Structure & Function of the Cerebral Cortex

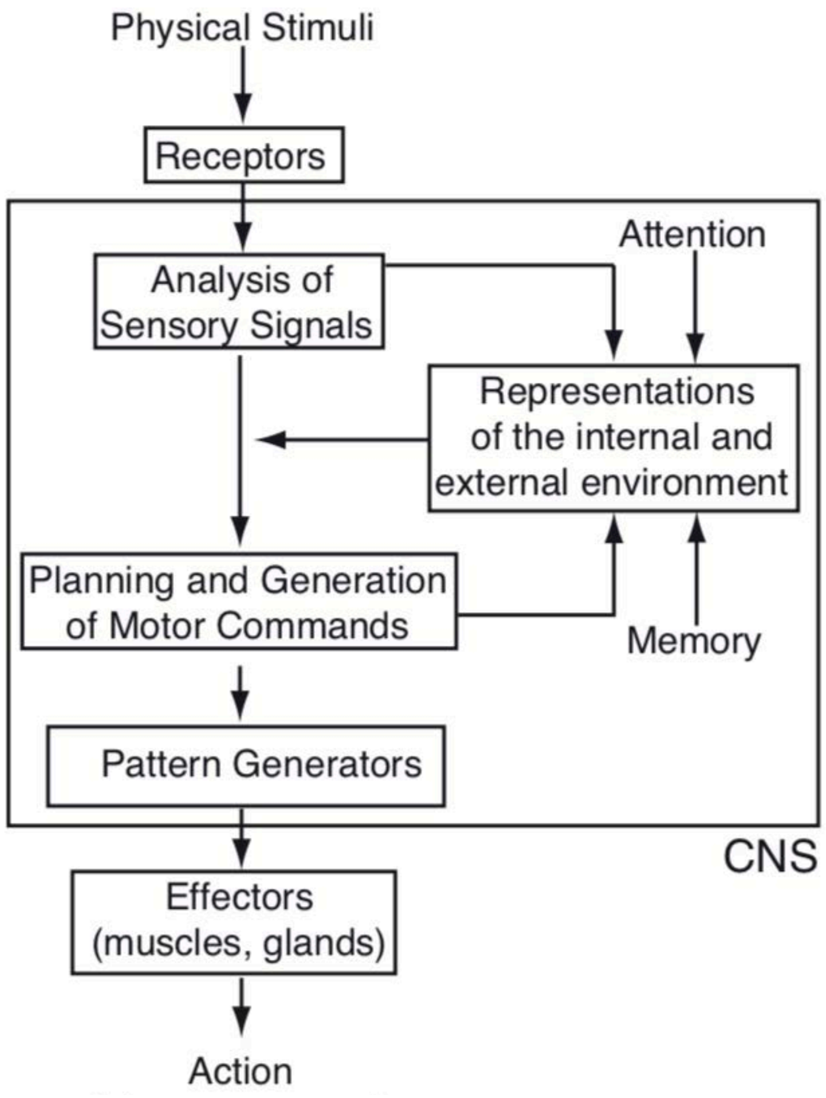
03/03/2021

Manolis Froudarakis
Group Leader
IMBB-FORTH

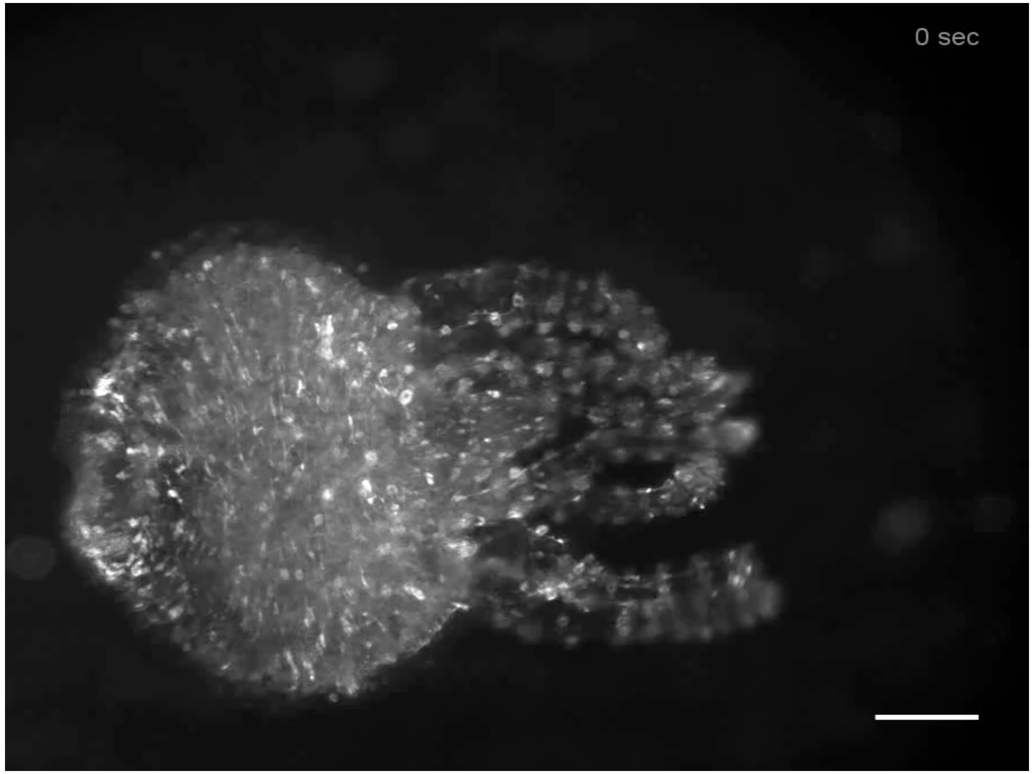
frouman@imbb.forth.gr / eflab.org

