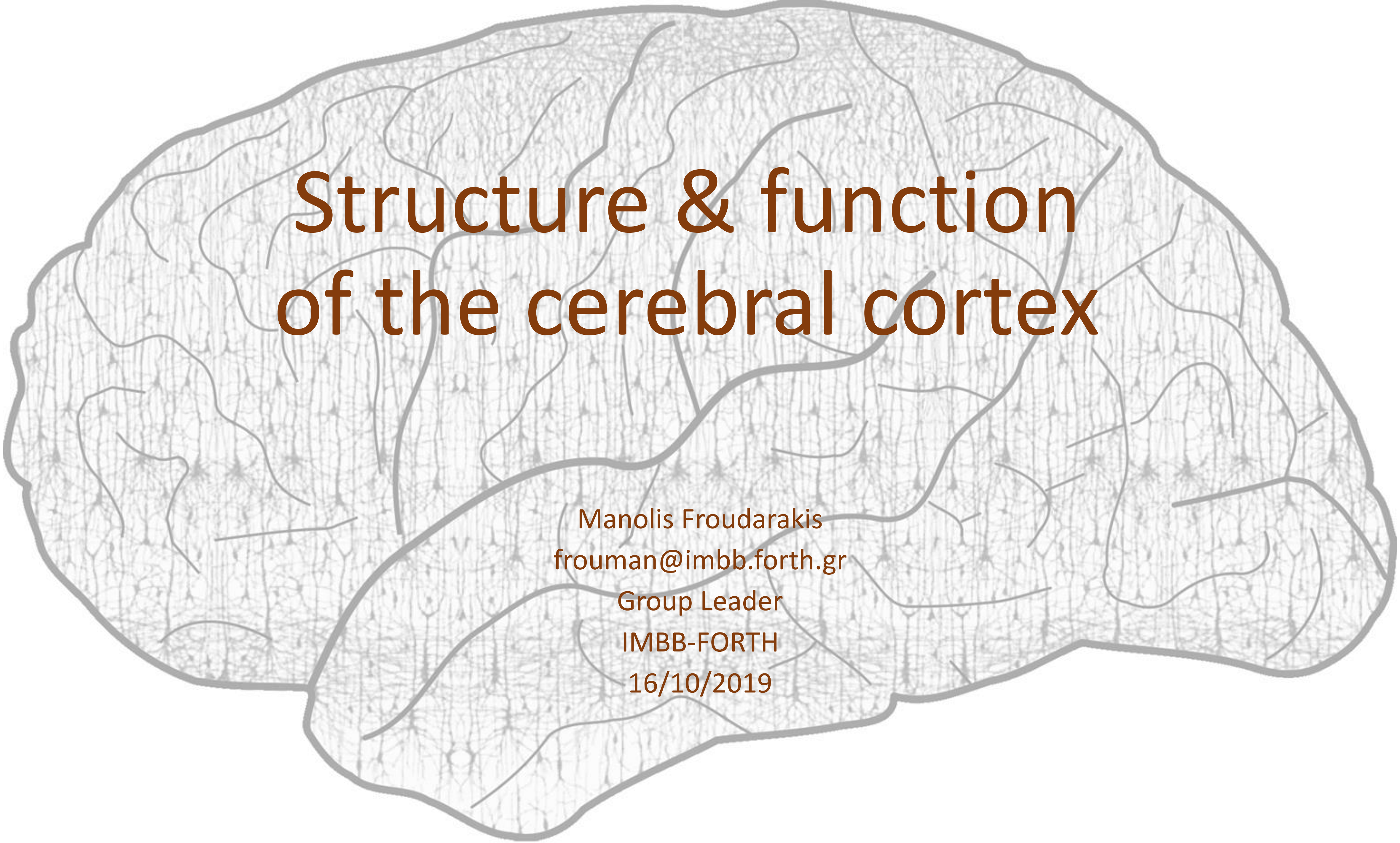

Structure & function of the cerebral cortex

Manolis Froudarakis

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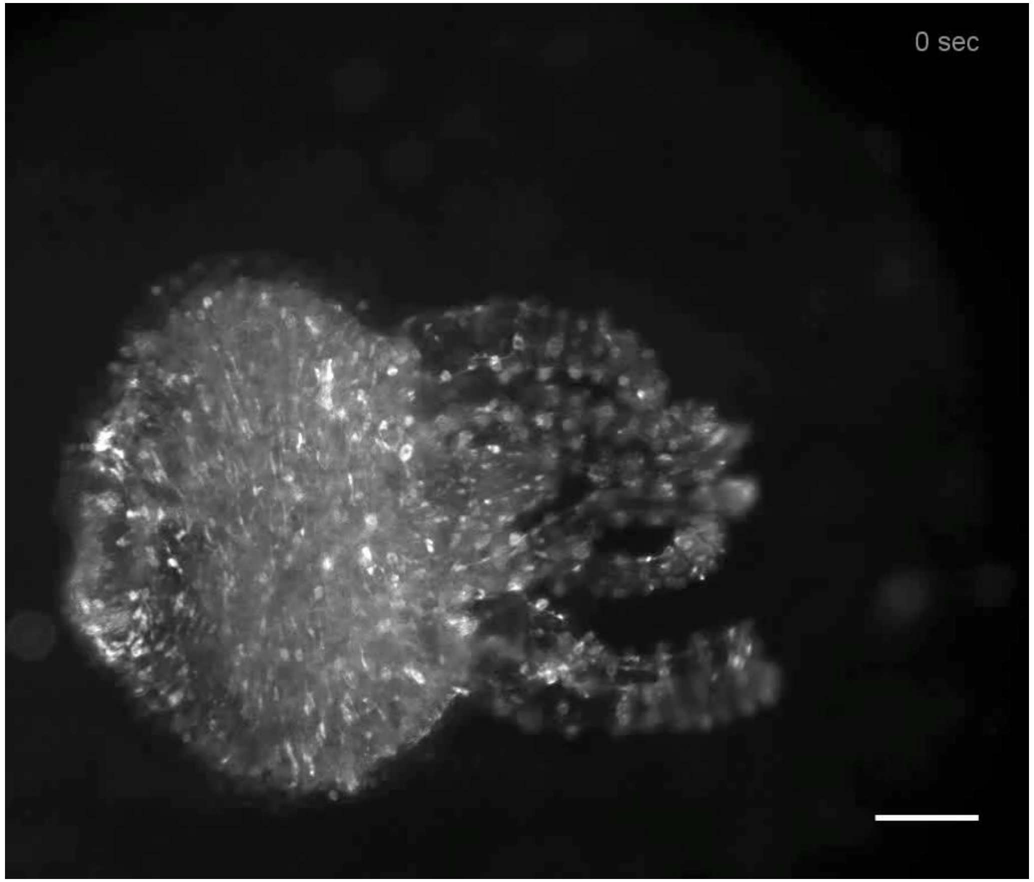
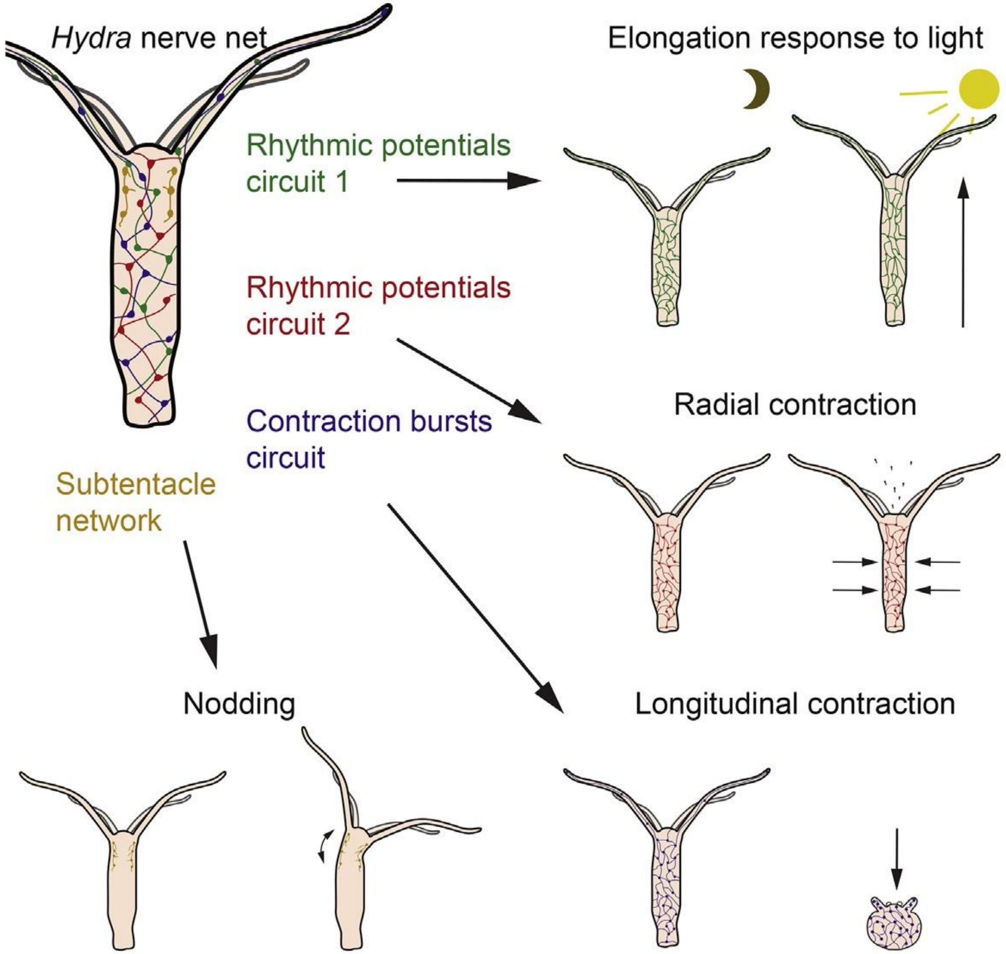
Group Leader

IMBB-FORTH

16/10/2019

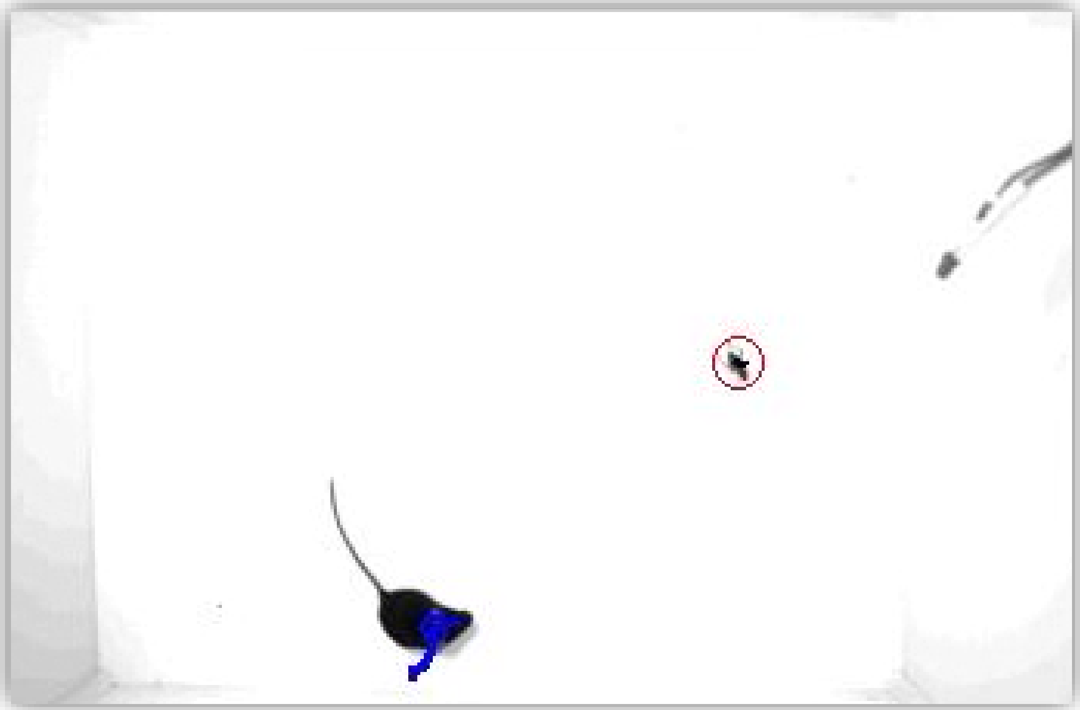
Neural Networks in Hydra vulgaris are associated with specific behaviors



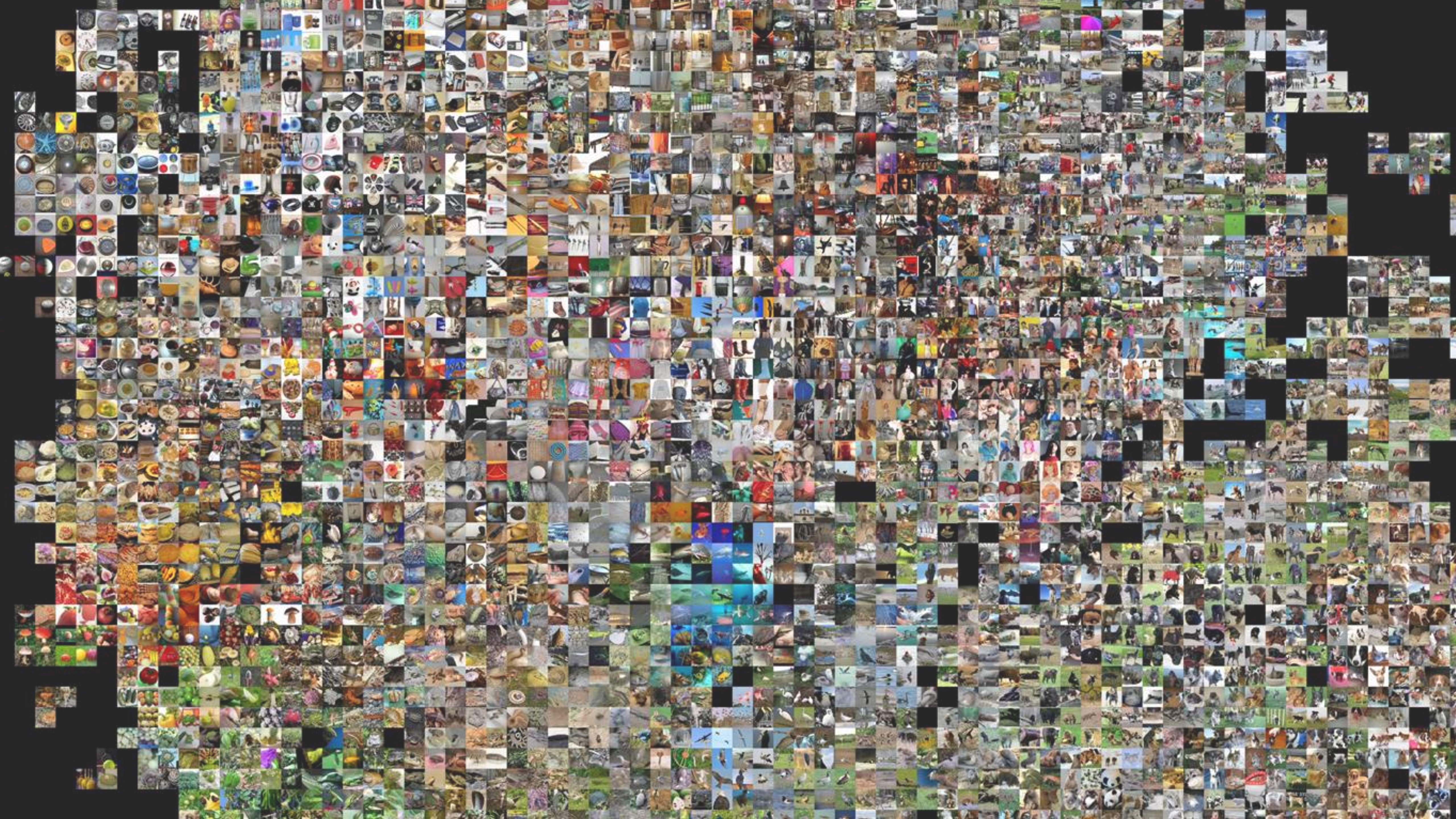


Dupre & Yuste 2017

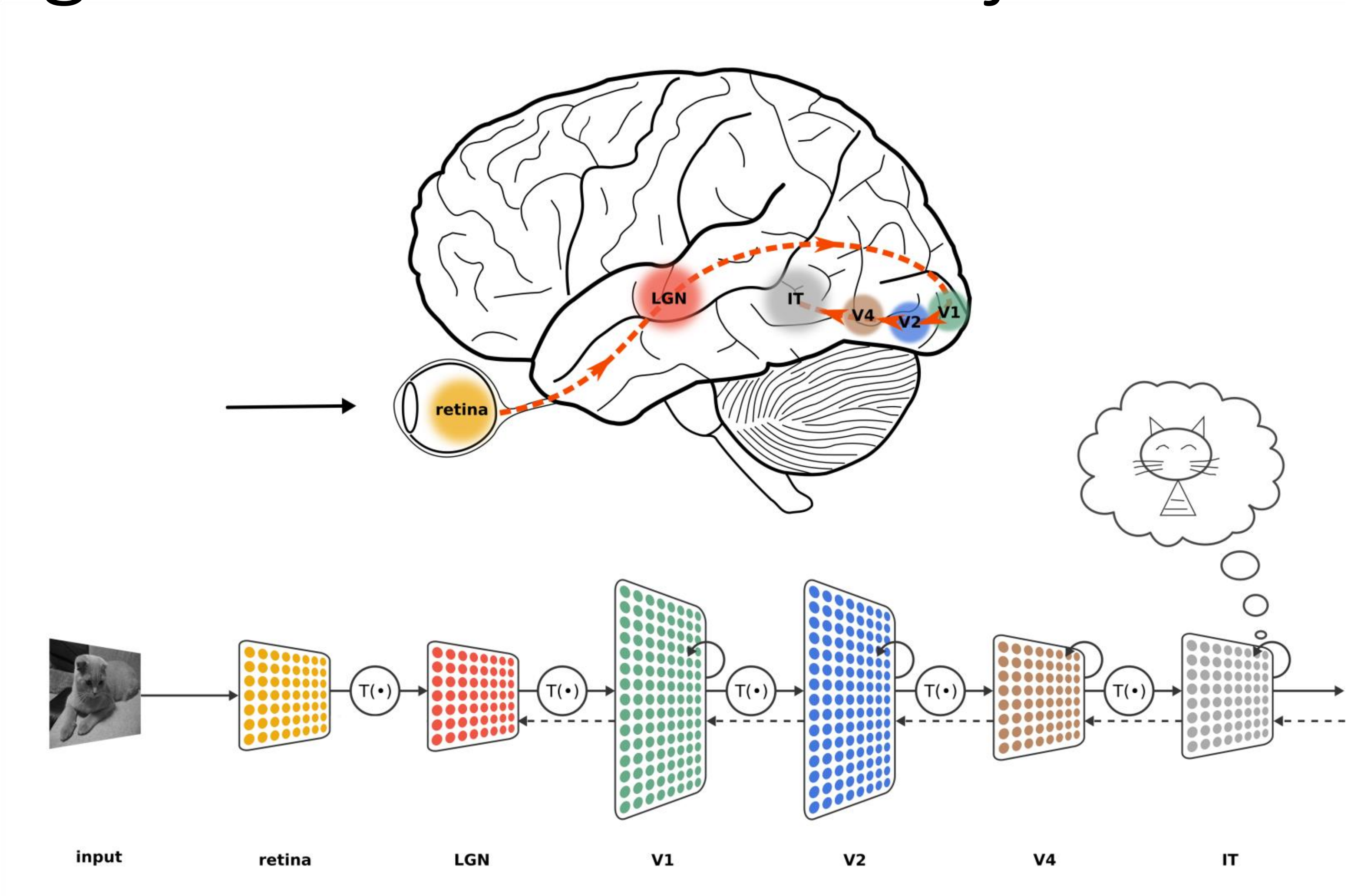
Or a highly integrated system to detect, process and respond to objects



