Synaptic vesicle loaded with XMTR
0. When action potential invades terminal

1. Voltage gated Ca++ channel opens

2. Ca++ enters into terminal
* Vesicle fuses because of Ca++ in terminal

**NOTE:**

\[ [Ca^{++}]_o = 10^{-3} M \]

vs

\[ [Ca^{++}]_i = 10^{-7} M \]

very steep concentration gradient

4. Vesicle fuses to terminal

5. Transmitter is released into synaptic cleft (exocytosis)
6 endocytosis
membrane
buds
new vesicles
(recycling
membrane
that was fused)

7 empty vesicles
are then
loaded with
transmitter
& await
another
action potential

note: ☀️ can
have more than 1 transmitter
synaptic cleft

pre synaptic

synapse

post synaptic

post synaptic receptors

*note: receptors are specific to xmtrs*
1. Neurotransmitter diffuses into synaptic cleft
2. XMTTR binds to post-synaptic receptor
3. Some XMTTR will diffuse out of cleft

enzyme degradation
5) Channel associated with receptor opens or
6) Channel closes (sometimes)

4) After XMTR binds to receptor something happens...

0) NOTE: THIS IS A XMTR INDUCED CURRENT FLOW

😊
1. Ions in the extracellular fluid

2. Ions will flow through channel when it opens.

3. Post-synaptic membrane potential will be altered.

4. Change in membrane potential will alter the probability that post-synaptic cell will fire an AP.
GLIA 1: REMOVE EXCESS XMTR

2: GLIA MODULATE EXTRACELLULAR ENVIRONMENT
   (e.g., $[K^+]_o$, $[Ca^{++}]_o$)

3: REMOVAL OF XMTR TERMINATES XMTR EFFECTS.

"INFORMATION IS TRANSIENT"
Recall

Electrical synapses
- GAP junctions
  - direct ionic current flow
  - bidirectional
  - immediate
  - failsafe

synchronize population of neurons!
Recall — most common

Chemical Synapse — slow

- neurotransmitter 
  - receptor
  - ion channel
Review of chemical synaptic transmission

10 STEPS
The activation of postsynaptic receptors by molecules of a neurotransmitter causes **neurotransmitter-dependent ion channels** to open, resulting in postsynaptic potentials.

Ionotropic receptors contain **ion channels**, which are directly opened when a ligand attaches to the binding site.

Metabotropic receptors are linked to G-proteins, which, when activated, open ion channels—usually by producing a chemical called a second messenger.

The nature of the postsynaptic potential depends on the type of ion channel that is opened by the postsynaptic receptors at a particular synapse.

For example, excitatory postsynaptic potentials occur when Na⁺ enters the cell.

For example, inhibitory postsynaptic potentials are produced when K⁺ leaves the cell or Cl⁻ enters it.

Postsynaptic potentials are normally brief. They are terminated by two means.

The most common mechanism is **reuptake**: retrieval of molecules of the neurotransmitter from the synaptic cleft by means of transporters located in the presynaptic membrane, which transport the molecules back into the cytoplasm.

Acetylcholine is deactivated by the enzyme **acetylcholinesterase**.
Chemical synaptic Transmission:
2 step process:
1. transmitting step
   - the release of a chemical messenger
2. receptive step
   - when transmitter binds to and activates the receptor in post synaptic side
Amplification \rightarrow chemical synapses

\rightarrow just one small vesicle

\rightarrow can release xmtR to open many ion channels in target cell.
Chemical Synapse

Synthesis of Neurotransmitter

• Need precursor materials, co-factors and enzymes
• Enzymes should be in the active form and
• Localized to the appropriate compartment

Synaptic cleft

• Release of neurotransmitter into cleft
• 20-50 nm wide
• 10x width of gap junction
• Filled with a matrix of fibrous extracellular protein to help align the pre and post synaptic elements

Synaptic vesicles

• Load neurotransmitter into vesicles using vesicular transporter proteins
• Store neurotransmitter
• 50nm diameter
• Membrane enclosed
• Protects neurotransmitter from enzymes
• Ready for quick release at terminal in response to repetitive stimulation
Active Zone

“On the presynaptic side, proteins jutting into the cytoplasm of the terminal along the intracellular face of the membrane sometimes look like a field of tiny pyramids. The pyramids, and the membrane associated with them, are the actual sites of neurotransmitter release.”