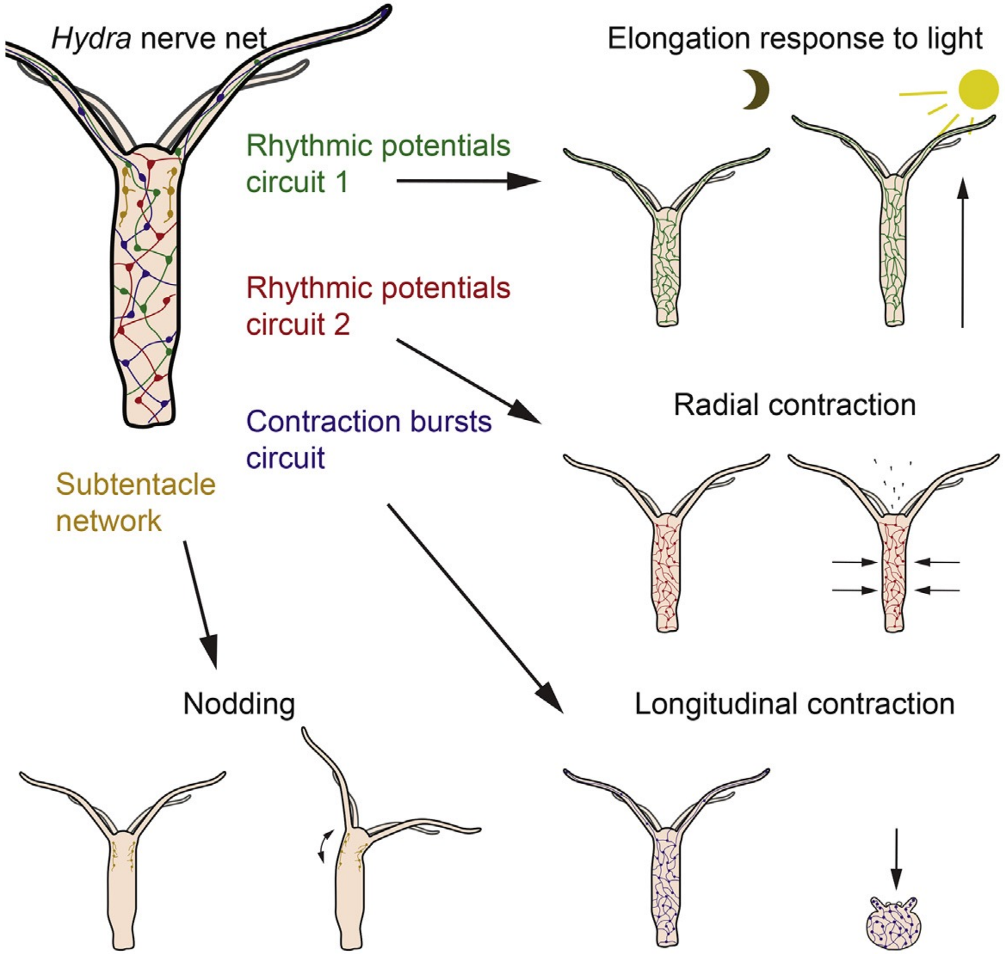
Information processing in neuronal networks

Goal: Interact with the environment



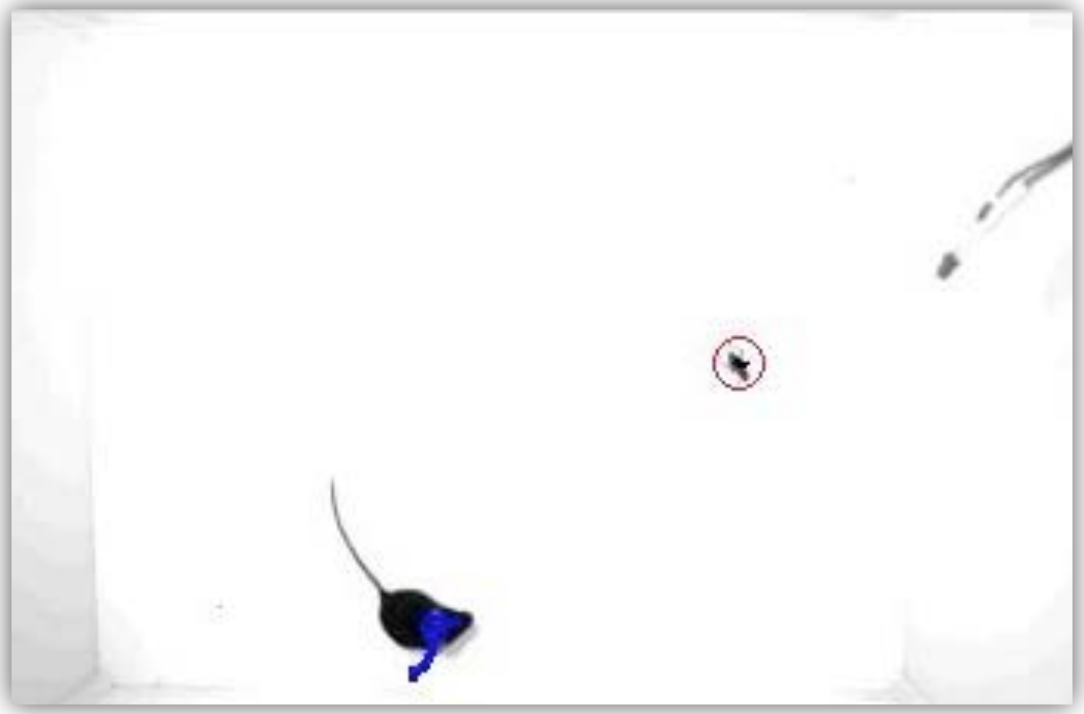
Neural Networks are associated with simple behaviors in Hydra