Hoy et al. 2016



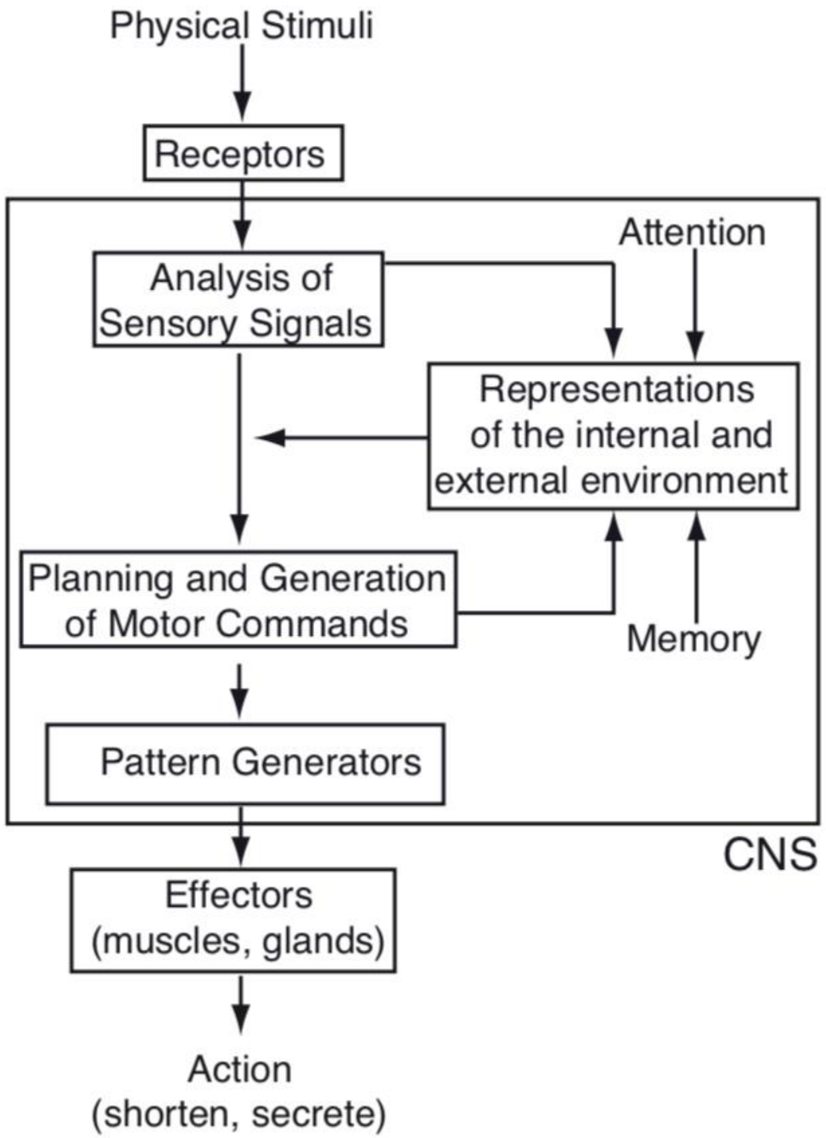
Extracting information about objects



DiCarlo & Cox 2017, J. Kubilius

Information processing in neuronal networks

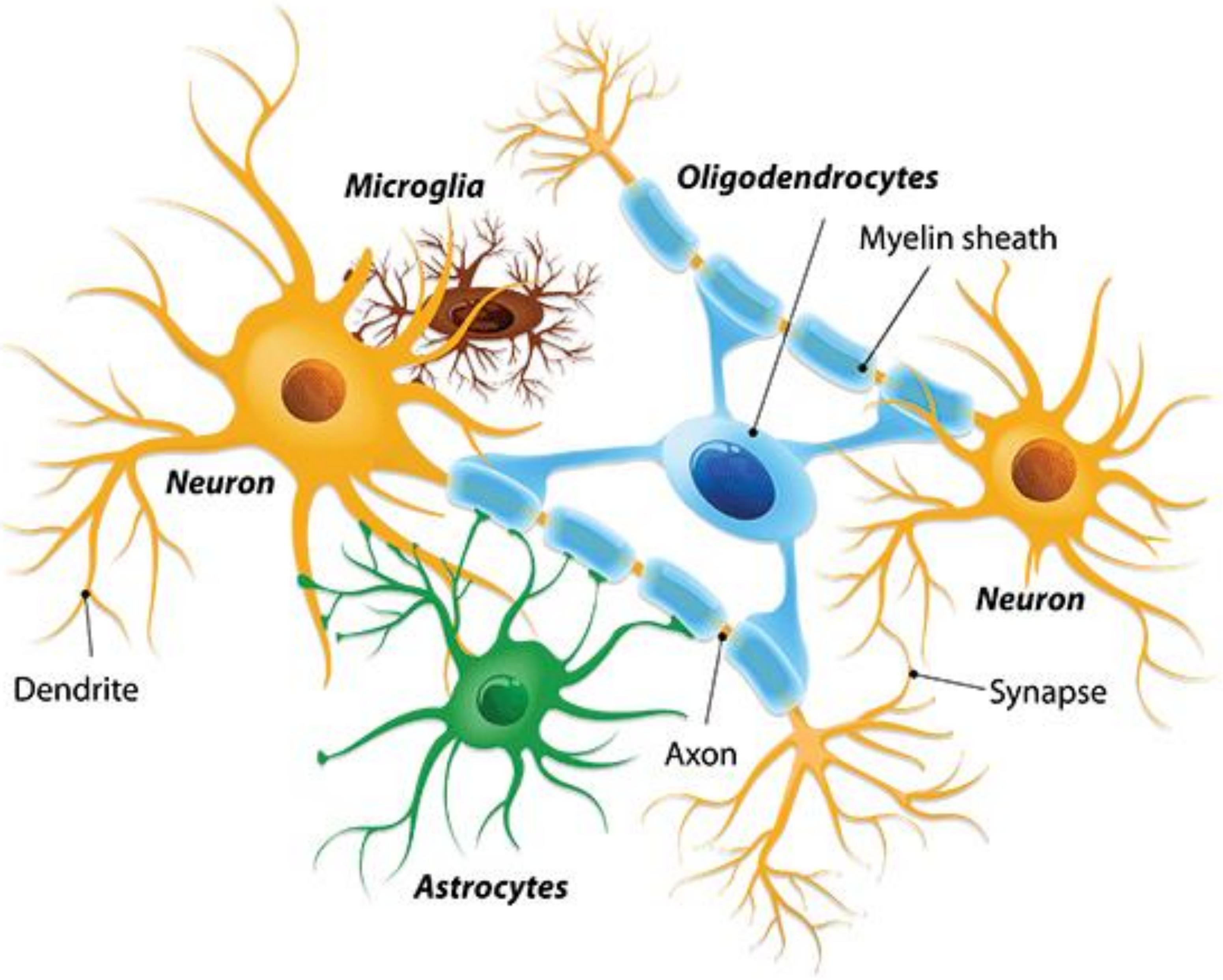
Goal: Interact with the environment



Brain cells

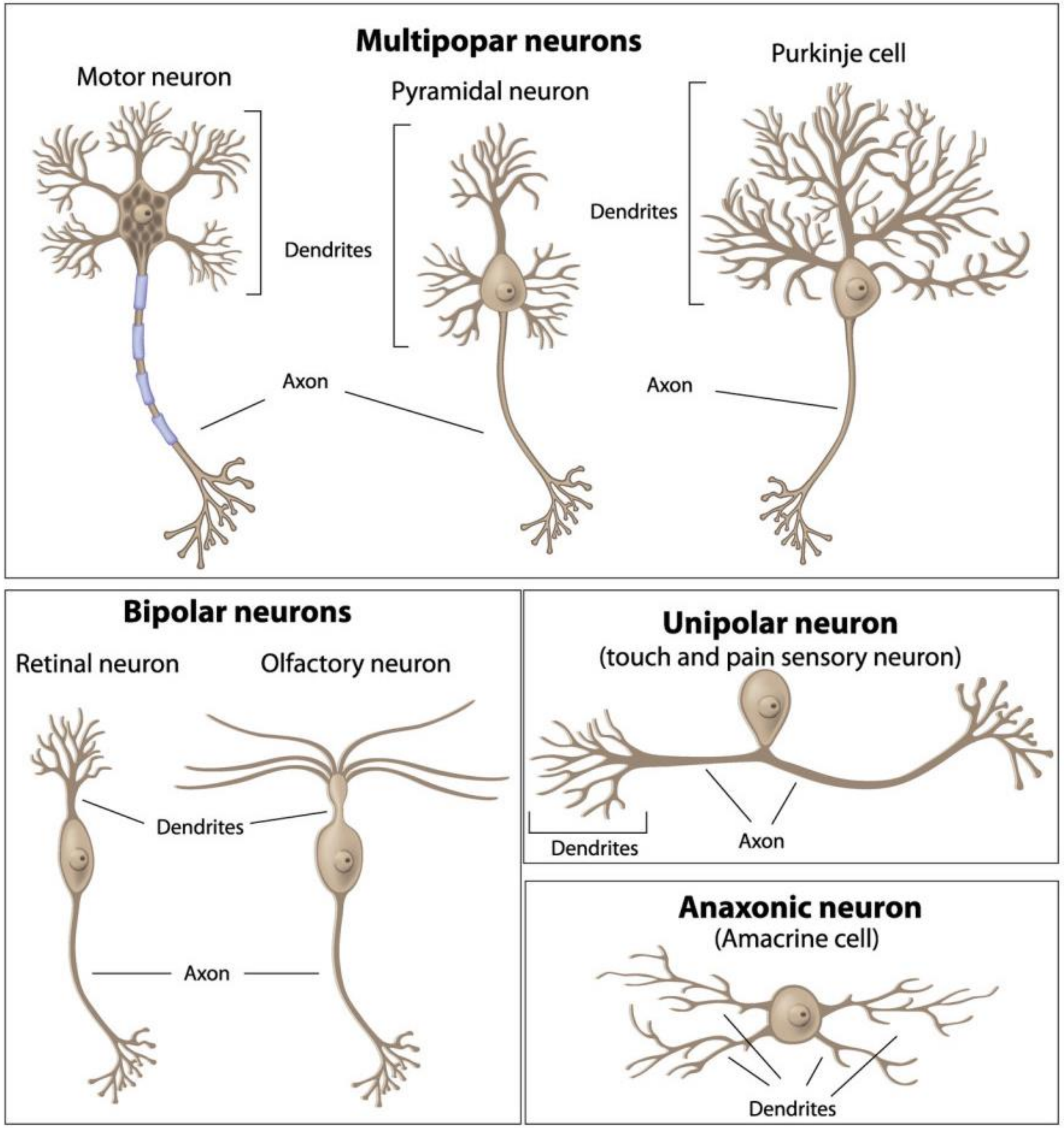
1. **Neurons**

2. **Glia cells**
   - Astrocytes
     extracellular homeostasis
   - Microglia
     immune response
   - Oligodendrocytes
     myelin sheath

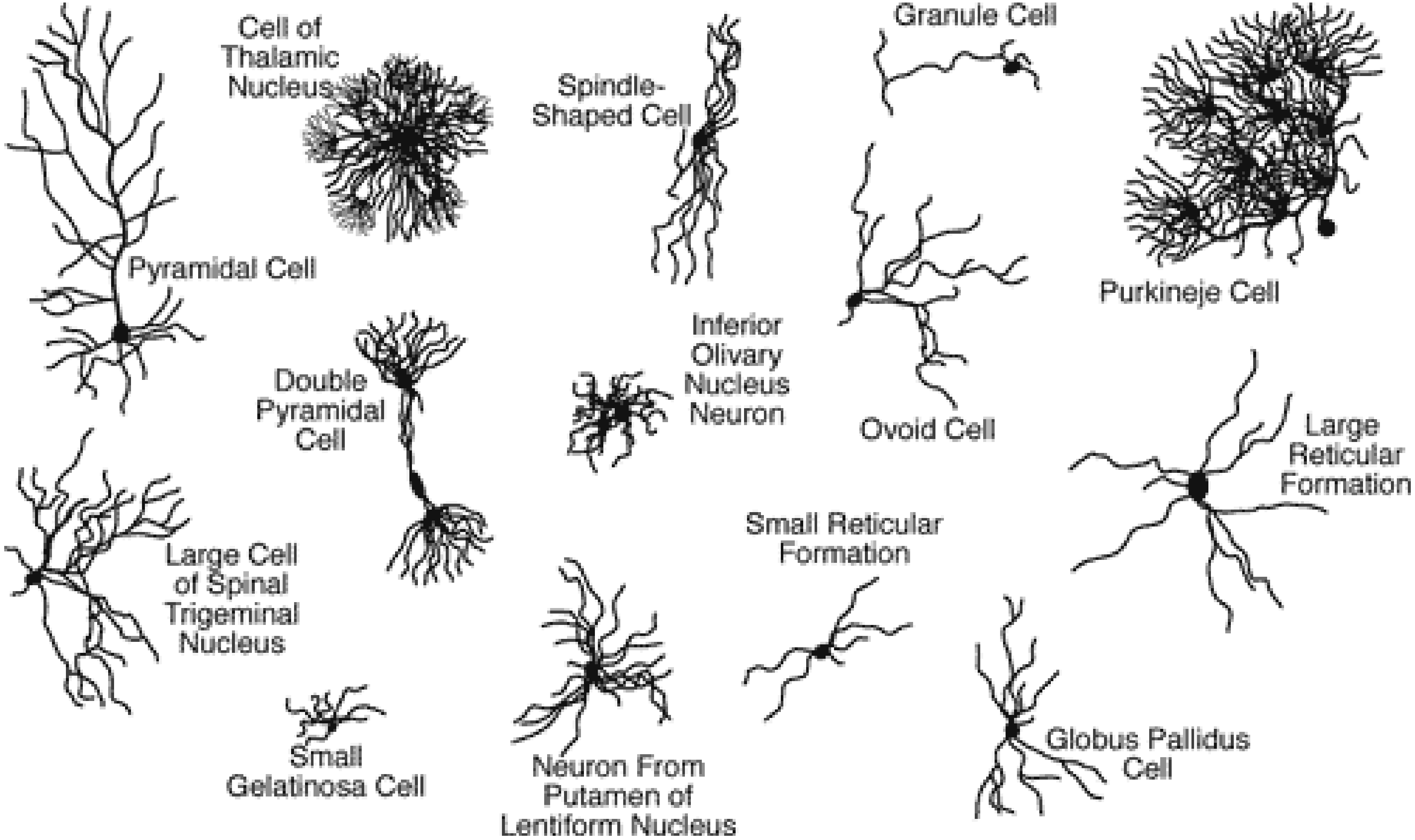


Γλία: Κόλλα

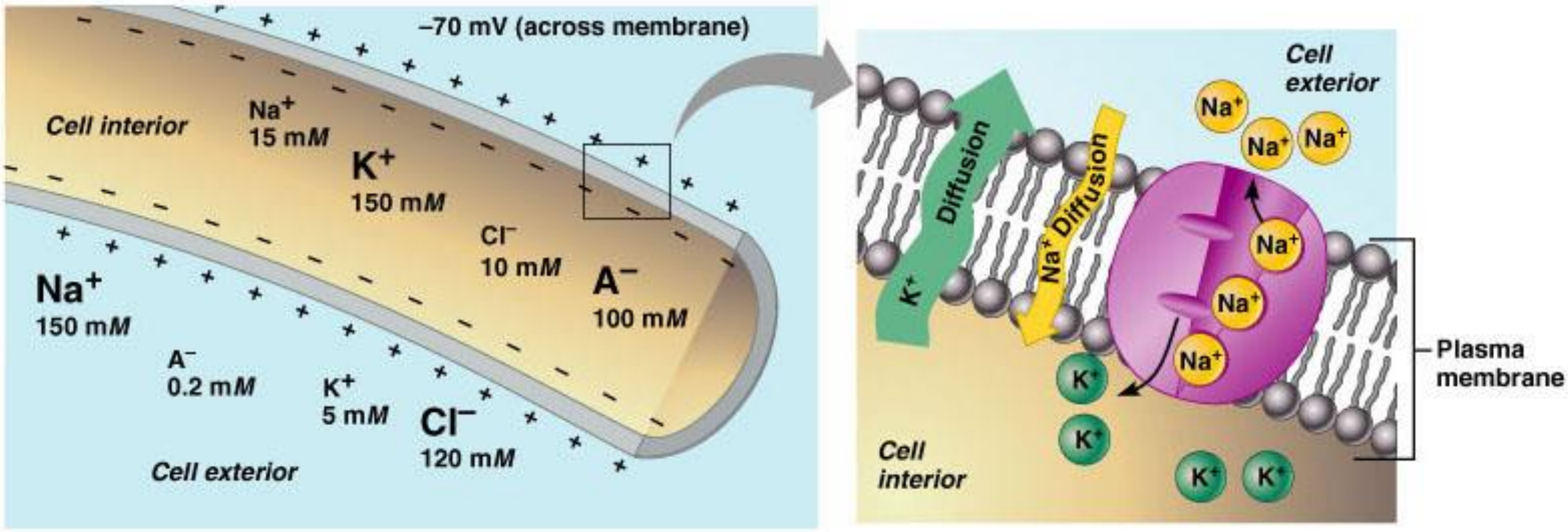
Types of Neurons
…based on polarity



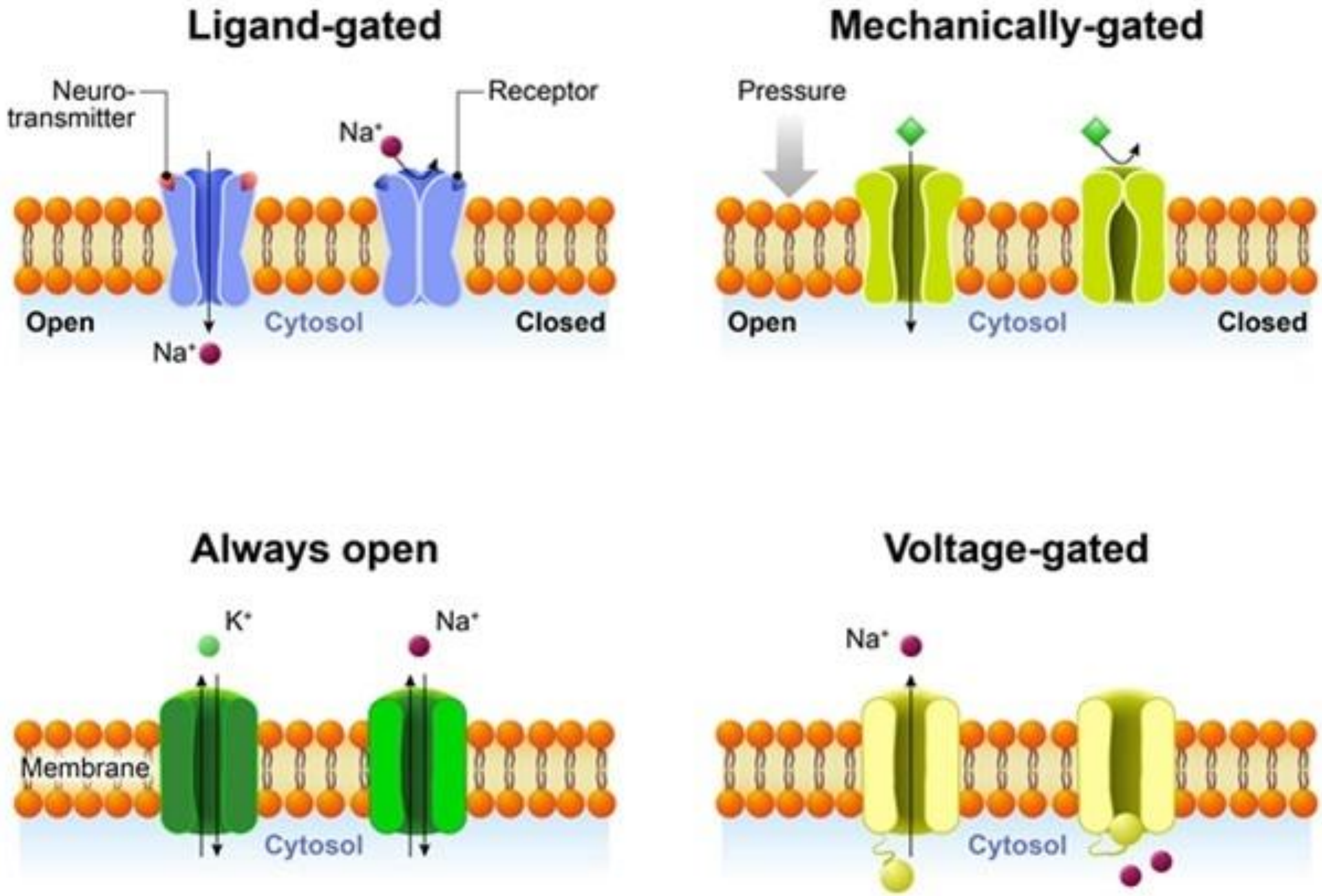
Types of Neurons …based on shape



Membrane as a capacitor

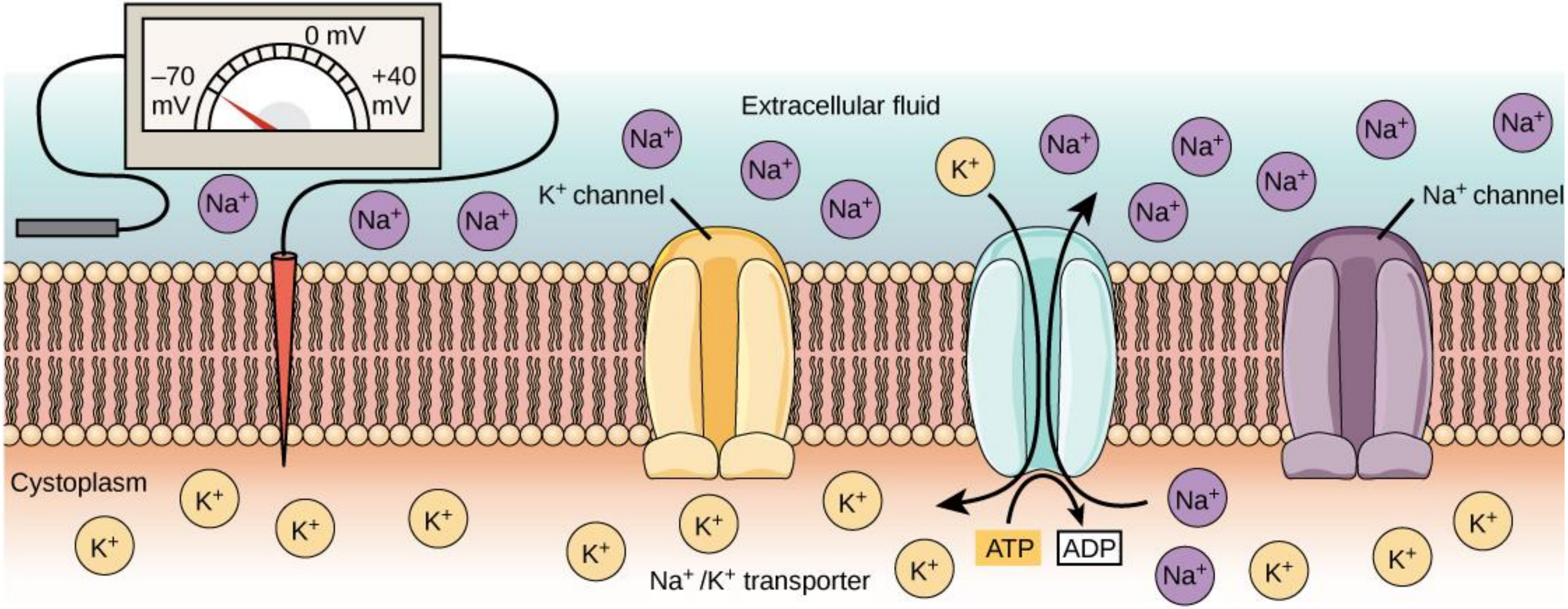


ION CHANNEL


Ligand-gated
Neuro-
transmitter
Receptor
Na⁺
Open
Cytosol
Closed
Na⁺
Mechanically-gated
Pressure
Open
Cytosol
Closed
Always open
K⁺
Na⁺
Membrane
Cytosol
Voltage-gated
Na⁺
Cytosol

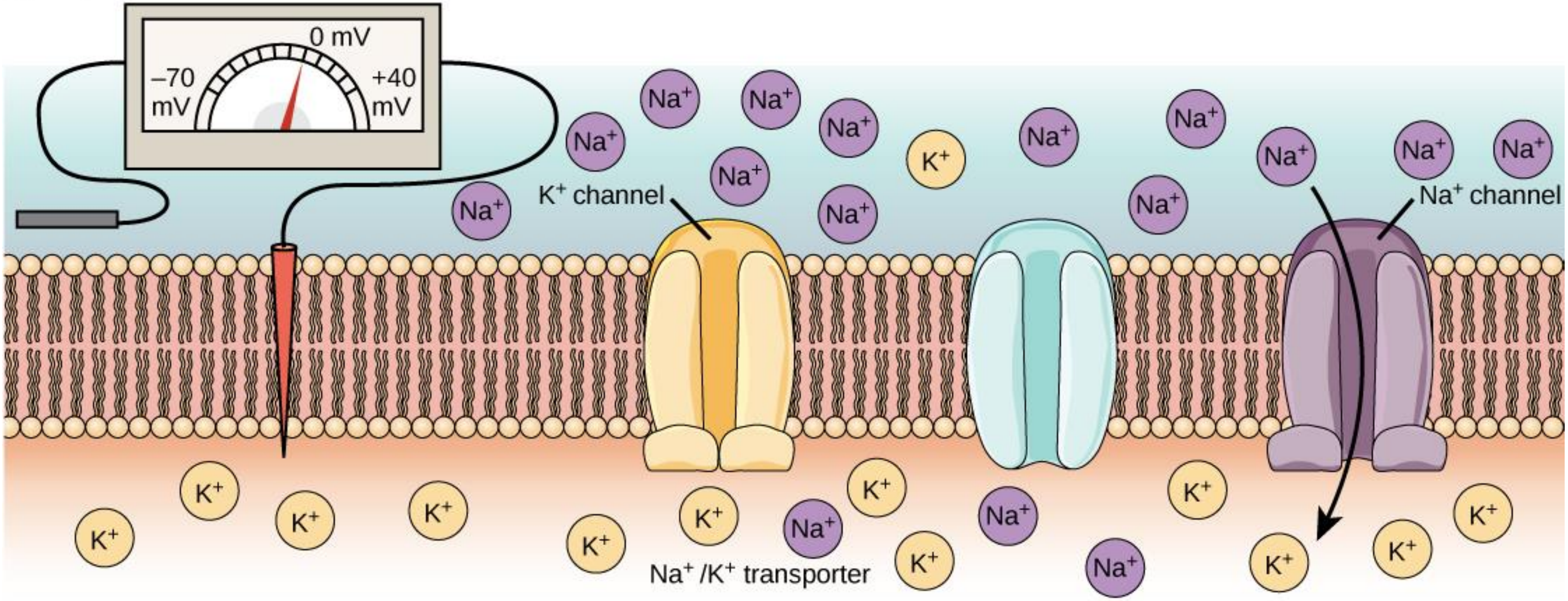
Resting membrane potential

results from the **separation of charges** across the cell membrane - **Electrochemical gradient**



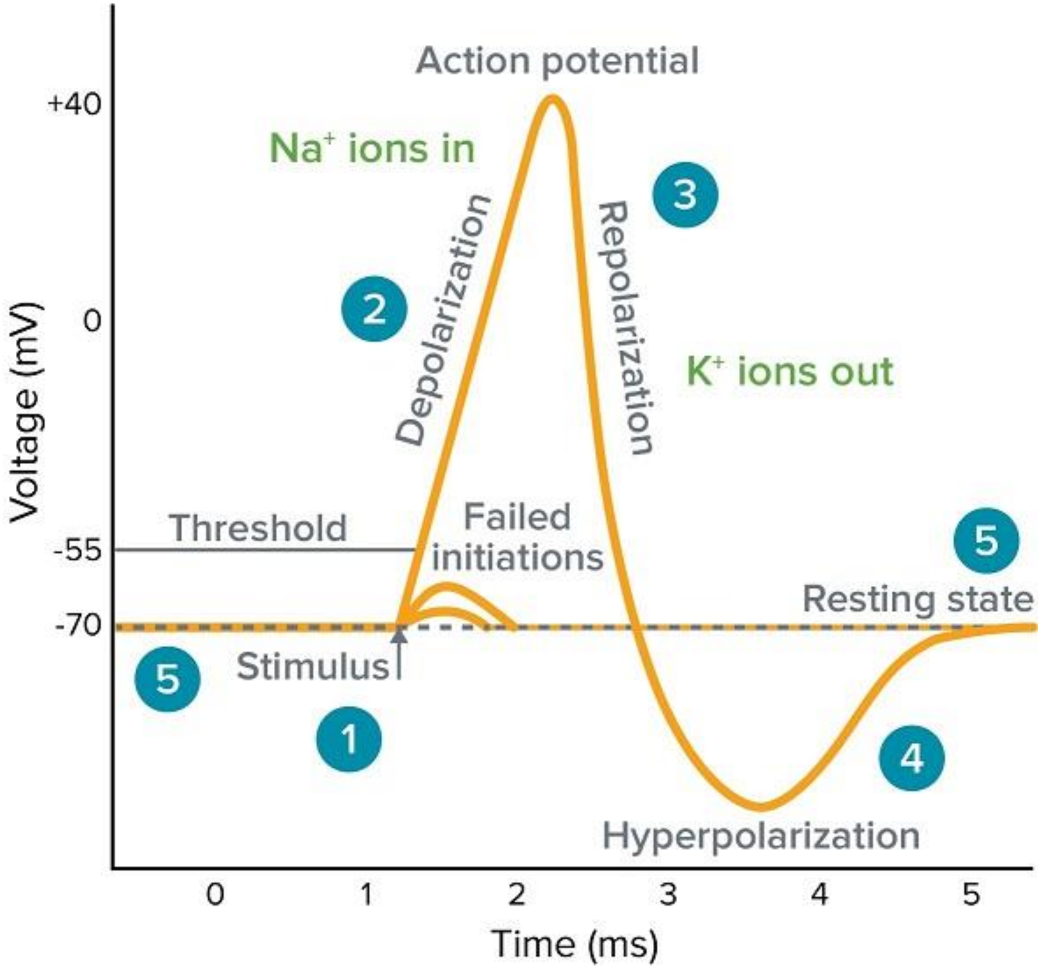
At the resting potential, all voltage-gated Na^+ channels and most voltage-gated K^+ channels are closed. The Na^+/K^+ transporter pumps K^+ ions into the cell and Na^+ ions out.

