

# Informatica Biomedica

## lezione20

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[www.dia.uniroma3.it/paoluzzi/web/did/biomed/](http://www.dia.uniroma3.it/paoluzzi/web/did/biomed/)

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# Informatica Biomedica: Lezione 20

## Neurotrasmettitori

- Definizione

- Classificazioni

- Neurotrasmettitori principali

- Eccitatori e inibitori

- Esempi di neurotrasmettitori

- Sistemi neurotrasmettitori

Peptides: neuropeptides

# Obiettivo

Estratto dall'articolo [Neurotransmitters](#) di [Wikipedia](#).

Si intende fornire delle linee guida rispetto alla costruzione di un repository locale, impiantato presso il DIA di Roma Tre, delle molecole biologiche con funzionalità di neurotrasmettitore.

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- ▶ I farmaci neuroattivi agiscono al livello dei neurotrasmettitori
- ▶ La presenza nel cervello di uno specifico farmaco cambia la quantità dei neurotrasmettitori disponibili per la trasmissione dei segnali di vario tipo.

## Neurotransmitter containers

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- ▶ Low level "baseline" release also occurs without electrical stimulation.

# Generalities

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- ▶ dividerli in aminoacidi, peptidi e monoamine è sufficiente per alcuni scopi
- ▶ Possono anche essere classificati in *eccitatori* e *inibitori*, sebbene spesso entrambe le funzioni possano essere svolte in funzione del contesto.



## UW FMA Classification

<http://sig.biostr.washington.edu/projects/fm/>

- Neurotransmitter receptor
  - Ionotropic receptor
  - Metabotropic receptor
- Acetylcholine receptor
  - Nicotinic acetylcholine receptor
  - Muscarinic acetylcholine receptor
- Catecholamine receptor
  - Alpha adrenergic receptor
  - Beta adrenergic receptor
- Dopamine receptor
  - D1 receptor
  - D2 receptor
- Histamine receptor
  - H1 receptor

# UW FMA Explorer

Select navigation tree type:

- Biological macromolecule
  - Protein
  - Lipid
  - Carbohydrate
  - Amino acid
  - Purine
  - Pyrimidine
  - Fatty acid
  - Lipoprotein
  - Cell pigment
  - Intercellular matrix component
  - Biogenic amine
  - Biogenic peptide
  - Protein complex
    - Component of protein complex
    - Ribonucleoprotein complex
    - Ribonucleic Acid
    - Hormone
    - Major histocompatibility complex gene
  - Deoxyribonucleic acid
  - Phospholipid
  - DNA molecule region
  - Preribosome
    - RNA molecule
    - Nucleoporin
    - Hydrophilic end of structural lipid molecule
    - Hydrophobic end of structural lipid molecule
    - Nucleotide
  - Glycosaminoglycan
  - Glycoconjugate
    - Peripheral microtubule doublet of axoneme of cilium
  - Ring protein subunit
    - Annular protein subunit
    - Column protein subunit
    - Luminal protein subunit
  - Microtubule doublet
  - Microtubule triplet
  - Neurotransmitter receptor
  - Cluster of differentiation transmembrane protein
  - Costamere
  - Structural gene
  - Structural lipid molecule

**SYNONYM:**

**NON-ENGLISH EQUIVALENT:**

name	language
Cellula	Latin
Zelle	German
Célula	Spanish

**FMAID:**

**DEFINITION:**  
Anatomical structure which has as its boundary the external surface of a maximally connected plasma membrane. Examples: lymphocyte, fibroblast, erythrocyte, neuron.