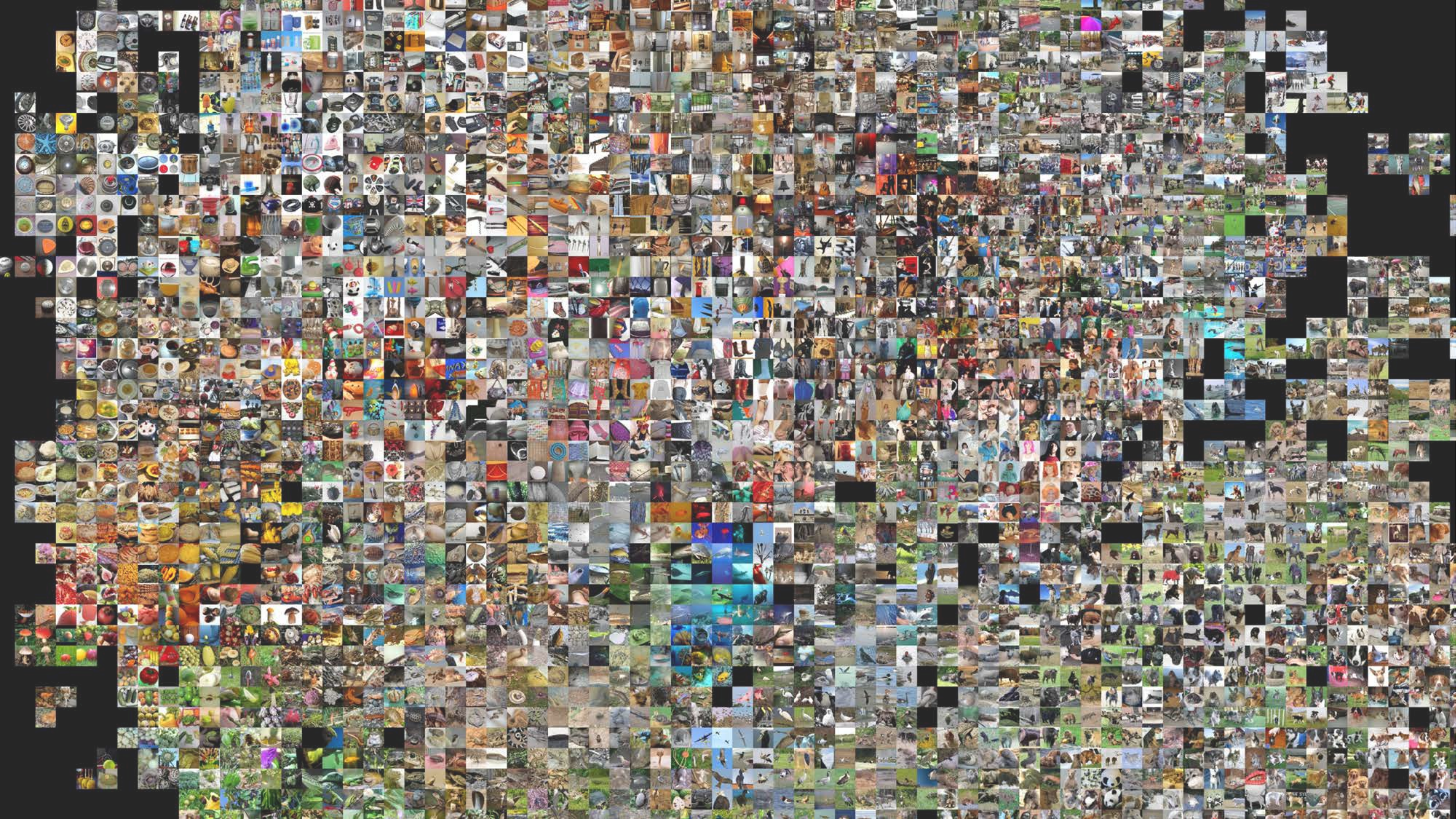


Dupre & Yuste 2017

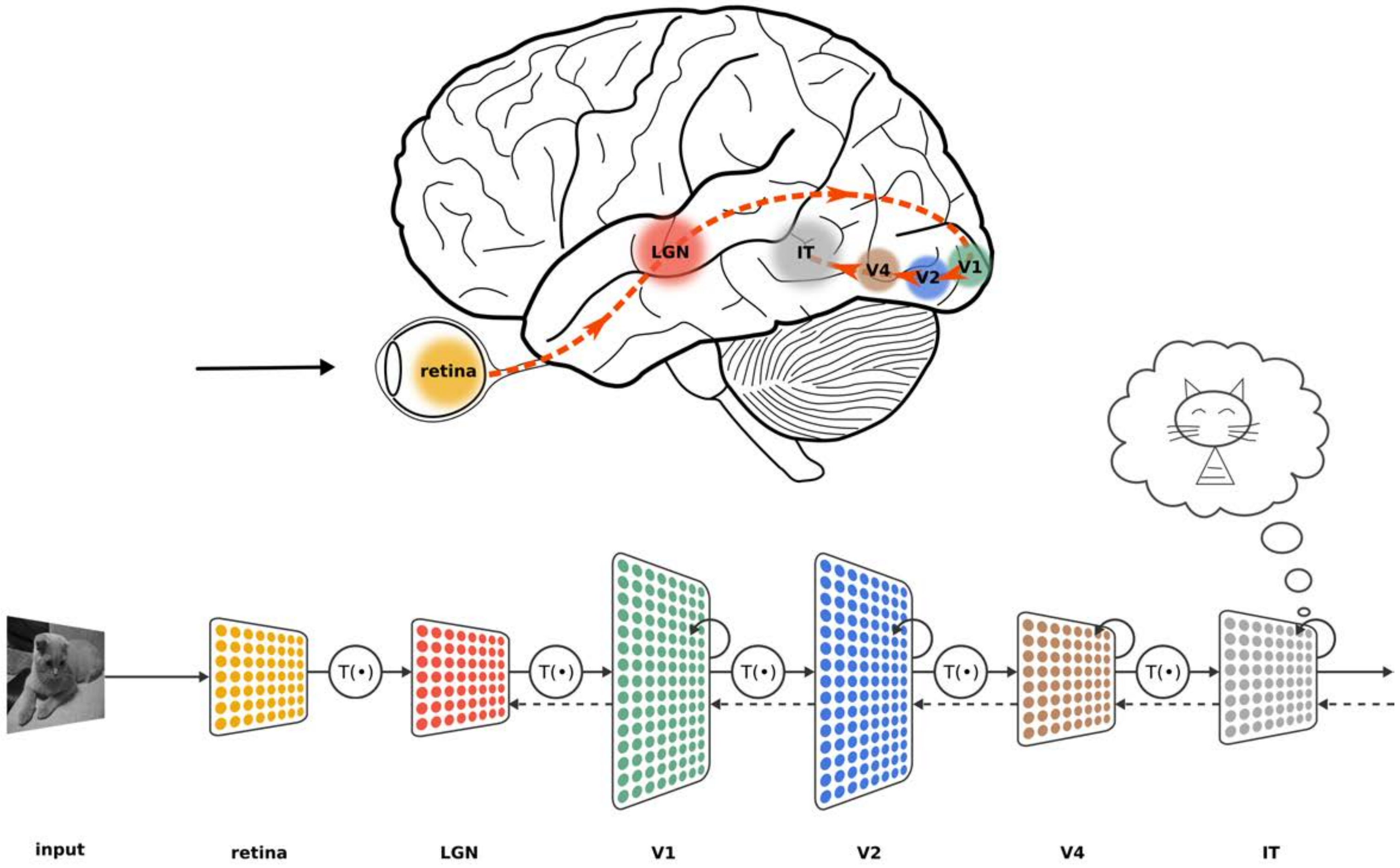
Or can form a highly integrated system to detect, process and respond to objects