Post synaptic density
- Just under post-synaptic membrane
- Contains neurotransmitter receptors

Kim & Sheng Current Biology Vol 19 No 17
Bear et al
SECRETORY GRANULES

- Store soluble protein
- 100nm diameter
- EM → dense-core vesicles
- Membrane enclosed
# PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

<table>
<thead>
<tr>
<th>AMINO ACIDS</th>
<th>AMINES</th>
<th>PEPTIDES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma-aminobutyric acid (GABA)</td>
<td>Acetylcholine (ACh)</td>
<td>Cholecystokinin (CCK)</td>
</tr>
<tr>
<td>Glutamate (Glu)</td>
<td></td>
<td>Dynorphin</td>
</tr>
<tr>
<td>Glycine (Gly)</td>
<td></td>
<td>Enkephalins (Enk)</td>
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<tr>
<td></td>
<td></td>
<td>N-acetylaspartylglutamate (NAAG)</td>
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<td></td>
<td>Neuropeptide Y</td>
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<td></td>
<td></td>
<td>Somatostatin</td>
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<td></td>
<td></td>
<td>Substance P</td>
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<td></td>
<td></td>
<td>Thyrotropin-releasing hormone</td>
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<td></td>
<td></td>
<td>Vasoactive intestinal polypeptide (VIP)</td>
</tr>
</tbody>
</table>

- All amino acids + ACh mediate FAST synaptic transmission.

**Amino Acids and Amines:**
- Small organic molecules
- Contain at least one nitrogen atom
- Stored in and released from synaptic vesicles

**Peptides:**
- Large molecules
- Stored and released from secretory granules.

- Neuropeptides tend to modulate slower, ongoing synaptic functions.

Both synaptic vesicles and secretory granules can be in the same axon terminal – but they are released under different conditions.

Small molecule neurotransmitters tend to mediate rapid synaptic actions.
"The Classical Neurotransmitters"

Characteristics

- Storage vesicles smaller
- Likely to have active presynaptic re-uptake
- XMTRS synthesized in the nerve terminal by enzymatic activity

ACh
Amino Acids
Amines
Amino acids:

Amine:

Peptide:
Glu & Gly
- Abundant in all cells of the body including neurons.

GABA & AMINES
- Made only by the neurons that release them.
- Neurons contain specific enzymes which are transported to the terminal to synthesize neurotransmitter.

**AMINO ACIDS**
- Gamma-aminobutyric acid (GABA)
- Glutamate (Glu)
- Glycine (Gly)

**AMINES**
- Acetylcholine (ACh)
- Dopamine (DA)
- Epinephrine
- Histamine
- Norepinephrine (NE)
- Serotonin (5-HT)

Made only by neurons that release them – neurons contain specific enzymes to synthesize them.

TRANSPORTED INTO VESICLES
- Transporter proteins
PEPTIDES:

1. Precursor peptide is synthesized in the rough ER
2. The precursor peptide is split in the Golgi apparatus to yield an active neurotransmitter.
3. Secretory vesicles containing the peptide bud off from the Golgi apparatus.
4. The secretory vesicles are transported down the axon to the terminal where the peptide is stored.

Cholecystokinin (CCK)
Dynorphin
Enkephalins (Enk)
N-acetylaspartylglutamate (NAAG)
Neuropeptide Y
Somatostatin
Substance P
Thyrotropin-releasing hormone
Vasoactive intestinal polypeptide (VIP)
Electron micrograph shows the fine structure of a synapse in the cerebellum.

Large dark structures are mitochondria.

The active zones are specialized areas that are thought to be docking and release sites for synaptic vesicles.

The many small round bodies are vesicles that contain neurotransmitter.