Depolarization



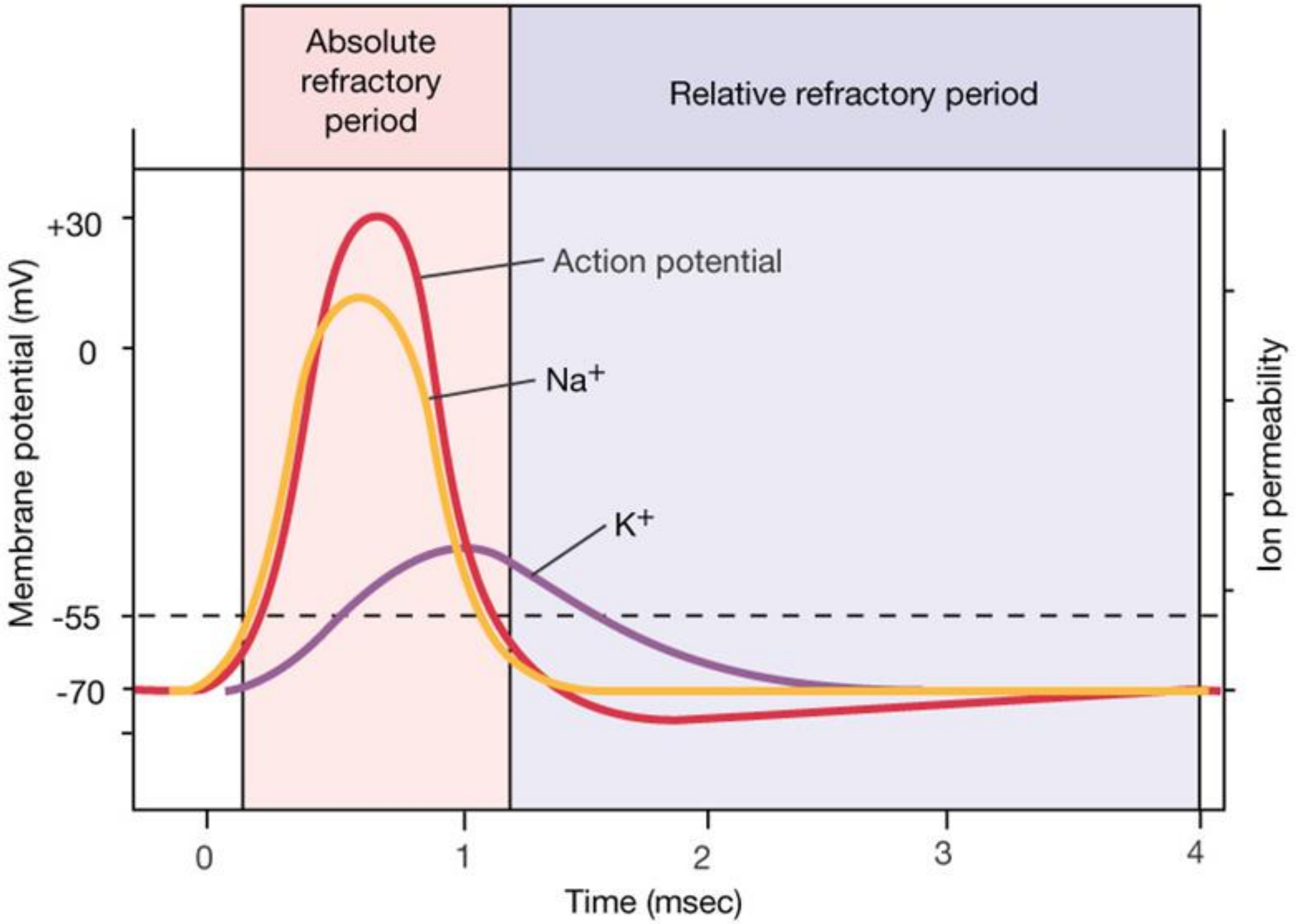
In response to a depolarization, some Na^+ channels open, allowing Na^+ ions to enter the cell. The membrane starts to depolarize (the charge across the membrane lessens). If the threshold of excitation is reached, all the Na^+ channels open.

Action potential (all or none!)



1. Stimulus starts and the voltage gated sodium channels begin to open and the membrane potential begins to slowly depolarizes and sodium enters the cell down its concentration gradient.
2. If sufficient drive raises the voltage above the threshold voltage, further depolarization is caused by a rapid rise in membrane potential opening of sodium channels in the cellular membrane, resulting in a large influx of sodium ions (**regenerative → all or none**).
3. Membrane repolarization results from rapid sodium channel inactivation as well as a large efflux of potassium ions resulting from activated potassium channels.
4. Hyperpolarization is a lowered membrane potential caused by the efflux of potassium ions due to the slow closing of the potassium channels.
5. Resting state is when membrane potential returns to the resting voltage that occurred before the stimulus occurred.

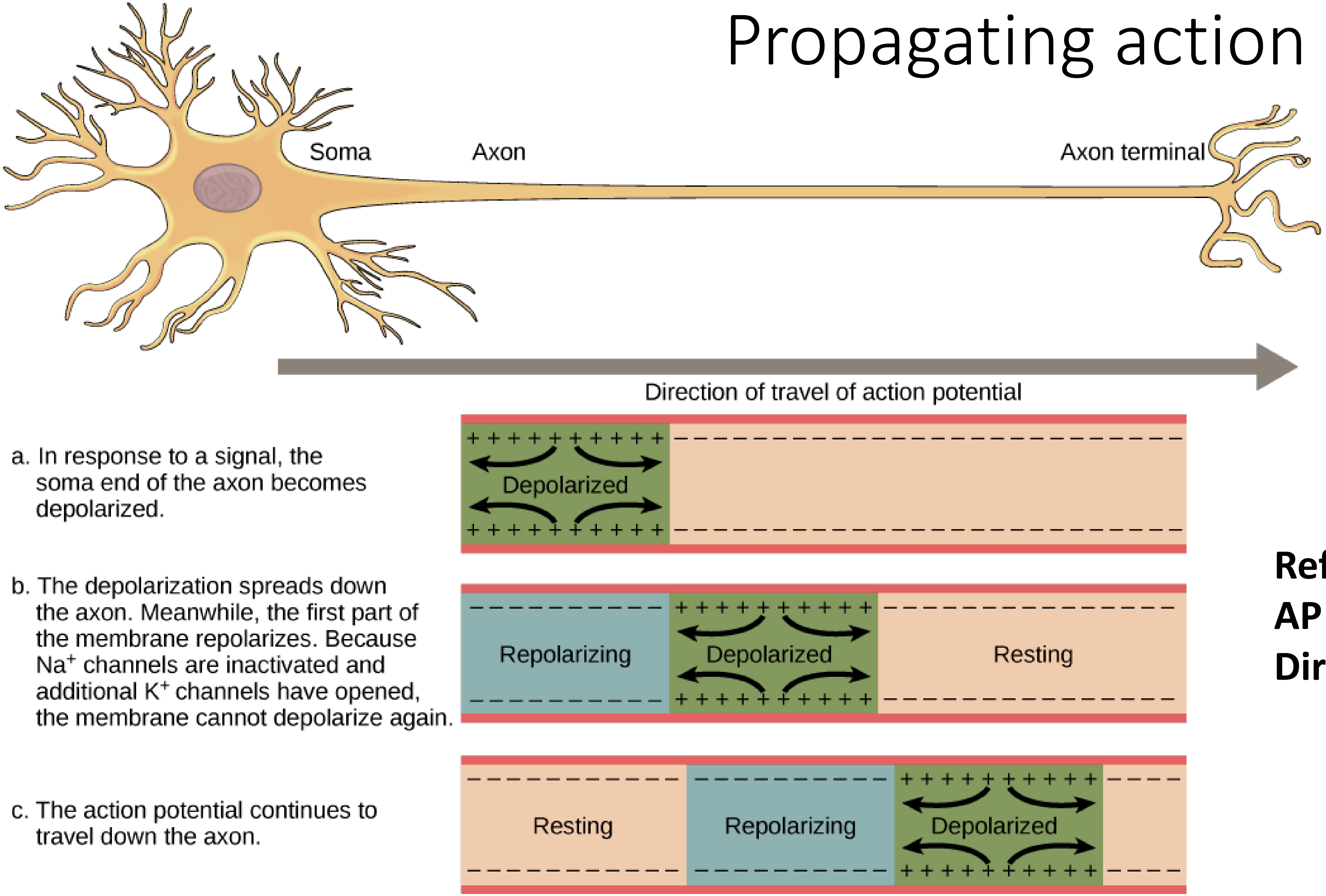
Refractory periods



Absolute refractory period: time during which another stimulus given to the neuron (no matter how strong) will not lead to a second action potential

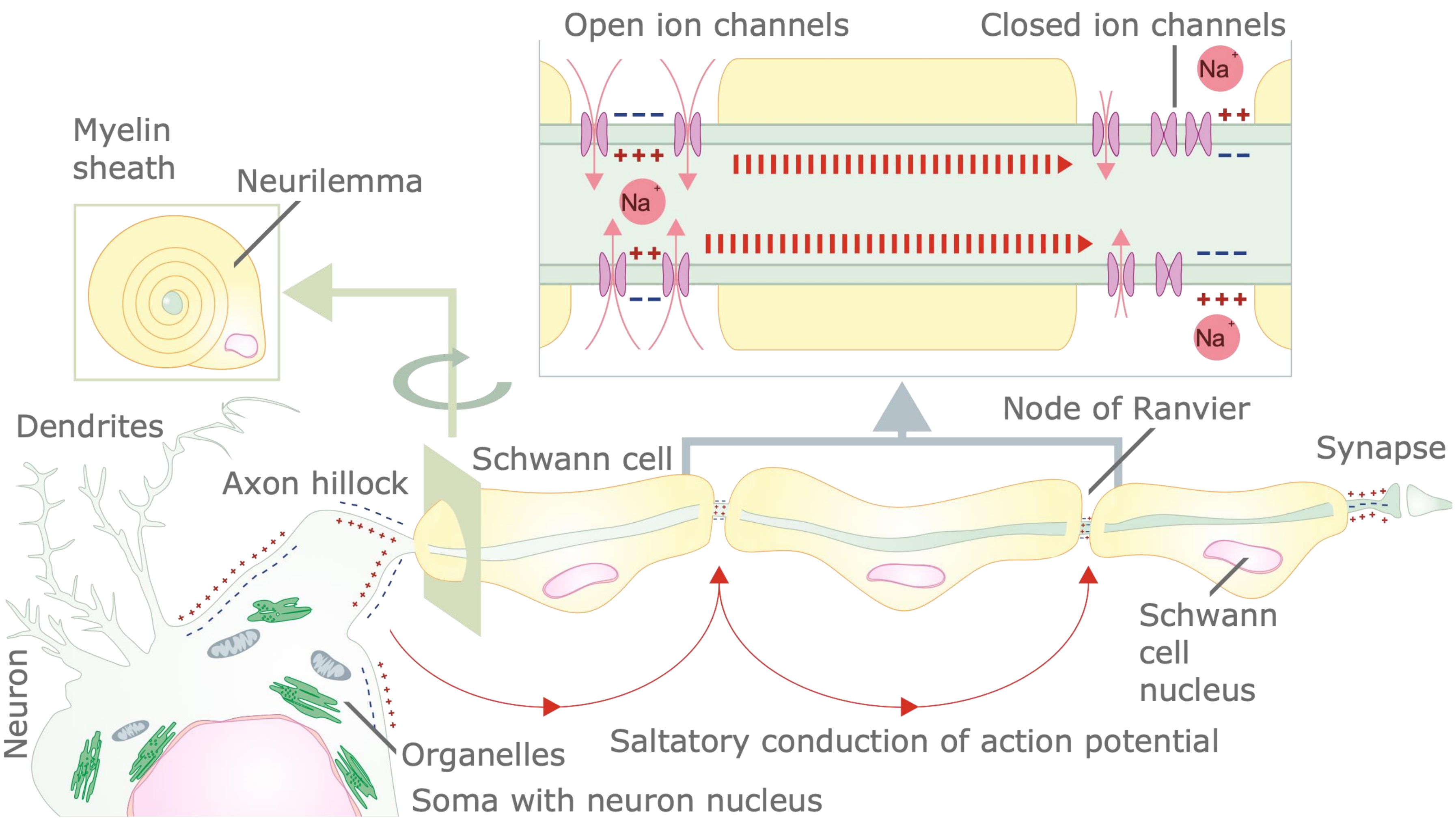
Relative refractory period: time during which a stronger than normal stimulus is needed to elicit neuronal excitation.

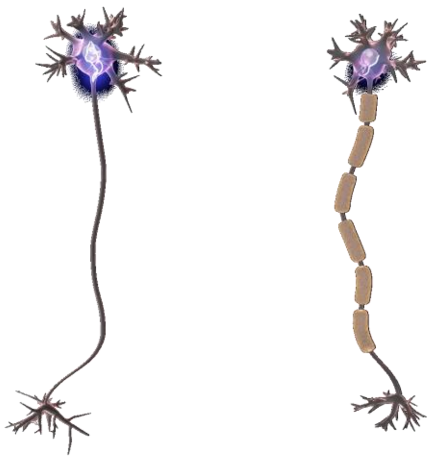
Propagating action potential



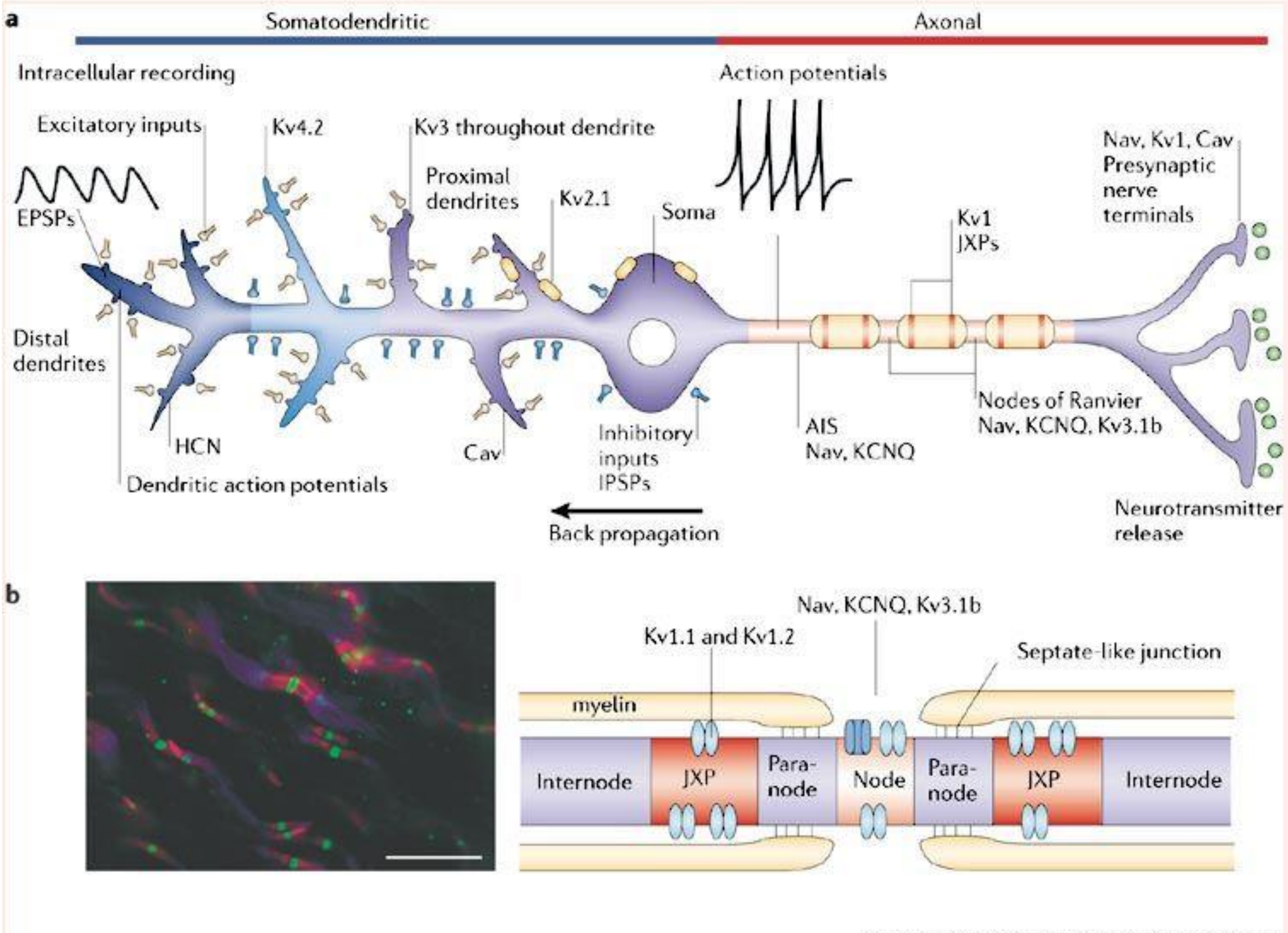
Refractory period → AP propagation Directionality!

Saltatory conduction

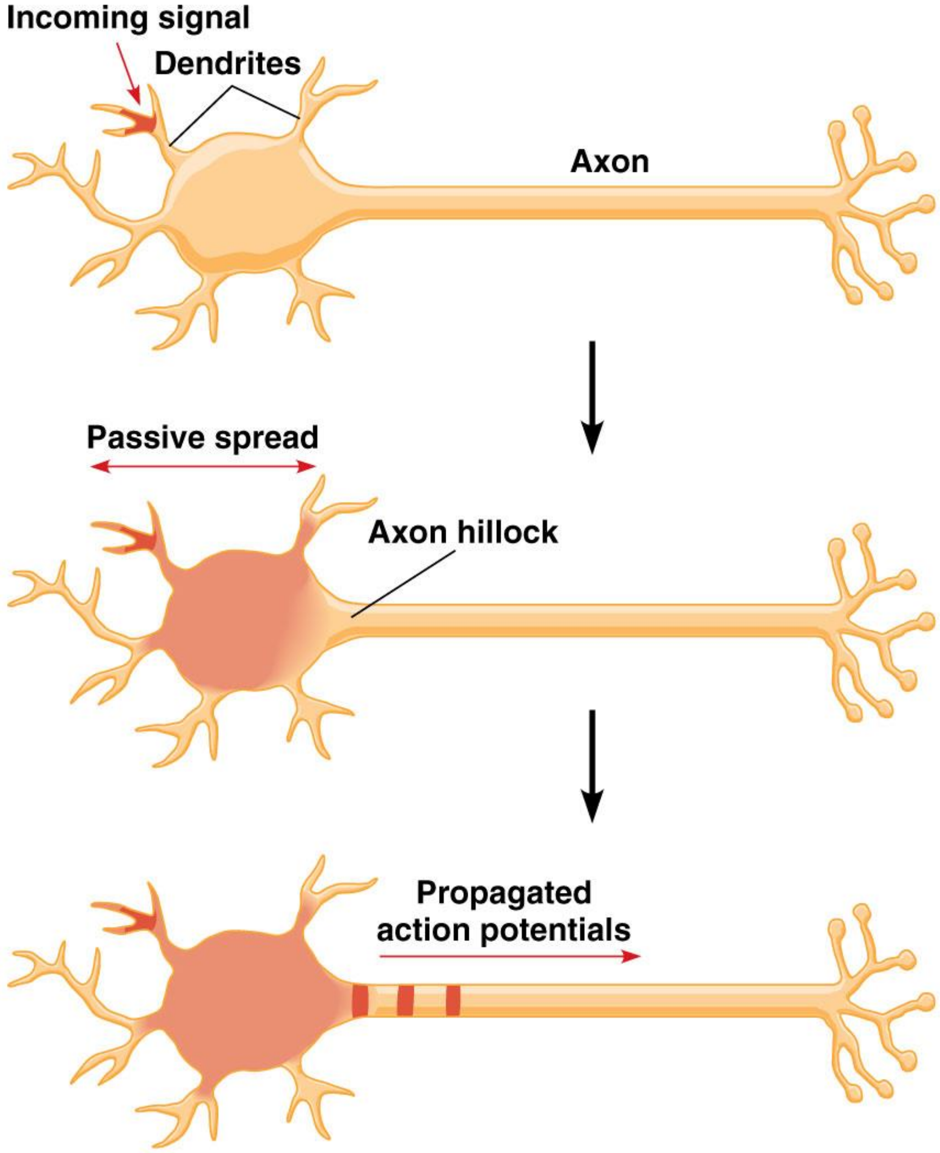


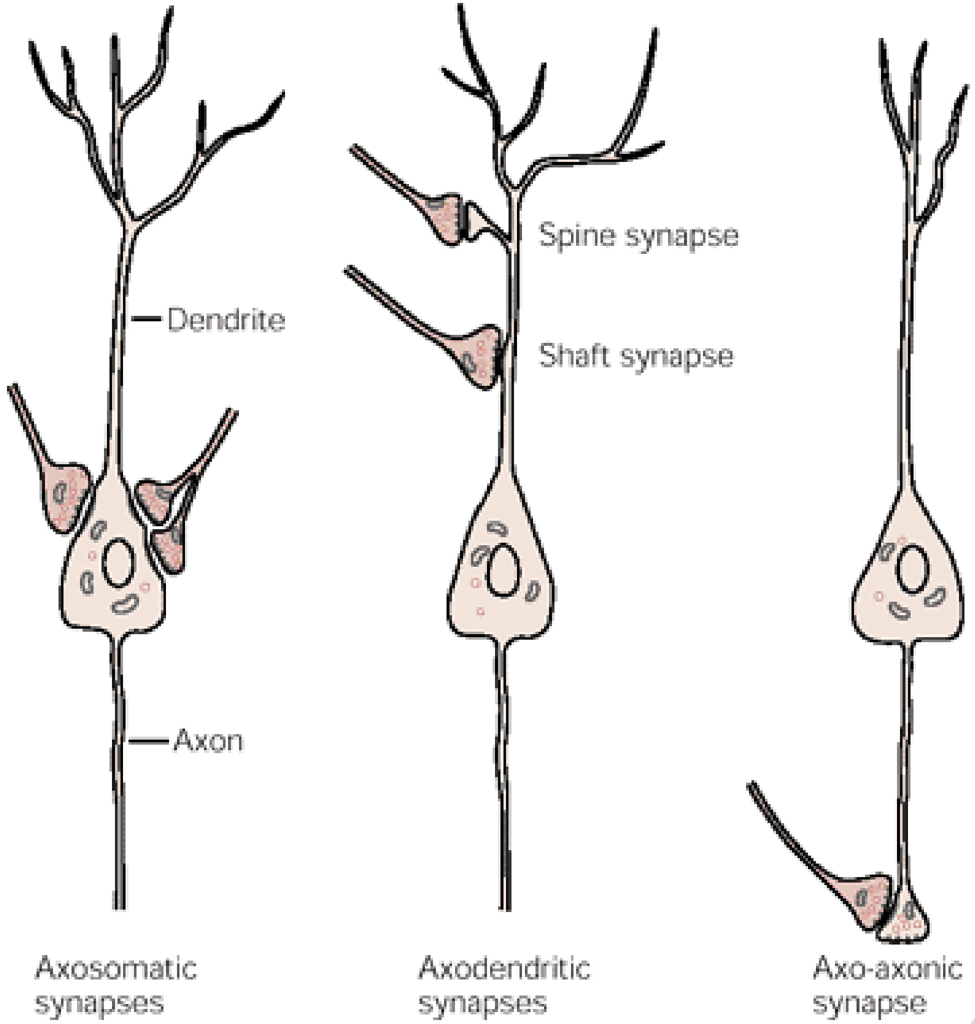


Functional properties of neurons



Nature Reviews | Neuroscience





Neuron communication Synapses - Neurotransmitters

Neurotransmitters

Neurotransmitters are endogenous chemicals that enable neurotransmission. It is a type of chemical messenger which transmits signals across a chemical synapse, such as a neuromuscular junction, from one neuron (nerve cell) to another "target" neuron, muscle cell, or gland cell.