Hoy et al. 2016



Extracting information about objects



DiCarlo & Cox 2017, J. Kubilius

Outline:

Neurons & Cortical Circuits

Part 1

- Classes of Neurons
- Spikes & Synapses
- Layered cortical organization & connectivity patterns
- Columnar organization
- Fine inhibitory control

Functional Properties of the Neocortex

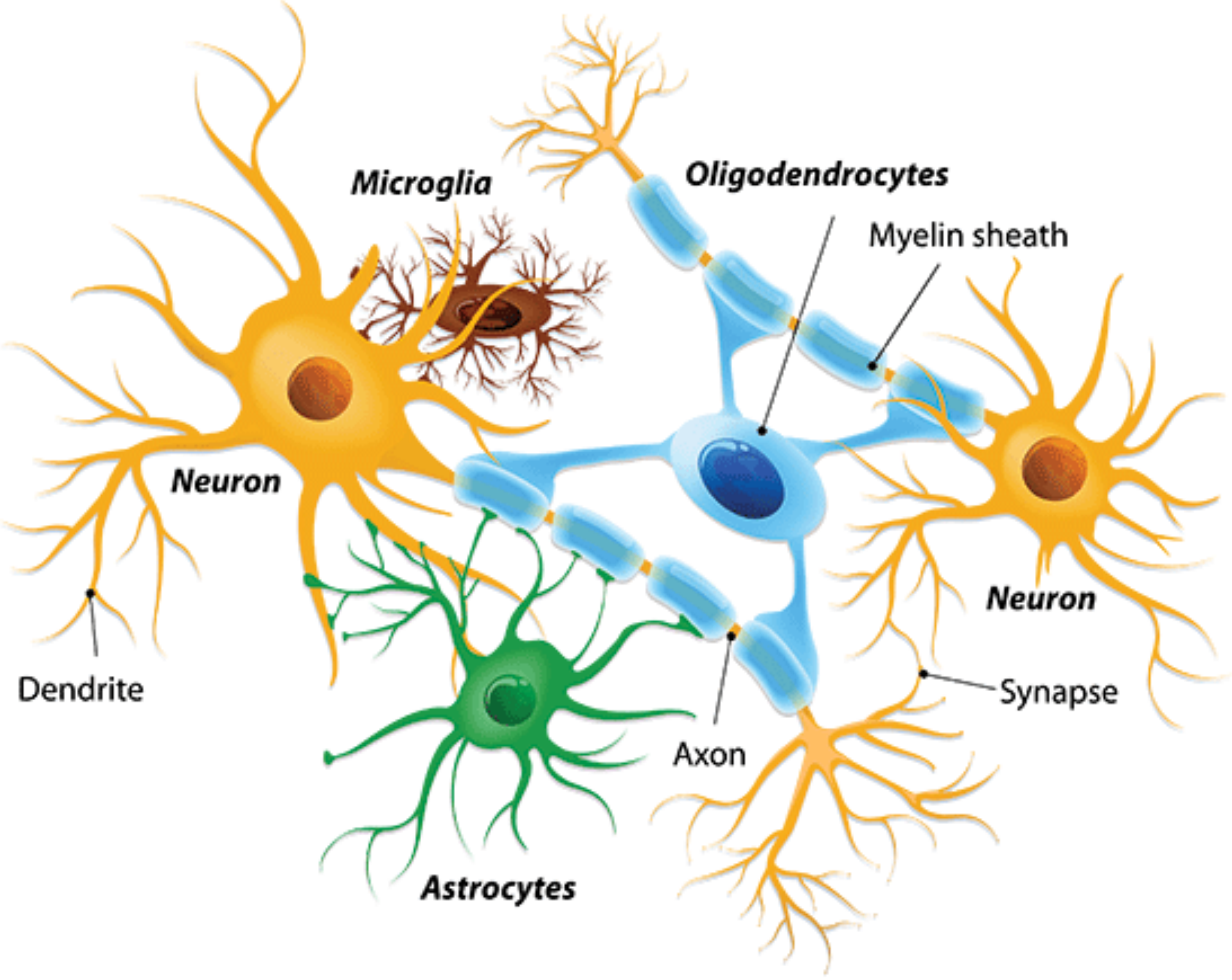
Part 2

- Receptive fields & Population representations
- Orientation columns
- Topographic maps
- Homunculus
- Hierarchical organization of the cortex

