

M260/NS M206/EE M255
Neuroengineering

**Basic neuroanatomy and neurophysiology
for neural engineering students**

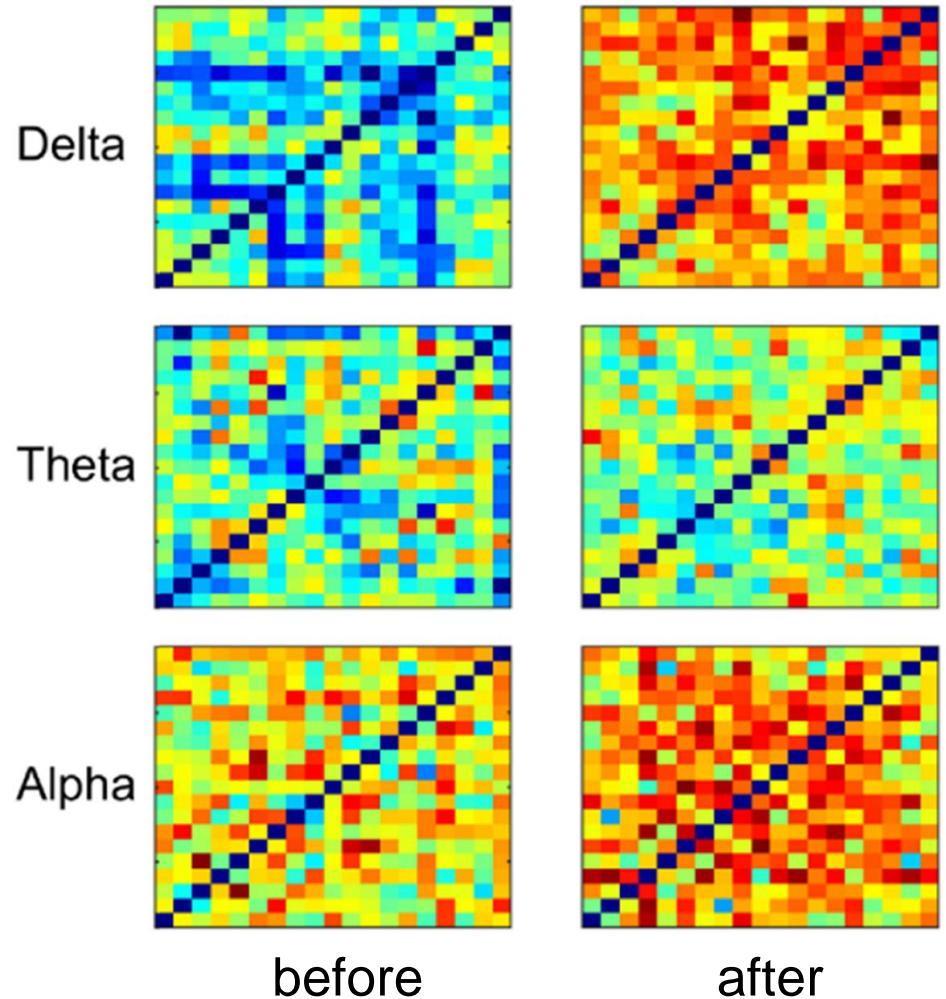
Dr. Victor Pikov
CEO, Medipace Inc
Pasadena, CA

How can we use neural interfaces: future versus now

BCI: connect to computers and AI

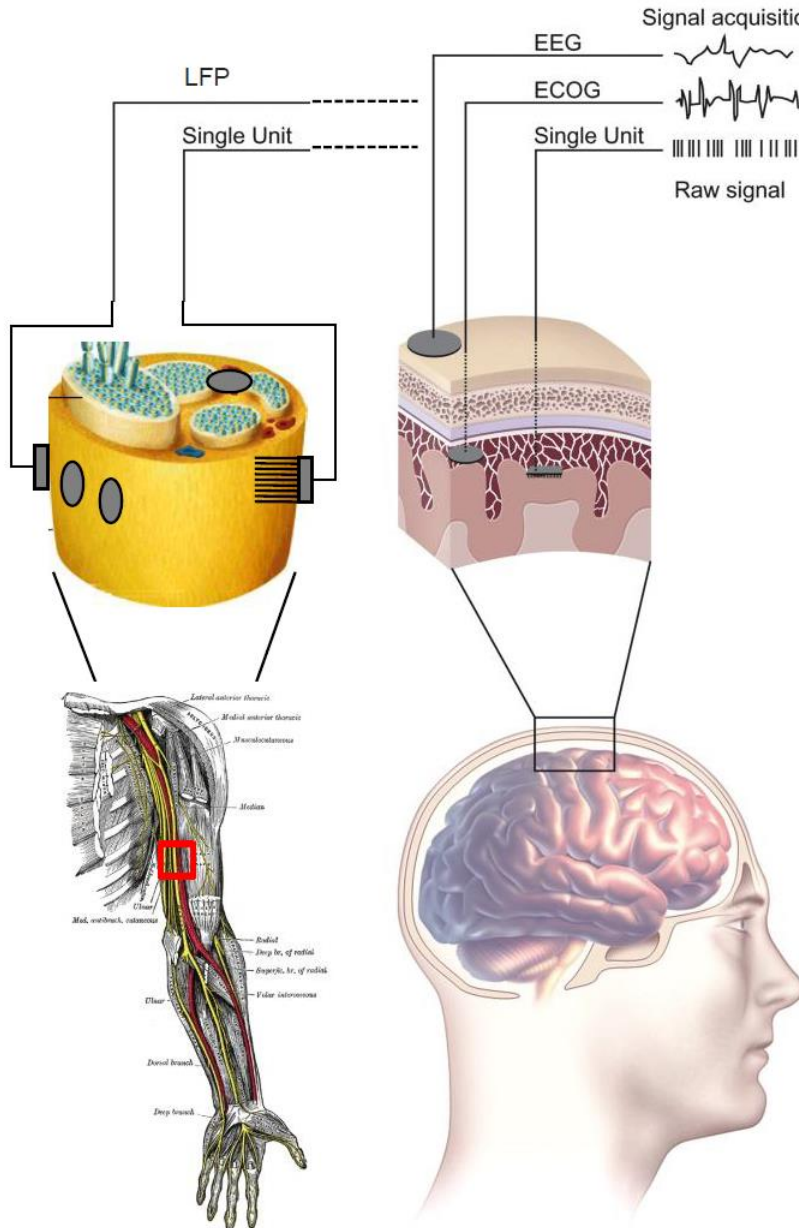


neuromodulation: restore balance and entropy in the aging brain

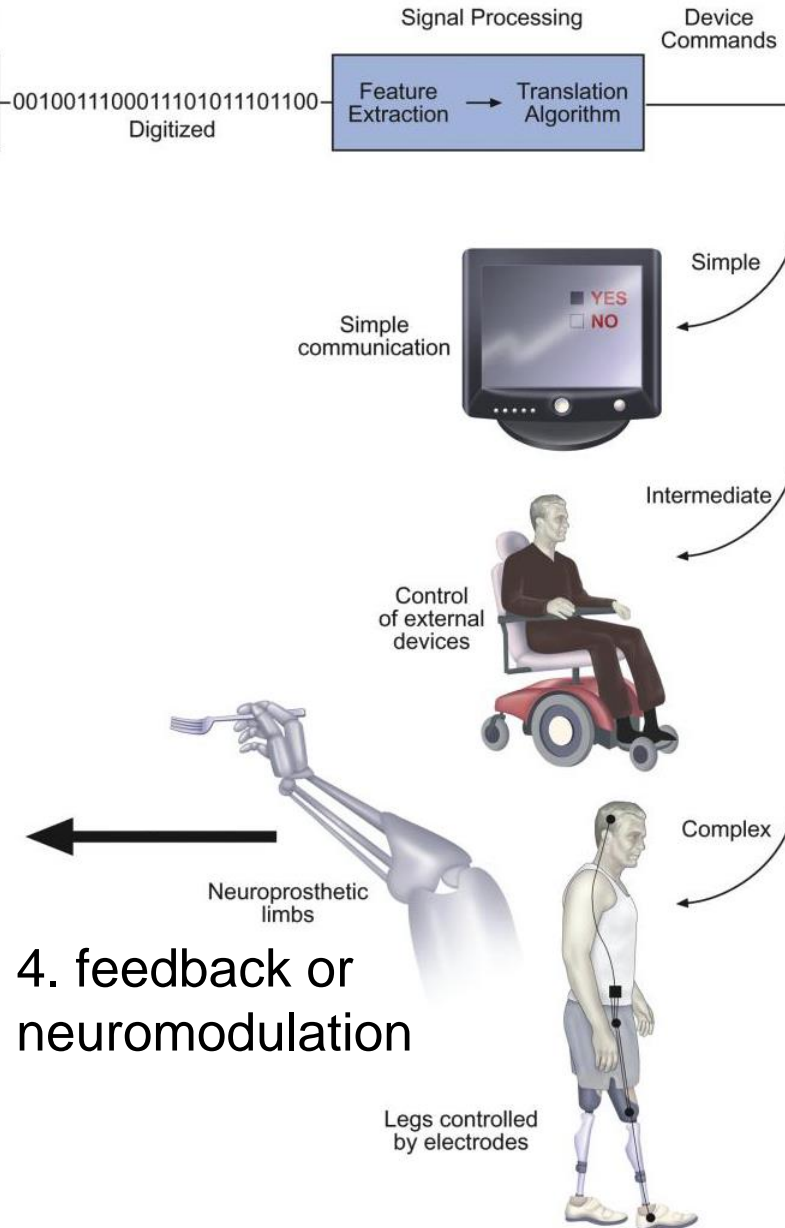


Key components of a neural interface

1. record



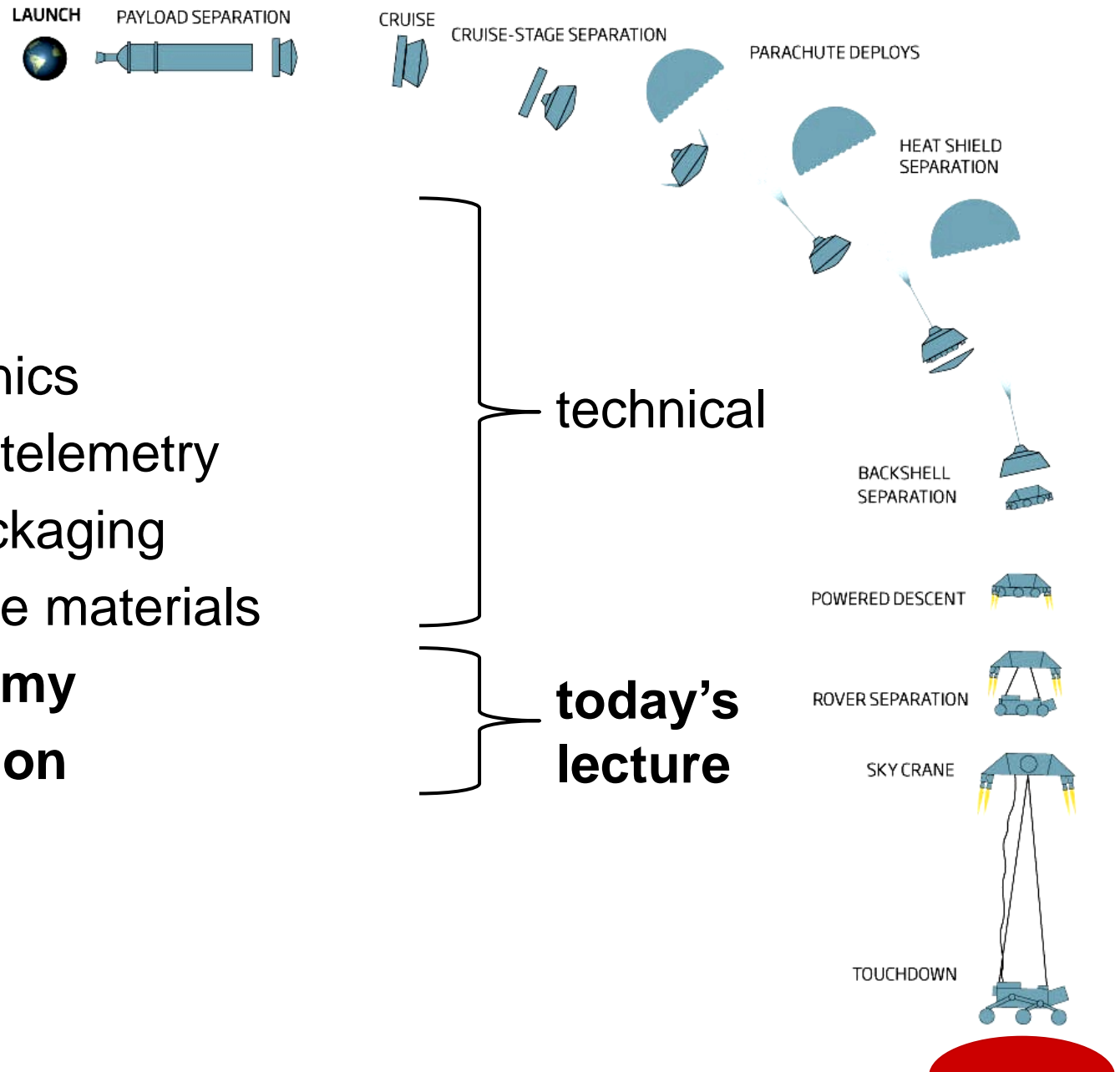
2. decode



3. control external devices

4. feedback or neuromodulation

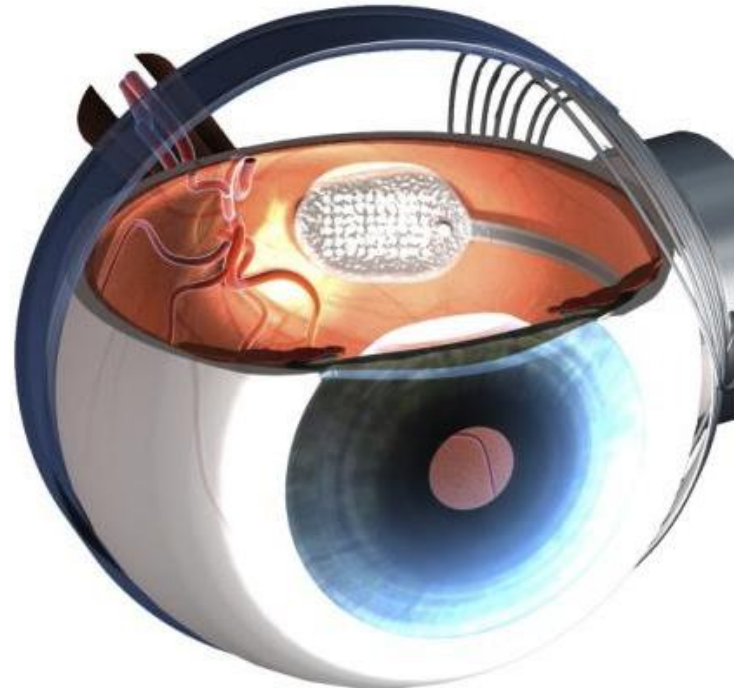
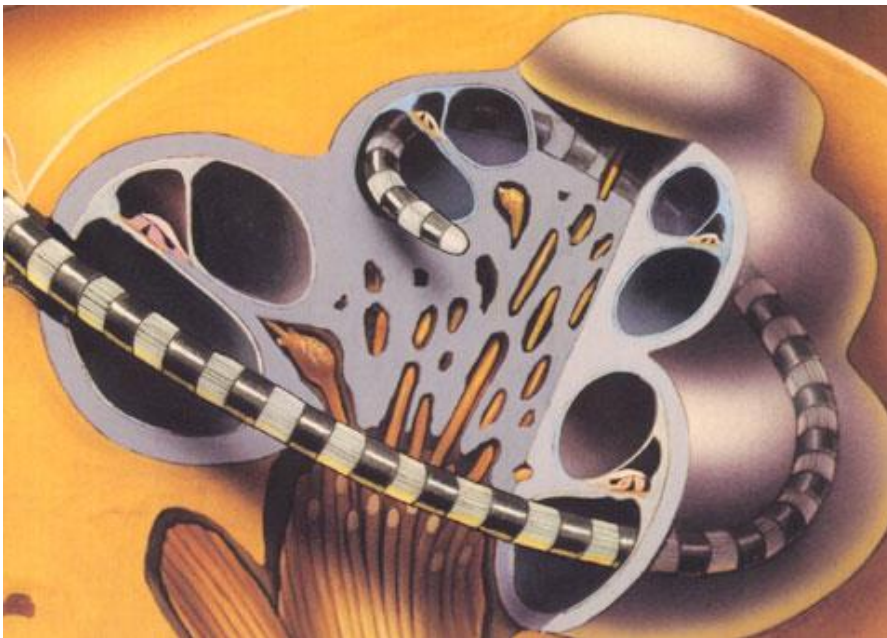
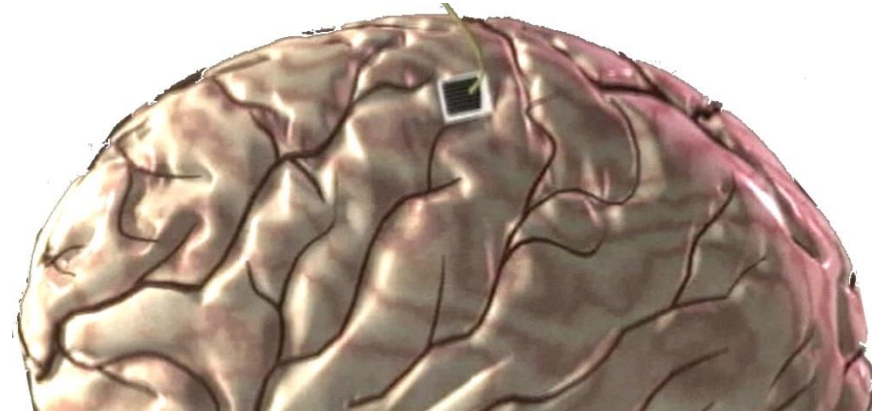
Challenges in the design of neural interfaces