Eric, Kandel, Schwartz, James, Jessell, Thomas, Siegelbaum, Steven, Hudspeth, J. Principles of Neural Science, Fifth Edition
The Active Zones:

- specialized secretary machinery
  - assist to focus the release location
Exocytosis: Process by which vesicles release their contents

**Vesicle loaded with transmitter**

**Influx** of Ca++ through voltage gated calcium channels (VGCC)

**Fusion** of the vesicle membrane with the presynaptic membrane

**Release** contents into the synaptic cleft

Transmitter recycled - endocytosis
Molecular model of protein mediated membrane fusion.

Shown are proteins involved in synaptic-vesicle fusion. According to the SNARE-hypothesis the SNAREs **Syntaxin 1A** and **SNAP-25** at the plasma membrane form a complex with the vesicle-associated SNARE **synaptobrevin 2**.

- The bilayers destined to fuse are pulled together as complex formation proceeds. SNARE-complex formation presumably is required to overcome the repulsive forces of the opposed bilayers.
- As SNAREs alone are able to fuse otherwise protein-free membrane bilayers, they may also induce membrane protrusions and trigger fusion. However, it is unclear if SNAREs have such functions in live systems.
- **Munc13** and **Munc18** are supposed to assist in the formation of the SNARE-complex.
- Once the SNARE-complex has formed completely it may be further stabilized by **Complexin**.
The sequence of events that underlie quantal transmission at central glutamatergic synapses

John E. Lisman*, Sridhar Raghavachari† and Richard W. Tsien§

Abstract | The properties of synaptic transmission were first elucidated at the neuromuscular junction. More recent work has examined transmission at synapses within the brain. Here we review the remarkable progress in understanding the biophysical and molecular basis of the sequential steps in this process. These steps include the elevation of Ca^{2+} in microdomains of the presynaptic terminal, the diffusion of transmitter through the fusion pore into the synaptic cleft and the activation of postsynaptic receptors. The results give insight into the factors that control the precision of quantal transmission and provide a framework for understanding synaptic plasticity.
Figure 1 | Steps in the process of chemical synaptic transmission. These steps occur in both vertebrates and invertebrates, at the neuromuscular junction and central synapses. Cartoons based on a drawing by J. A. Ernst and A. Brunger.
Two potential mechanisms of formation of the fusion pore between the synaptic vesicle (upper membrane; pink) and the plasma membrane (lower membrane; green). In the top left panel the vesicle is in the ‘docked’ state in which it is held near the plasma membrane by the SNARE complex. In the top right panel, the vesicle and plasma membrane have their distal leaflets in a hemifused state that is primed for release. During the release process, a protein-lined pore (lower left panel) is formed by two of the SNARE proteins, syntaxin and synaptobrevin. This step may be reversible, or may be followed by a transition to a lipid-lined pore (bottom right panel). An alternative model is that fusion pore opening always involves the formation of a lipid-lined pore.

Figure 1. Protein components of the synaptic exocytotic machinery. The synaptic vesicle cycle at the nerve terminal involves vesicle docking, priming, fusion, endocytosis, and recycling (see text for details). Indicated are proteins that have been implicated in the docking, priming, and fusion steps. Conserved protein components of the general fusion machinery are shown in green, whereas unique components of synaptic vesicle exocytosis are shown in red.
Neurotransmitter Release Recap: Mechanisms

- Process of exocytosis stimulated by release of intracellular calcium, \([Ca^{2+}]_i\)
- Proteins alter conformation - activated
- Vesicle membrane incorporated into presynaptic membrane
- Neurotransmitter released
- Vesicle membrane recovered by endocytosis
Recall: Ion channels have important properties:

1. recognize and select specific ions
2. the open & close in response to signals
electrical, mechanical, chemical
3. conduct ions across the membrane
TRANSMITTER - GATED ION CHANNELS
IONOTROPIC
Quantal Analysis of EPSPs

- Synaptic vesicles: Elementary units of synaptic transmission
- Quantum: An indivisible unit
- Miniature postsynaptic potential ("mini")
- Quantal analysis: Used to determine number of vesicles that release during neurotransmission
- Neuromuscular junction: About 200 synaptic vesicles, EPSP of 40mV or more
- CNS synapse: Single vesicle, EPSP of few tenths of a millivolt
An impulse arriving in the presynaptic terminal causes the release of neurotransmitter.