Cells in the brain

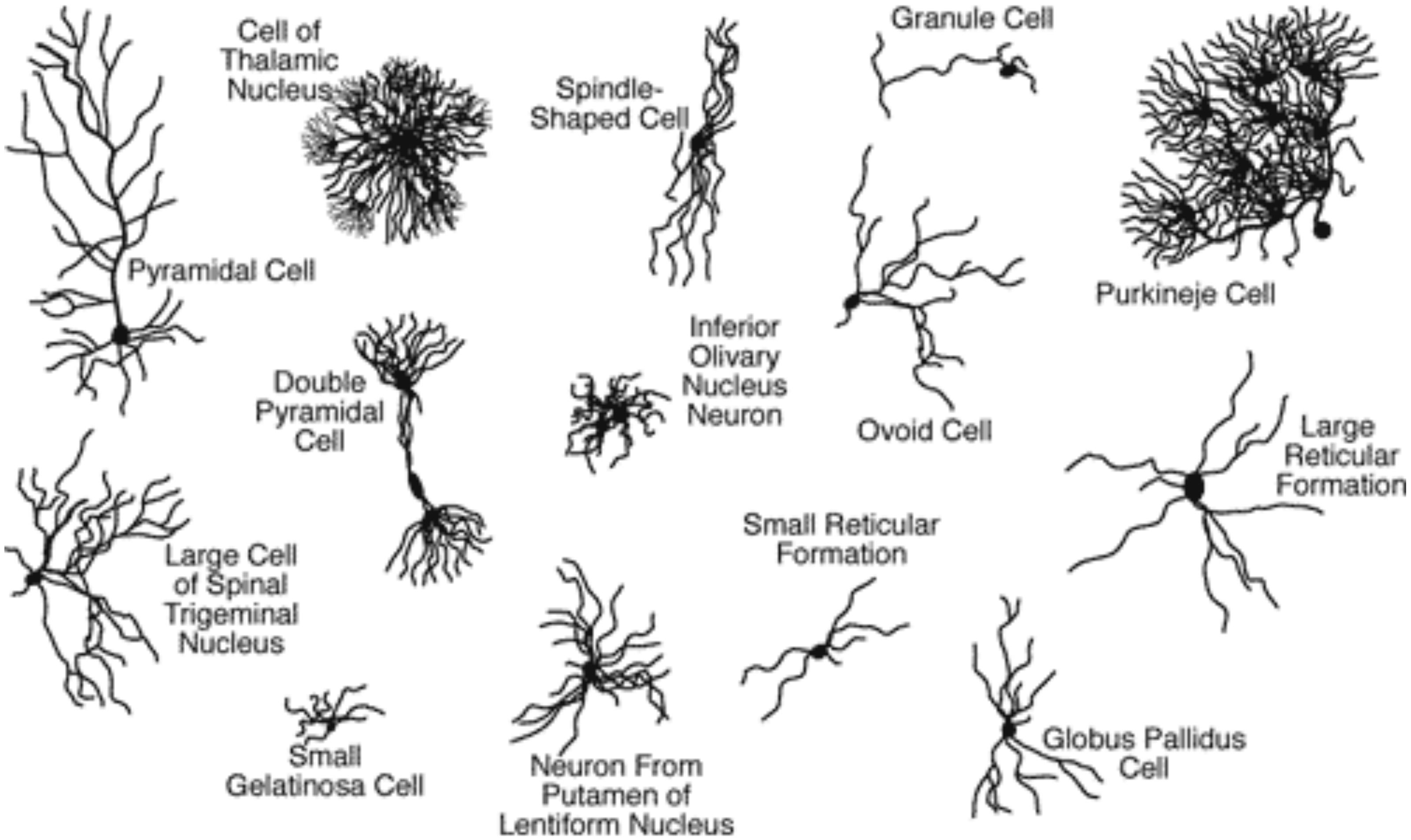
1. **Neurons**

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

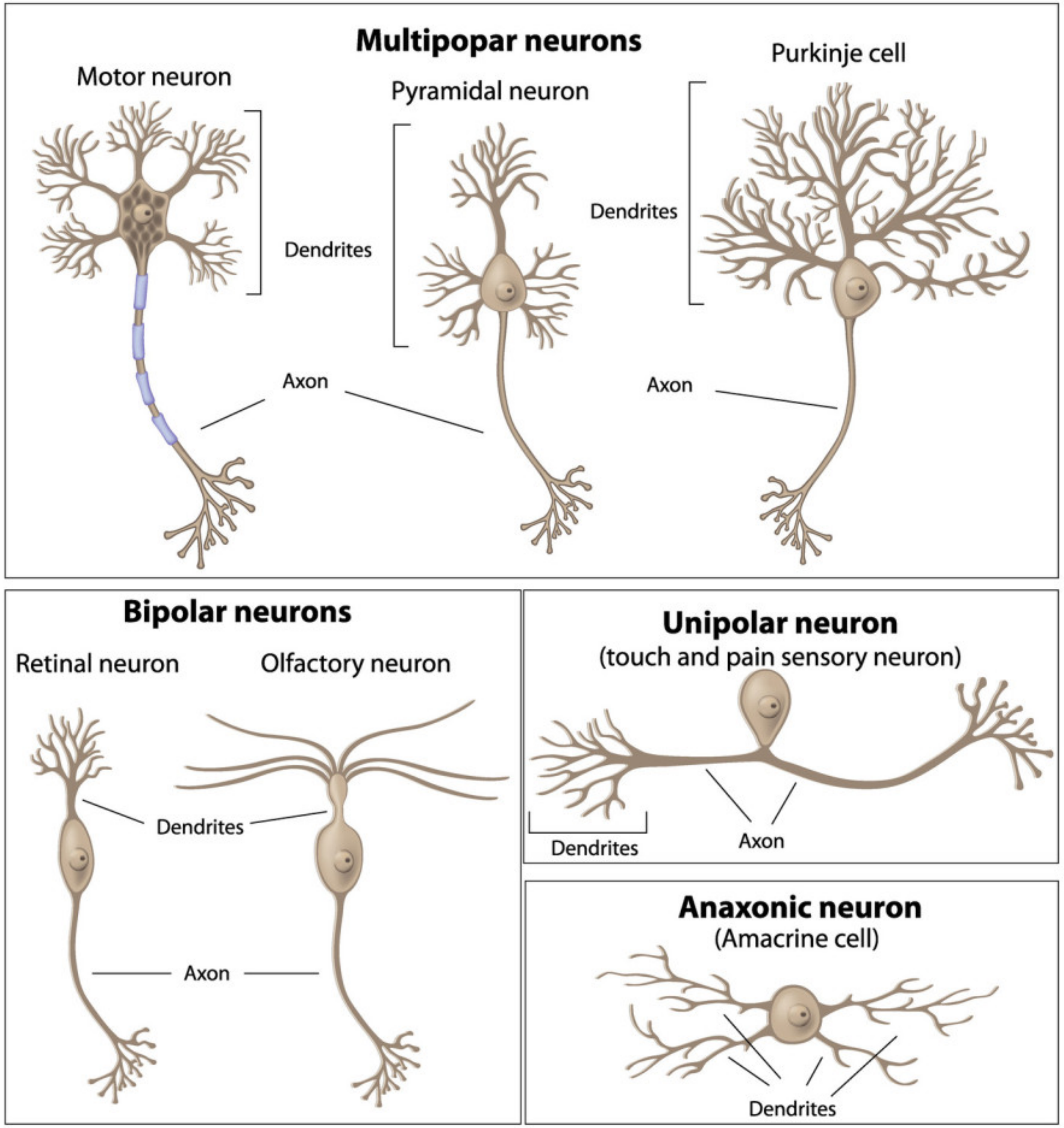


Γλία: Κόλλα

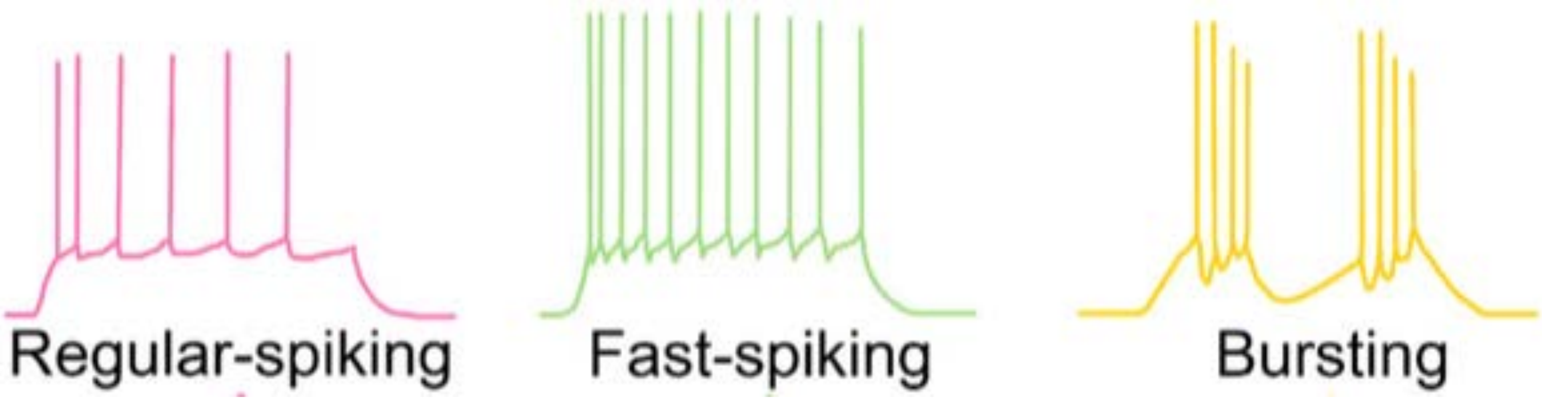
Types of Neurons