Transmitter	Receptor subtypes	Receptor types	Effect: Ion conductance Na^+	K^+	Ca^{2+}	Cl^-	Second messenger: cAMP	IP_3/DAG
Acetylcholine	Nicotinic	🟠	↑	↑	↑			
	Muscarinic:							
	M_1,	🟢						↑
	M_2, M_3	🟢		↑			↓	
ADH (= vasopressin)	V_1	🟢						↑
	V_2	🟢					↑	
Dopamine	D_1, D_5	🟢					↑	
	D_2	🟢		↑	↓		↓	
GABA (= gamma-aminobutyric acid)	$GABA_A$,	🟠				↑		
	$GABA_B$	🟢		↑	↓		↓	
Glutamate (aspartate)	AMPA	🟠	↑	↑				
	Kainic acid	🟠	↑	↑				
	NMDA	🟠	↑	↑	↑			
	mGlu	🟢					↓	↑
Glycine	–	🟠				↑		
Histamine	H_1	🟢						↑
	H_2	🟢					↑	
Norepinephrine, epinephrine	$\alpha_{1\,(A–D)}$	🟢		↑				↑
	$\alpha_{2\,(A–C)}$	🟢		↑	↓		↓	
	β_{1-3}	🟢					↑	
Opioid peptides	μ, δ, κ	🟢		↑	↓		↓	
Oxytocin	–	🟢						↑
Serotonin (5-hydroxytryptamine)	5-HT_1	🟢		↓			↓	
	5-HT_2	🟢						↑
	5-HT_3	🟠	↑	↑				
	5-$HT_{4–7}$	🟢					↑	
Somatostatin (GHIH)	SRIF	🟢		↑	↓		↓	
Tachykinin	NK1–3	🟢						↑

- Amino acids
- Catecholamines
- Peptides
- Others

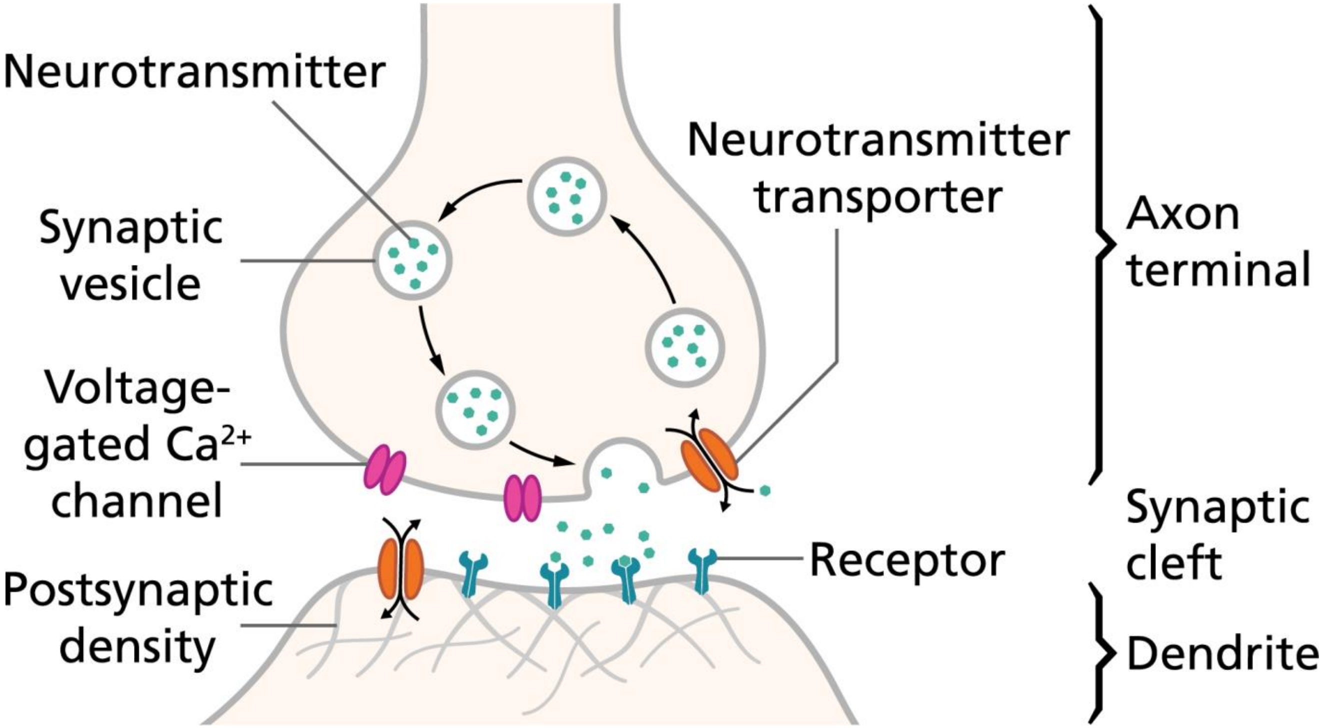
🟠 = ligand-gated ion channel (ionotropic) receptor

🟢 = G-protein coupled (metabotropic) receptor

↓ = inhibits

↑ = promotes

Synaptic transmission

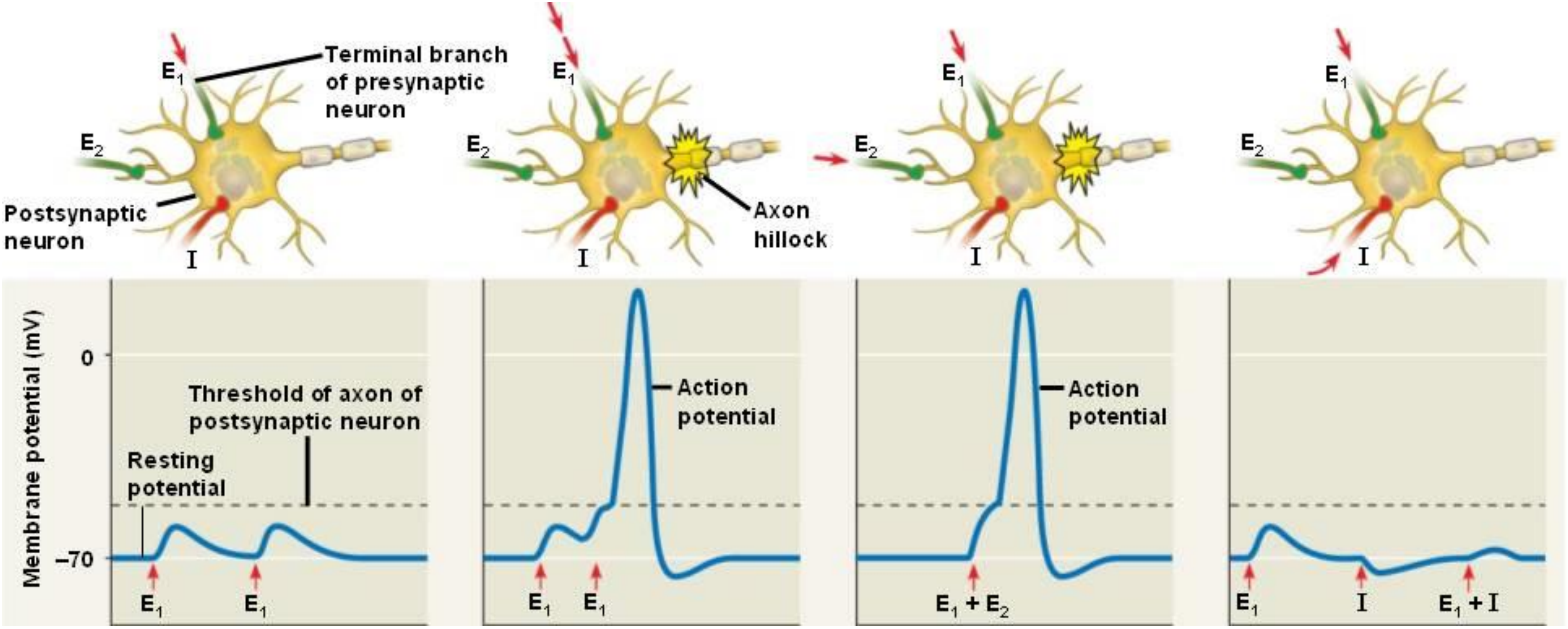


1. Action potential reaches axon terminal and depolarizes membrane
2. Voltage-gated Ca^{+2} channels open and Ca^{+2} flows in
3. Ca^{+2} influx triggers synaptic vesicles to fuse with the membrane and release neurotransmitter
4. Neurotransmitter binds to receptors on target cell
5. Depending on the synapse it can lead to depolarization (Na^{+2} influx) or hyperpolarization (Ca^{-1} influx)

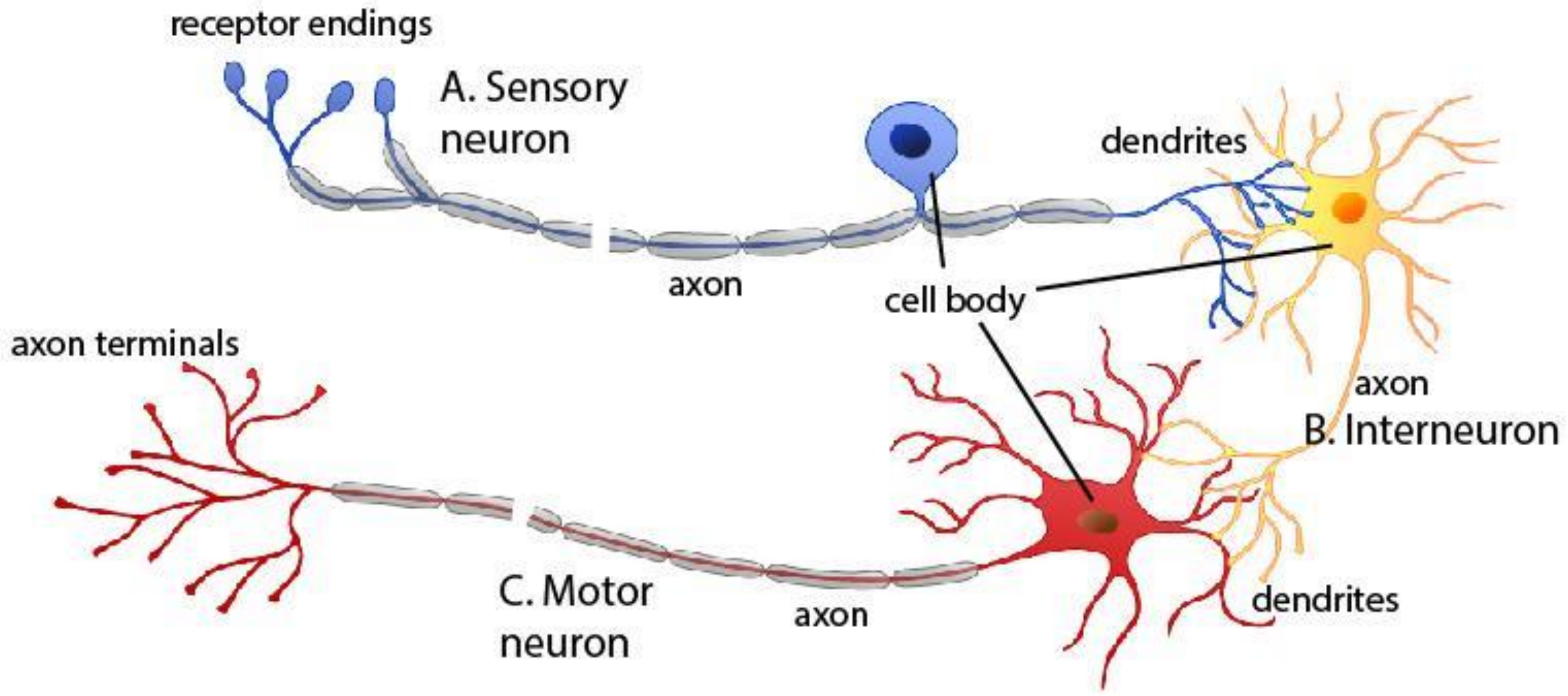
Functional classification of neurons

- Action on other neurons (Excitatory – Inhibitory)
- Discharge patterns (Regular spiking, Fast spiking, Bursting
- Neurotransmitter (GABAergic, Glutamatergic, Dopaminergic, …)

Spatial and temporal summation



Networks of neurons



Transduction is the process of converting that sensory signal to an electrical signal in the sensory neuron.

Sensory receptors – Each type is optimized to respond to different kind of stimuli:

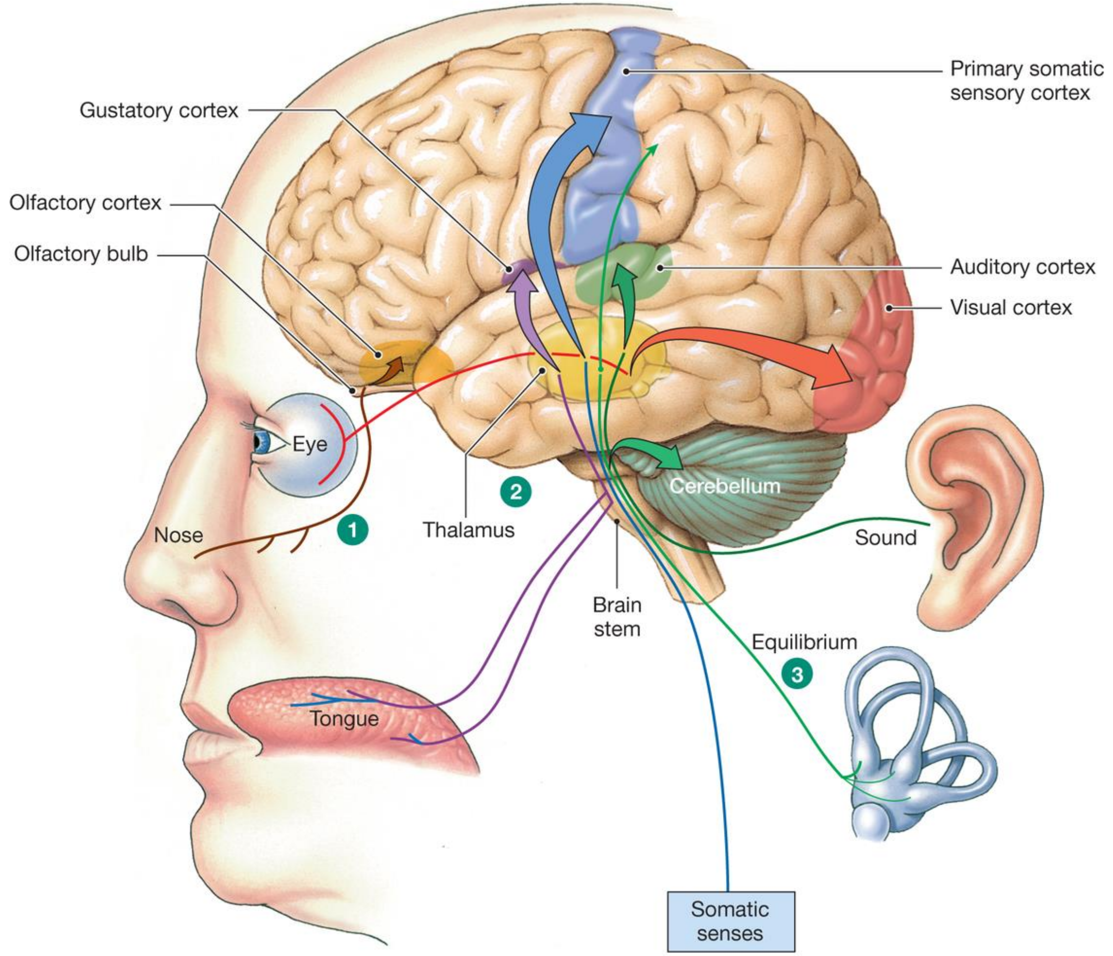
- Thermoreceptors – Respond to changes in temperature
- Photoreceptors – react to light
- Chemoreceptors – Respond to chemicals
- Mechanoreceptors – Respond to pressure, touch and vibration
- Nociceptors – pain

Sensory modalities & primary sensory areas

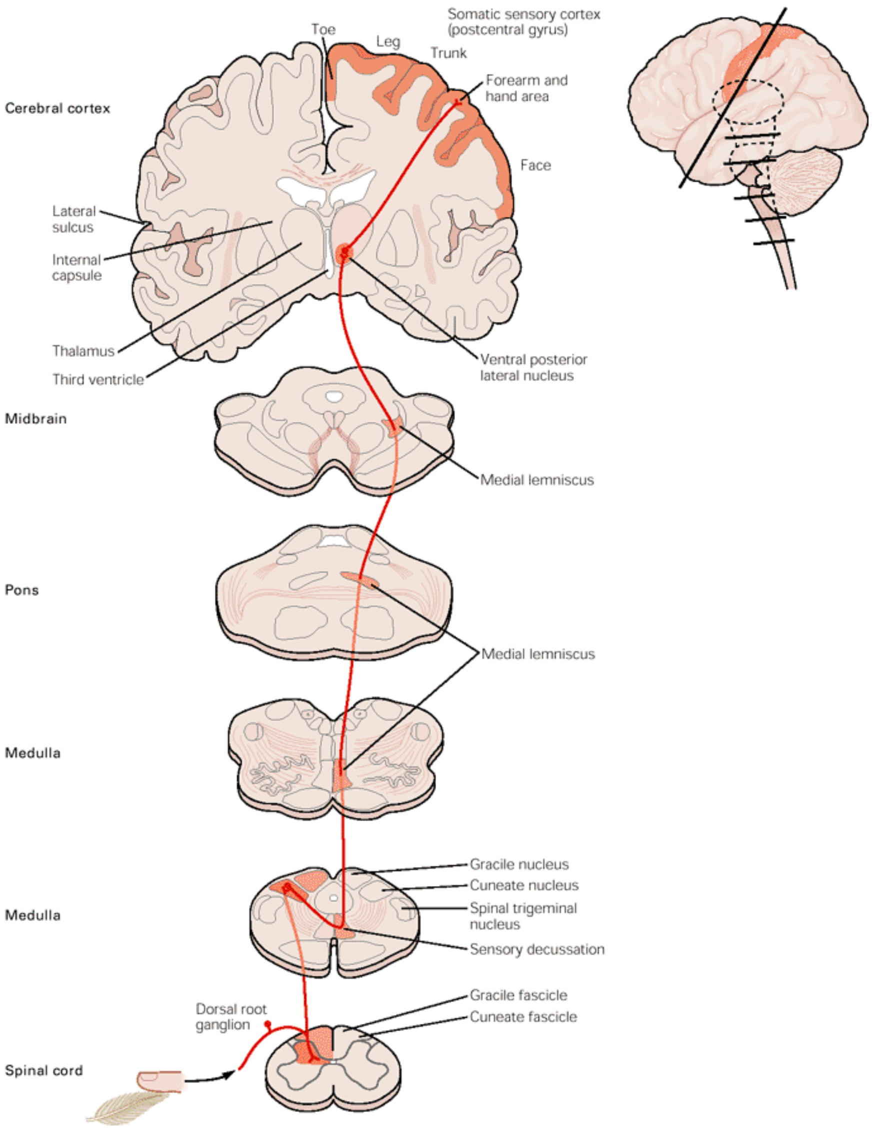
Labelled line theory

- Individual receptors preferentially transduce information about an adequate stimulus

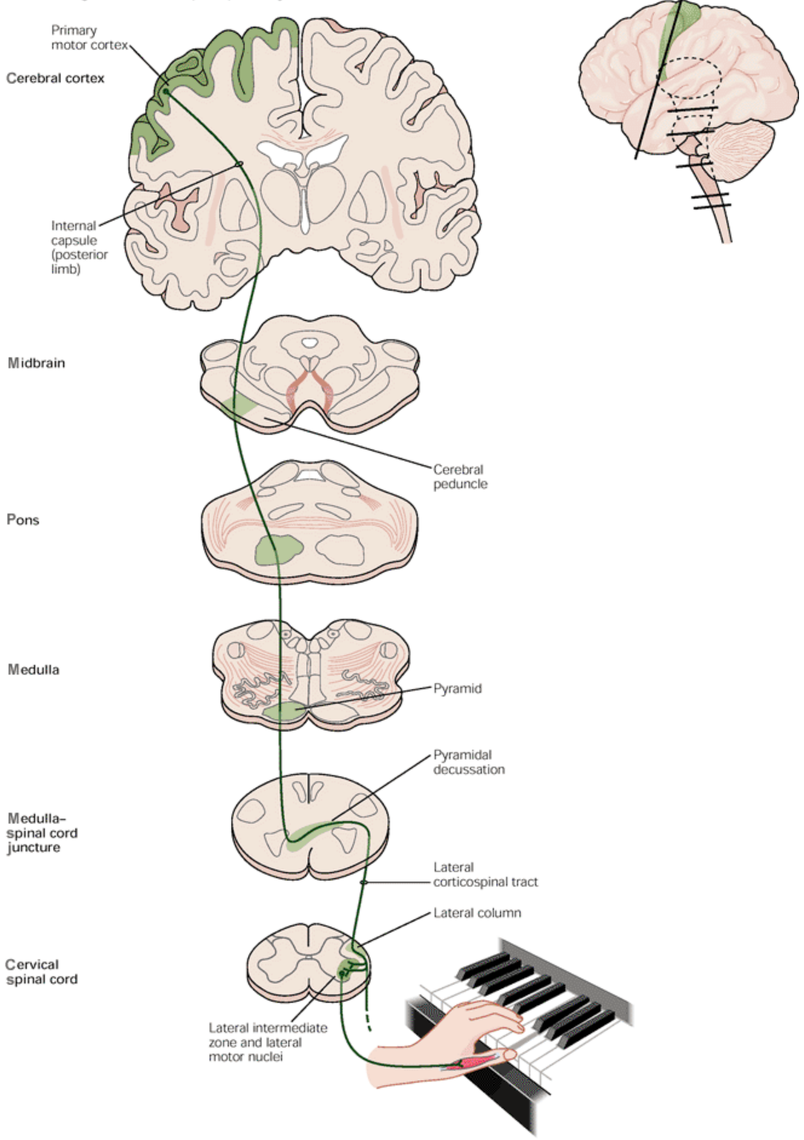
- Individual primary afferent fibers carry information from a single type of receptor



Ascending dorsal column–medial lemniscal pathway to primary sensory cortex

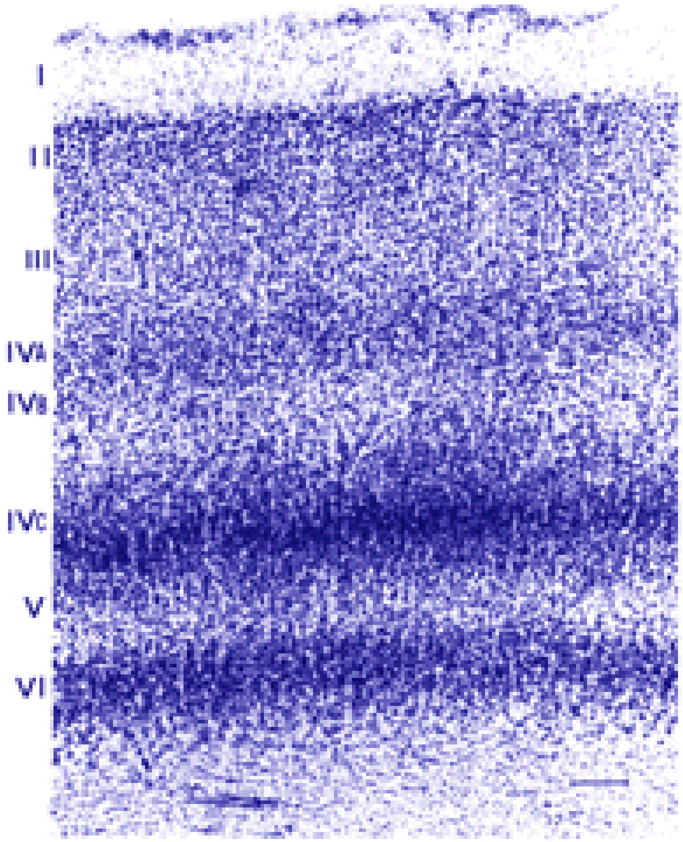


Descending lateral corticospinal pathway

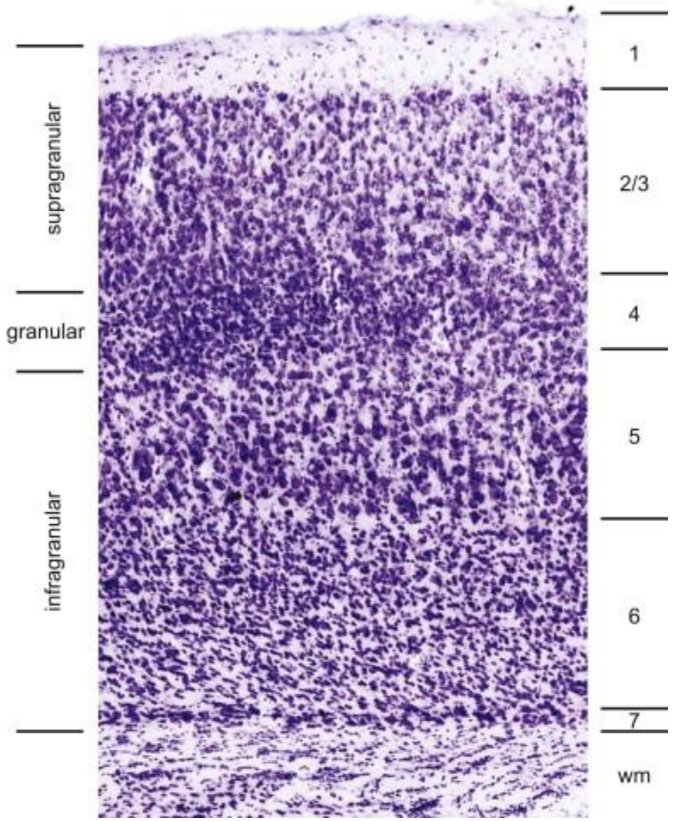


The layered structure of neocortex

Monkey

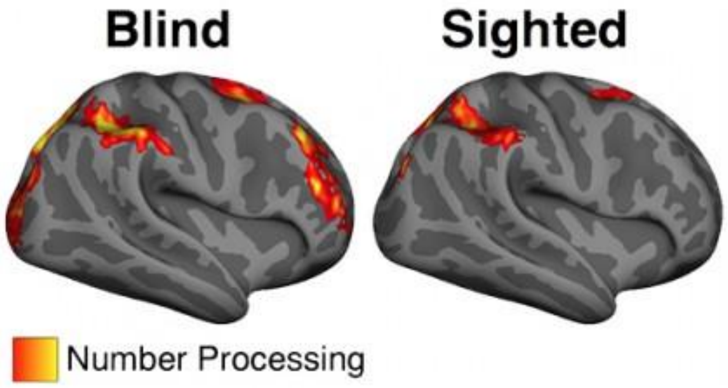


Mouse



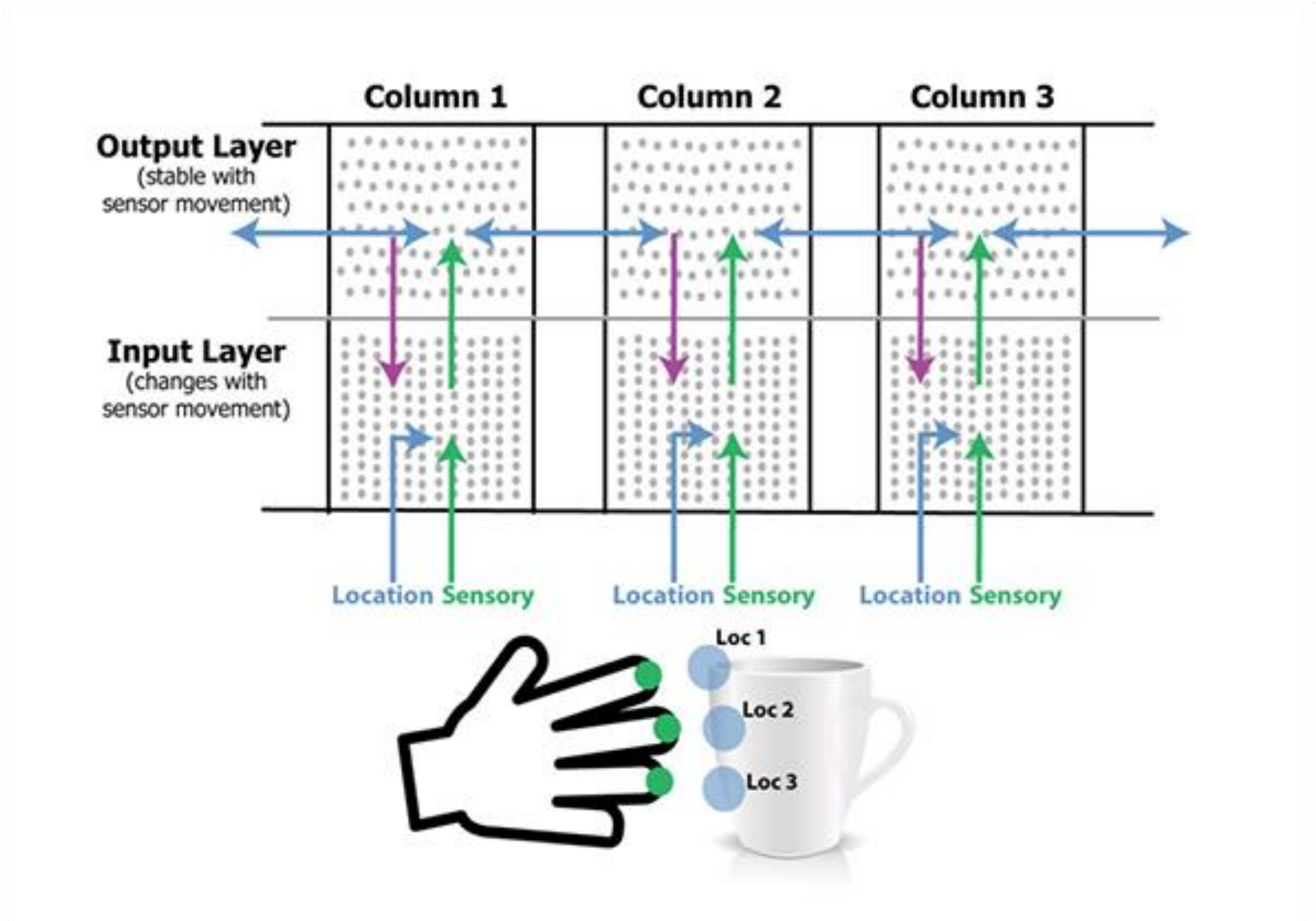
The function of a given cortical area is not fixed! Cortical flexibility