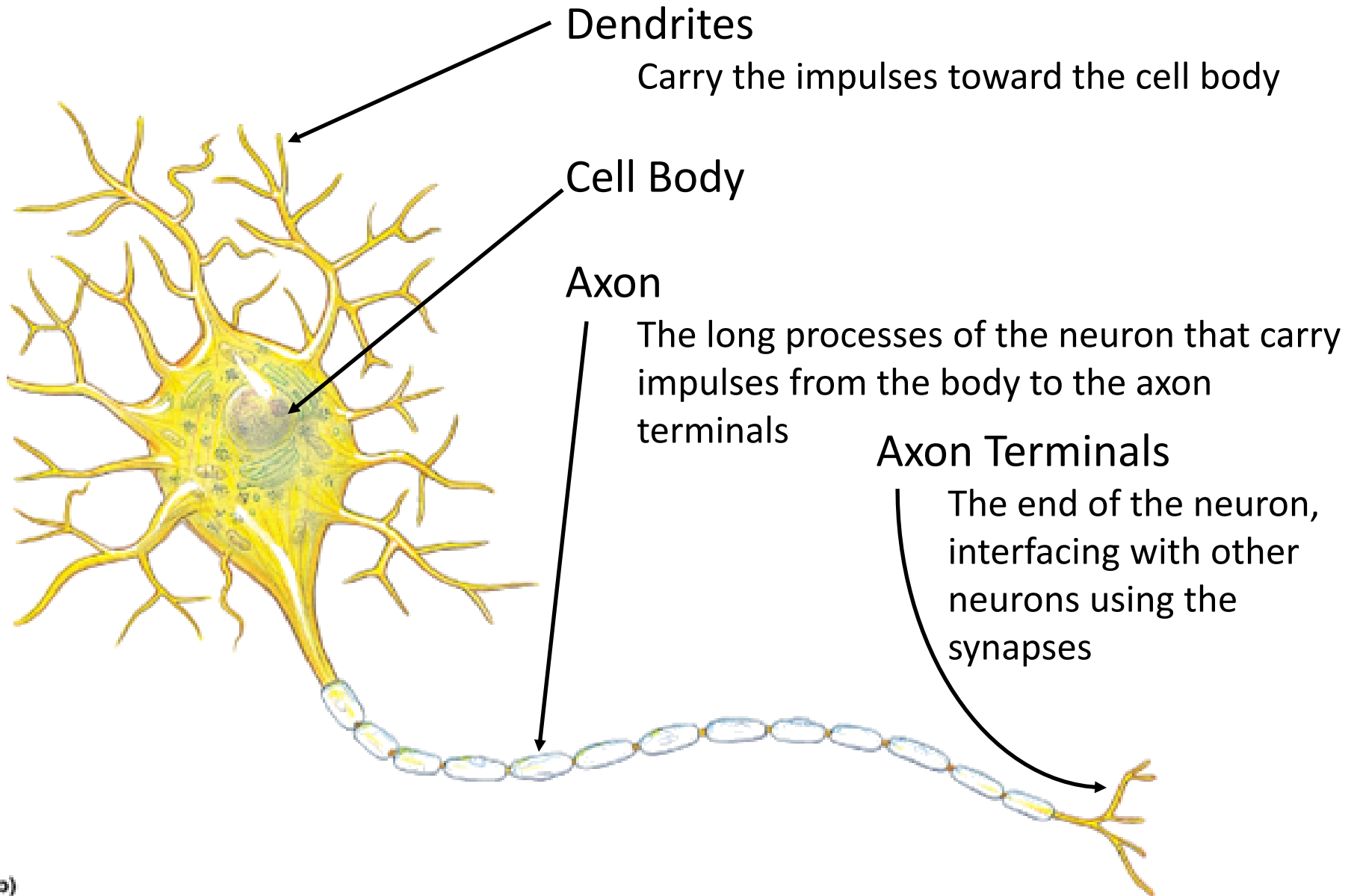
- Electrodes
- Connectors
- Microelectronics
- Bidirectional telemetry
- Hermetic packaging
- Biocompatible materials
- **target anatomy**
- **target function**

target anatomy drives the neural interface design

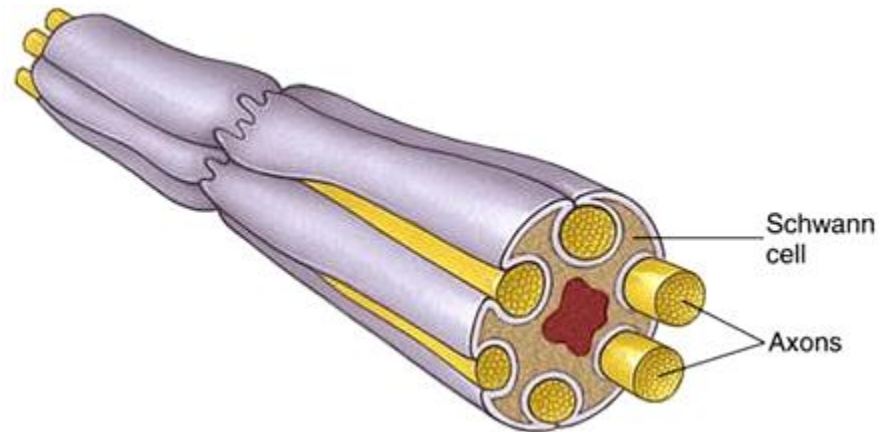
- one size/shape **does not** fit all targets
- **recording** versus **stimulation**
- different requirements for the **number of electrodes** and **data throughput**



Neuron

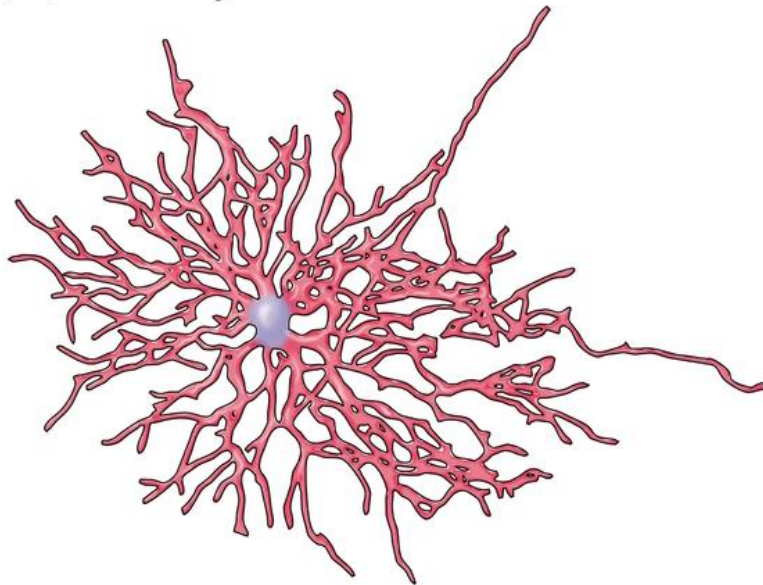


inside nerves: Schwann cells

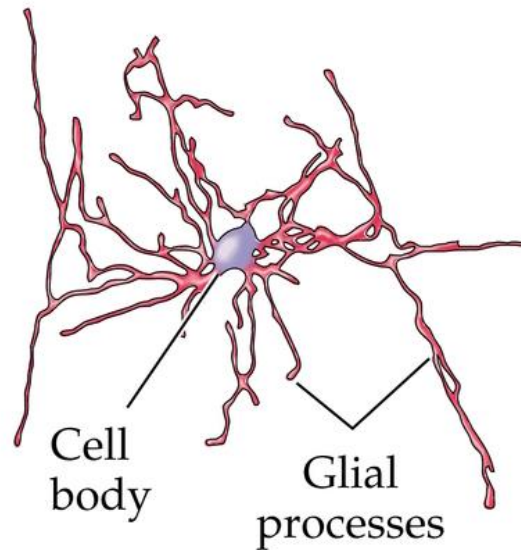


inside brain:

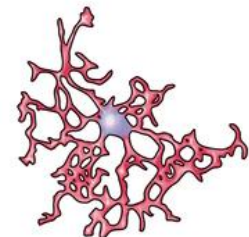
(A) Astrocyte



(B) Oligodendrocyte



(C) Microglial cell



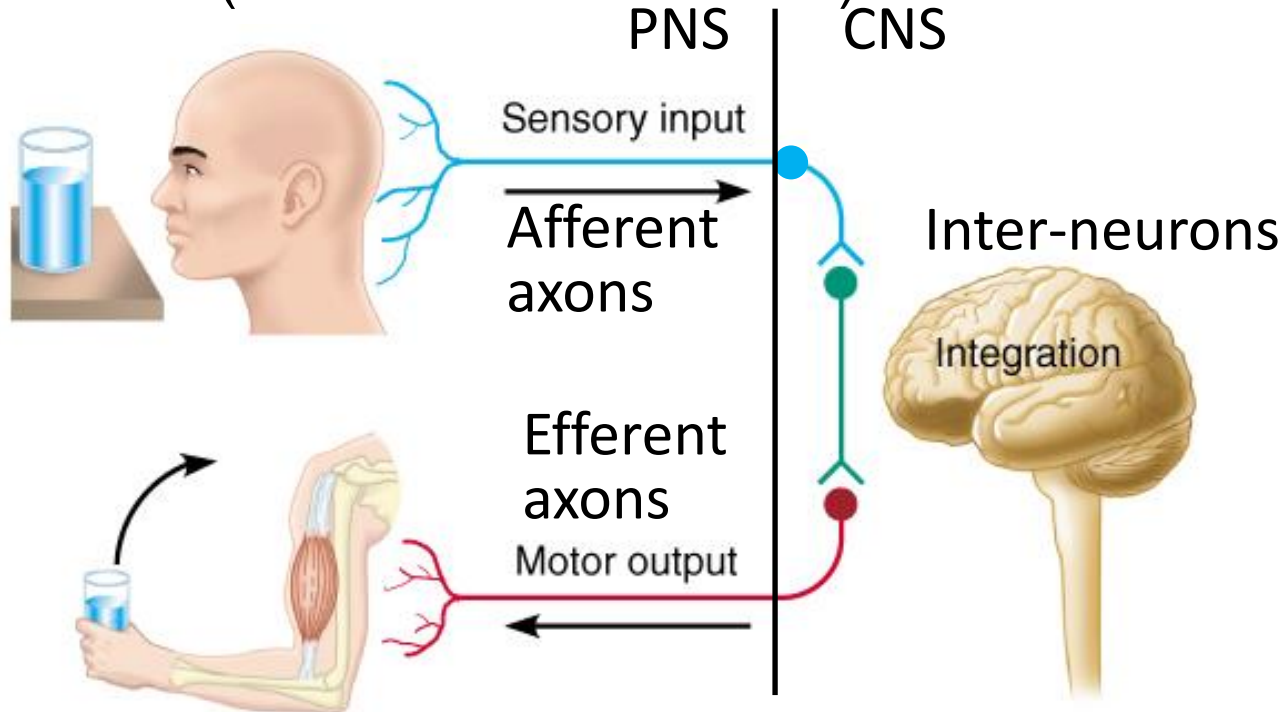
Nervous system subdivision

Central Nervous System (CNS)

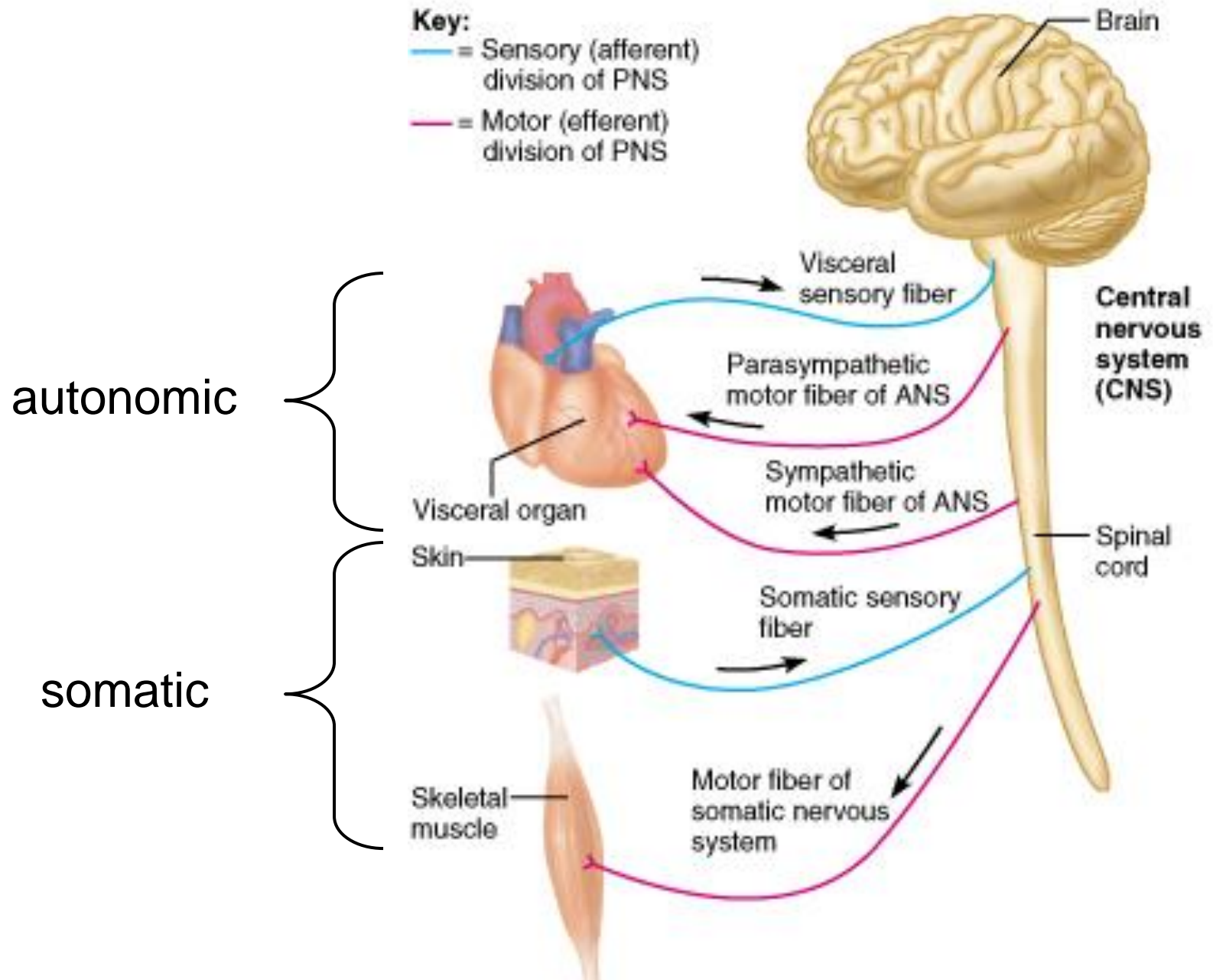
- Brain (cortex, brainstem, cerebellum)
- Spinal cord

Peripheral Nervous System (PNS)

- Afferent (sensory) axonal fibers
- Efferent (motor and autonomic) axonal fibers