The bind to transmitter-gated ion channels in the post-synaptic membrane.

If Na+ enters the post-synaptic cell through the open channels, the membrane will become depolarized.

The resulting change in membrane potential (Vm) is the EPSP.

Triggered by the arrival of an action potential in the axon terminal.
Triggered by the arrival of an action potential in the axon terminal.

An **impulse** arriving in the presynaptic terminal causes the **release of neurotransmitter**

The **bind to transmitter-gated ion channels in the post-synaptic membrane.**

If **Cl⁻** enters the post-synaptic cell through the open channels, the membrane will become **hyperpolarized.**

The resulting change in membrane potential \( (V_m) \) is the **IPSP**
Inhibition

- Action of synapses to take membrane potential away from action potential threshold
- Exerts powerful control over neuron output
All receptors for chemical xmitrs have:

1. They are membrane spanning proteins
   - the region exposed to the external environment recognizes and binds the xmitr from the pre-synaptic cell

   ... AND ...
Receptors carry out an effector function within the target cell.

E.g., opening or closing an ion channel.
DIRECT GATING:

THE RECEPTOR IS PART OF THE CHANNEL

Eric, Kandel, Schwartz, James, Jessell, Thomas, Siegelbaum, Steven, Hudspeth, J.  *Principles of Neural Science, Fifth Edition*
INDIRECT GATING

*separate molecules control receptor & channel control

The **binding of neurotransmitter** to the receptor leads to **activation of G-proteins**.

G-proteins can **activate an ion-channel**
The binding of neurotransmitter to the receptor leads to activation of G-proteins. G-proteins can activate enzymes that generate intracellular second messengers.
Comparison - Ionotropic receptor

1. Produce relatively fast actions
   → last only msec
2. Used in circuits to mediate rapid signaling
   e.g. stretch reflex
METABOTROPIC RECEPTORS

1. Slower synaptic actions → seconds to minutes
2. Alter the strength or excitability of connections
3. Used in reinforcing pathways - e.g., learning

Diagram details:
- Transmitter
- Receptor
- G protein
- Adenylyl cyclase
- Channel
- Pore
- Effector function
- cAMP
- GTP
- PKA
- Extracellular side
- Cytoplasmic side

SLOW!!
NMJ neuro-muscular junction

→ most studied synapse!

motor neuron → skeletal muscle
Most studied synapse ever!

- Chemical synapse.
- Clinical significance.
- *Fast* and reliable!
- AP motor axon always causes an AP in muscle cell it innervates.
- It is all about the size of the synapse and the high number of active zones!
Reasons why to study NMJ:

1. Simple & accessible to experimentation
2. Muscle cell - can hold multiple electrodes
3. Muscle cell receives input from 1 axon
4. Signaling mechanism is simple

\[ \text{xnr} \rightarrow \text{ion channel opens} \]
① Motor neuron (MN) innervates muscle end plate

② Each bouton is positioned over a junctional fold

③ Junctional folds contain receptors
has everything it needs to release ACh!

organizes the synapse

Mitochondrion

Synaptic vesicle (ACh)

Presynaptic membrane

Synaptic cleft

Postsynaptic membrane

Active zone

Ca^{2+} channel

Basal lamina

Junctional fold

Voltage-gated Na^{+} channel

ACh receptor-channels

(4) basal lamina
→ connective tissue
→ collagen & glycoproteins
→ permeable to ions & xmr

(5) AChE
acetylcholinesterase
→ inactivates ACh
Summary:
1. Open ACh receptor channels at endplate causes
2. Opens neighboring Vg Na⁺ channels

Opening of voltage-gated Na⁺ channels
- Na⁺ inflow
- Depolarization
- Action potential

ACh binding to receptor-channel molecule
- Channel opening
- Na⁺ inflow
- K⁺ outflow
- Depolarization (end-plate potential)
The Neuromuscular Junction
The Classic Model of Synaptic Excitation

This tutorial simulates the responses of a muscle fiber to acetylcholine (ACh) released from the motoneuron's presynaptic terminal.
The simulations model the postsynaptic (or "end plate") membrane of the well-known neuromuscular junction (NMJ) of the frog. At the NMJ, ACh binds to its postsynaptic (nicotinic) receptors, which are also ion channels. The channels open, causing a postsynaptic "end plate current" (EPC) to flow that leads to a postsynaptic, depolarizing "end plate potential" (EPP) in the muscle fiber.