- In arm amputees, the hand area of somatosensory cortex responds to stimulation of the face
- The auditory cortices of deaf individuals respond to visual stimuli
- In congenitally blindness visual areas show responses to
  - language
  - mathematical processing

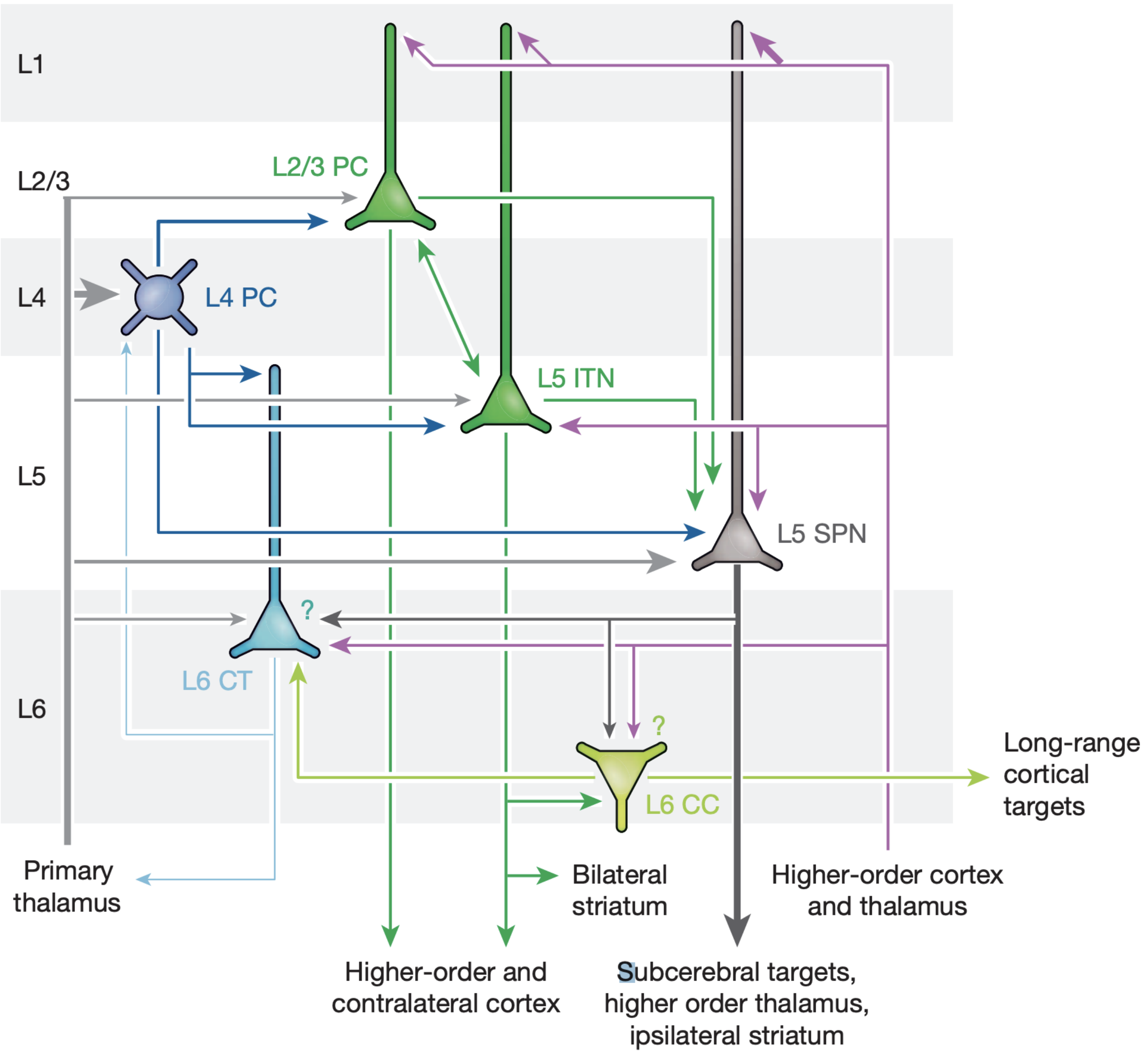


Kanjliaa et al. (2016)

Cortical columns as canonical computations



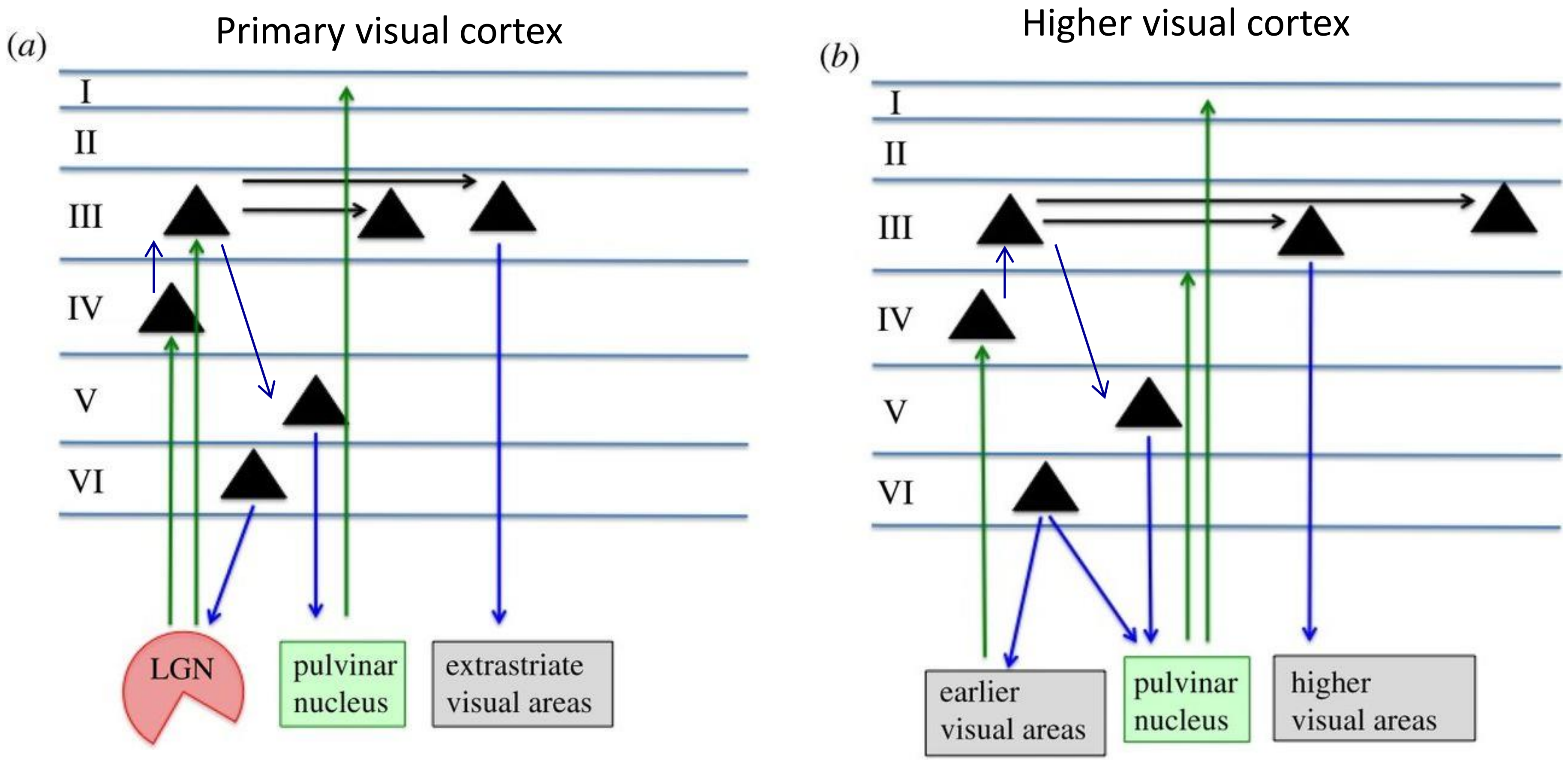
Canonical connectivity of cortical principal cells



feedforward input to a given area, which either comes from thalamus or from ‘lower’ cortical areas, comes dominantly into layer 4 (L4);
L4 projects strongly to layers 2/3 (L2/3);

L2/3 provides feedforward input to L4 of ‘higher’ cortical areas, and also projects to L5; L5 provides the only output from cortex other than feedback to thalamus, and also projects to L6; L6 projects up to layers 2 through 4, completing a loop through the layers; and L6, and more generally layers other than L4, provide feedback to areas projecting feedforward input to the given area

Connectivity between neocortical layers in sensory areas (excitatory)



Primary sensory thalamus

Higher order thalamus

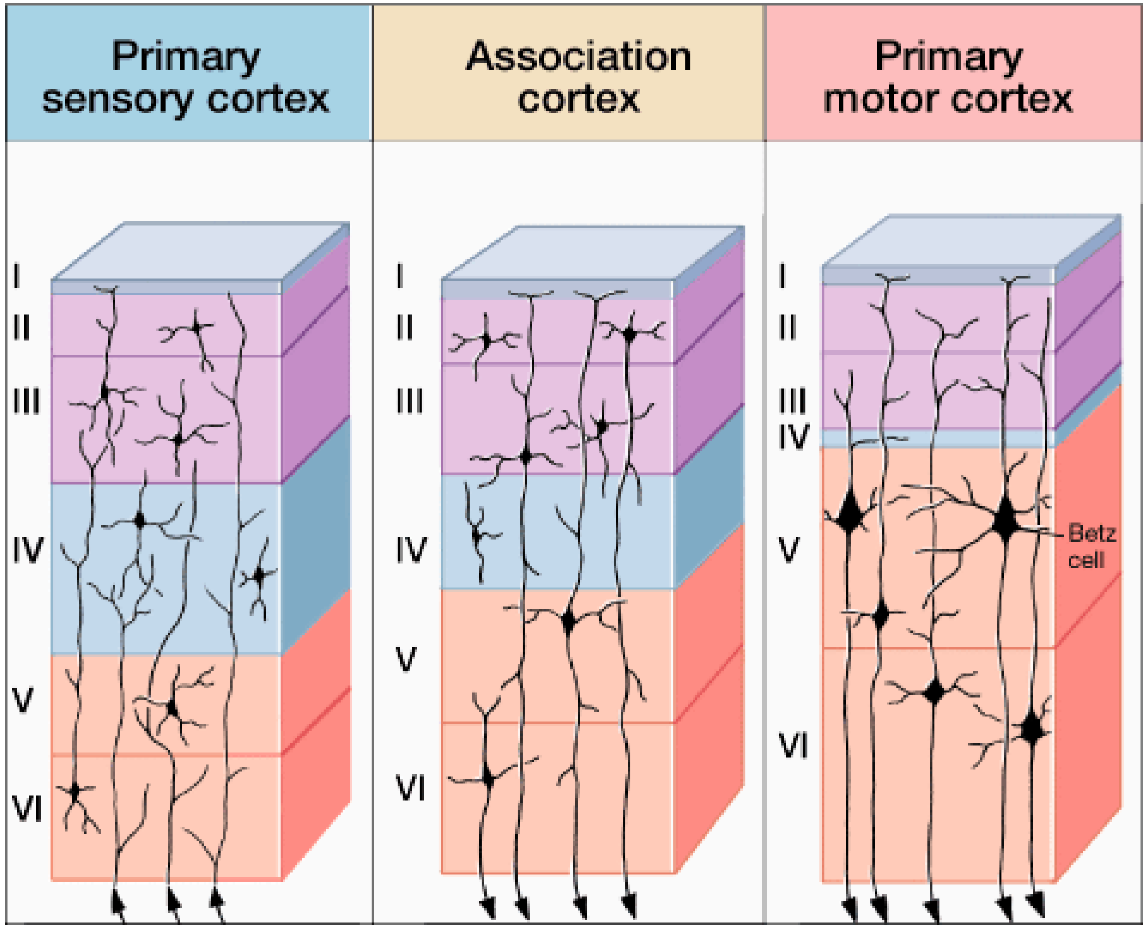
Higher order sensory cortex

Early sensory areas

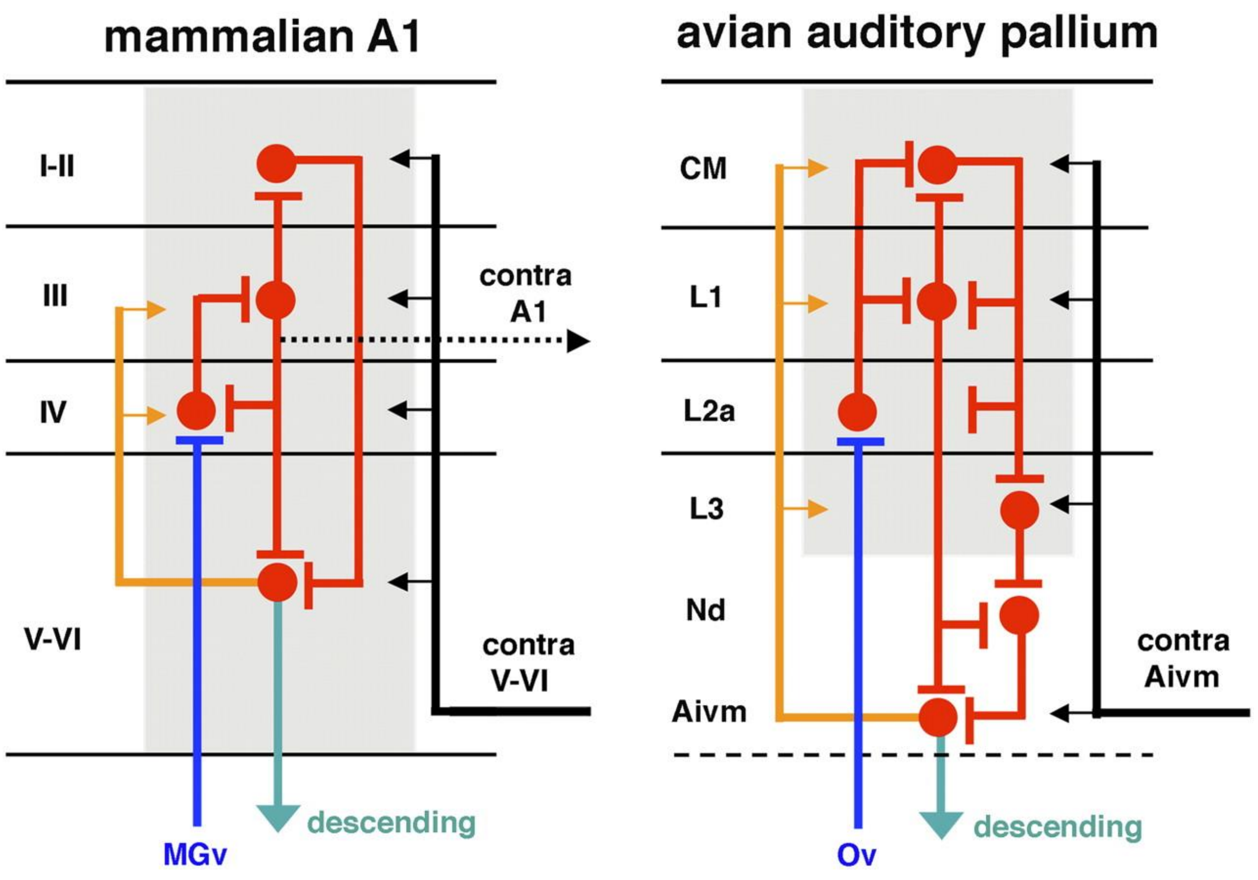
Higher order thalamus

Higher order sensory cortex

Connectivity within a functional unit

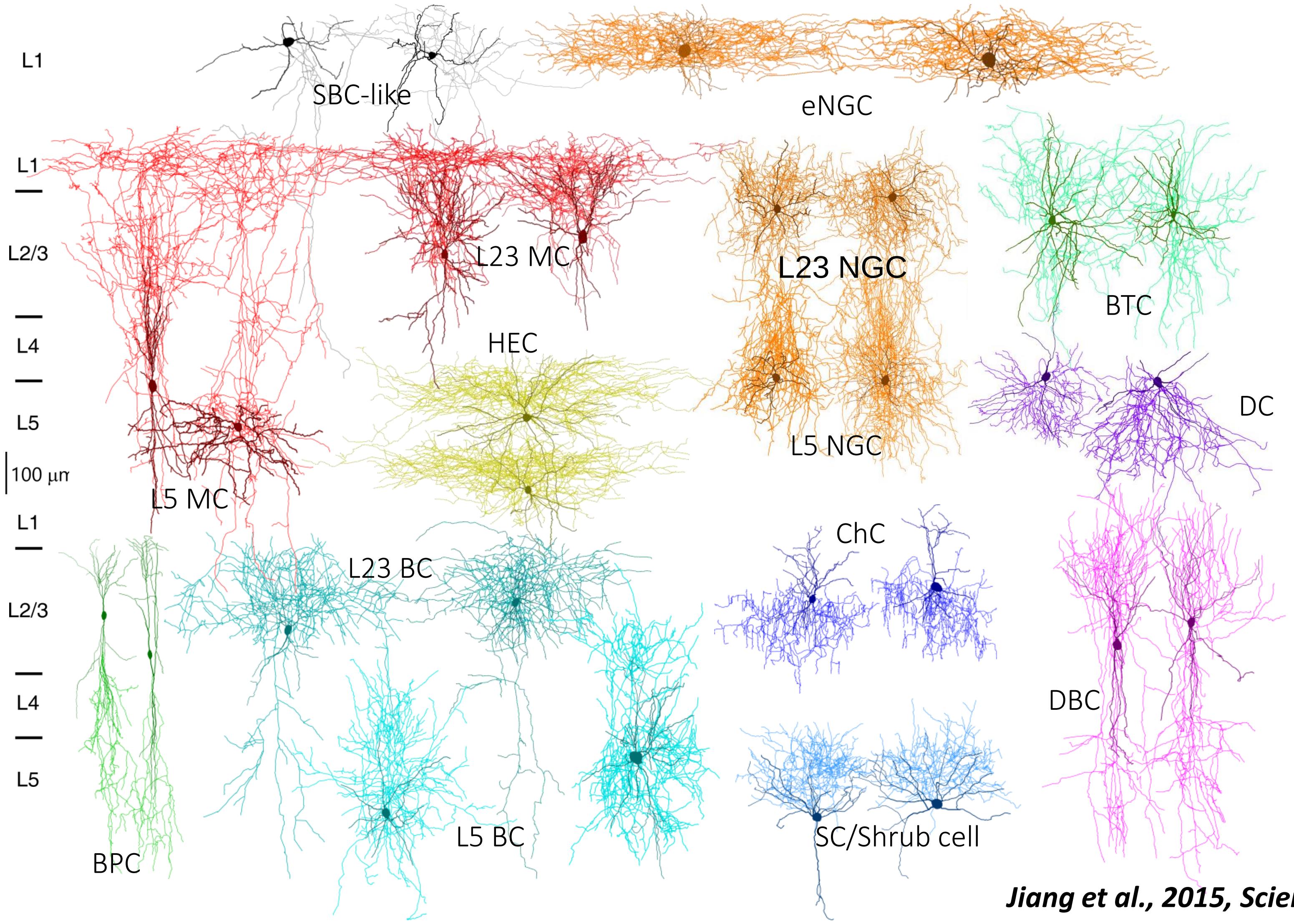


Comparable laminar and columnar organization across species



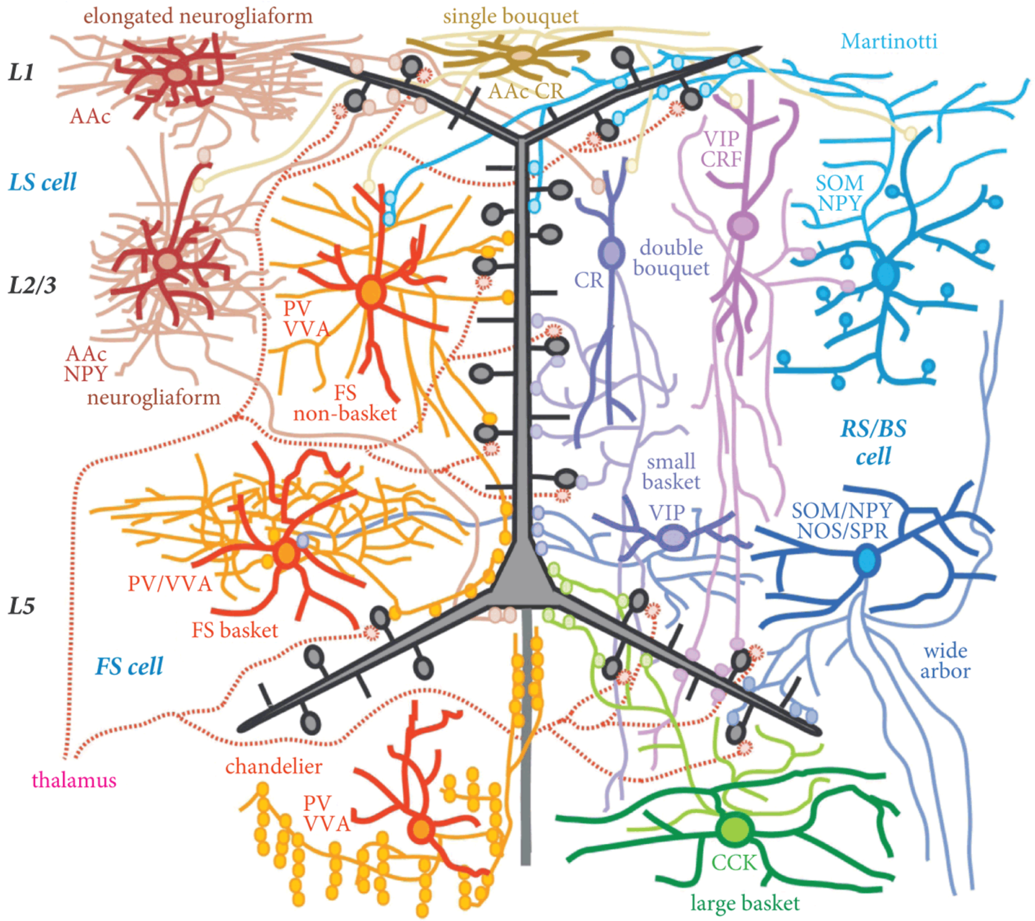
Yuan Wang et al. 2010

Large number of inhibitory subtypes in the cortex

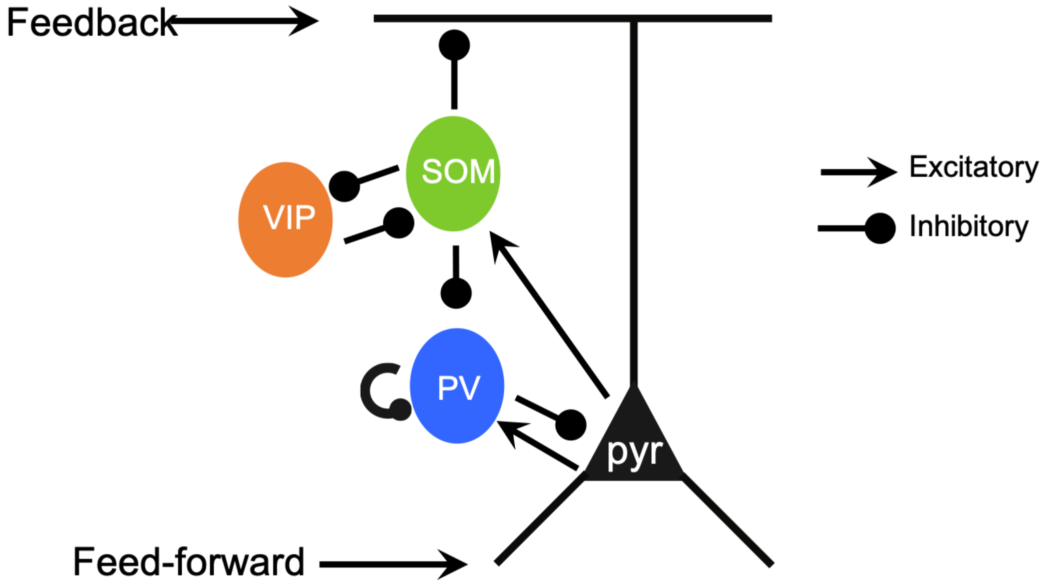


Jiang et al., 2015, Science

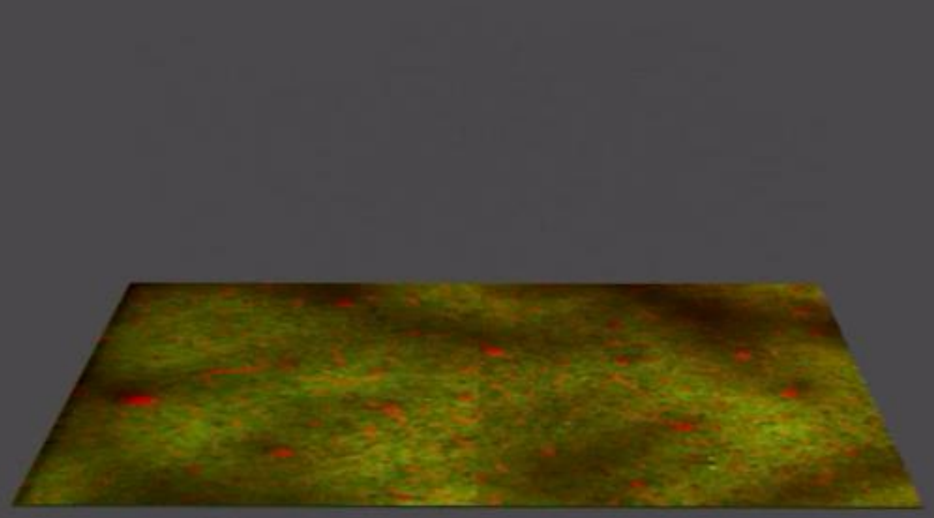
Local connectivity with inhibitory neurons—simplified version