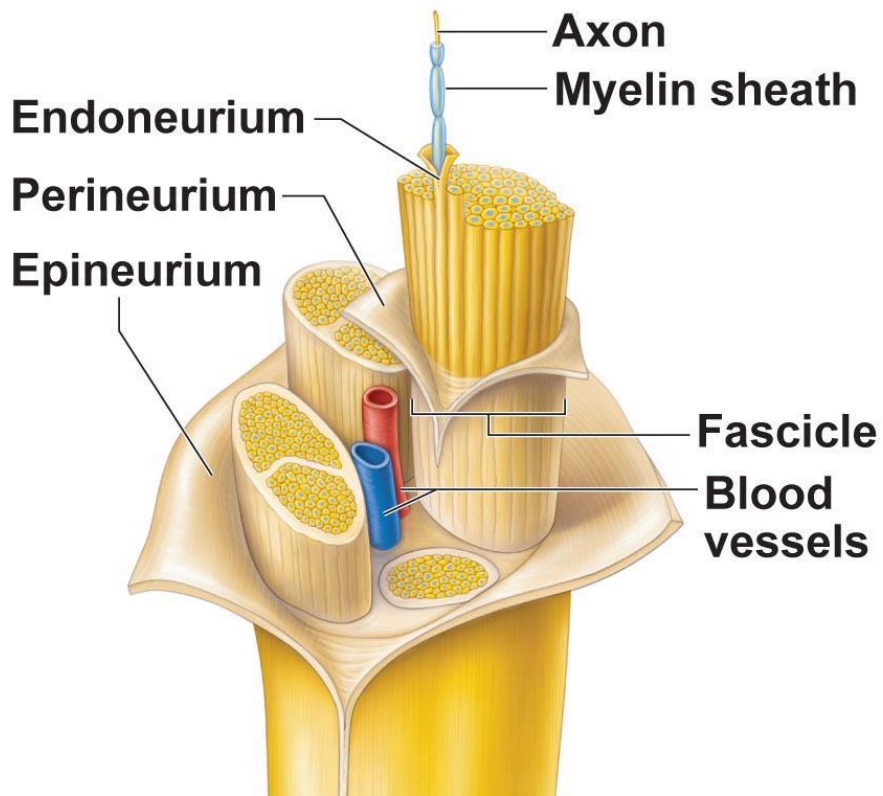


Peripheral Nervous System (PNS) subdivision

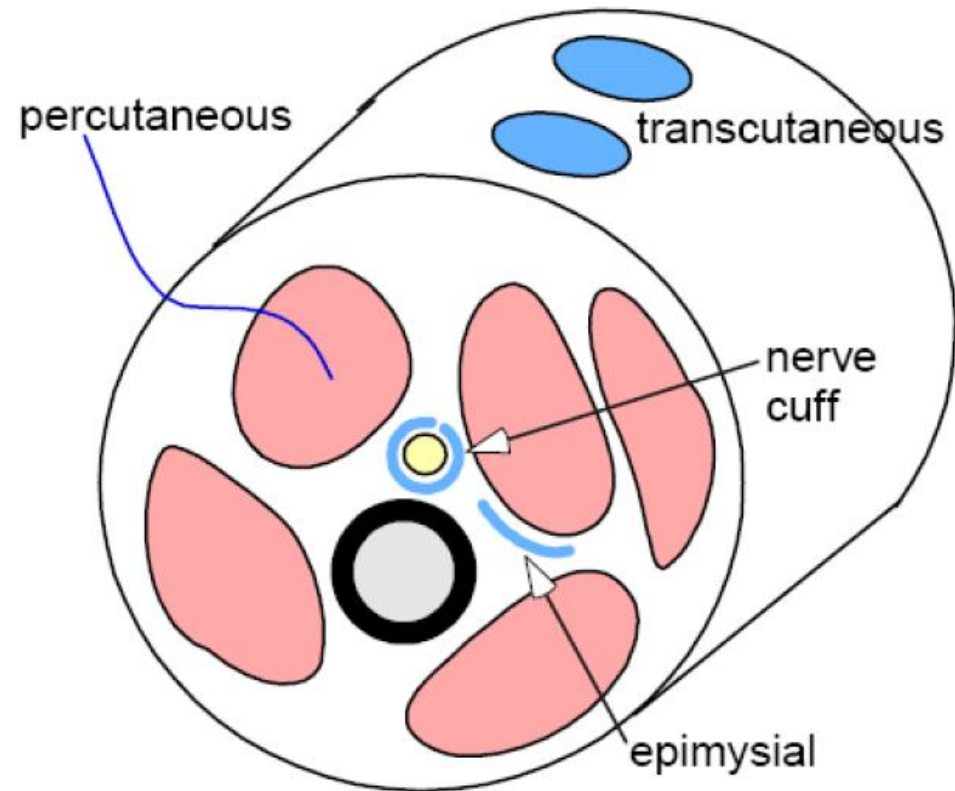


PNS: Nerve structure and nerve interfaces

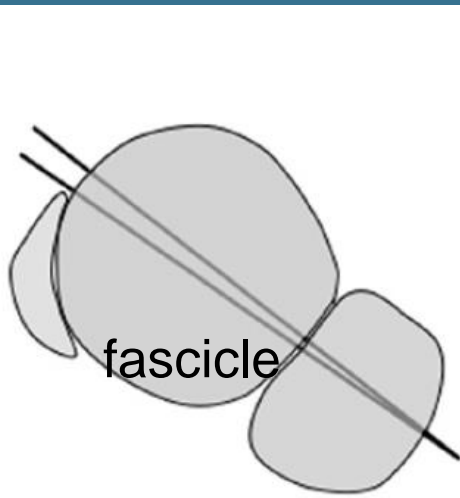
Multi-fascicular nerve



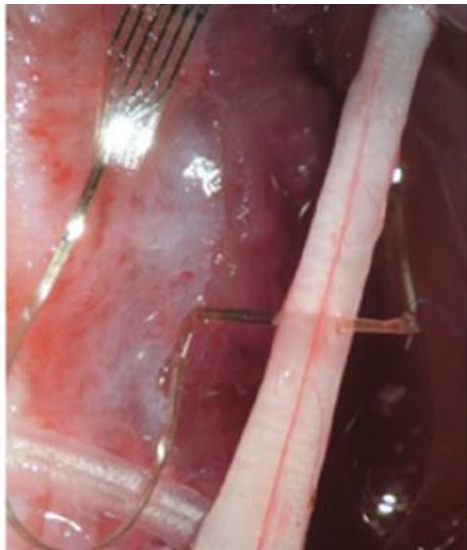
Nerve interfaces in the arm



Comparison of key nerve interfaces



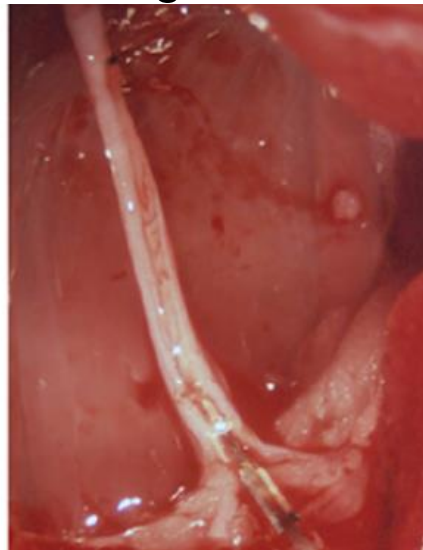
transverse



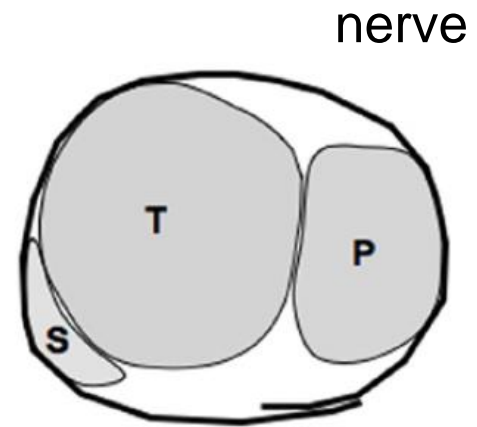
access to
multiple fascicles



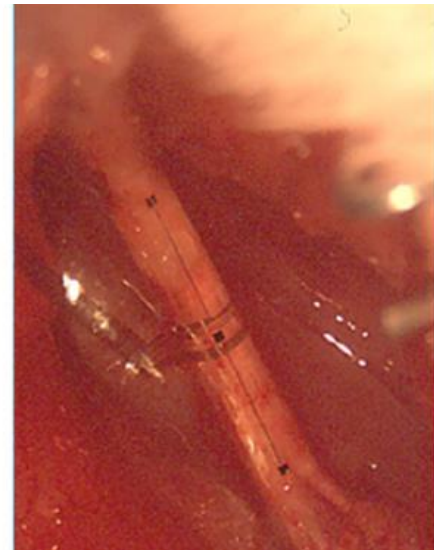
longitudinal



low stimulation
voltage



cuff

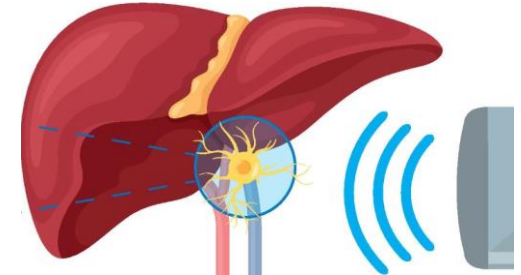


minimal nerve
trauma

Key components of the nerve interface

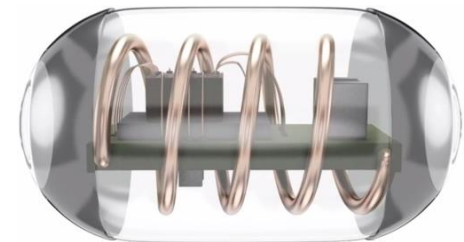
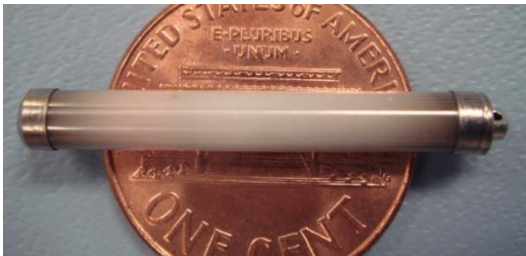
Front-end:

- electrical/optical/ultrasound electrodes for nerve recording/stim
- coatings to reduce impedance



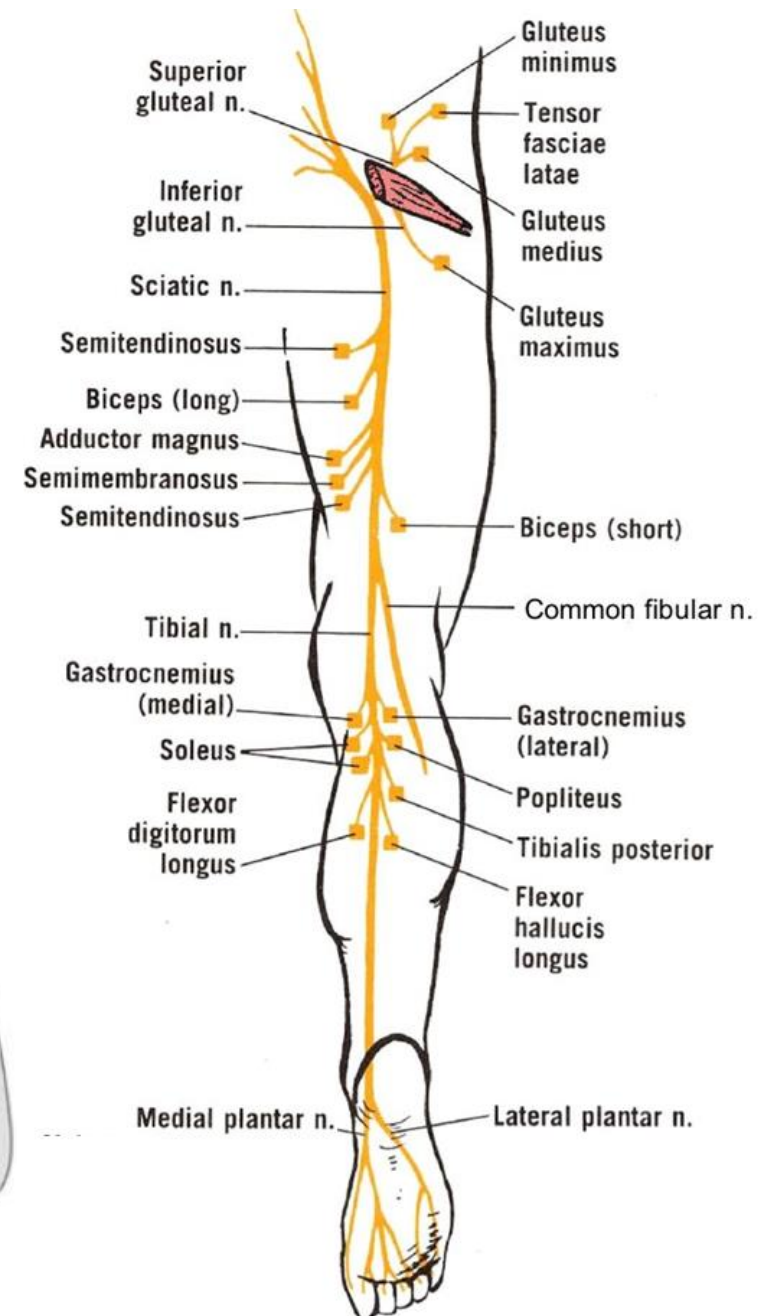
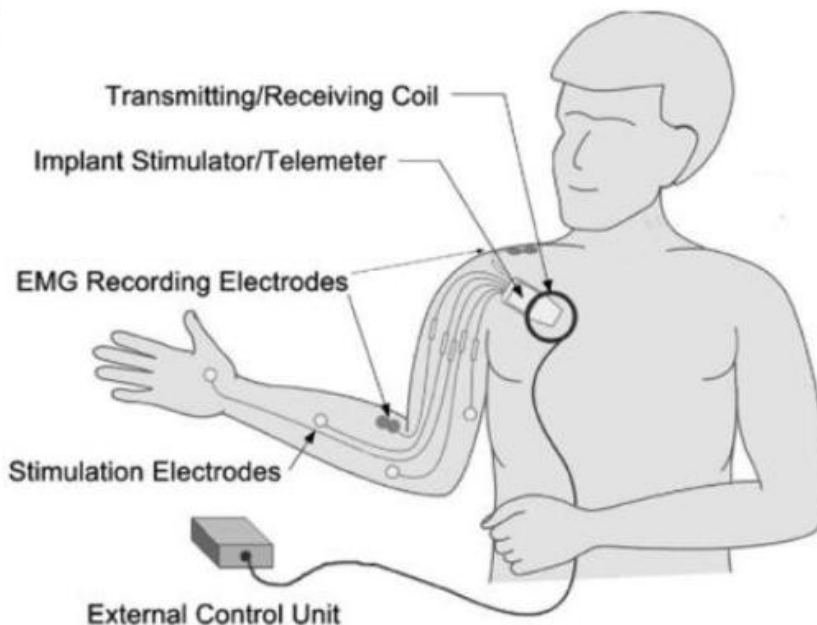
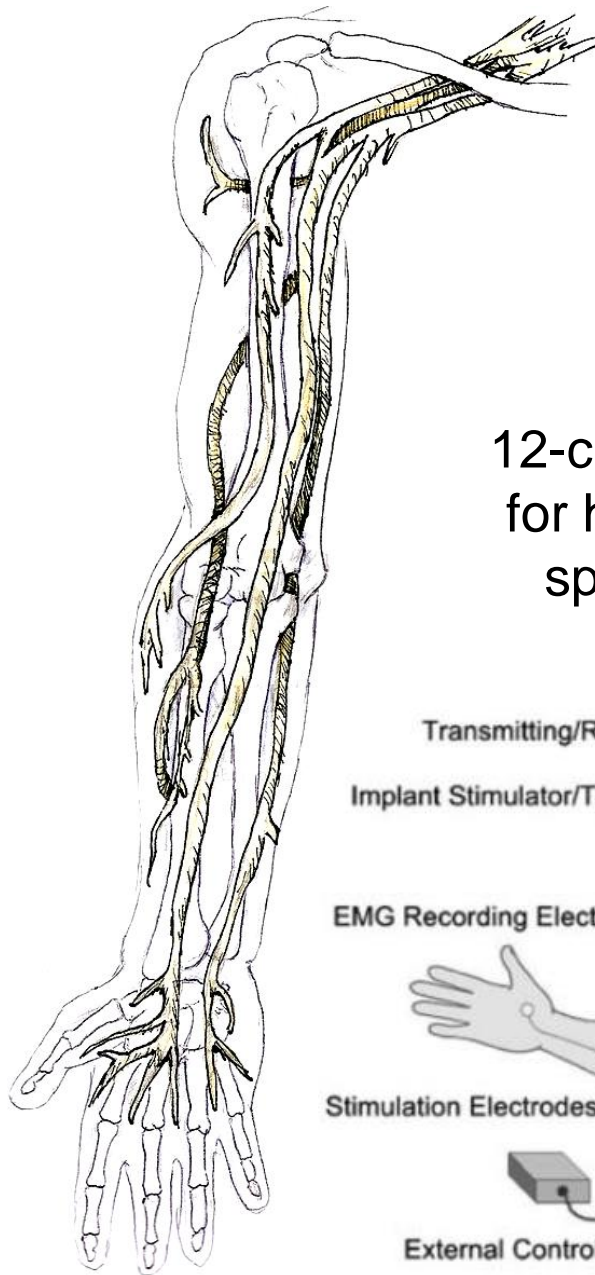
Back-end:

- Data and power telemetry
- Low-noise ($<1\ \mu\text{V}$), low-power amplifiers
- Signal processing and artifact suppression
- Miniature hermetic packaging