**BOUNDED BY:**

**PART:**

<input type="text" value="Apical part of cell"/>
<input type="text" value="Basal part of cell"/>
<input type="text" value="Plasma membrane"/>
<input type="text" value="Compartment of cell"/>

**HAS DIMENSION:**

**HAS MASS:**

**HAS BOUNDARY:**

<input type="text" value="true"/>
<input type="text" value="false"/>

## Amino acid neurotransmitter (1/2)

glutamate, aspartate, serine,  $\gamma$ -aminobutyric acid (GABA), glycine

**An amino acid neurotransmitter**

is a chemical substance which is able to transmit a **nerve message** across a synapse

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- ▶ Neurotransmitters (chemicals) are packaged into **vesicles** that cluster beneath the axon terminal membrane on the presynaptic side of a synapse in a process called **endocytosis**
- ▶ Amino acid neurotransmitter release (**exocytosis**) is dependent upon calcium ions ( $\text{Ca}_2^+$ ) and is a **presynaptic response**

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- ▶ There are **inhibitory** amino acids (**IAA**) or **excitatory** amino acids (**EAA**)

### **Some EAA**

*L-Glutamate, L-Aspartate, L-Cysteine, and  
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## Some IAA

*$\gamma$ -aminobutyric acid (GABA), Glycine,  $\beta$ -Alanine, and Taurine*

1. *The IAA depress the activity of post-synaptic cells*

# Monoamine neurotransmitters:

## Monoamine neurotransmitters

are neurotransmitters and neuromodulators that contain one amino group that is connected to an aromatic ring by a two-carbon chain ( $-CH_2 - CH_2-$ ).

All monoamines are derived from aromatic amino acids like phenylalanine, tyrosine, tryptophan, and the thyroid hormones by the action of aromatic amino acid decarboxylase enzymes.

They include:

dopamine (DA), norepinephrine (noradrenaline; NE, NA), epinephrine (adrenaline), histamine, serotonin (SE, 5-HT), melatonin

## Peptides:

over 50 neuroactive peptides have been found ([trovarli tutti](#)), and new ones are discovered regularly

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over 50 neuroactive peptides have been found ([trovarli tutti](#)), and new ones are discovered regularly

- ▶ Many of these are "co-released" along with a small-molecule transmitter, but in some cases a peptide is the primary transmitter at a synapse.

See [Peptide Neurotransmitters](#) extracted from book [Neuroscience, Fourth Edition](#)

Others:

acetylcholine (ACh), adenosine, anandamide, nitric oxide, etc.

single ions:

such as synaptically released zinc, are also considered neurotransmitters by some, as are some gaseous molecules such as nitric oxide (NO) and carbon monoxide (CO)



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- ▶ These are not classical neurotransmitters by the strictest definition, however, because although they have all been shown experimentally to be released by presynaptic terminals in an activity-dependent way, they are not packaged into *vesicles*

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- ▶ The effect on the postsynaptic cell depends, therefore, entirely on the properties of those receptors. It happens that for some neurotransmitters (for example, glutamate), the most important receptors all have excitatory effects: that is, they increase the probability that the target cell will fire an action potential.

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- ▶ For other neurotransmitters (such as GABA), the most important receptors all have inhibitory effects.
- ▶ There are, however, other neurotransmitters, such as acetylcholine, for which both excitatory and inhibitory receptors exist;
- ▶ and there are some types of receptors that activate complex metabolic pathways in the postsynaptic cell to produce effects that cannot appropriately be called either excitatory or inhibitory.

# Glutamate

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- ▶ It is also used at most synapses that are "modifiable", i.e
- ▶ capable of increasing or decreasing in strength
- ▶ Modifiable synapses are thought to be the main memory-storage elements in the brain.

# GABA

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- ▶ Correspondingly glycine is the inhibitory transmitter in the spinal cord.

# Acetylcholine

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- ▶ The paralytic arrow-poison curare acts by blocking transmission at these synapses
- ▶ Acetylcholine also operates in many regions of the brain, but using different types of receptors.



# Dopamine

has a number of important functions in the brain

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- ▶ It plays a critical role in the reward system, but dysfunction of the dopamine system is also implicated in Parkinson's disease and schizophrenia.