…based on shape



Types of Neurons
…based on polarity

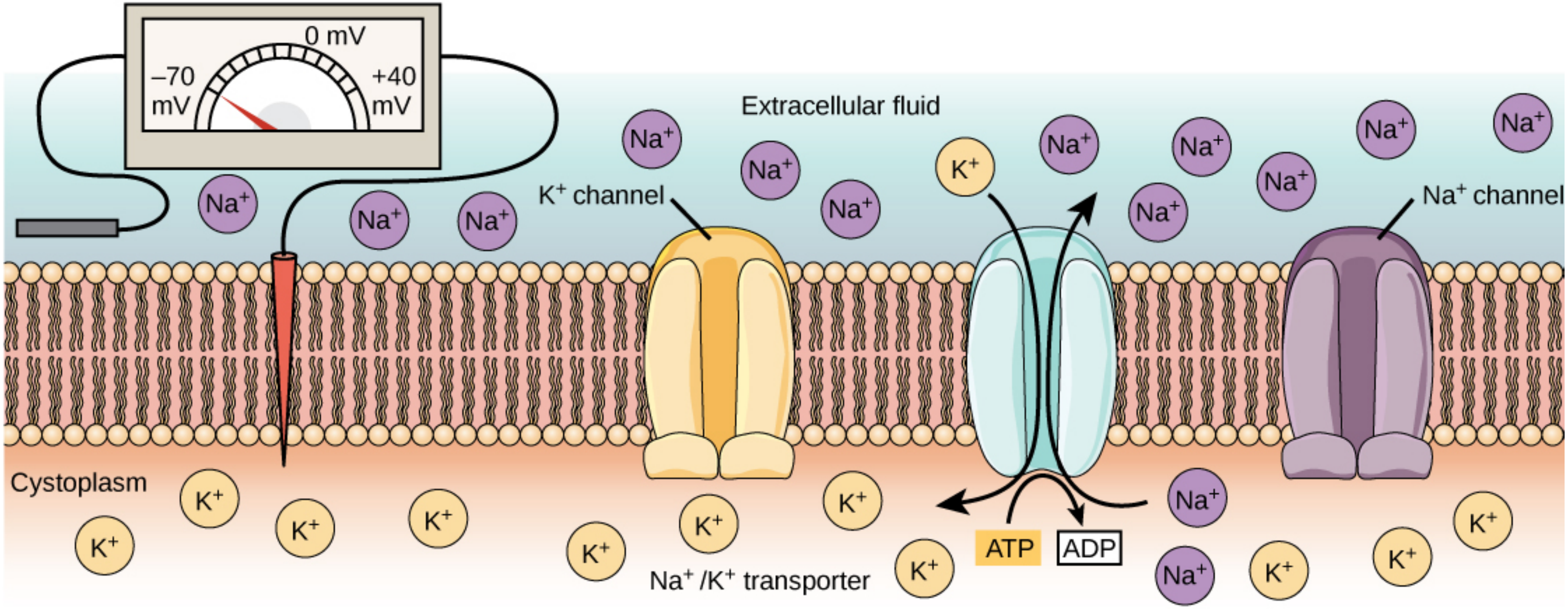


Or based on activity



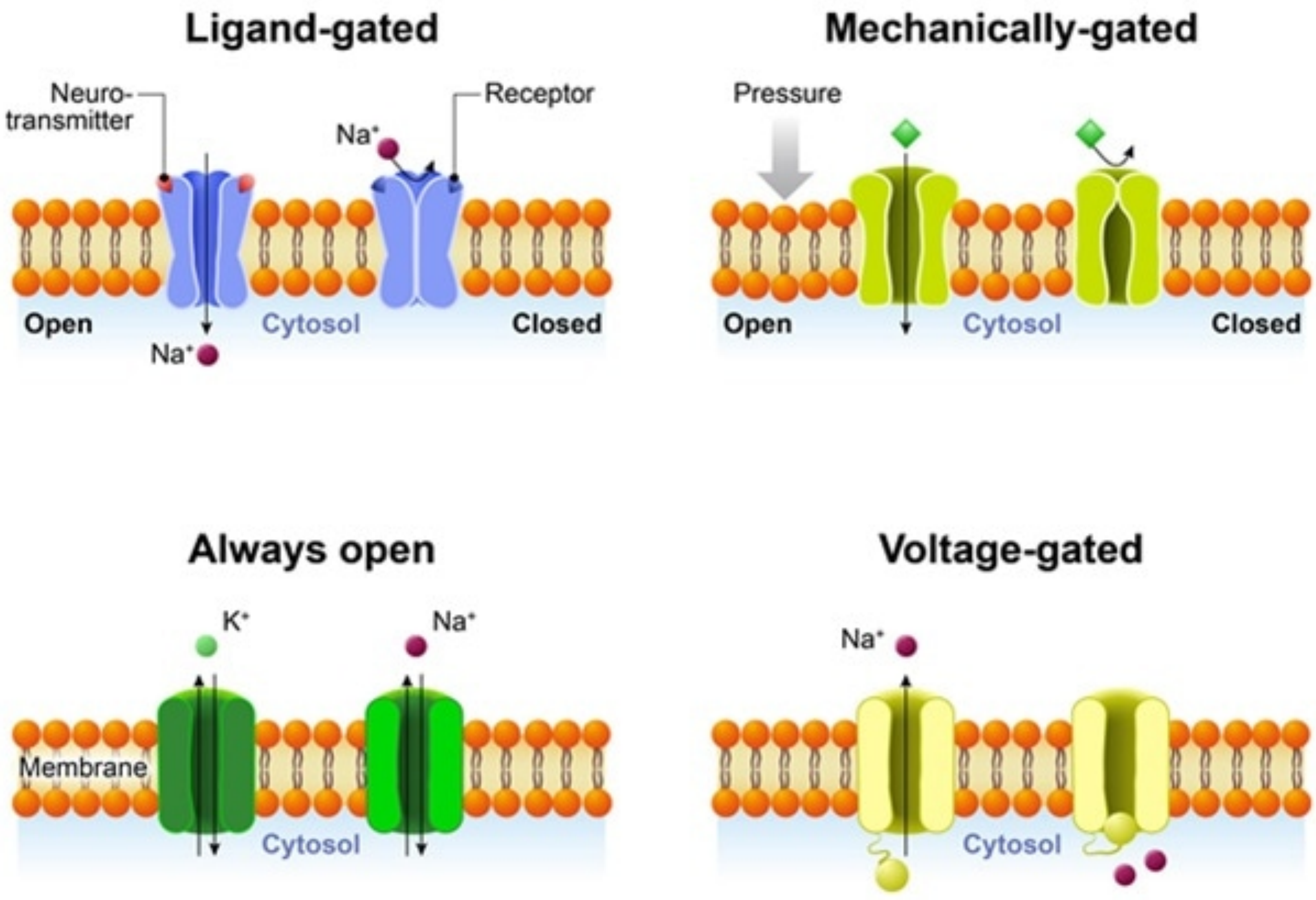
Resting membrane potential

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