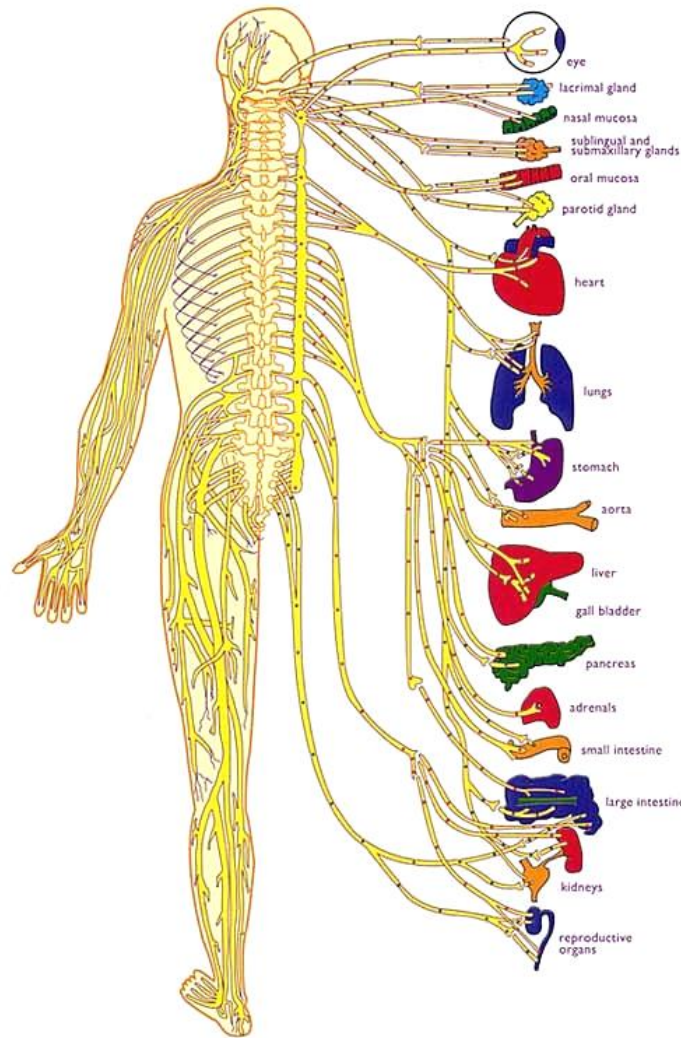


Clinical applications of somatic nerve interfaces

12-channel stimulator
for hand paralysis in
spinal cord injury



Future clinical applications of autonomic nerves



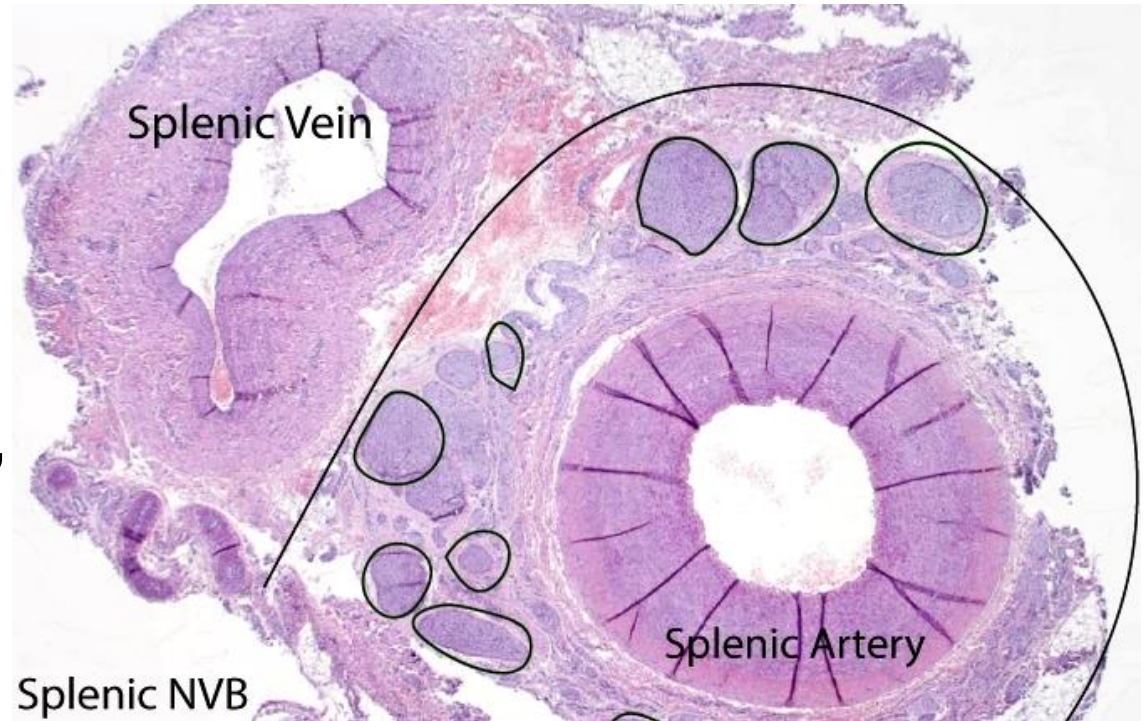
- eye: dry eye, macular degeneration, glaucoma
- tongue: obstructive sleep apnea
- carotid sinus in the neck: type 2 diabetes
- thyroid gland: hypothyroid syndrome, osteoporosis
- lungs: asthma, COPD, long COVID
- GI tract: IBD, IBS, gastroparesis, fecal incontinence
- pancreas: type 1 diabetes
- heart: heart failure, arrhythmia
- blood vessels: hypertension
- spleen: rheumatoid arthritis, lupus
- adrenal gland: psychosis, asthma, hypertension
- kidney: chronic kidney disease, central sleep apnea
- bladder: incontinence
- ovary: polycystic ovarian syndrome

by 2033, expected to treat 2 billion patients, 25% of people

Challenges in developing autonomic nerve interfaces

Surgical challenges:

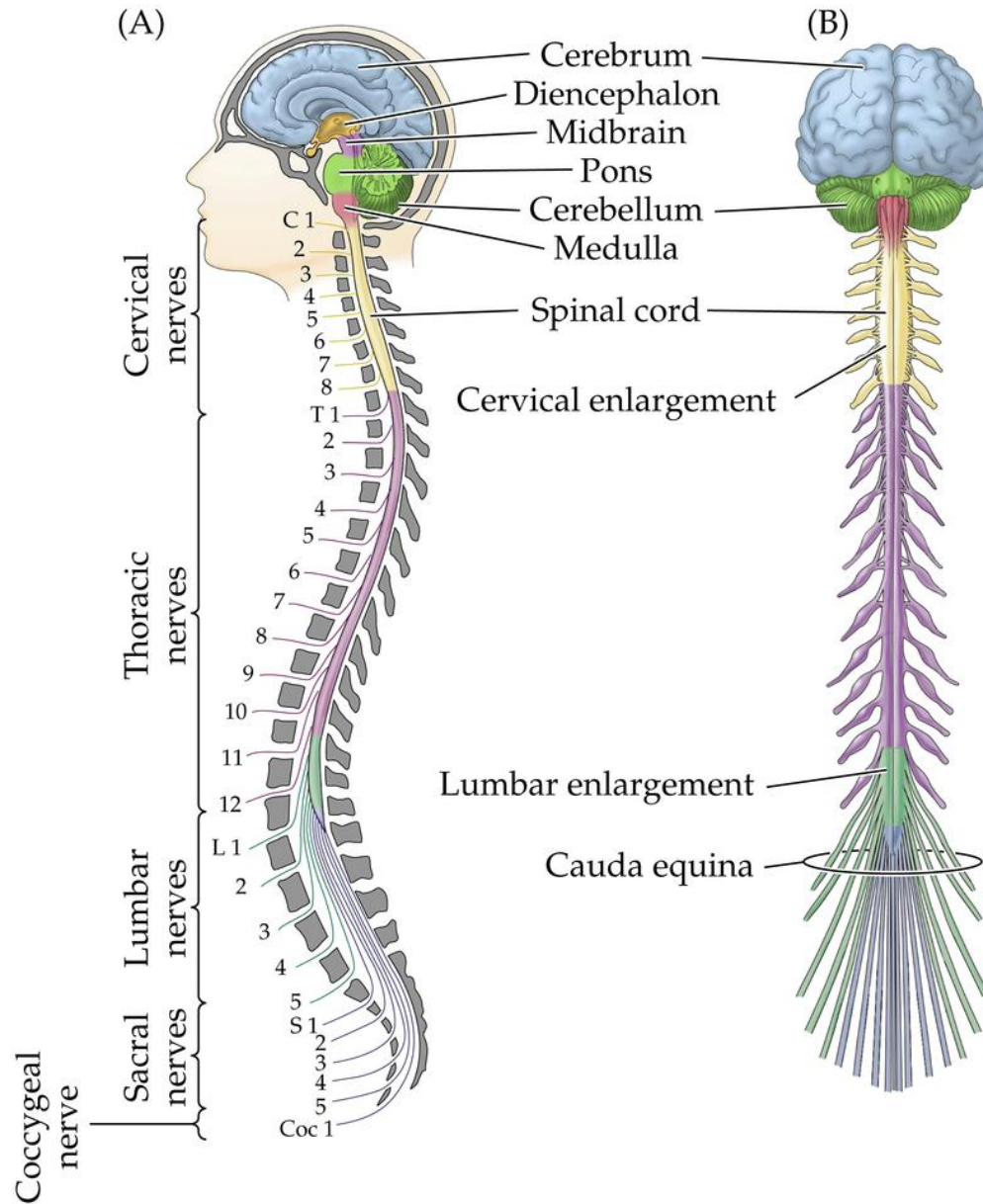
- small transparent nerves are difficult to visualize
- nerves are buried inside vessel walls, ligaments, or adipose tissue



Technical challenges:

- nerve cuff requires soft materials to avoid compression
- difficult to stimulate, as majority of axons are unmyelinated
- Difficult to record, as nerve is surrounded by electrically-noisy organs, e.g. heart, lungs, intestines, and bladder

CNS subdivision

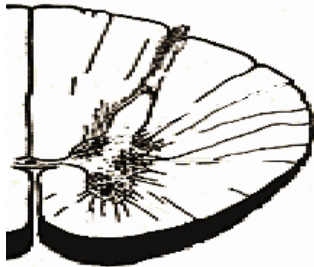


Spinal segments have different functions

Spinal level - Motor Functions



Low cervical - Movement of arms and hands



Mid-thoracic - Respiration



Low lumbar - Movement of legs



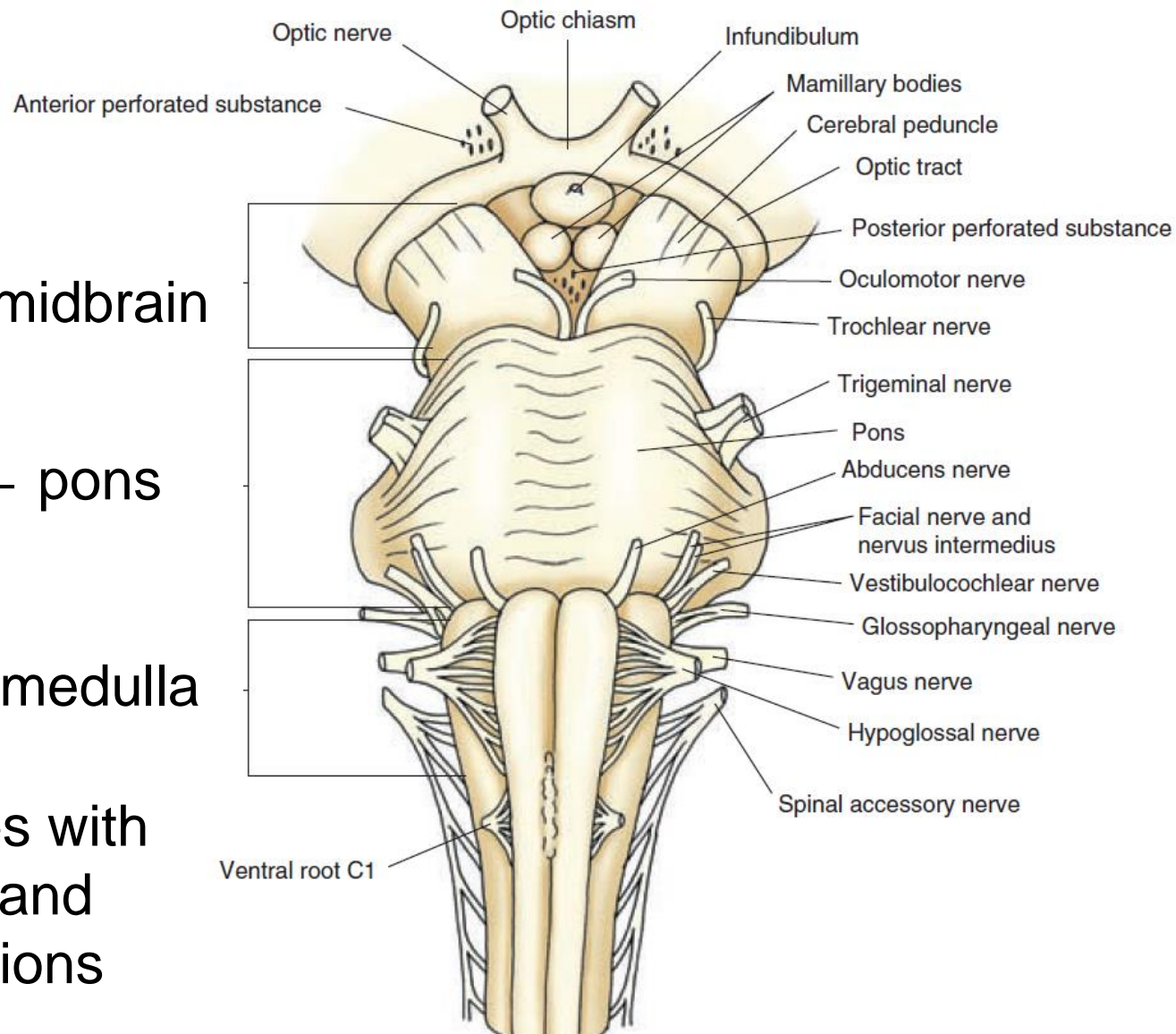
**Sacral - Bladder voiding, Bowel emptying,
and Sexual function**

Brainstem has many functions

Brainstem has:

- 3 major parts
 - midbrain
 - pons
 - medulla

- 12 cranial nerves with sensory, motor, and autonomic functions



Cranial nerves and nuclei: anatomy

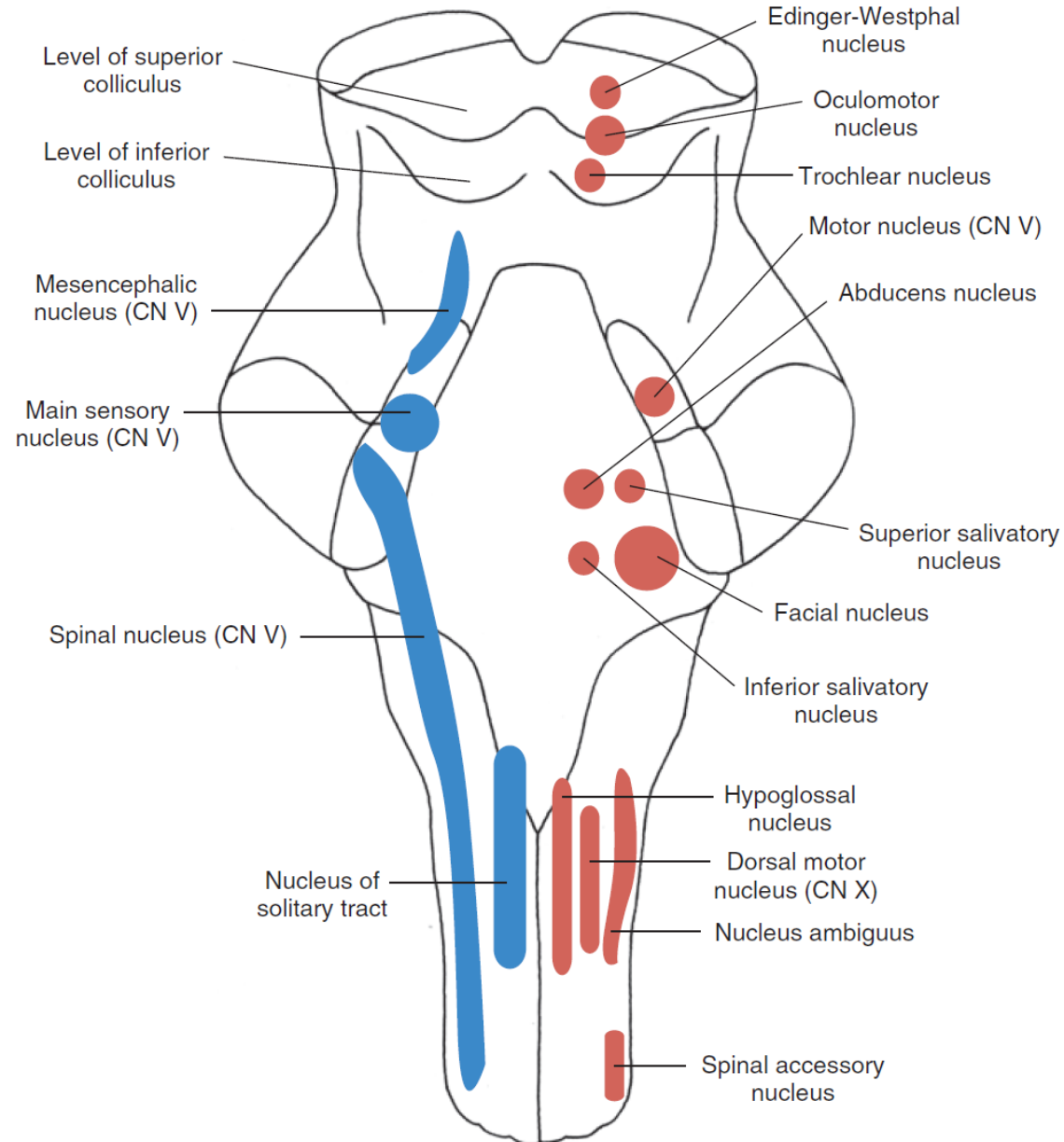
Sensory only:
olfactory (I), optic (II)

Mixed (motor/autonomic):
oculomotor (III)

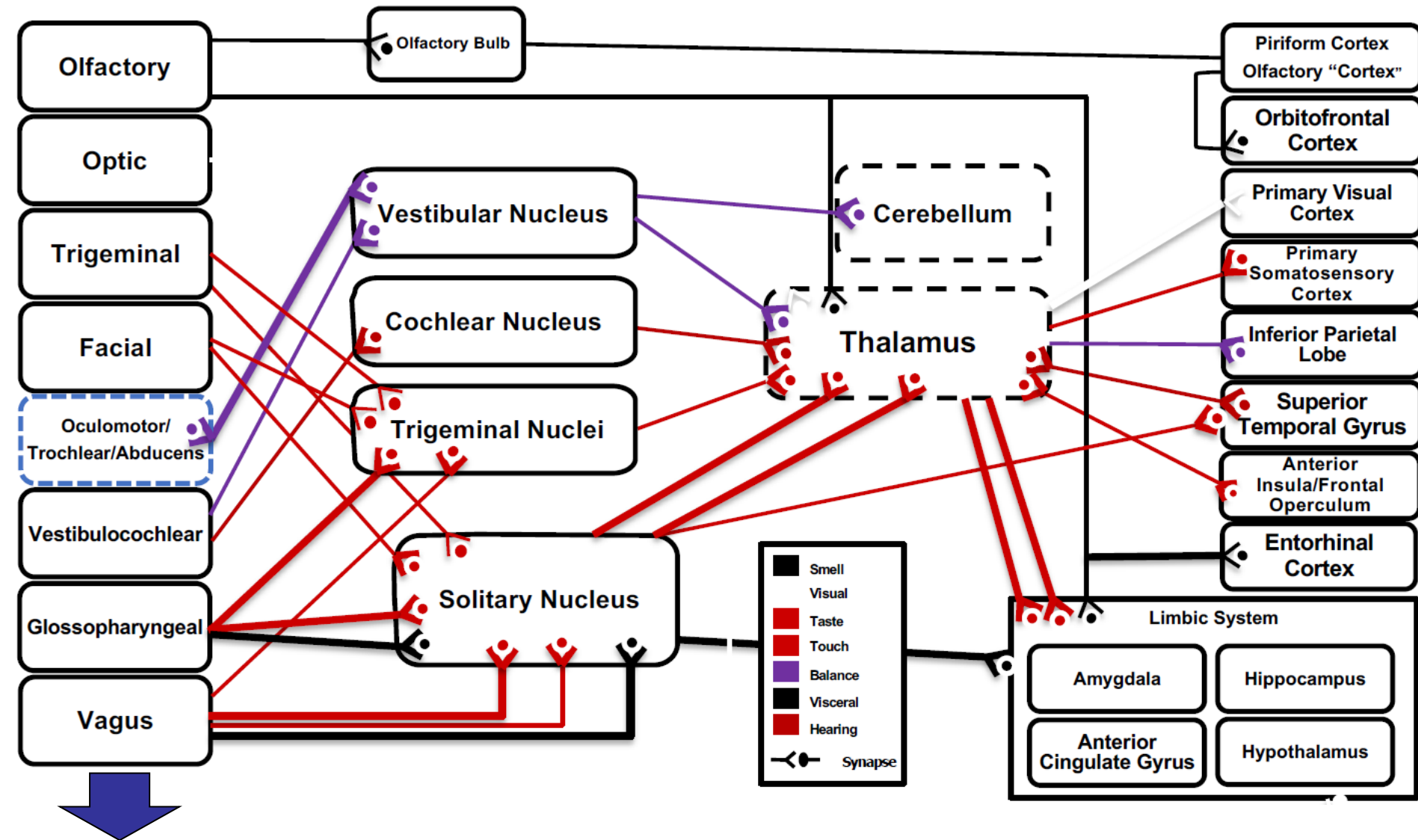
Mixed (sensory/motor):
trigeminal (V)