ACh-gated receptors are permeable to both Na and K ions.
Activation of ACh receptors causes a simultaneous and equal increase in the postsynaptic conductance to both Na and K ions. In this tutorial you will see the relationships between the ACh-gated conductance, the resulting EPC, and the EPP.

Studying the NMJ reveals general principles of excitatory synapses.
In later tutorials you will experiment with excitatory postsynaptic potentials (EPSPs) in neurons, such as: the interaction of EPSPs in a patch, the spread of an EPSP along a dendrite to the soma and axon, and the temporal integration of more than one EPSP.

Goals of this Tutorial
- To observe the relationships between the ACh-gated conductance, the resulting current (the EPC), and the voltage change in the muscle fiber (the EPP)
- To experiment with the reversal potential of the ACh-gated EPC and EPP
- To discover the effect on the EPP of adding voltage-gated channels to the muscle fiber
End-plate potential  Total end-plate current  Single-channel current

Resting membrane potential $-90 \text{ mV}$

ACh receptor channels $I_{Na^+}$ $I_{K^+}$ $I_{net}$

Figure adapted from: Kandel, Schwartz, Jessell (2015)
End-plate potential  Total end-plate current  Single-channel current
ACh receptor channels  \[ I_{Na} \quad I_{K} \quad I_{net} \]

Figure adapted from: Kandel, Schwartz, Jessell (2015)
End-plate potential | Total end-plate current | Single-channel current

$E_{EPSP}$: 0 mV

$-30$ mV

Figure adapted from: Kandel, Schwartz, Jessell (2015)
Recap:

1. At resting potential (-90 mV), the current through single AChR is large & inward.

   b/c: Large inward driving force on Na\(^+\) & small outward driving force on K\(^+\)

   \[ \implies \text{Total = large depolarizing potential} \]
Recap:
(2) At more positive levels of membrane potential, the inward driving force on Na⁺ is less and the outward driving force on K⁺ is ↑.

Result:
Decrease in size of the end plate current & therefore a reduction in the end plate potential.
Recap:

- At the reversal potential (0 mV) the inward $\text{Na}^+$ flux is balanced by the outward $\text{K}^+$ flux.

Result:
- No net current at the end plate and no change in $V_m$
Recap:

4. Further depolarization to +30mV inverts the direction of the endplate current. The larger outward driving force on K⁺ & smaller inward force on Na⁺.

At $E_{Na}$, therefore $I_{Na} = 0$. 

Diagram: 

- $E_{Na} + 55$ mV 
- +30 mV
Chemical Transmission - 4 steps:

1. Synthesis & storage of a transmitter substance
2. Release of the transmitter
3. Interaction with the receptor
4. Removal of transmitter from cleft.
SELF REGULATION MECHANISMS: AUTORECEPTOR

- **Neurotransmitter synthesis**
  - Load neurotransmitter into synaptic vesicles
  - Vesicles fuse to presynaptic terminal

- **Neurotransmitter spills into synaptic cleft**
  - Binds to postsynaptic receptors

- **Biochemical/Electrical response elicited in postsynaptic cell**

- **Feedback & Control**
  - Removal of neurotransmitter from synaptic cleft

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**Autoreceptor**: sensitive to the neurotransmitter it can control synthesis and release of transmitter.
Neurotransmitter Recovery and Degradation

- Diffusion: Away from the synapse
- Reuptake: Neurotransmitter re-enters presynaptic axon terminal
- Enzymatic destruction inside terminal cytosol or synaptic cleft
- Desensitization: e.g., AChE cleaves Ach to inactive state
Recall: Excitatory and Inhibitory Postsynaptic Potentials:

**EPSP**: Transient postsynaptic membrane depolarization by presynaptic release of neurotransmitter

**IPSP**: Transient hyperpolarization of postsynaptic membrane potential caused by presynaptic release of neurotransmitter
**Quantal Analysis of EPSPs**

- Synaptic vesicles: Elementary units of synaptic transmission
- Quantum: An indivisible unit
- Miniature postsynaptic potential ("mini")
- Quantal analysis: Used to determine number of vesicles that release during neurotransmission
- Neuromuscular junction: About 200 synaptic vesicles, EPSP of 40mV or more
- CNS synapse: Single vesicle, EPSP of few tenths of a millivolt
An action potential invades the presynaptic terminal

Depolarization of presynaptic terminal causes opening of V Ca²⁺ channels

Influx of Ca²⁺ through channels

Ca²⁺ causes vesicles to fuse with presynaptic membrane

Transmitter is released into synaptic cleft via exocytosis

Transmitter binds to receptor molecules in postsynaptic membrane

Postsynaptic channels open or close

Postsynaptic current causes excitatory or inhibitory postsynaptic potential that changes the excitability of the cell.

Removal of neurotransmitter by glial uptake or enzyme degradation.

Retrieval of vesicular membrane from plasma membrane

Transmitter is synthesized and stored in vesicle

Review:
Synaptic Integration

• Process by which multiple synaptic potentials combine within one postsynaptic neuron
EPSP Summation

• Allows for neurons to perform sophisticated computations
• Integration: EPSPs added together to produce significant postsynaptic depolarization
• Spatial: EPSP generated simultaneously in different spaces
• Temporal: EPSP generated at same synapse in rapid succession
The Contribution of Dendritic Properties to Synaptic Integration

• Dendrite as a straight cable
• Membrane depolarization falls off exponentially with increasing distance
  • \( V_x = V_o/e^{x/\lambda} \)
• Dendritic length constant (\( \lambda \))
• In reality, dendrites are very elaborate structures that contribute to more complex integrative properties
Decreasing depolarization as a function of distance along a dendritic cable.

- Current is injected into a dendrite and the depolarization is recorded.
- As this current spreads down the dendrite, much of it dissipates across the membrane.
- Therefore, the depolarization measured at a distance from the site of current injection is smaller than that measured right under it.
- Plot membrane depolarization as a function of distance along the dendrite.
- At the distance $\lambda$, one length constant, the membrane depolarization $V_{\lambda}$ is 37% of that at the origin.
The Contribution of Dendritic Properties to Synaptic Integration

Excitable Dendrites
Dendrites of neurons of voltage-gated sodium, calcium, and potassium channels
   Can act as amplifiers (vs. passive)
Dendritic sodium channels:
   May carry electrical signals in opposite direction, from soma outward along dendrites
Shunting Inhibition: Inhibiting current flow from soma to axon hillock

**IPSPs and Shunting Inhibition**

- Excitatory vs. inhibitory synapses: Bind different neurotransmitters, allow different ions to pass through channels
- Membrane potential less negative than -65mV = hyperpolarizing IPSP

*Shunting Inhibition: Inhibiting current flow from soma to axon hillock*
Modulation

- Synaptic transmission that modifies effectiveness of EPSPs generated by other synapses with transmitter-gated ion channels
- Example: Activating NE β receptor

1. Binding NE to receptor activates G-protein in membrane
2. The G-protein activates the enzyme adenylyl cyclase
3. Adenylyl cyclase converts ATP into second messenger cAMP.
4. cAMP activates a protein kinase.
5. The protein kinase causes a potassium channel to close by attaching a phosphate group to it.
Neuropharmacology

Effect of drugs on nervous system tissue
- Receptor antagonists:
  Inhibitors of neurotransmitter receptors
  - Curare
- Receptor agonists:
  Mimic actions of naturally occurring neurotransmitters
  - Nicotine
- Defective neurotransmission:
  Root cause of neurological and psychiatric disorders
Chemical synaptic transmission
Rich diversity allows for complex behavior
Provides explanations for drug effects
Defective transmission is the basis for many neurological and psychiatric disorders
Key to understanding the neural basis of learning and memory