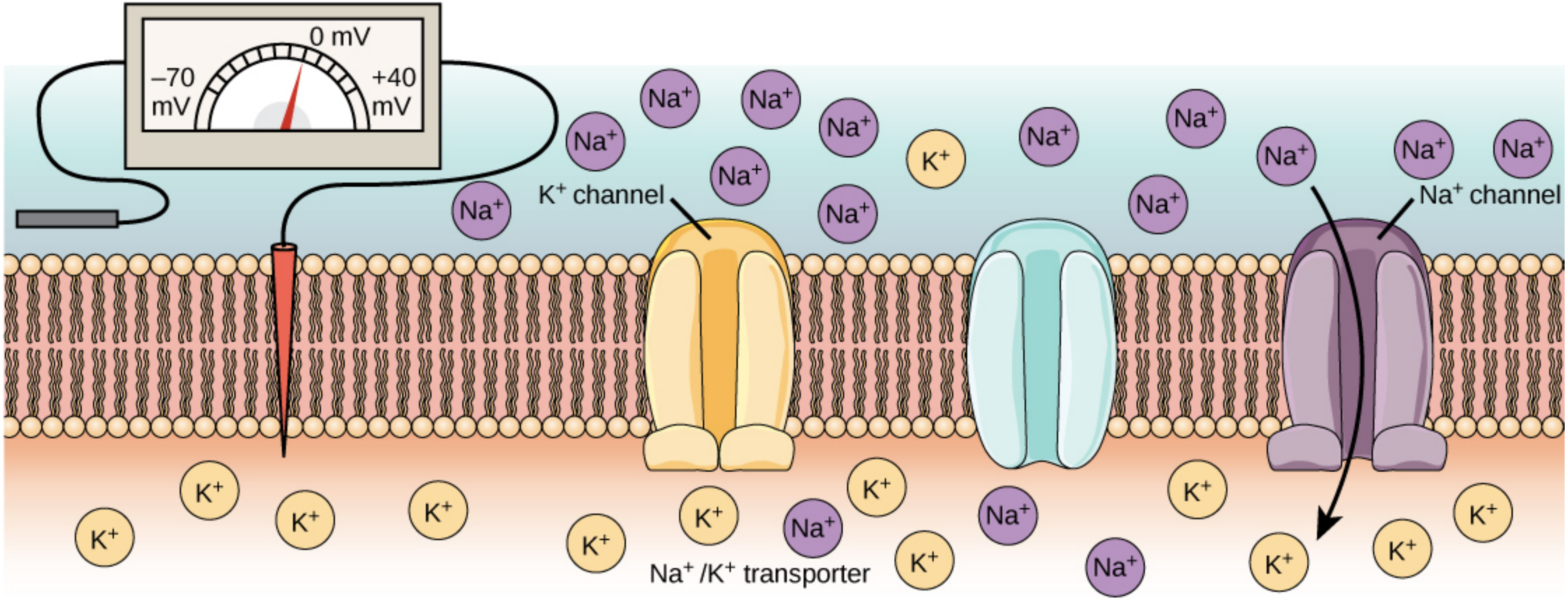
At the resting potential, all voltage-gated Na^+ channels and most voltage-gated K^+ channels are closed. The Na^+/K^+ transporter pumps K^+ ions into the cell and Na^+ ions out.