**Mixed (sensory/motor/
autonomic):**
glossopharyngeal (IX)

Motor only:
hypoglossal (XII)

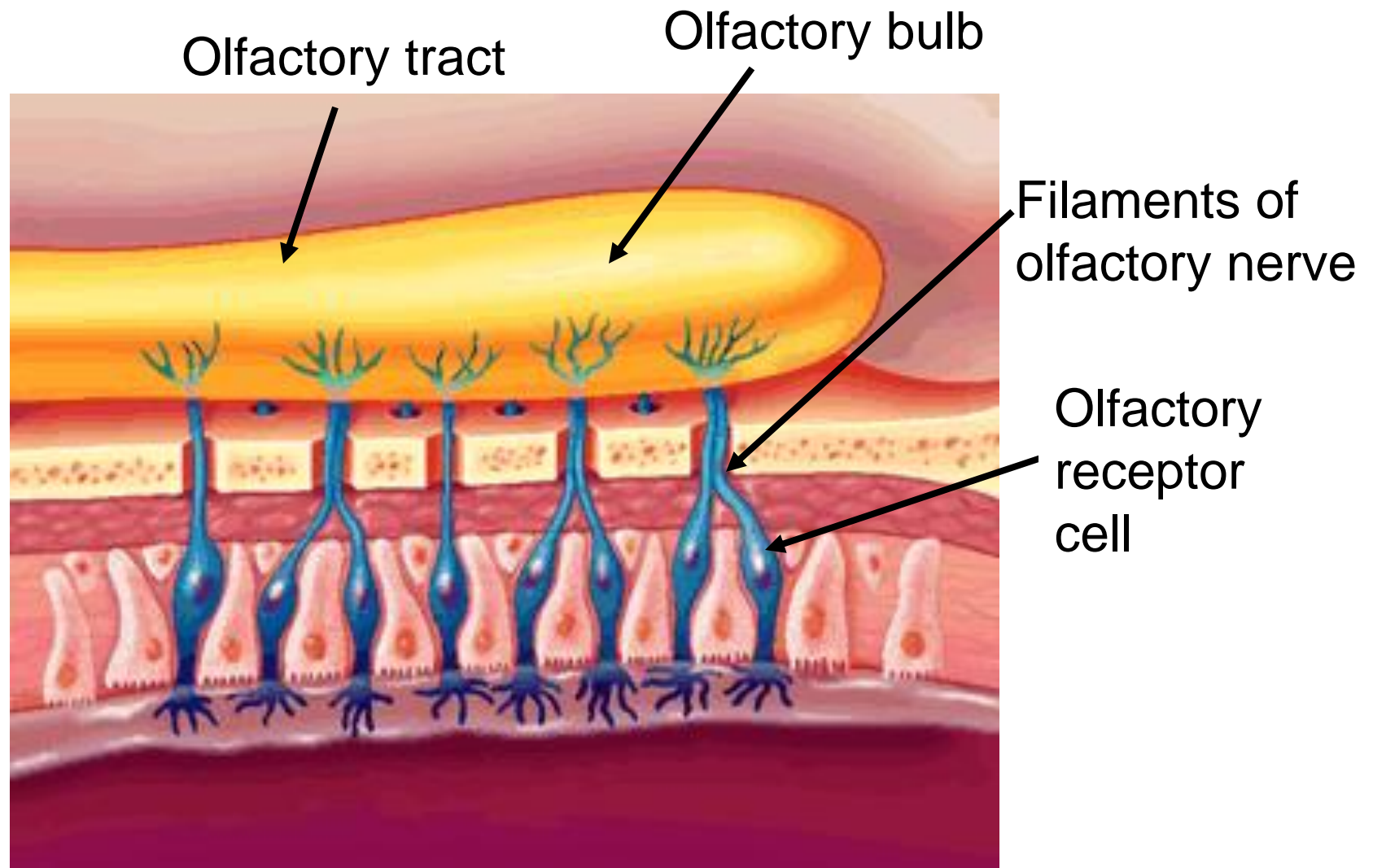


Cranial nerves and nuclei function as a gateway to the brain

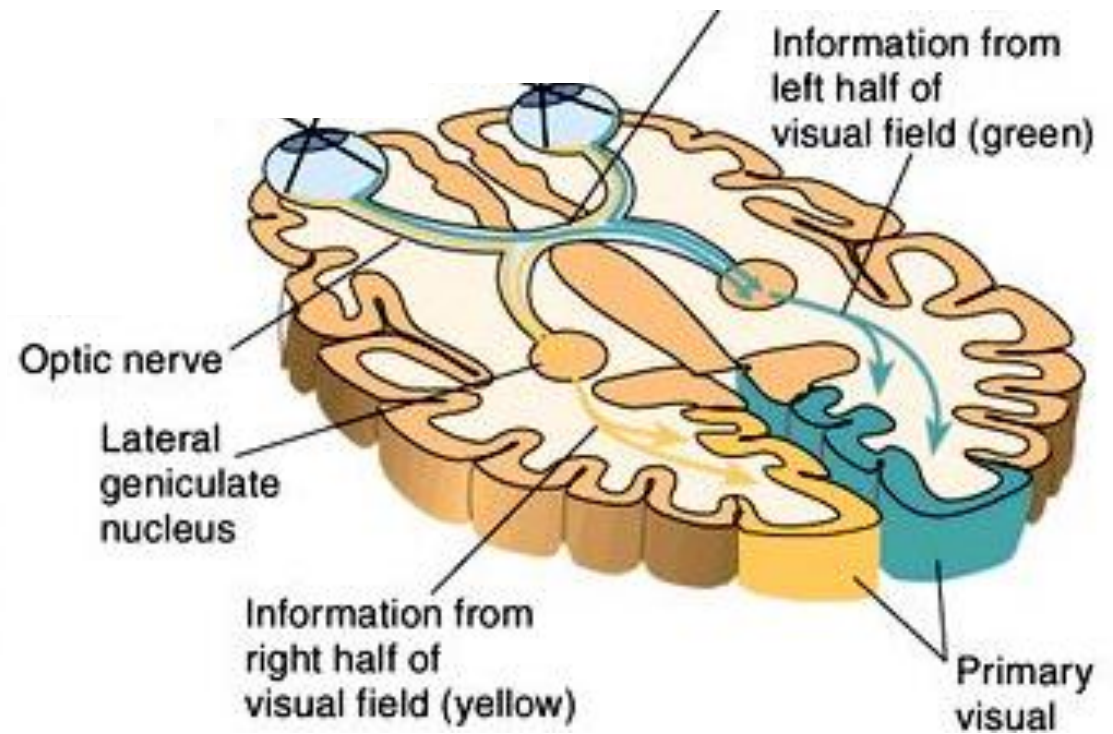
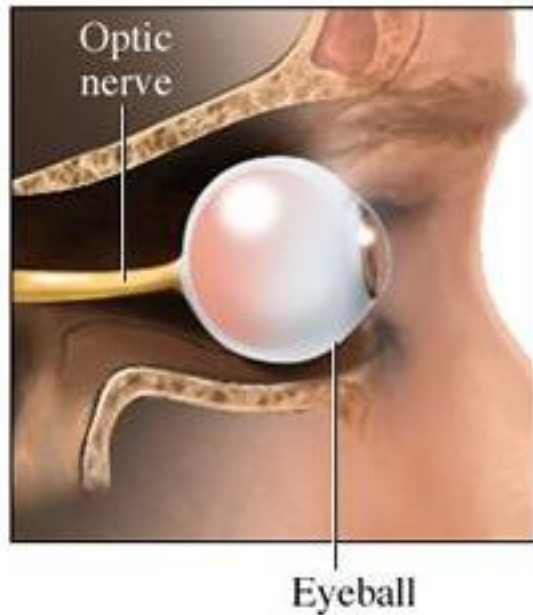


sensory organs, muscles, internal organs

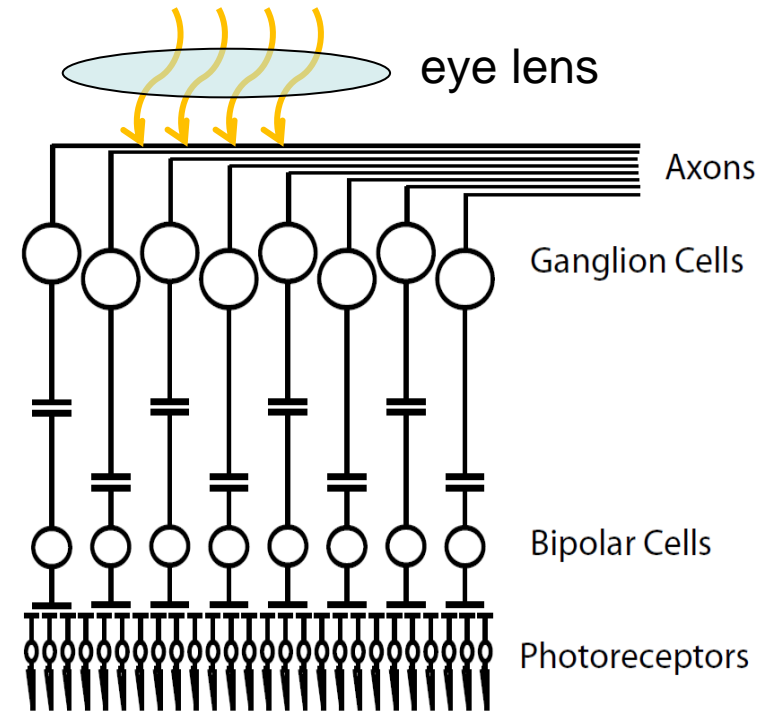
Olfactory nerve: sense of smell



Optic nerve: vision

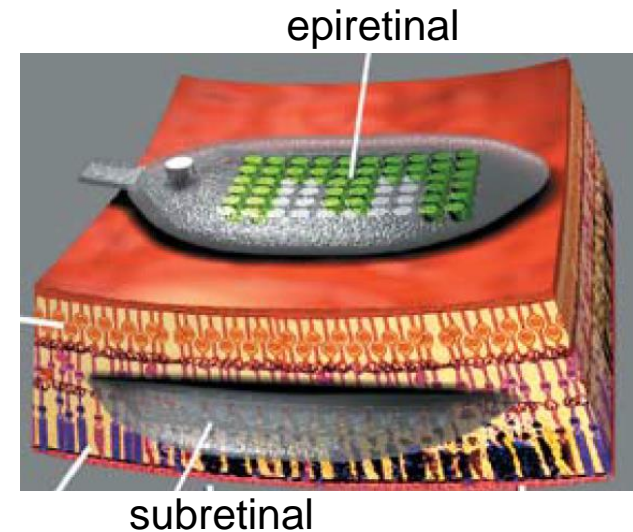


Retinal implants

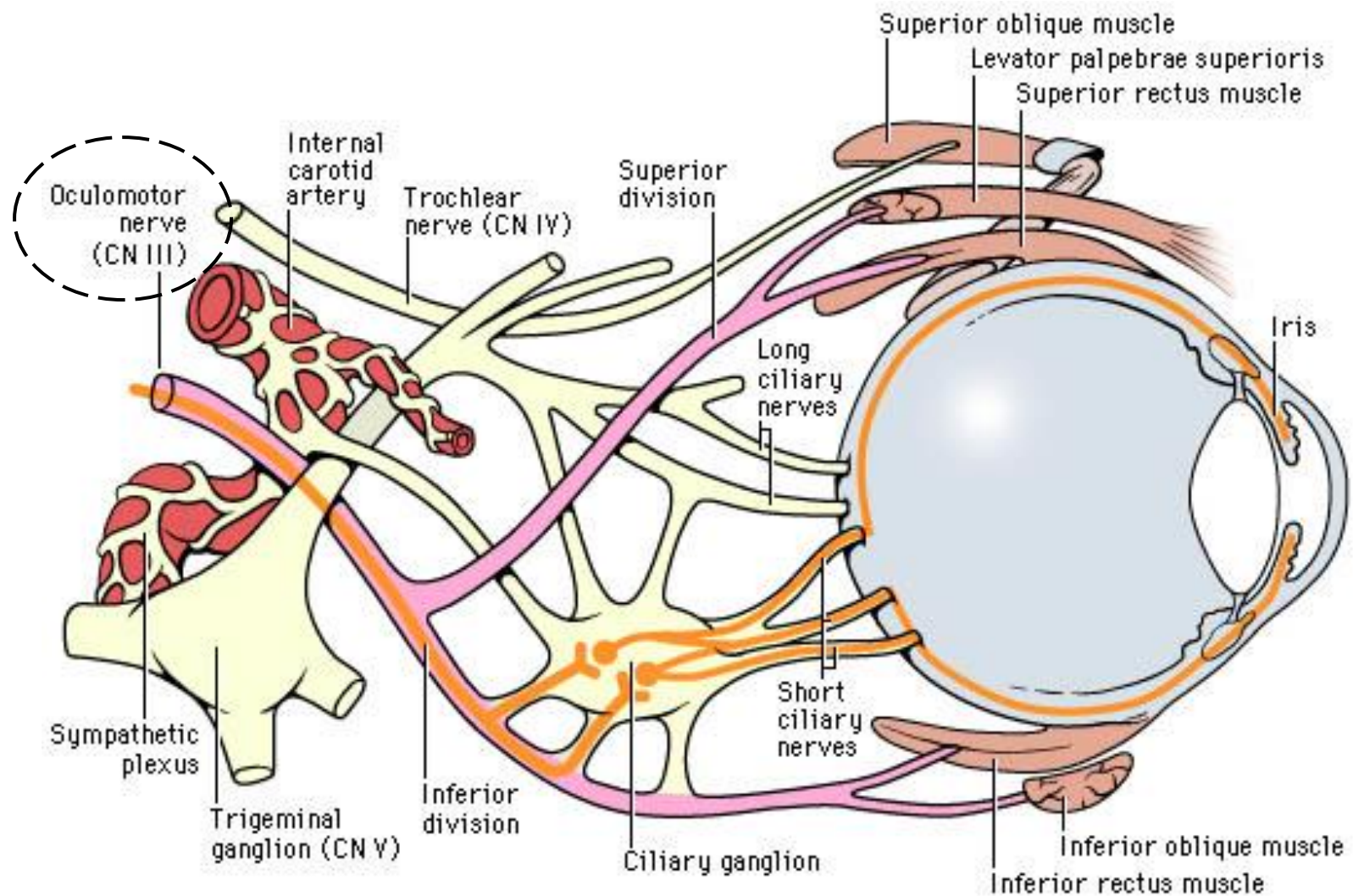


Surgical placement in the eye:

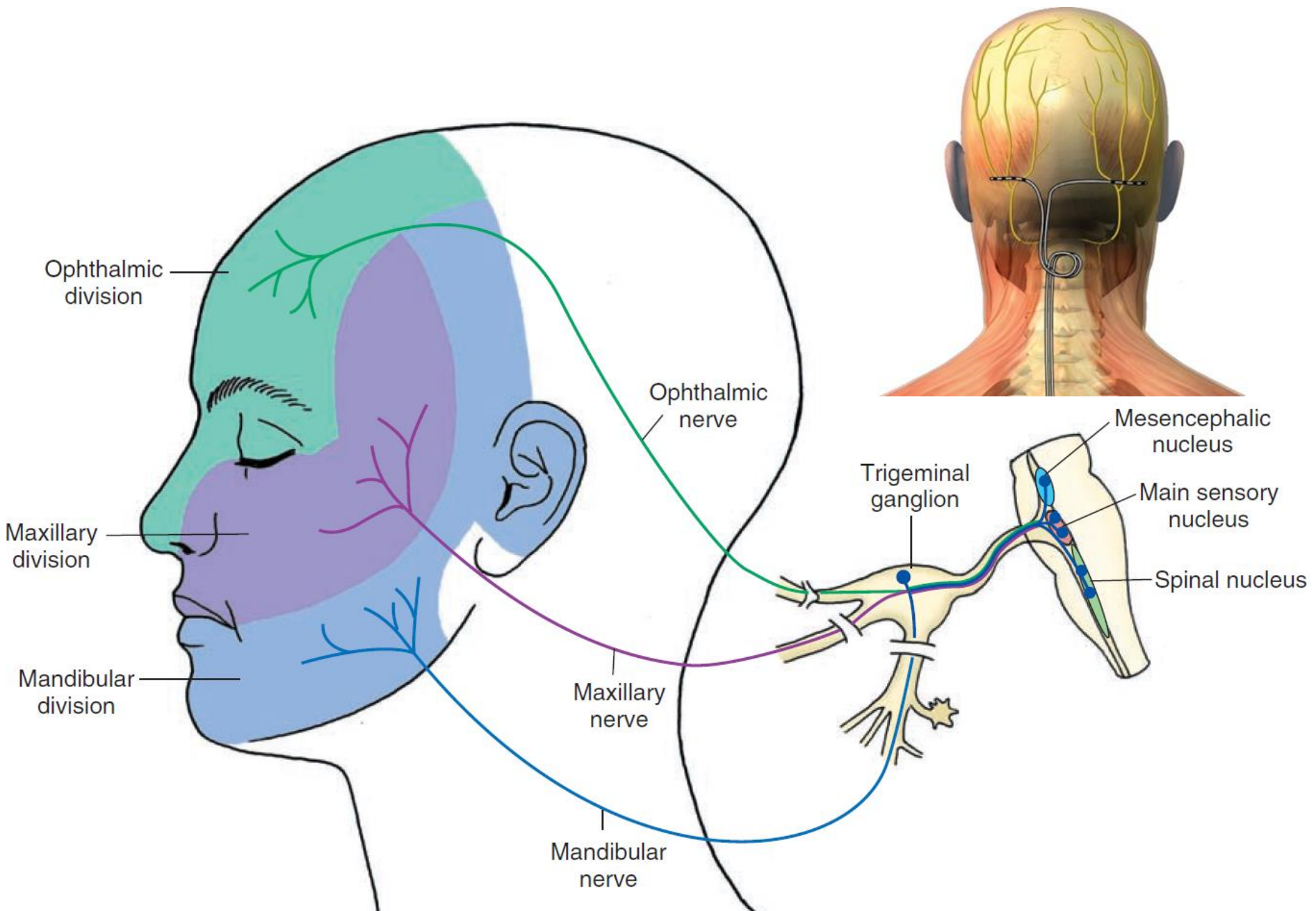
- epiretinal (attached with tacks)
- subretinal