# Serotonin

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# Serotonin

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- ▶ Most is produced by and found in the intestine (approximately 90
- ▶ It functions to regulate appetite, sleep, memory and learning, temperature, mood, behaviour, muscle contraction, and function of the cardiovascular system and endocrine system
- ▶ It is speculated to have a role in depression, as some depressed patients are seen to have lower concentrations of metabolites of serotonin in their cerebrospinal fluid and brain tissue.

## Substance P

undecapeptide responsible for transmission of pain from certain sensory neurons to the central nervous system.

## Neurotransmitter systems

Neurons expressing certain types of neurotransmitters sometimes form distinct systems, where activation of the system affects large volumes of the brain, called volume transmission



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Neurons expressing certain types of neurotransmitters sometimes form distinct systems, where activation of the system affects large volumes of the brain, called volume transmission

- ▶ Major neurotransmitter systems include the **noradrenaline** (norepinephrine) system, the **dopamine** system, the **serotonin** system and the **cholinergic** system.

## Serotoning receptors

<b>Type</b>	<b>Distribution</b>	<b>Postulated Roles</b>
5-HT1	Brain, instetinal nerves	Neuronal inhibition, behavioural effects, cerebral vasoconstriction
5-HT2	Brain, heart, lungs, smooth muscle control, GI system, blood vessels, platelets	Neuronal excitation, vasoconstriction, behavioural effects, depression, anxiety
5-HT3	Limbic system, ANS	Nausea, anxiety
5-HT4	CNS, smooth muscle	Neuronal excitation, GI
5-HT5, 6, 7	Brain	Not known

# Noradrenaline receptors

<b>Type</b>	<b>Distribution</b>	<b>Postulated Roles</b>
Alpha1	Brain, heart, smooth muscle	Vasoconstriction, smooth muscle control
Alpha2	Brain, pancreas, smooth muscle	Vasoconstriction, presynaptic effect in GI (relaxant)
Beta1	Heart, brain	Heart rate (increase)
Beta2	Lungs, brain, skeletal muscle	Bronchial relaxation, vasodilatation
Beta3	Postsynaptic effector cells	Stimulation of effector cells

## Dopamine receptors

<b>Type</b>	<b>Distribution</b>	<b>Postulated Roles</b>
D1, 5-like	Brain, smooth muscle	Stimulatory, role in schizophrenia?
D2, 3, 4-like	Brain, cardiovascular system, presynaptic nerve terminals	Inhibitory, role in schizophrenia?

# Acetylcholine receptors

<b>Type</b>	<b>Distribution</b>	<b>Postulated Roles</b>
M1	Nerves	CNS excitation, gastric acid secretion
M2	Heart, nerves, smooth muscle	Cardiac inhibition, neural inhibition
M3	Glands, smooth muscle, endothelium	Smooth, muscle contraction, vasodilation
M4	?CNS?	Not known
M5	?CNS?	Not known
NM	Skeletal muscles neuromuscular junction	Neuromuscular transmission
NN	Postganglionic cell body dendrites	Ganglionic transmission

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# neuropeptides

Hypothalamic	Somatostatin, CRH, GnRH, GHRH, Orexins, TRH, POMC (ACTH, MSH, Lipotropin)
Gastrointestinal hormones	Cholecystokinin, Gastric inhibitory polypeptide, Gastrin, Motilin, Secretin, Vasoactive intestinal peptide
Other hormones	Calcitonin, Oxytocin, Vasopressin
Neuromedins	B, N, S, U
Opioid peptides	Dynorphin, Endomorphin, Endorphin, Enkephalin, Nociceptin, Opiorphin
Other neuropeptides	Angiotensin, Bombesin, Calcitonin gene-related peptide, Carnosine, Cocaine and amphetamine regulated transcript, Delta sleep-inducing peptide, FMRFamide, Galanin, Galanin-like peptide, Gastrin releasing peptide, Kinins (Bradykinin, Tachykinins), Neuropeptide S, Neuropeptide Y, Neurophysins, Neurotensin, Pancreatic polypeptide, Pituitary adenylate cyclase activating peptide, RVD-Hp $\alpha$ , VGF