Kubota (2014)



Pfeffer et. al (2013)

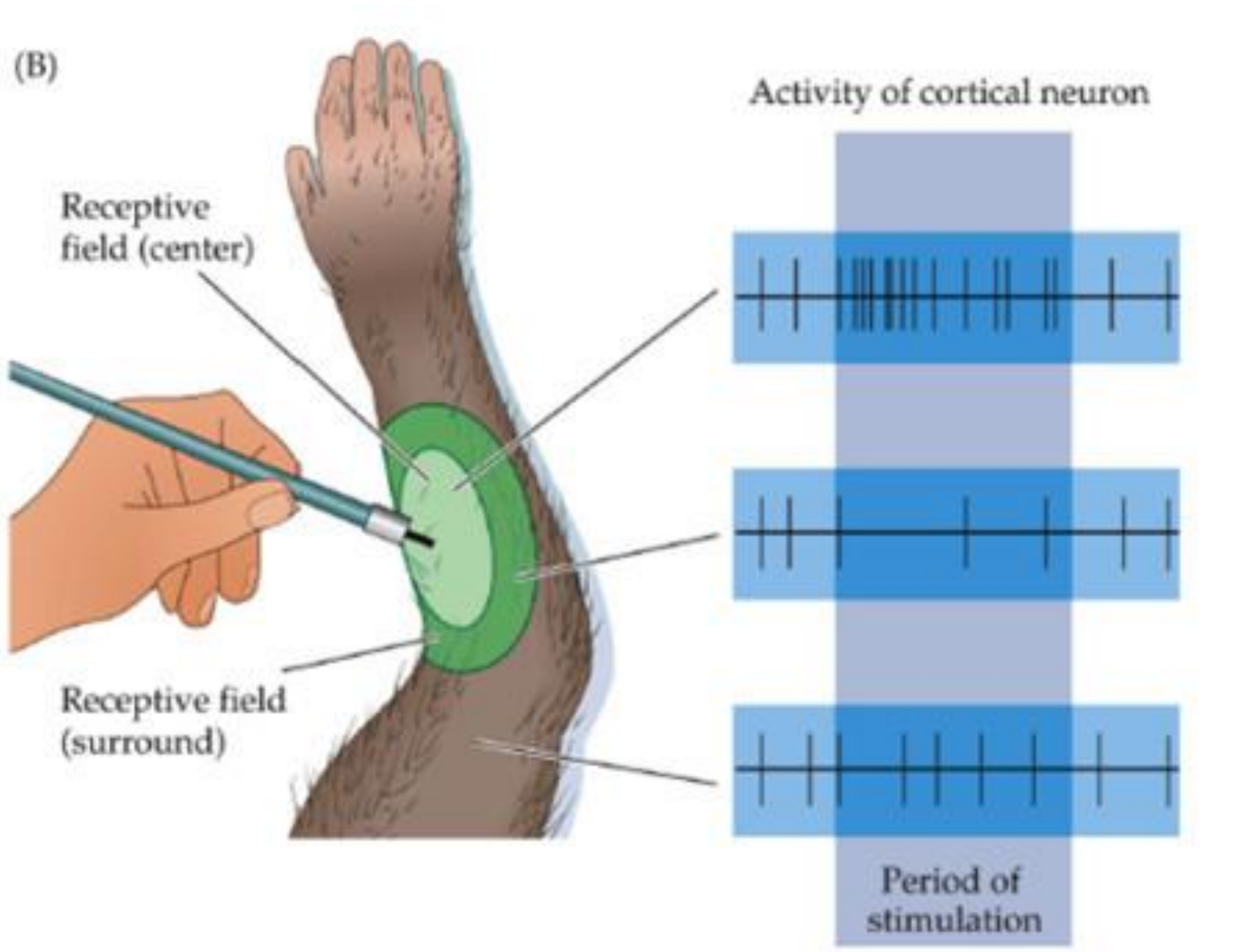


Receptive field

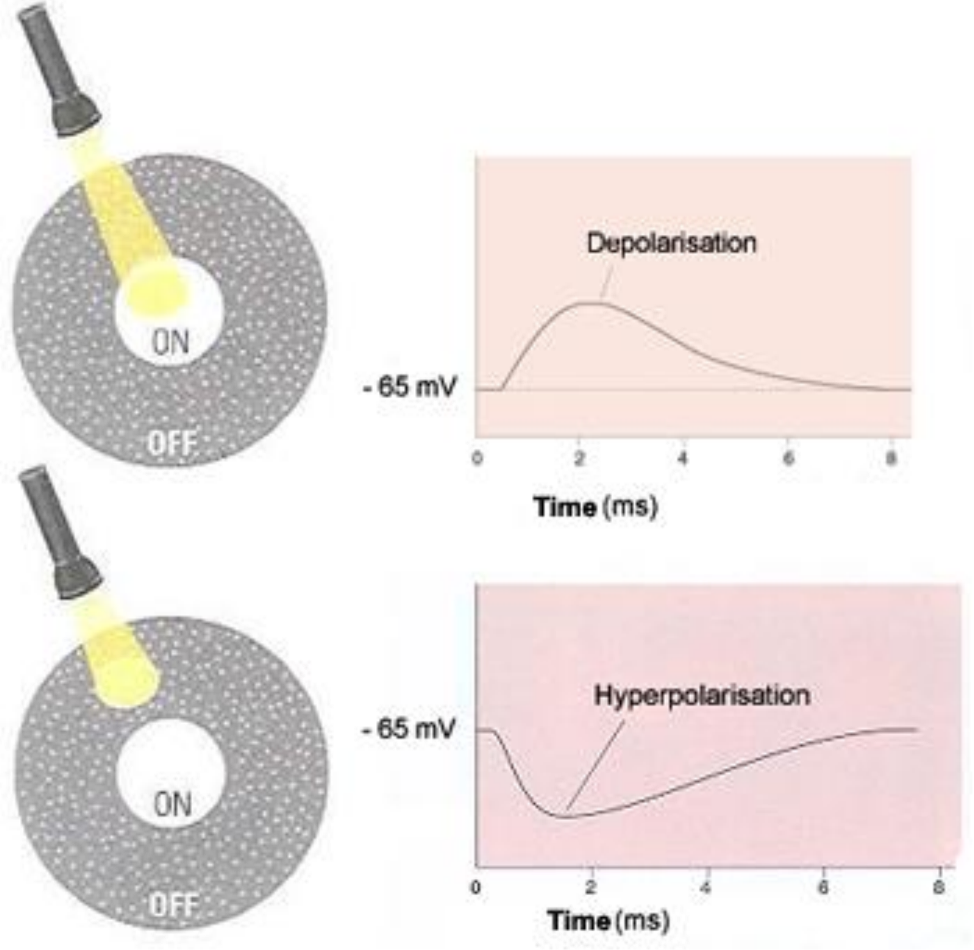
- The **receptive field** of a sensory neuron is the particular region of the sensory space in which a stimulus will elicit neuronal response.

- The sensory space can be defined in a single dimension (e.g. carbon chain length of an odorant), two dimensions (e.g. skin surface) or multiple dimensions (e.g. space, time and tuning properties of a visual receptive field)