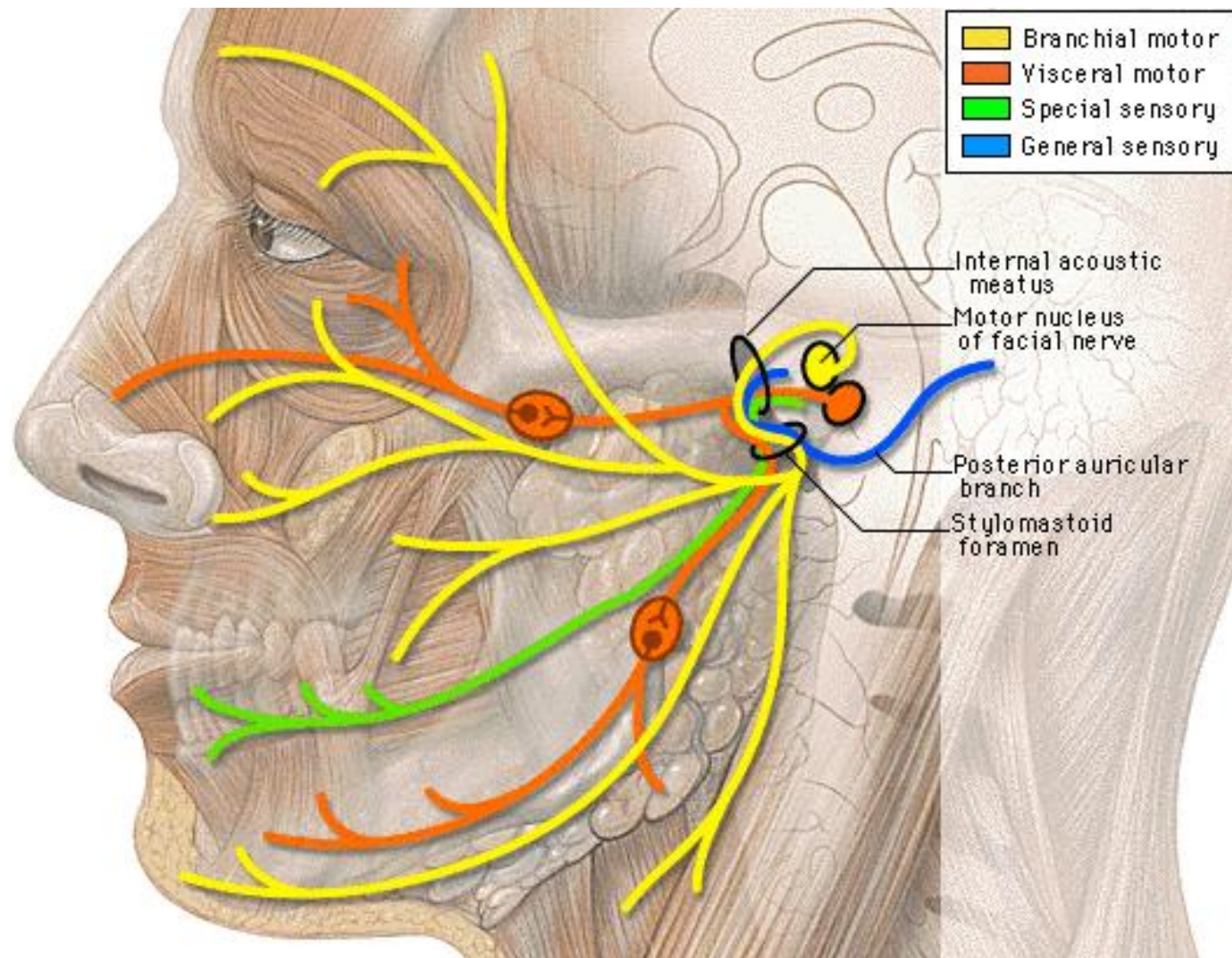
Oculomotor nerve: movement of eye muscles



Trigeminal and occipital nerves: sensory input from the head

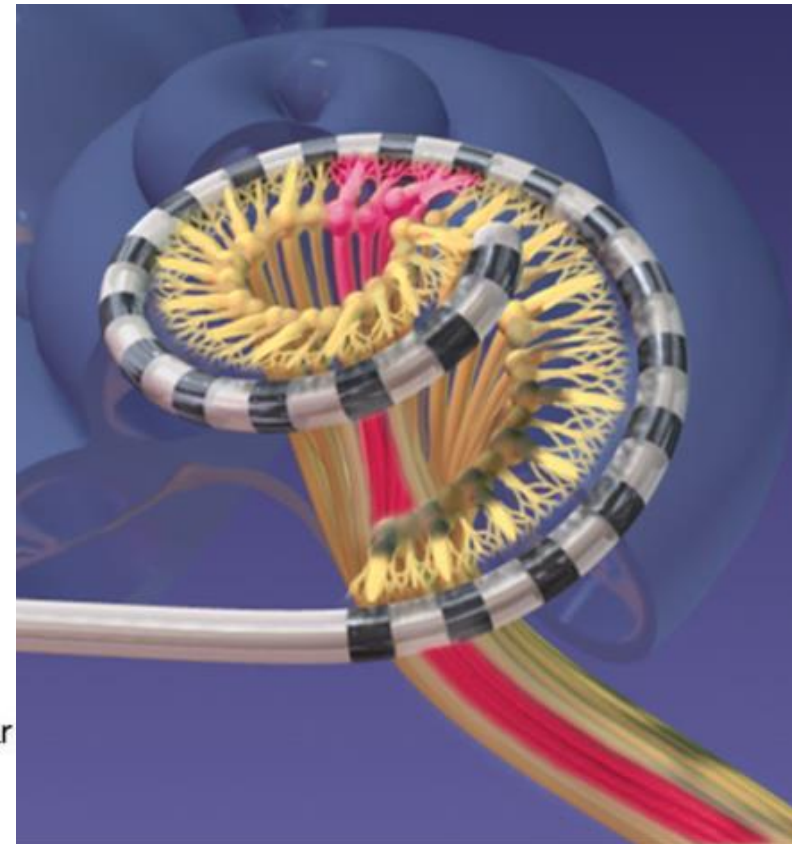
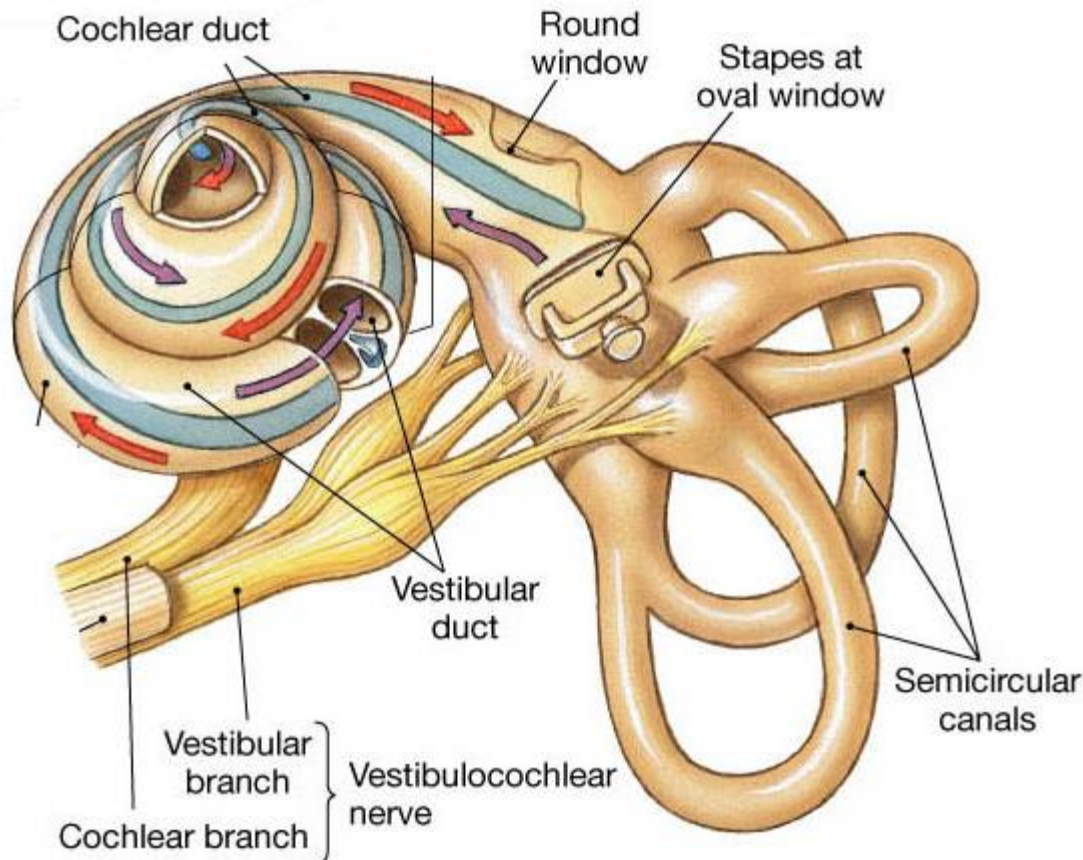


Facial nerve: control of facial expressions



Vestibulocochlear nerve: hearing and balance

- Speech perception can be restored with 10-20 electrodes stimulating 30,000 axons in the cochlear nerve (no need for selective stimulation of every axon)
- Better hearing restoration soon after hearing loss



Vagus nerve: parasympathetic control of nearly all internal organs



- eye: dry eye, macular degeneration, glaucoma
- tongue: obstructive sleep apnea
- carotid sinus in the neck: type 2 diabetes
- thyroid gland: hypothyroid syndrome, osteoporosis
- lungs: asthma, COPD, long COVID
- GI tract: IBD, IBS, gastroparesis, fecal incontinence
- pancreas: type 1 diabetes
- heart: heart failure, arrhythmia
- blood vessels: hypertension
- spleen: rheumatoid arthritis, lupus
- adrenal gland: psychosis, asthma, hypertension
- kidney: chronic kidney disease, central sleep apnea
- bladder: incontinence
- ovary: polycystic ovarian syndrome

by 2033, expected to treat 2 billion patients, 25% of people

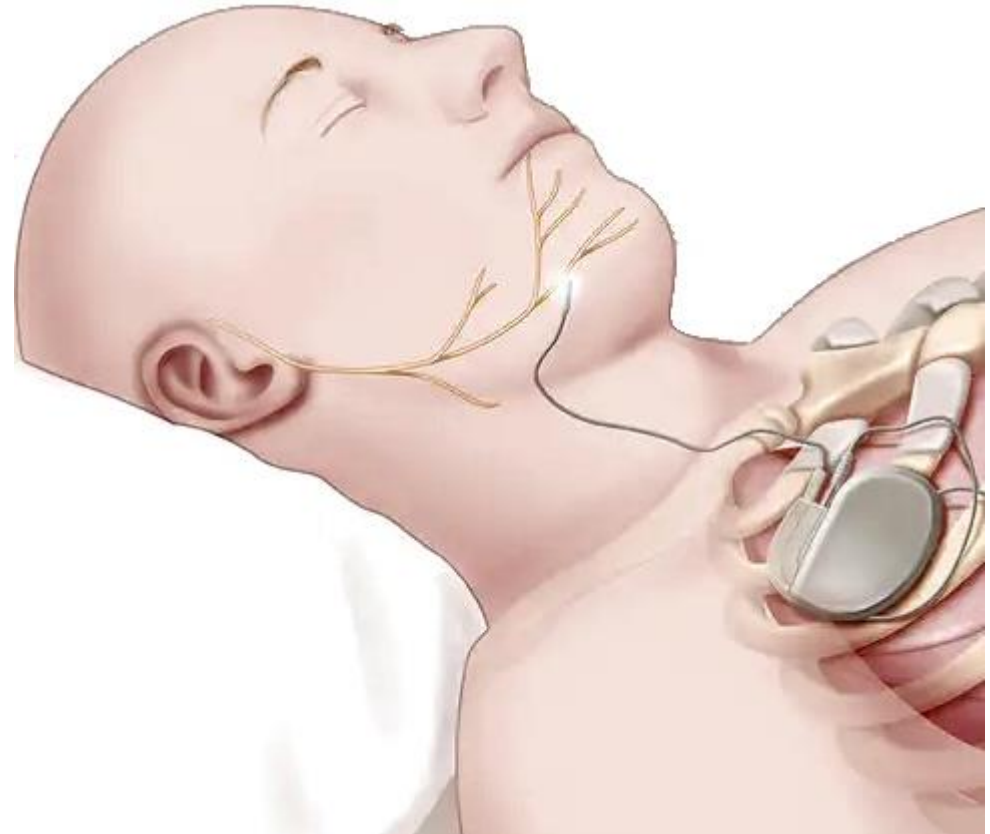
Hypoglossal nerve: tongue contraction for obstructive sleep apnea

“Apnea” = “without breath”

Tongue muscle relaxes during sleep and falls back, obstructing the airway

During each episode of hypoxia (lack of oxygen) neurons in the brain die

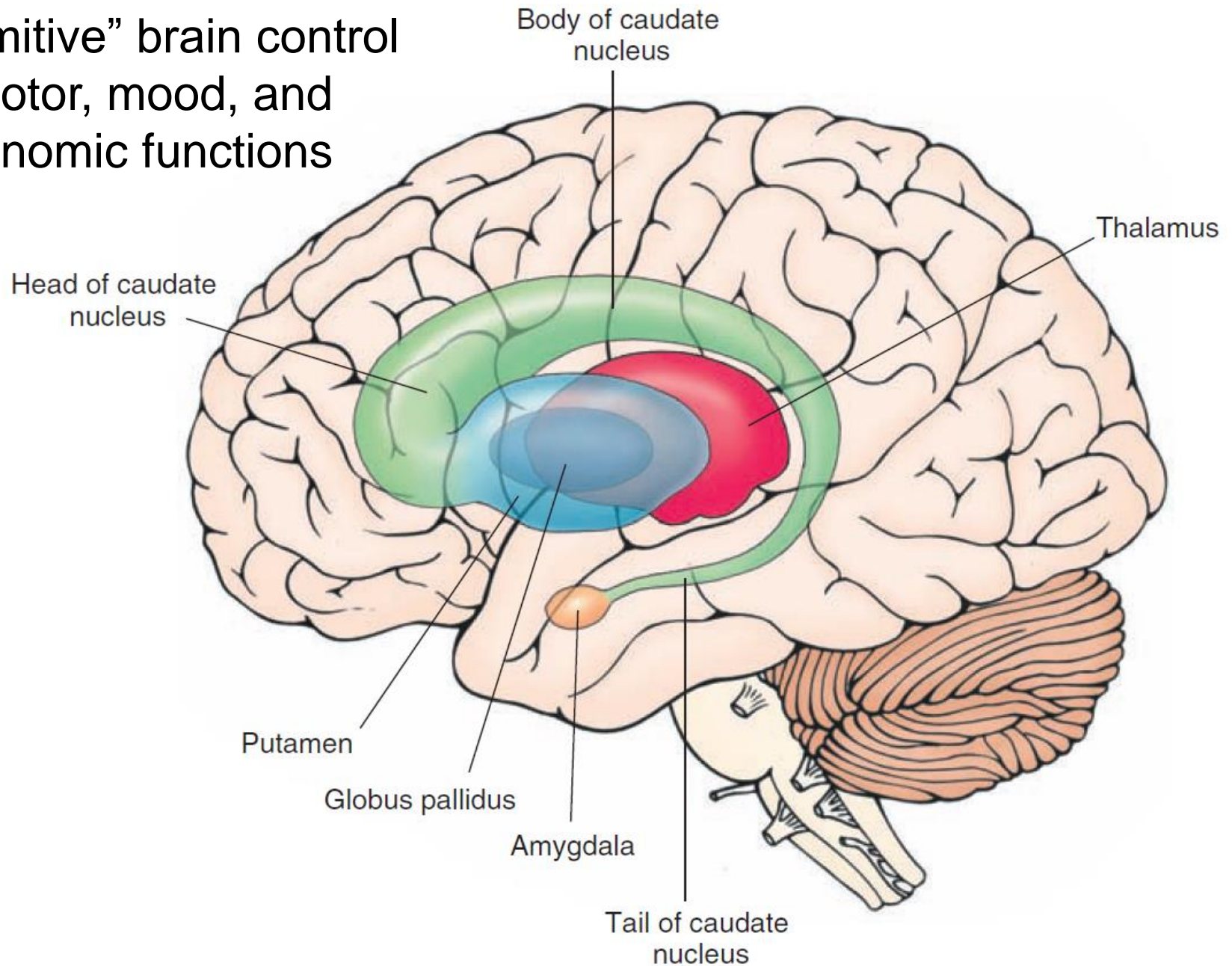
Over time, this can lead to dementia and Alzheimer's disease



In the US, 5% have diagnosed OSA, 30% – undiagnosed

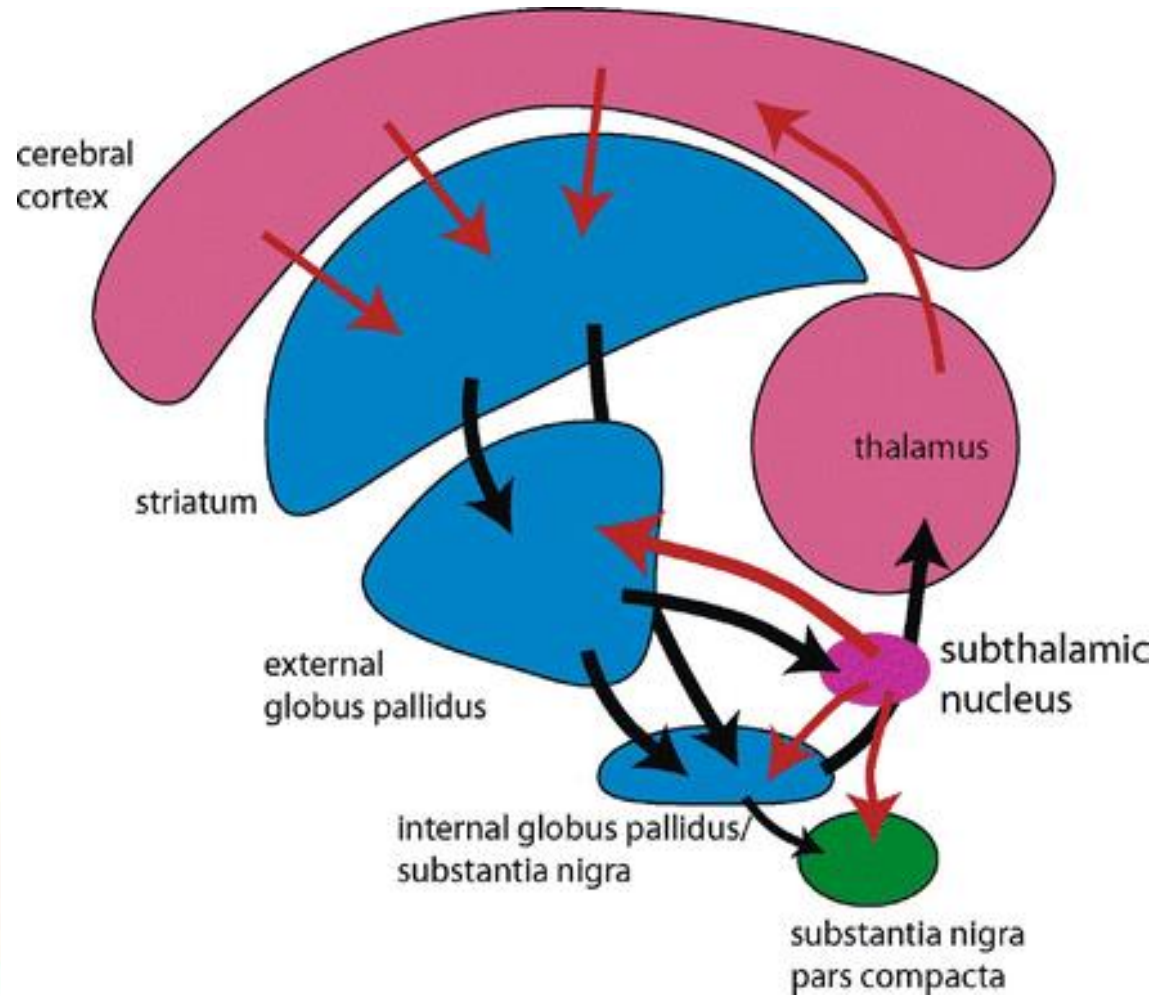
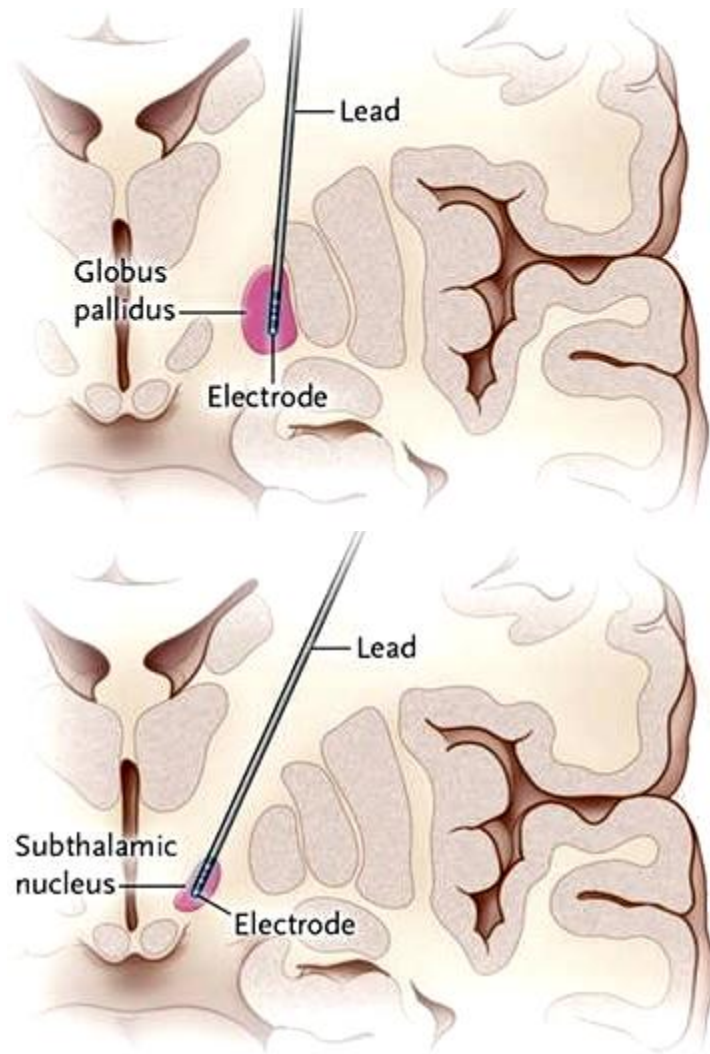
Thalamus + basal ganglia (caudate nucleus, putamen, globus pallidus)

“Primitive” brain control
of motor, mood, and
autonomic functions



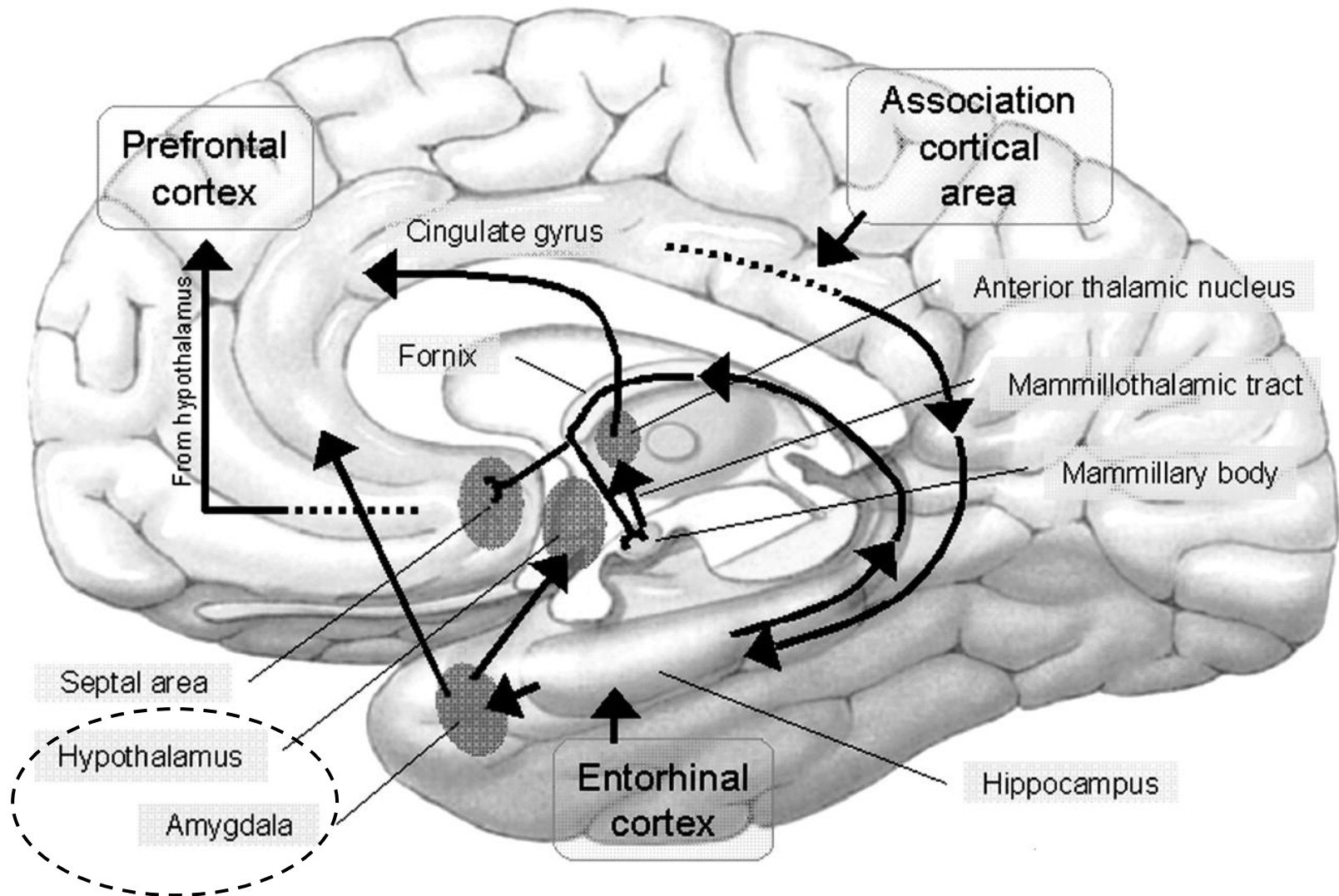
Restoring motor and mood control with deep brain stimulation

High-frequency stimulation (150 Hz) of globus pallidus or subthalamic nucleus can reducing tremor in Parkinson's disease and essential tremor patients (7 million in the US)



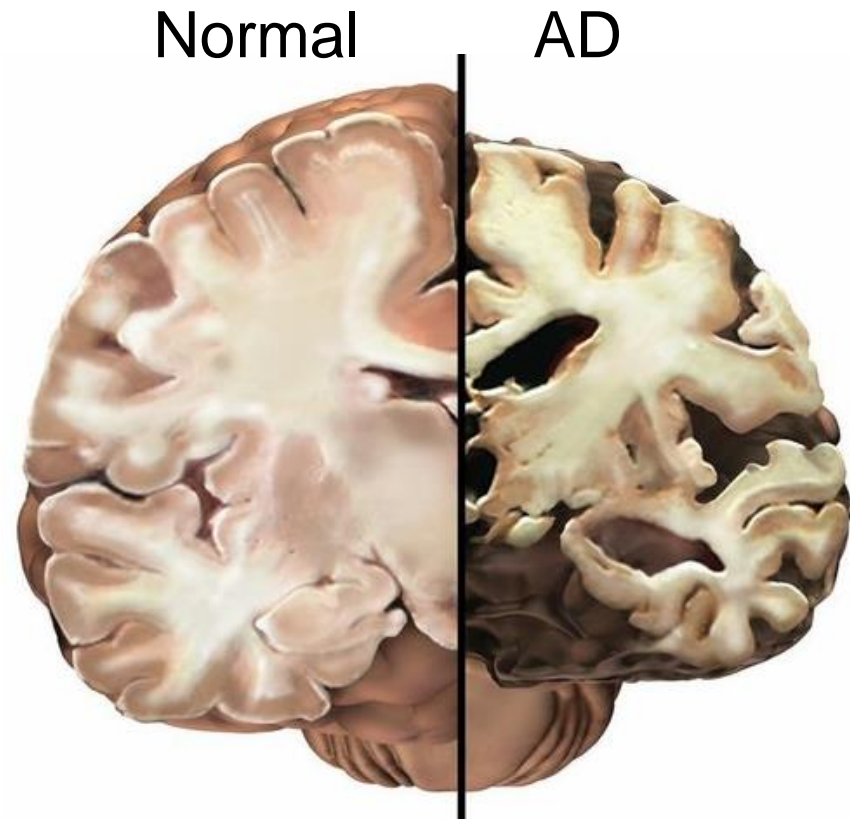
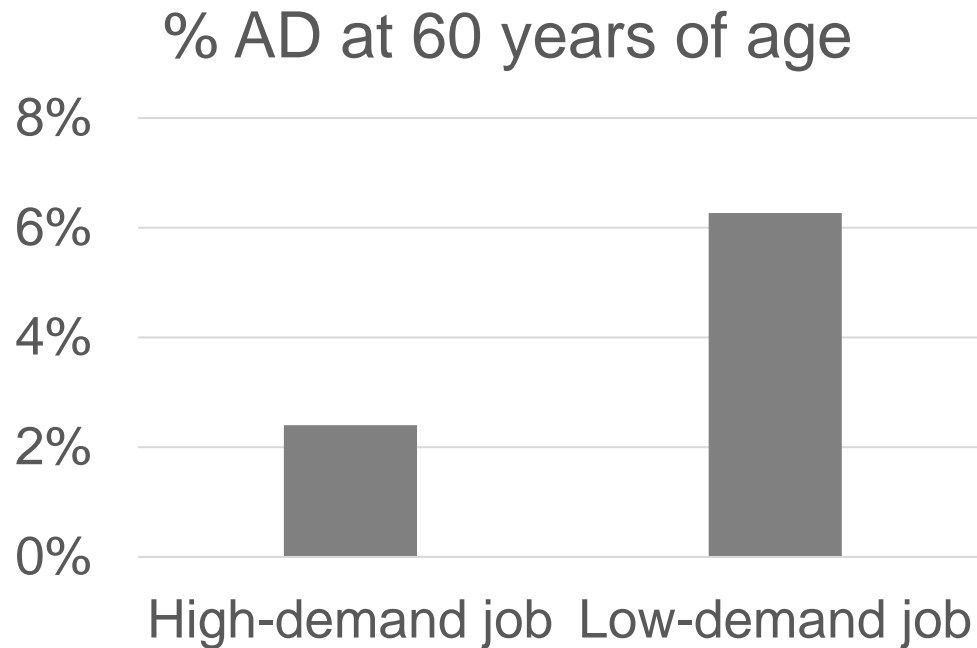
Limbic system: “primitive” brain control of emotions and learning

Limbic system: hippocampus, septal area, amygdala, n. accumbens and adjoining regions of cortex



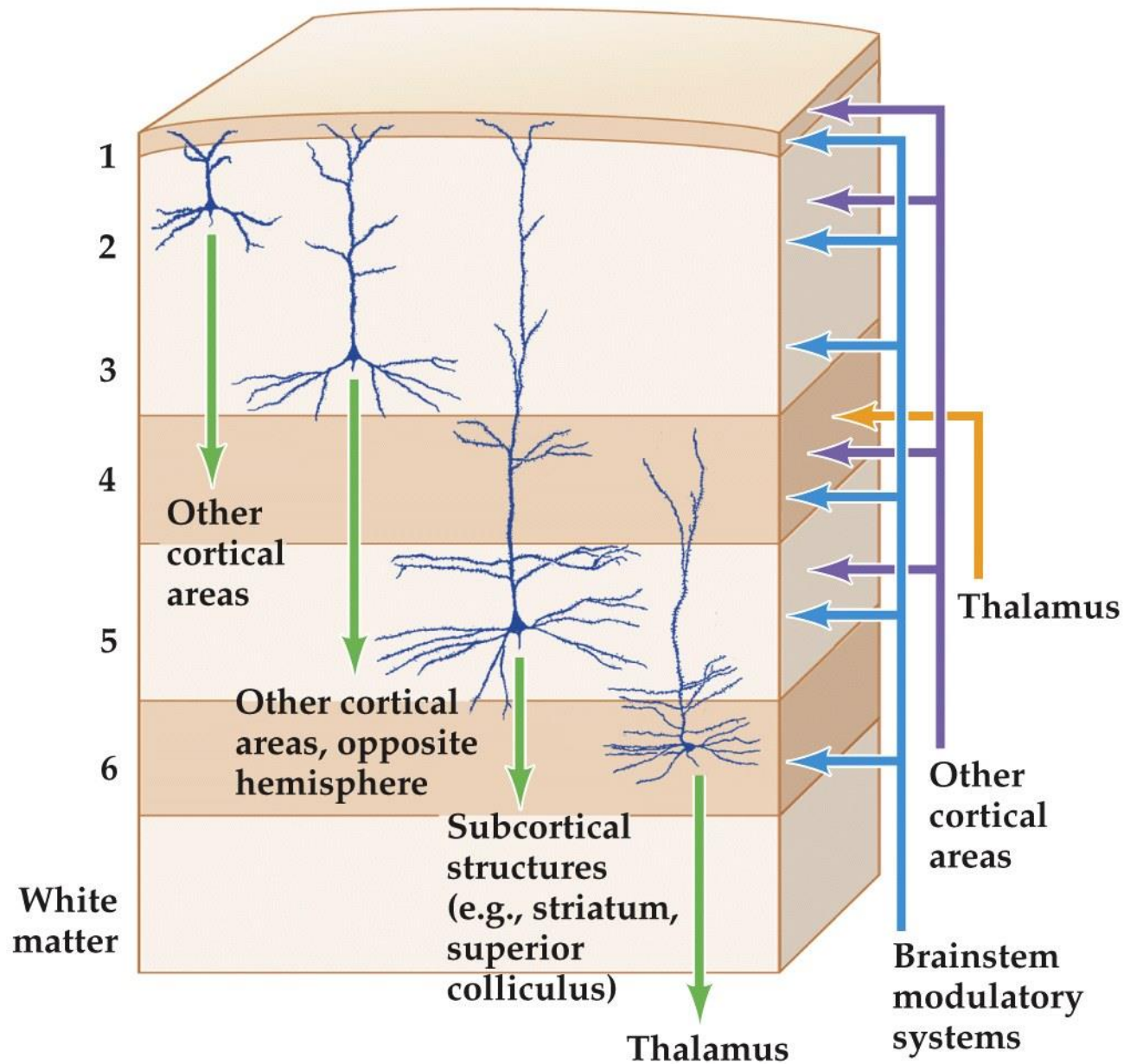
Brain tissue degeneration: Alzheimer's disease