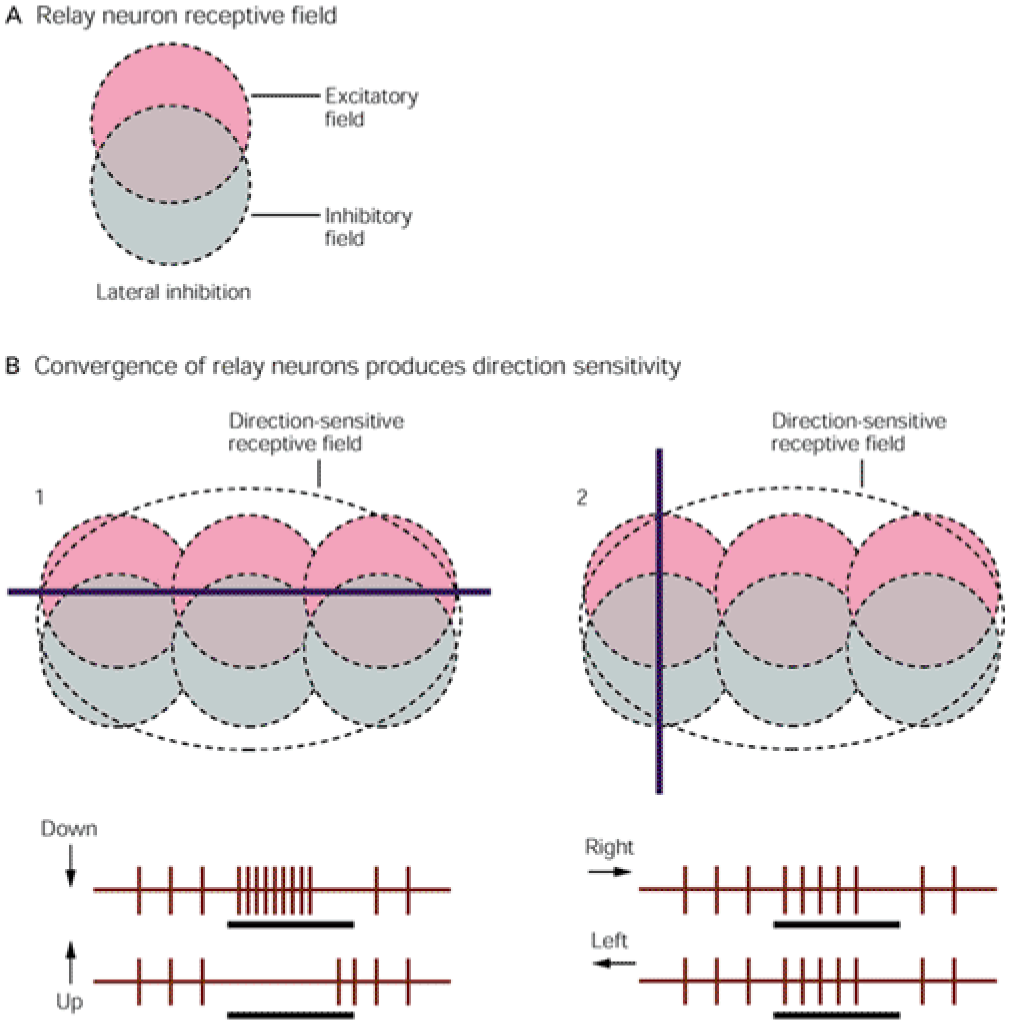
Receptive field examples

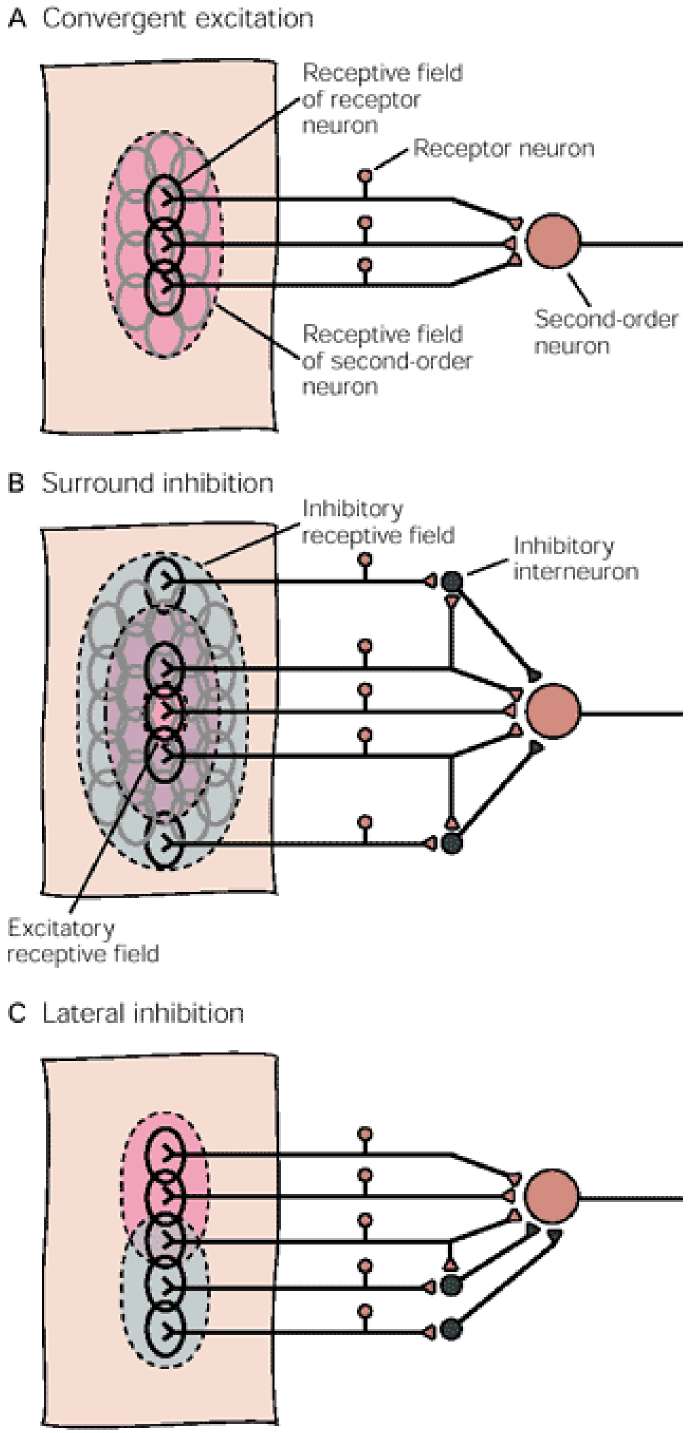


***NEUROSCIENCE*, Fourth Edition, Figure 1.13 (Part 2)**

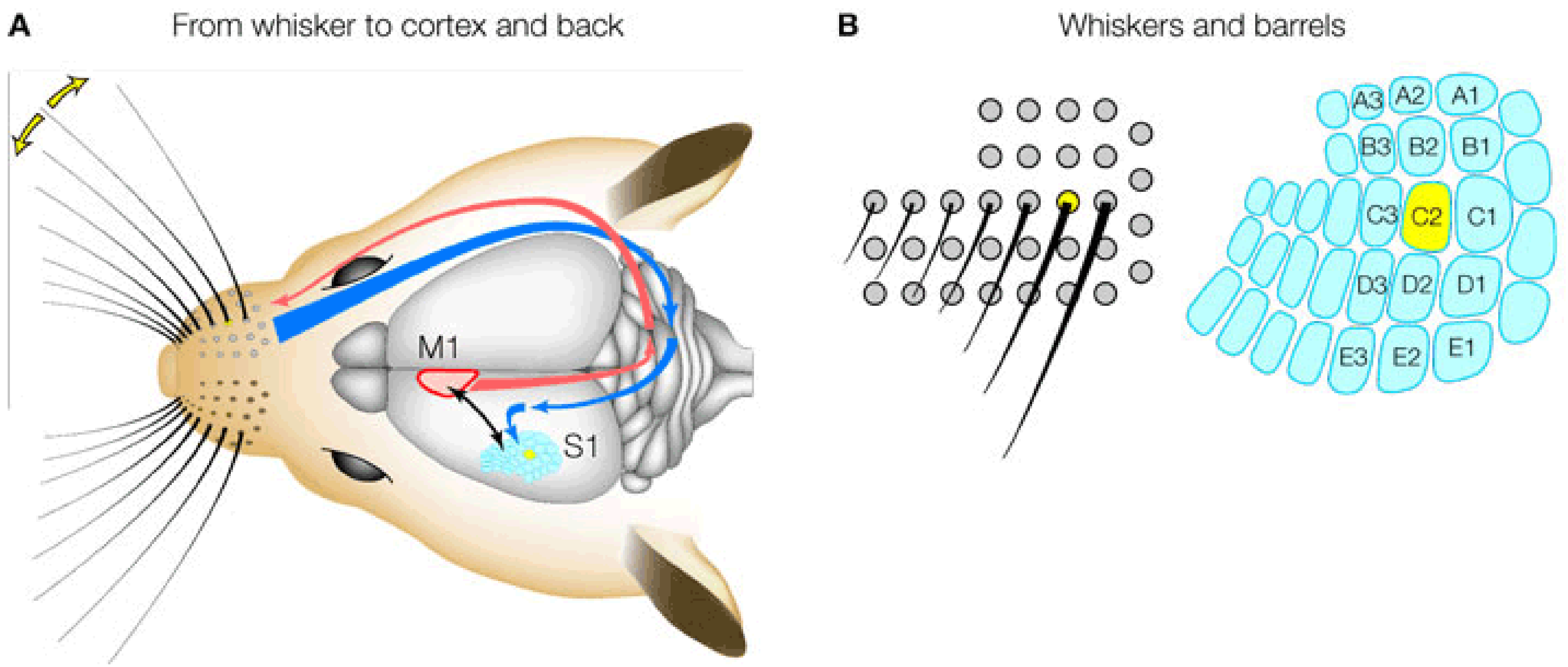


Cortical coding



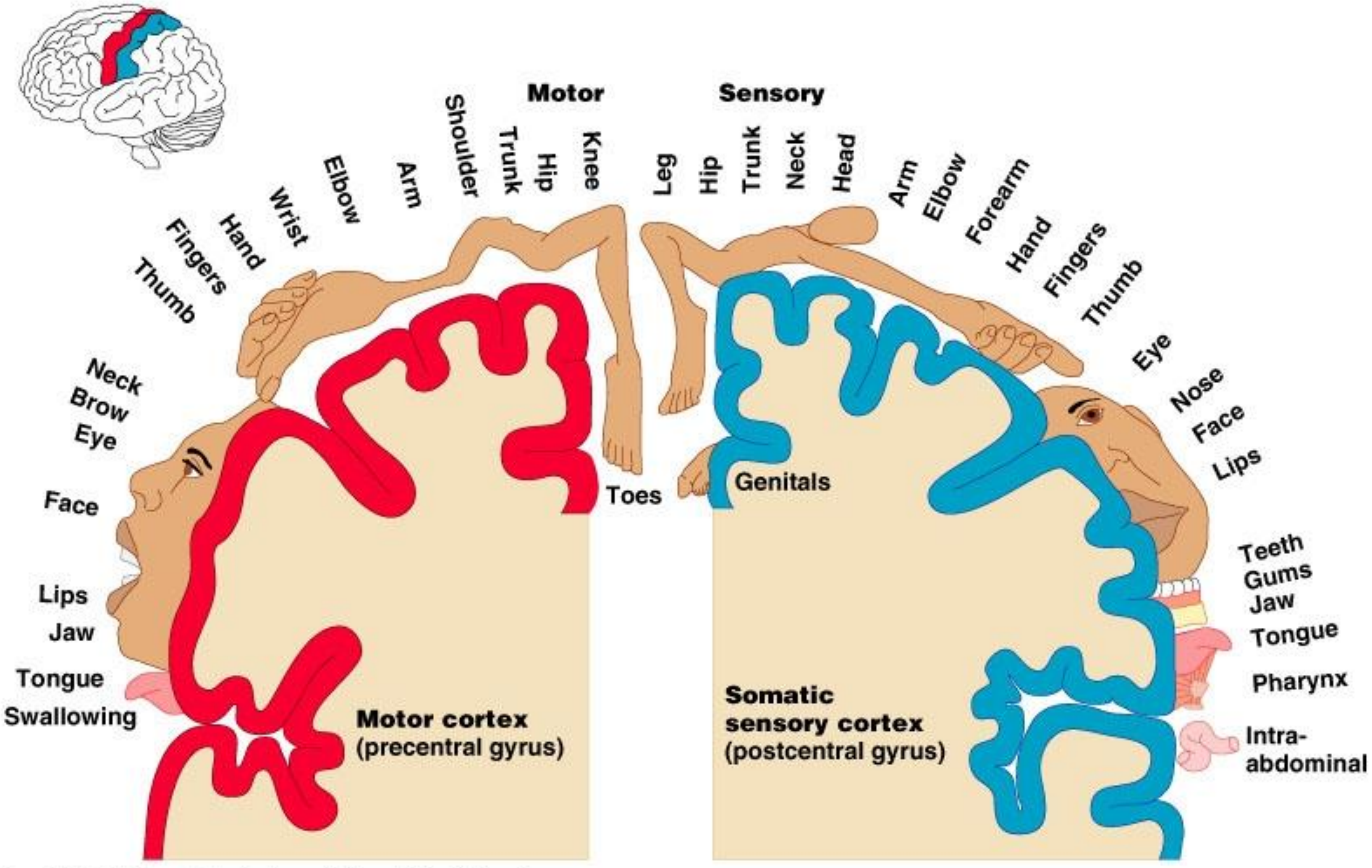


Barrel columns in the mouse somatosensory system



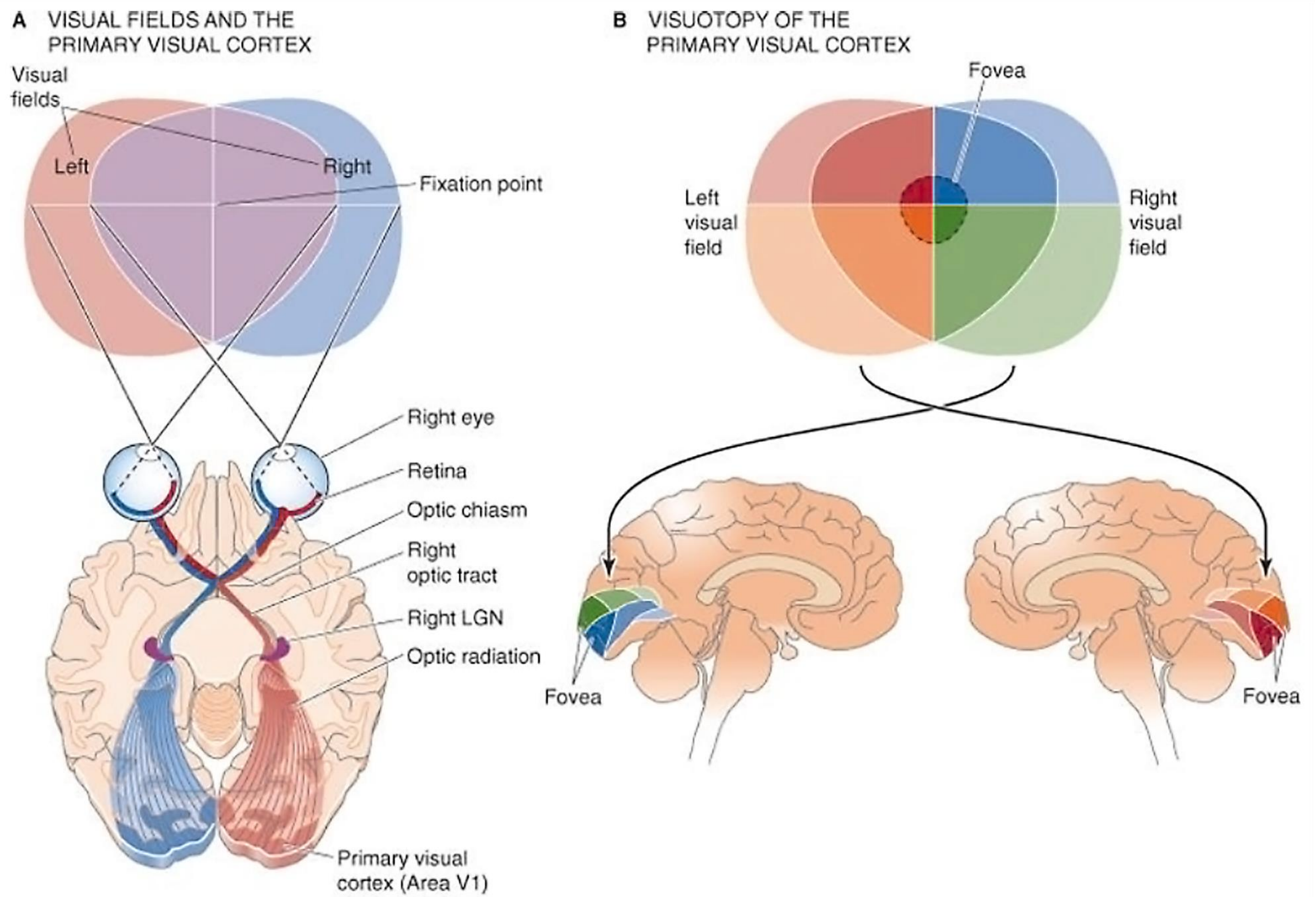
Aronoff and Petersen 2008

Body maps in somatosensory and motor areas

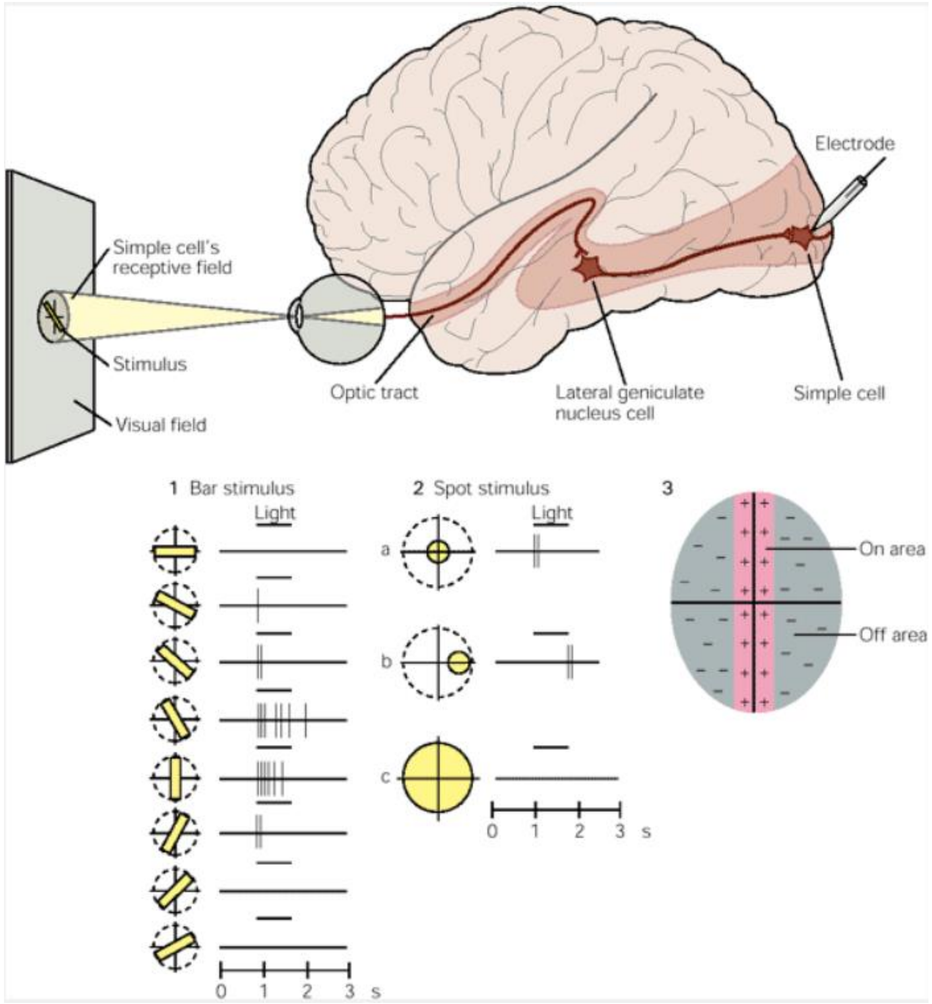


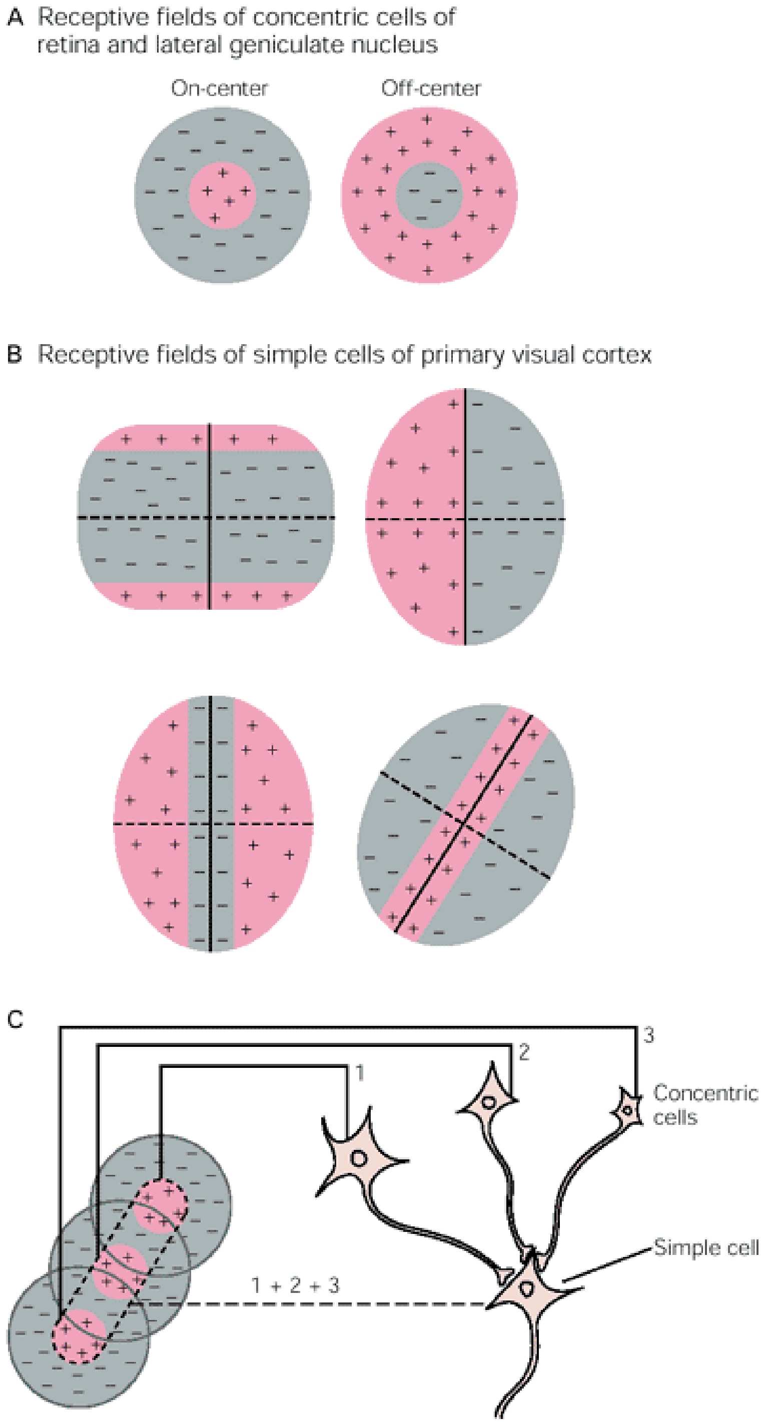
homunculus

Topographic maps in the visual system



Convergence of excitatory input





Orientation columns in primary visual cortex

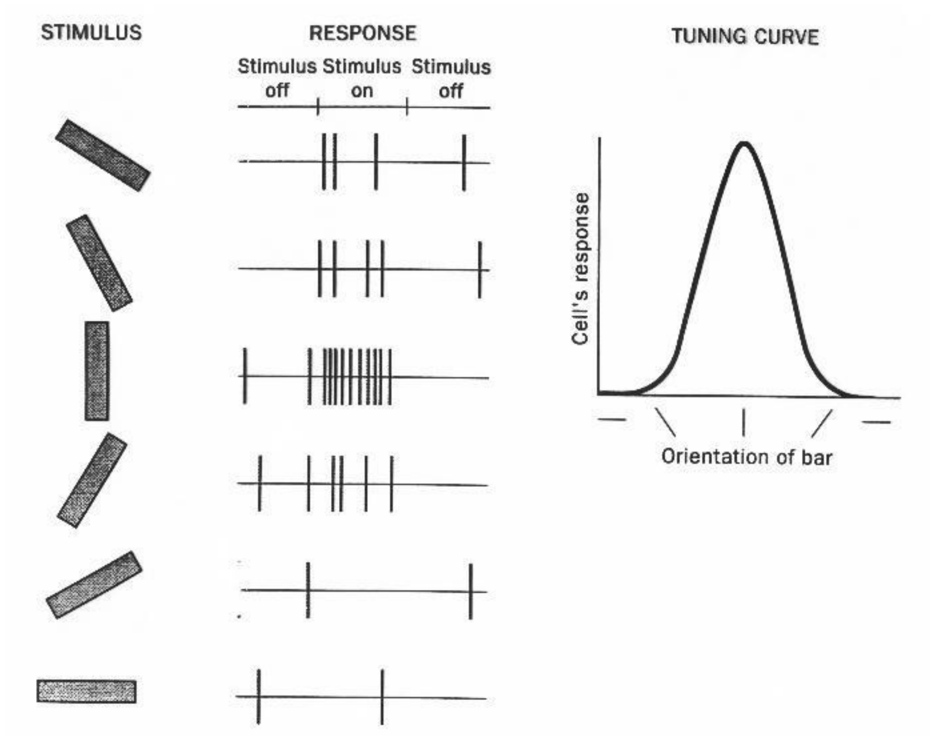
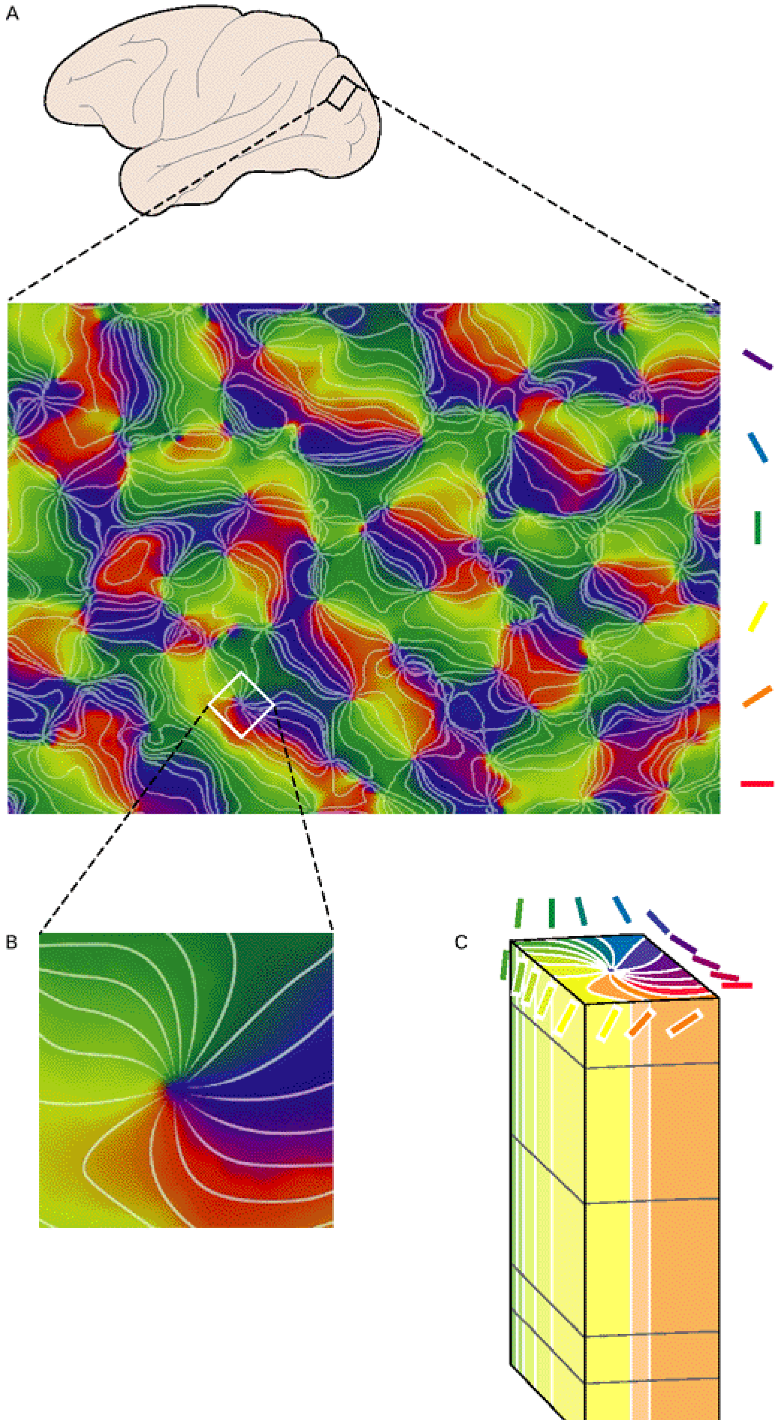
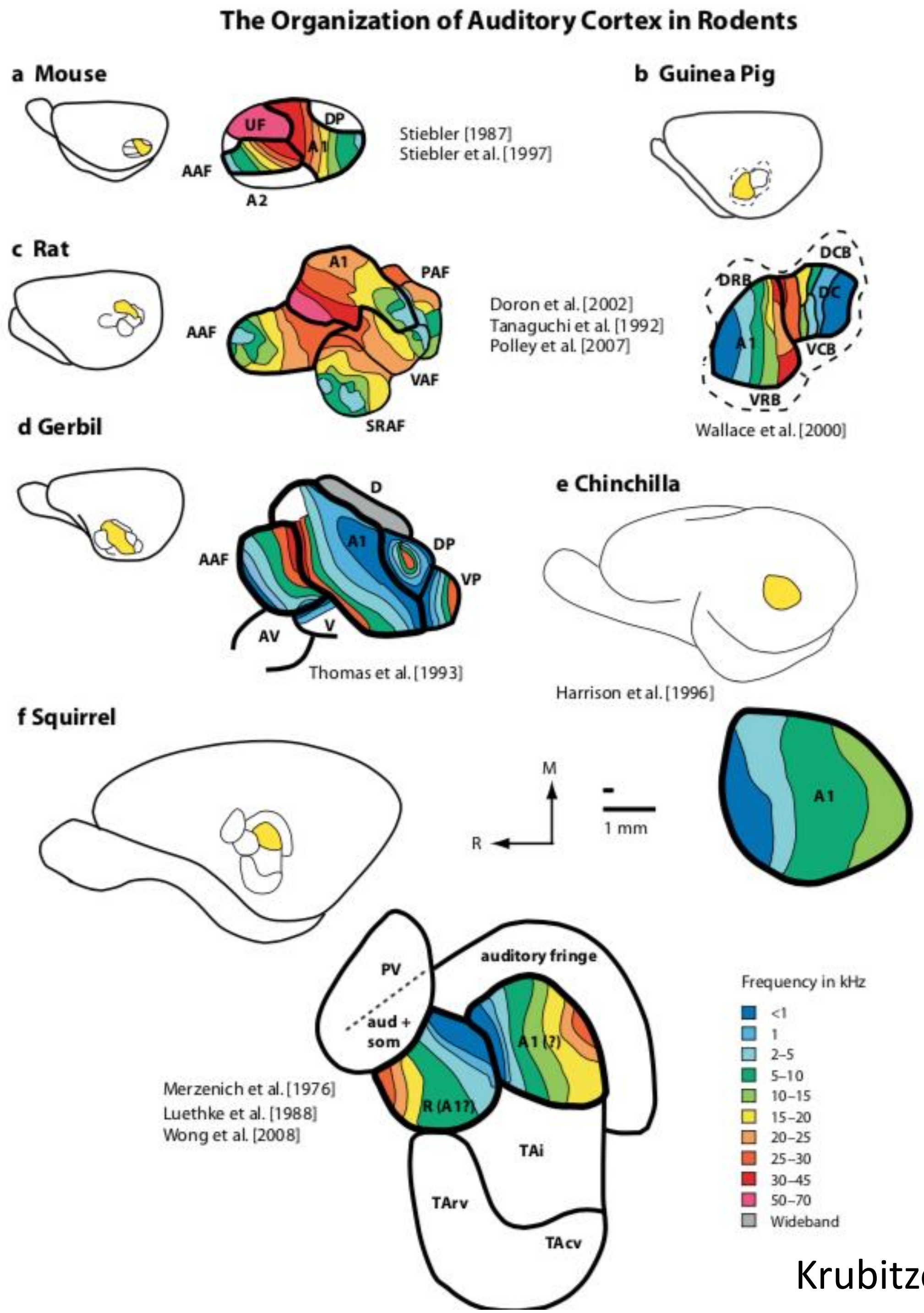


FIGURE 4.8 Response of a single cortical cell to bars presented at various orientations.

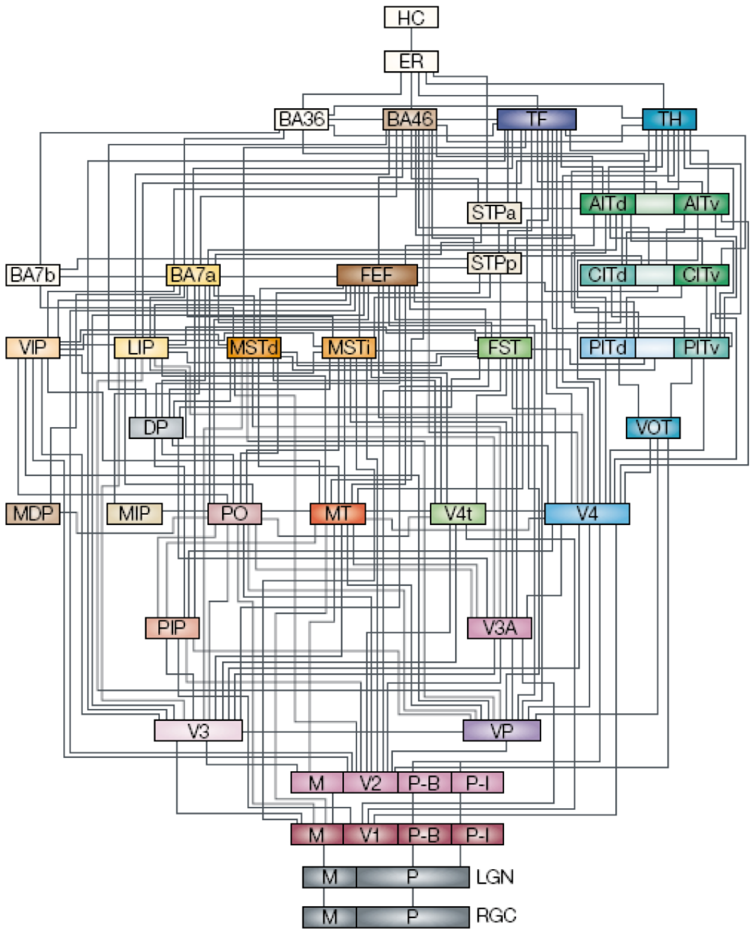


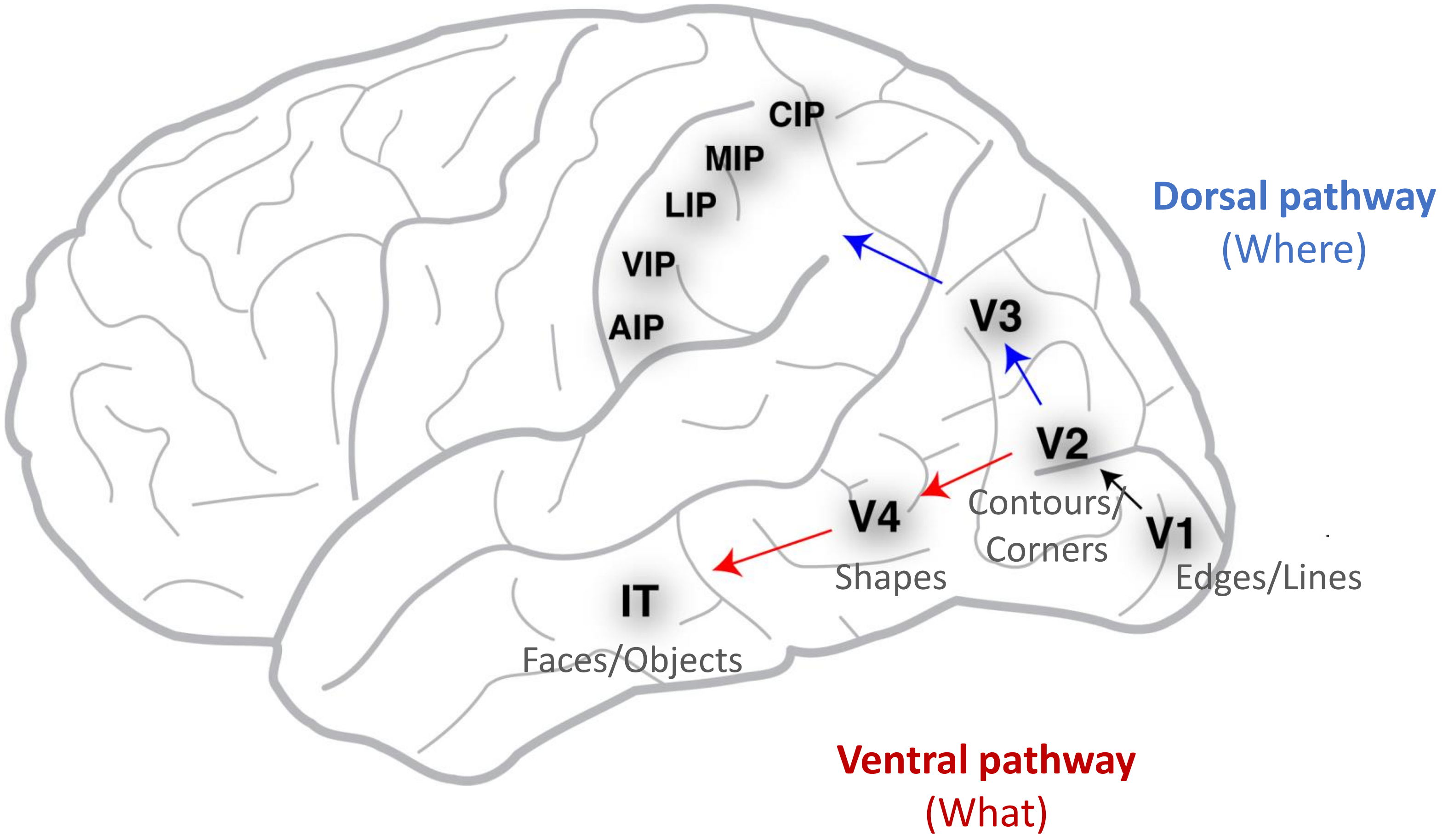
Tonotopic maps in auditory system



Krubitzera et al. 2011

Hierarchical processing in the visual system



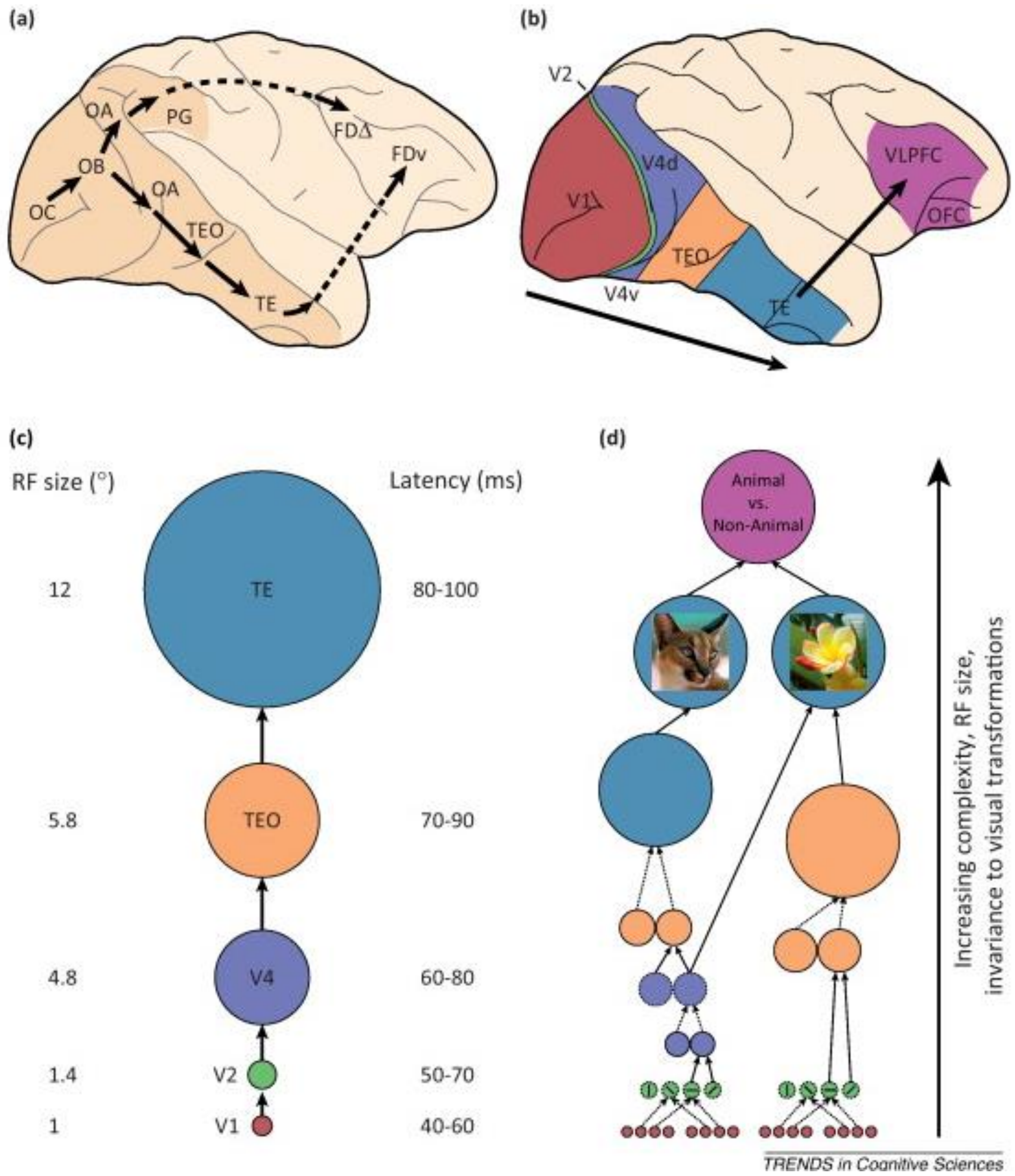


Hierarchical processing:

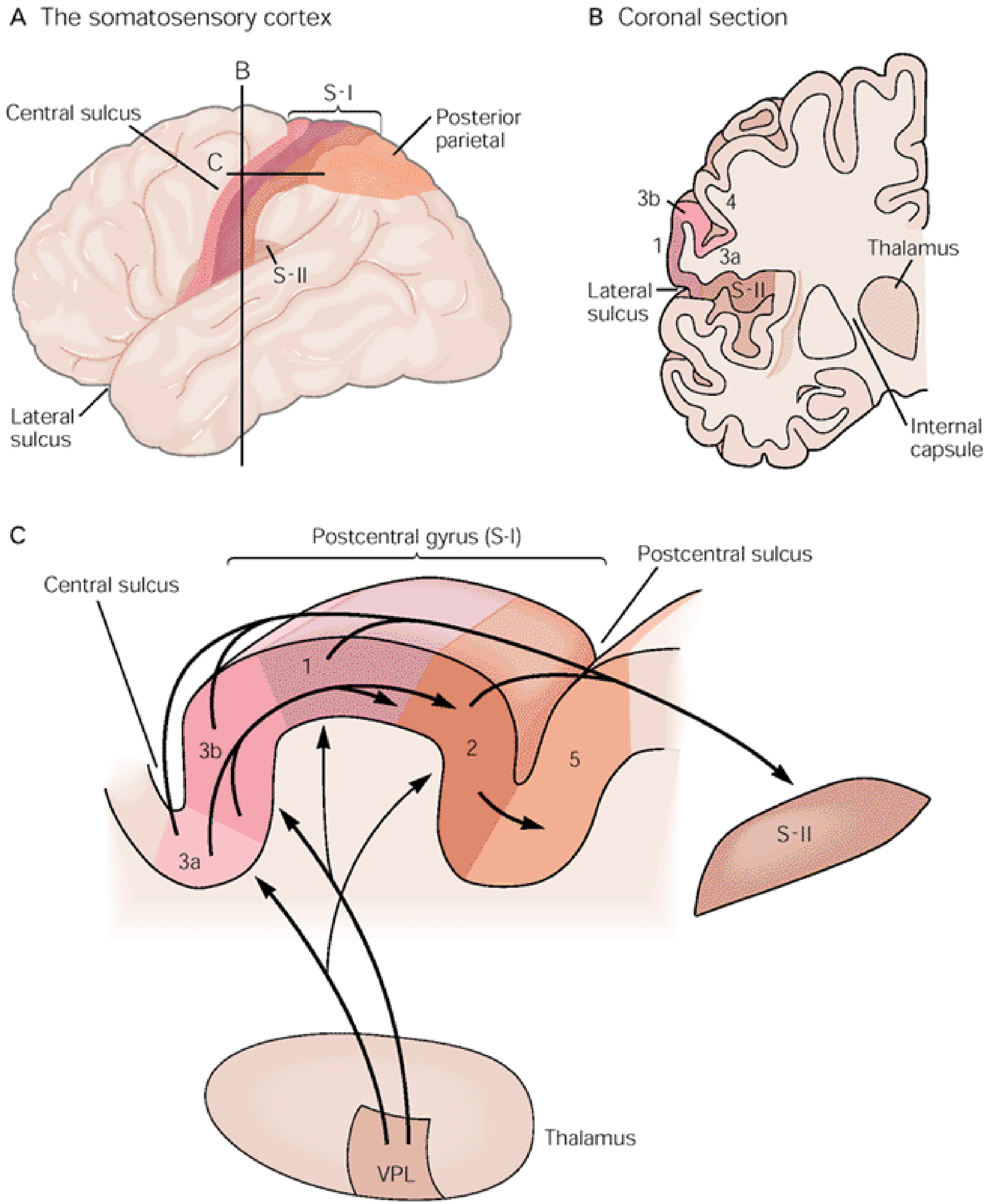
Through selectivity, each neuron responds to a narrow range of stimuli, across time, space, frequency, etc.

At each processing step, signals from previous neurons converge and activate another neuron.

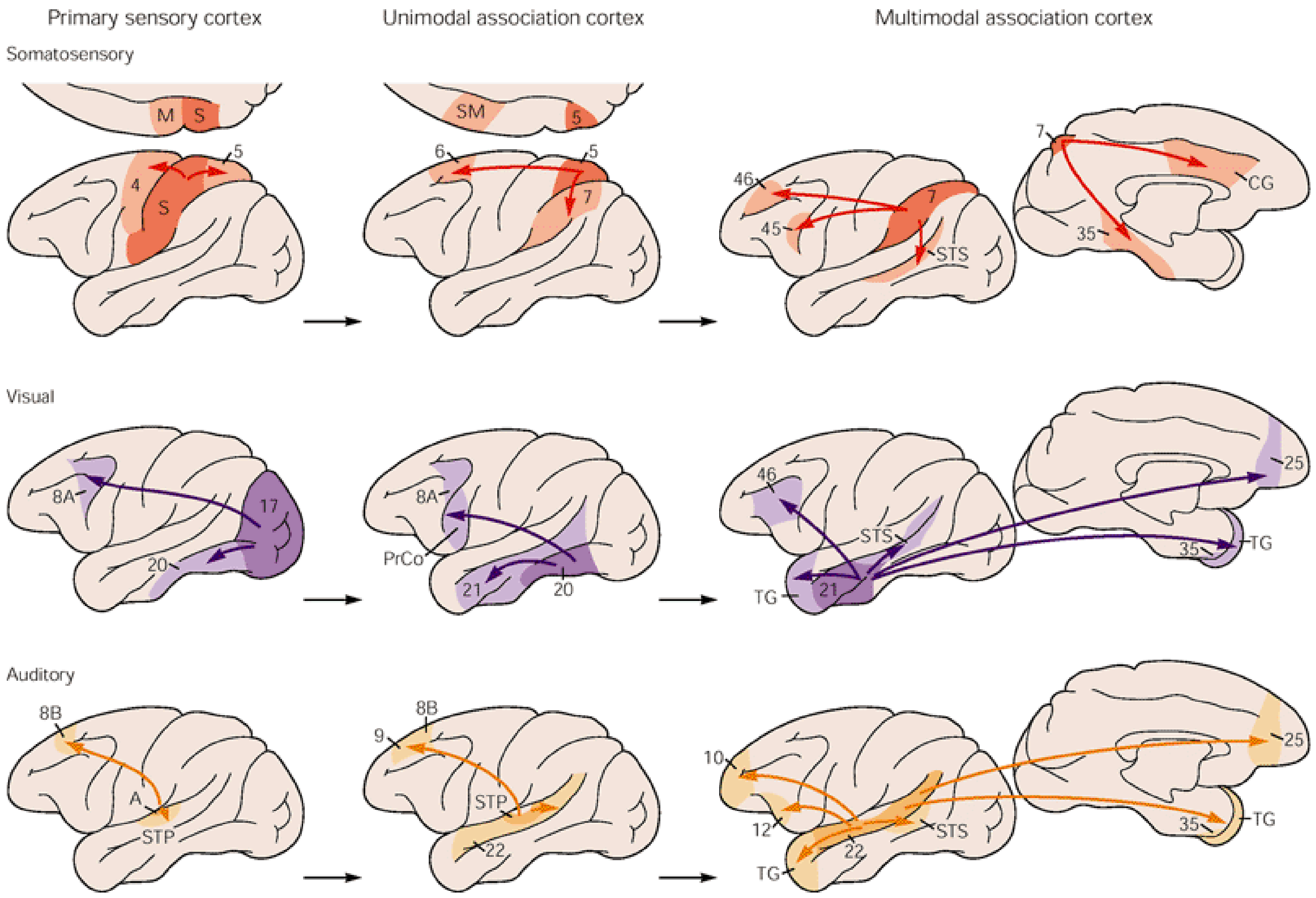
This allows increasingly complex patterns to be detected in the stimulus.



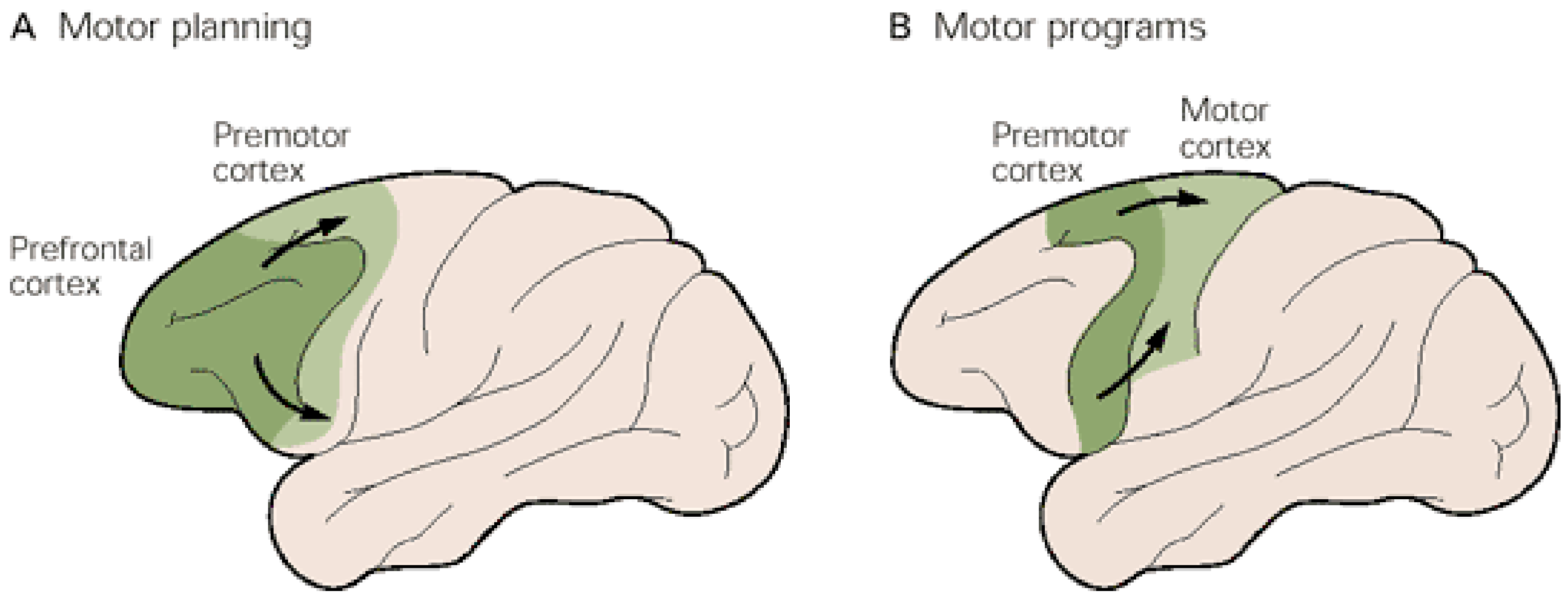
Hierarchical processing in the somatosensory cortex



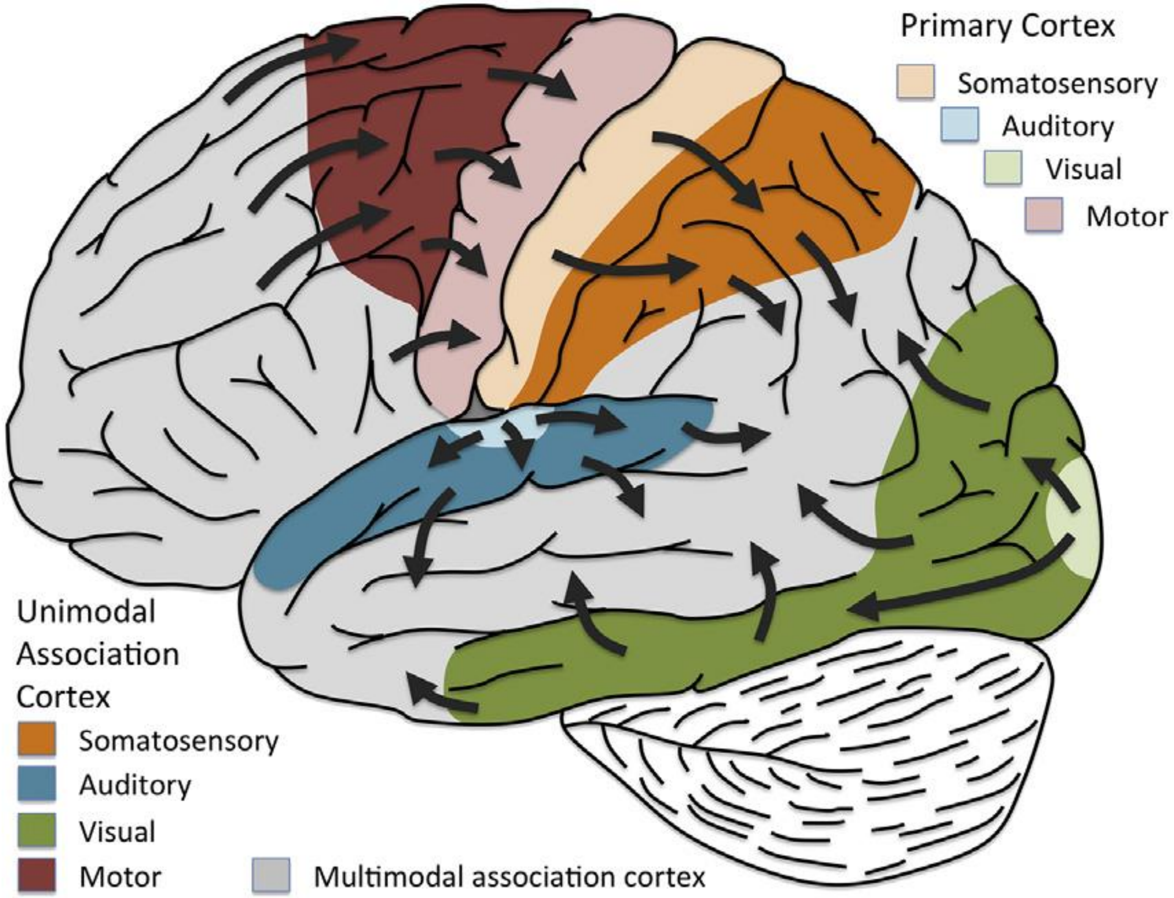
Stages of sensory information processing

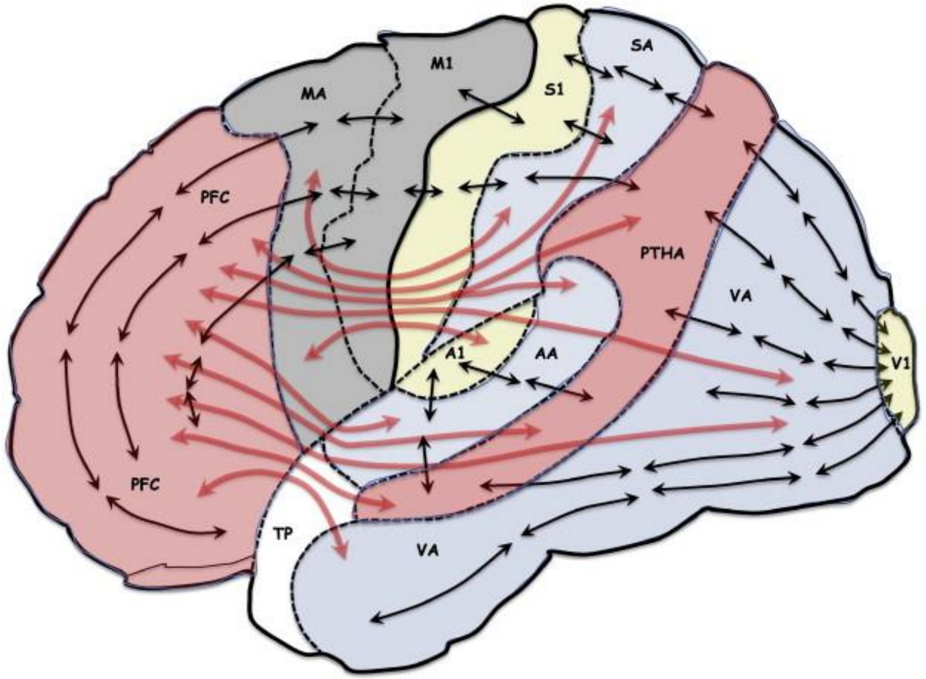


The flow of information in the motor system is the reverse of that in the sensory systems



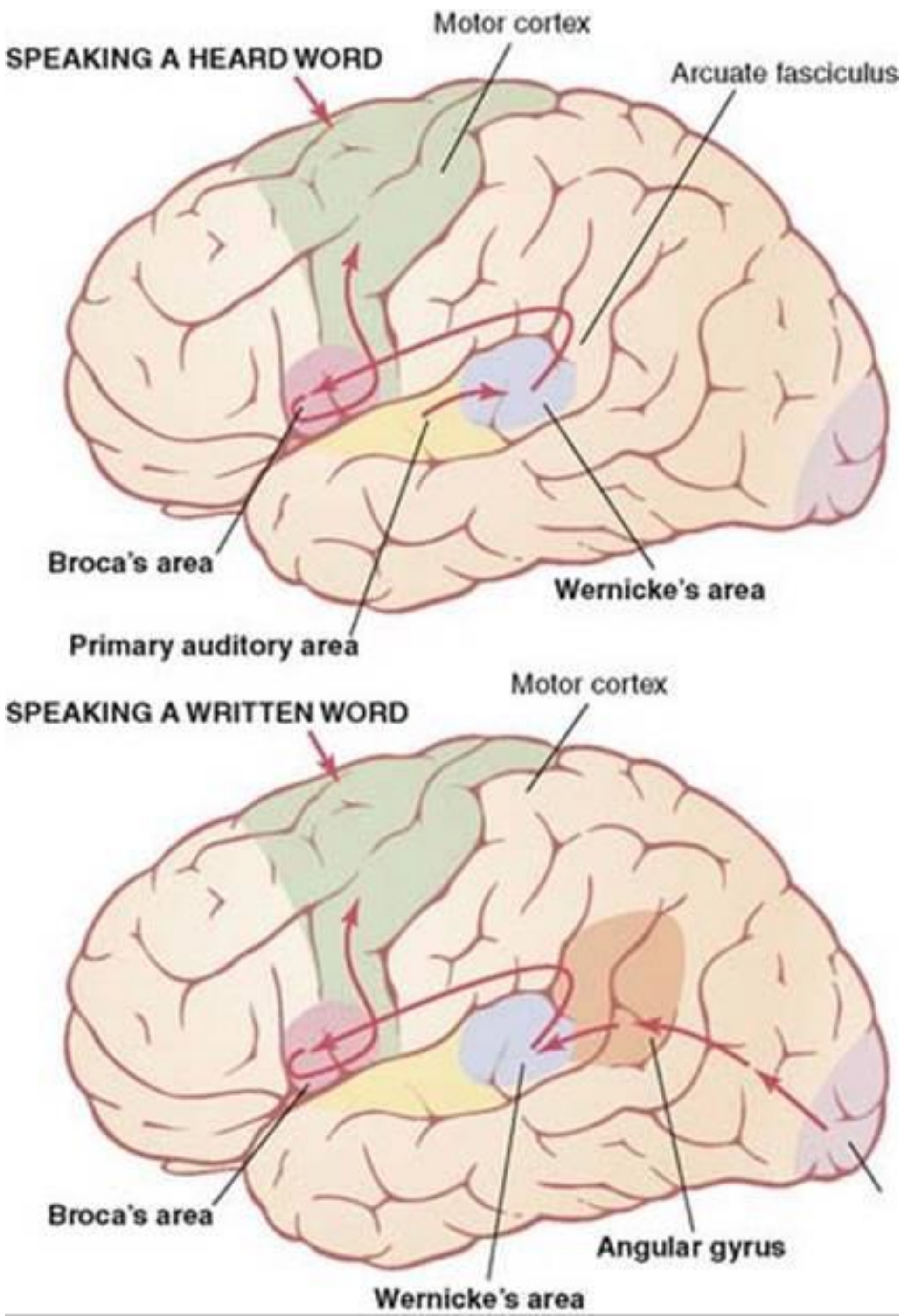
Convergence on multimodal association areas



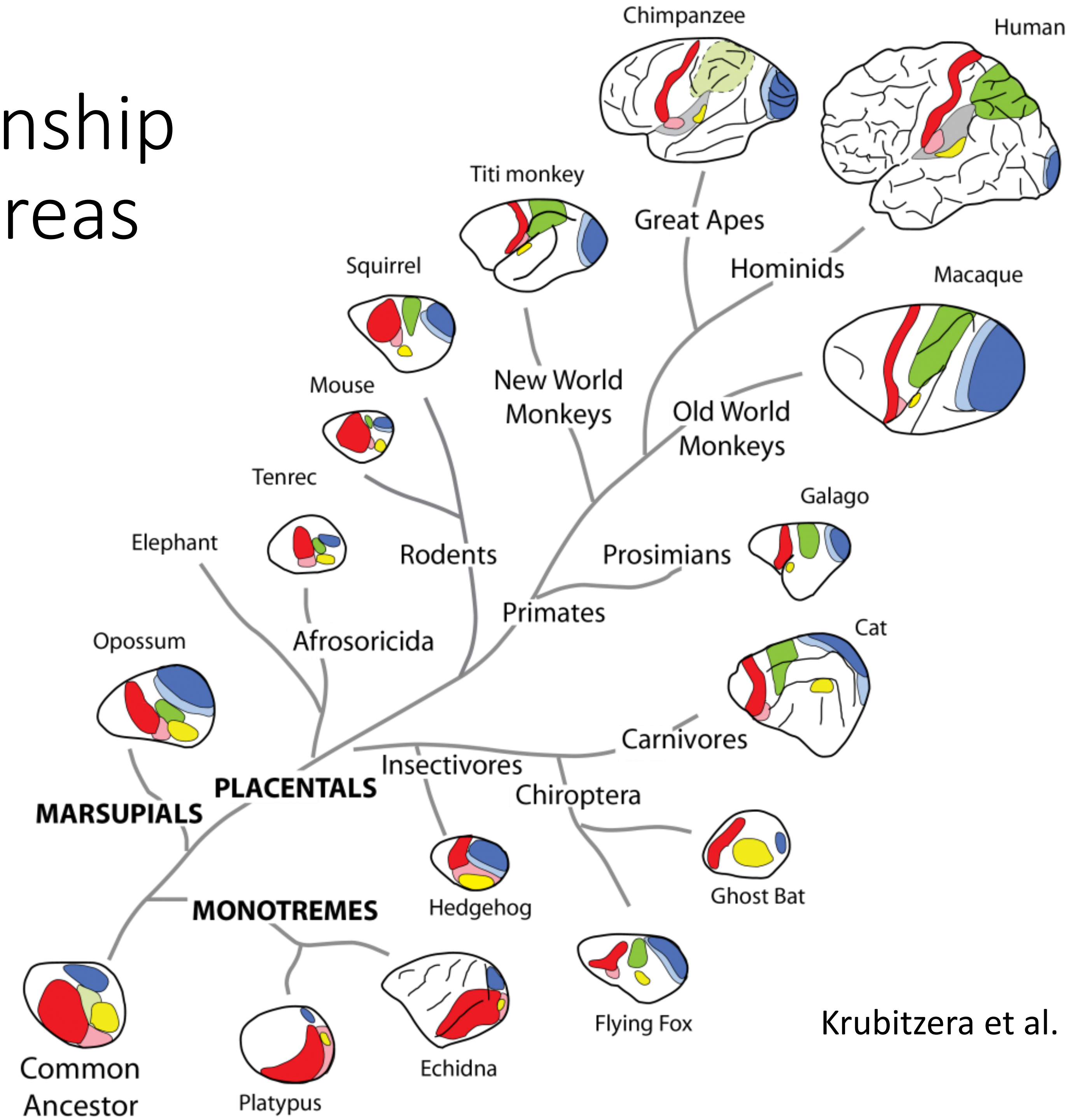


Cortical areas & speech

- **Wernicke's area:** Comprehension of speech
- **Broca's area:** Production of speech



Phylogenetic relationship between sensory areas



Primary visual area (V1)
Second visual area (V2)
Auditory cortex
Primary somatosensory area (S1)
Second somatosensory area (S2)
Parietal association areas

Krubitzera et al. 2011