- 8% of the US healthcare budget
- 6 million people in the US



Electrical stimulation of limbic networks controlling emotions and learning may soon be approved (study to finish in 2024)

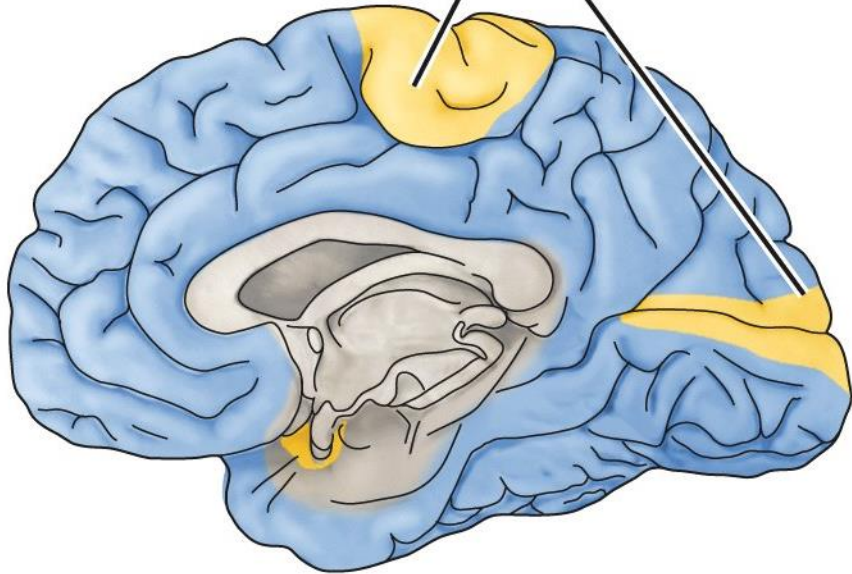
Cortex: layered structure and key connections



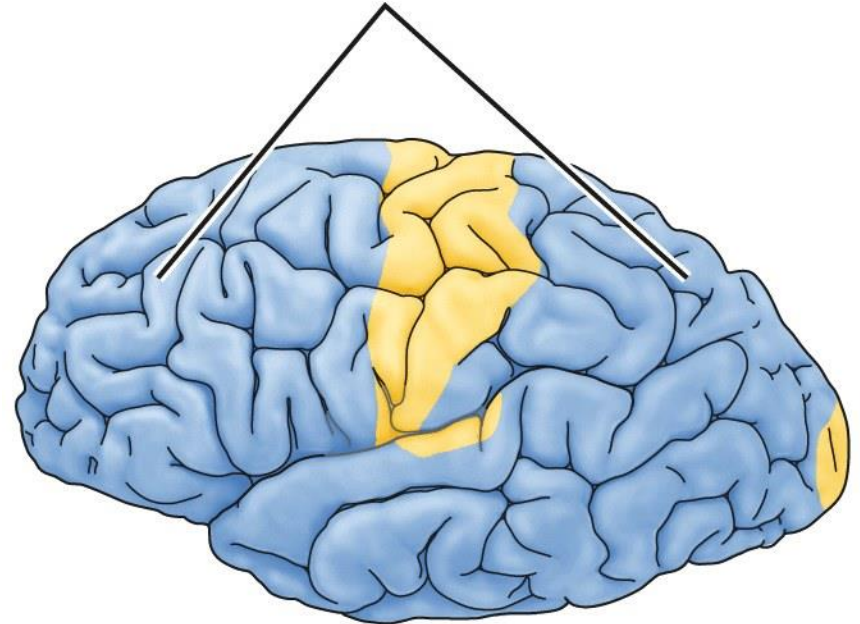
Sensory, motor, and association cortices

Targets of existing neuroprosthetic devices

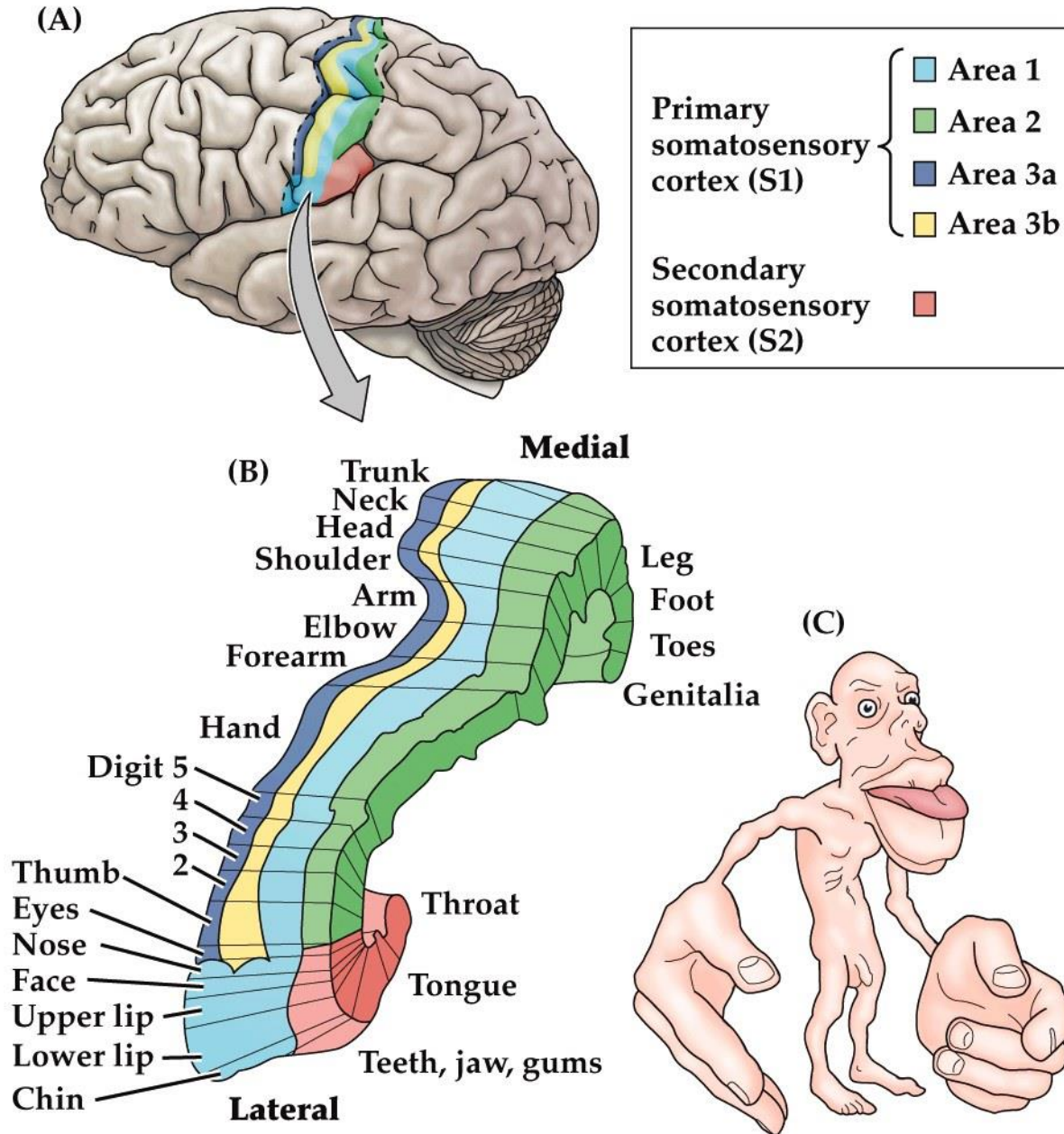
Primary sensory
and motor areas



Association cortices

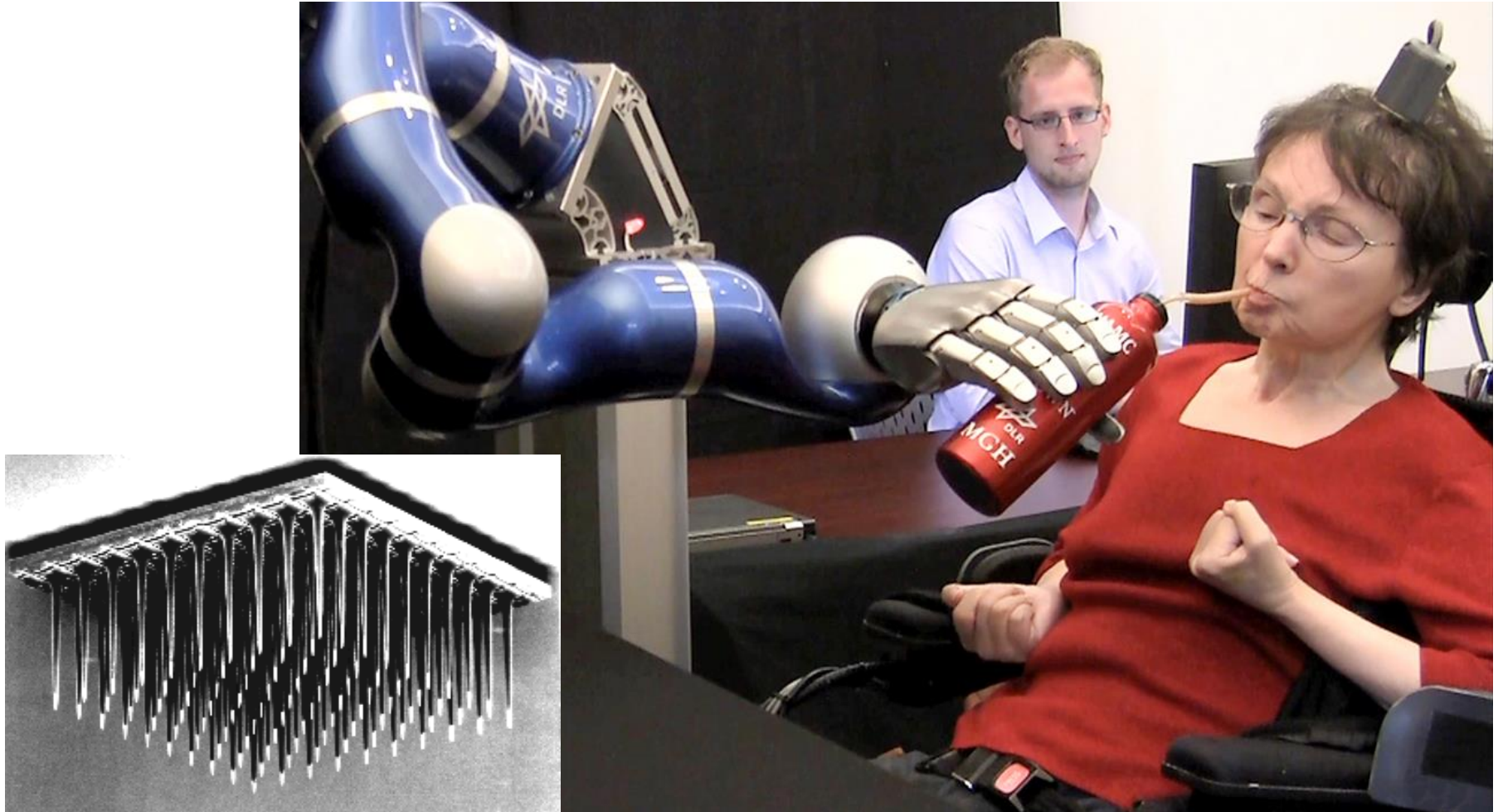


Body maps in the somatosensory and motor cortex



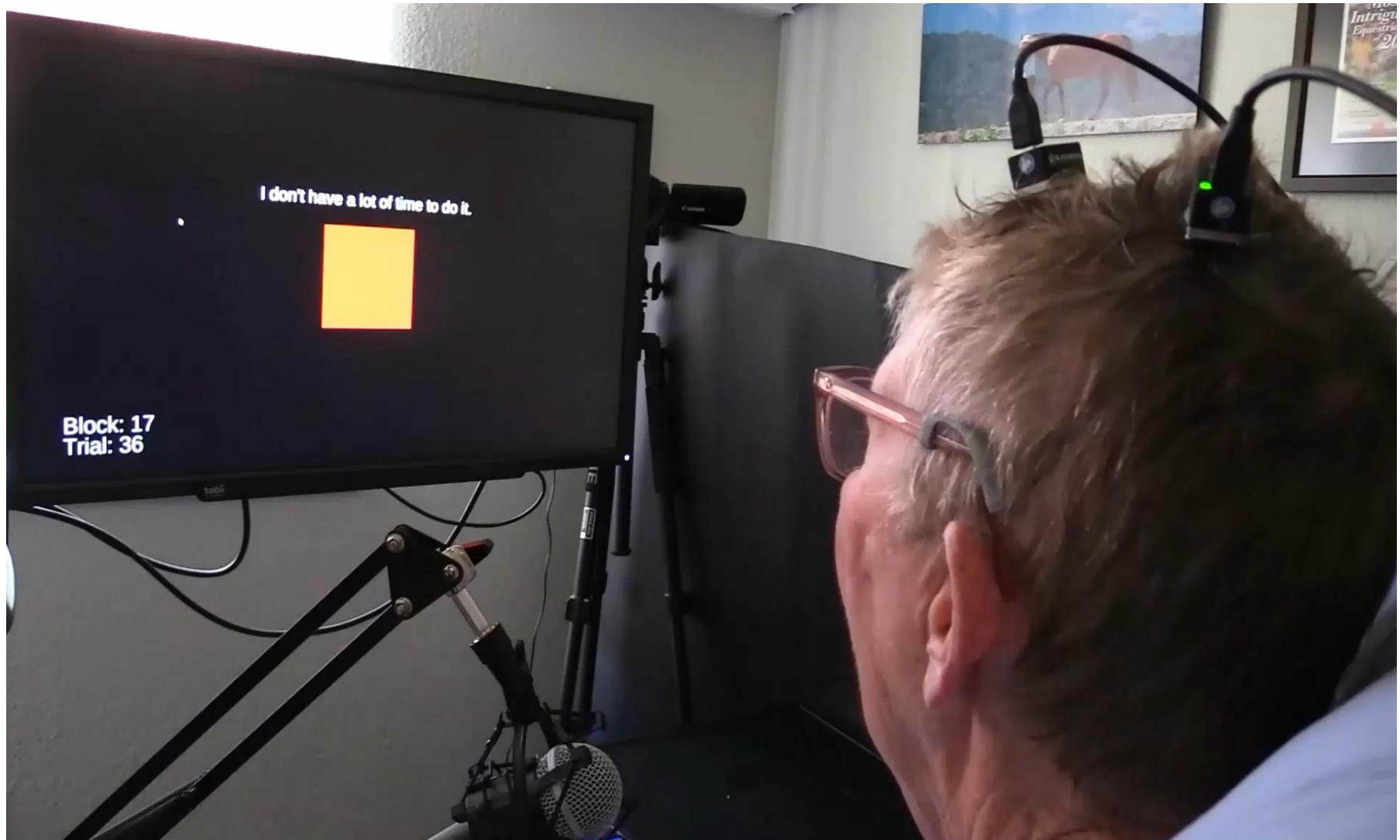
Motor cortex interface

Recording movement intent with one 100-electrode array in paralyzed patients



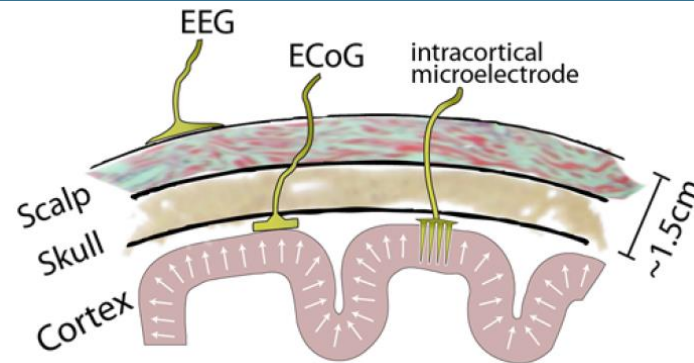
Motor cortex interface

Recording face and tongue movement with two 100-electrode arrays in paralyzed patients at 62 words per minute!

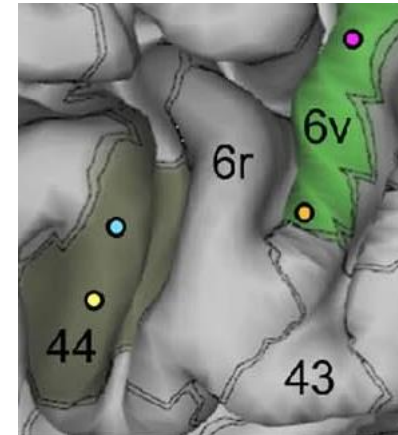
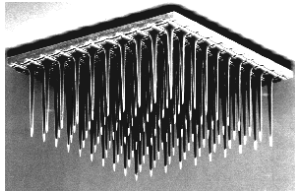


<https://www.nature.com/articles/s41586-023-06377-x>

BCI interfaces: getting close to cortical neurons



2x100 intracortical
electrodes:
62 words per minute



2x64 subdural
electrodes:
2 words per minute