Ion Channels



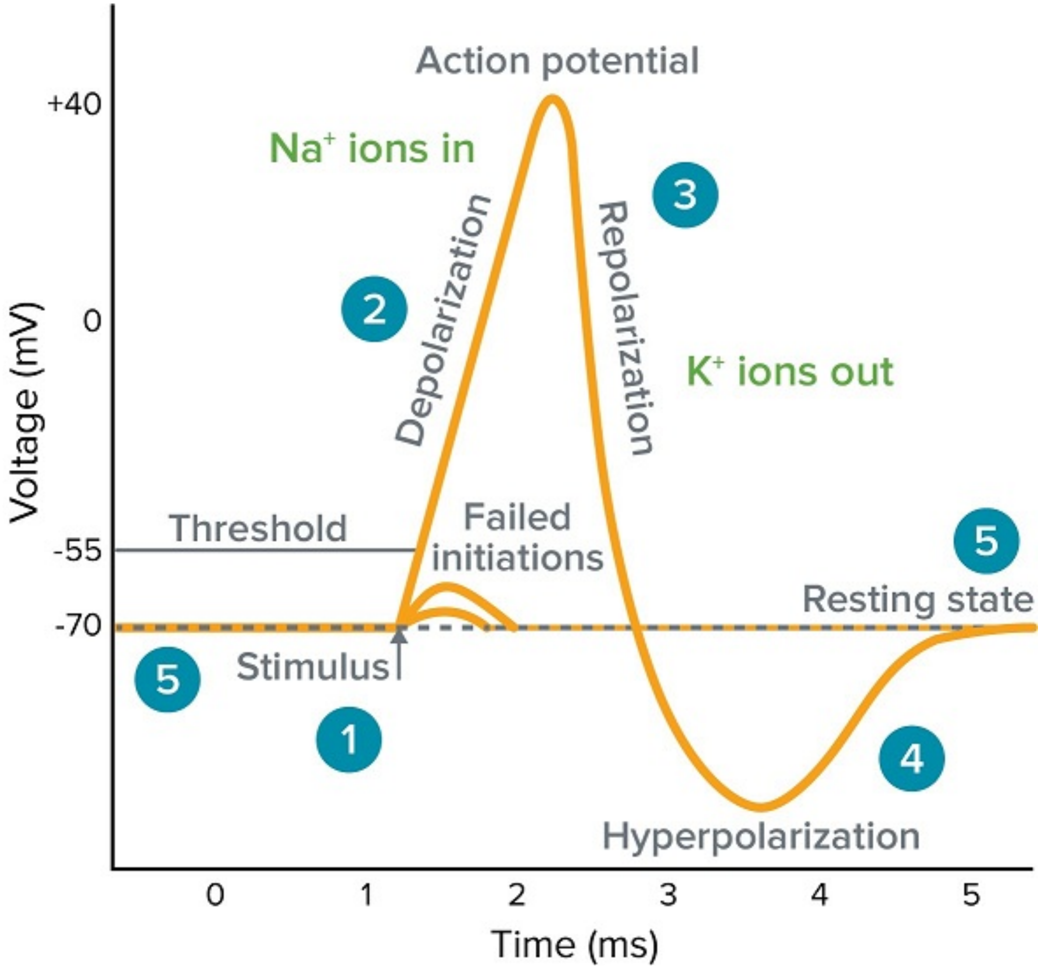
Ion channels allow ions to move across the membrane down those concentration gradients.

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



1. Stimulus starts and the voltage gated sodium channels begin to open and the membrane potential begins to slowly depolarize and sodium enters the cell down its concentration gradient.

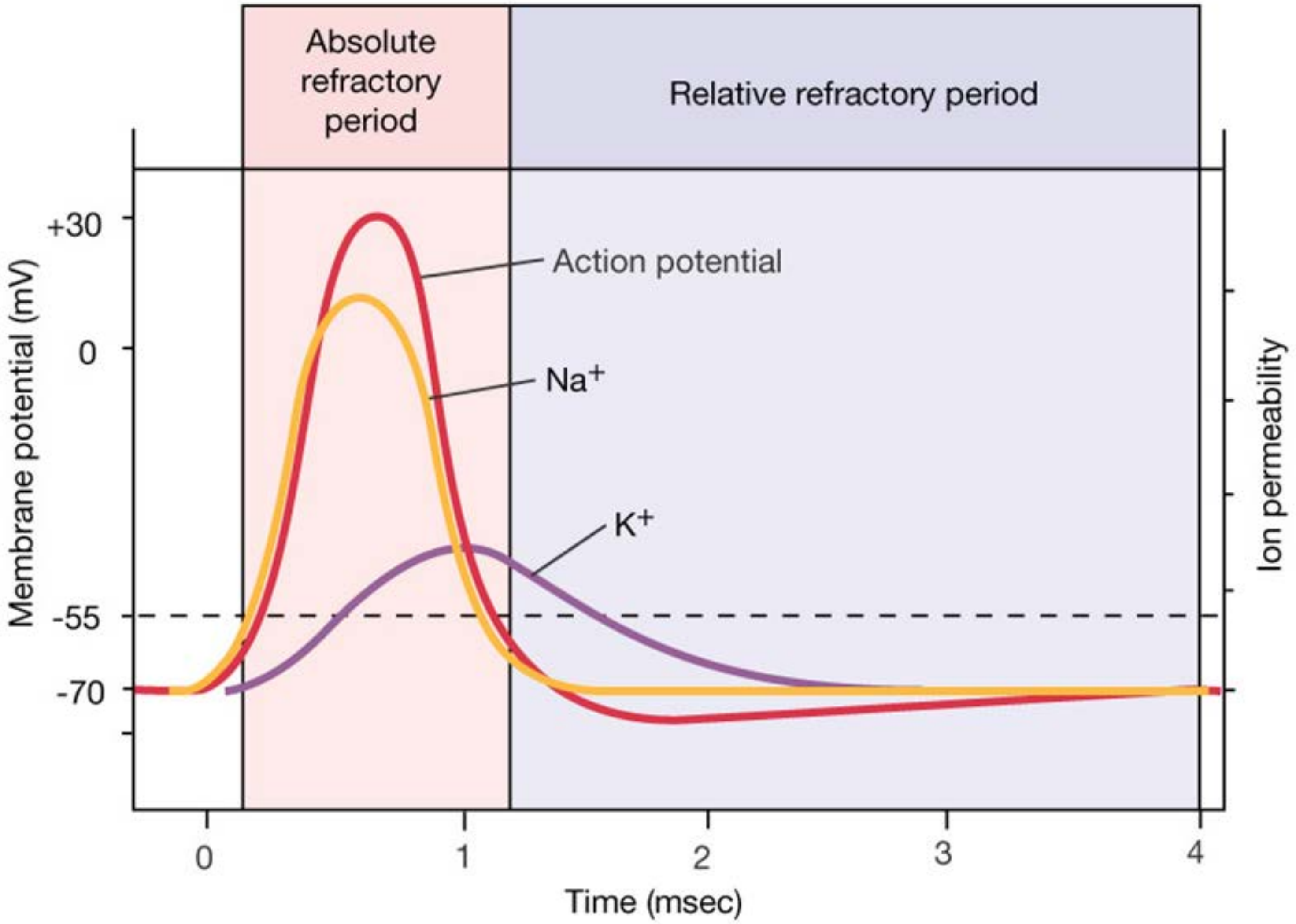
2. If sufficient drive raises the voltage above the threshold voltage, further depolarization is caused by a rapid rise in membrane potential opening of sodium channels in the cellular membrane, resulting in a large influx of sodium ions (**regenerative → all or none**).

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.

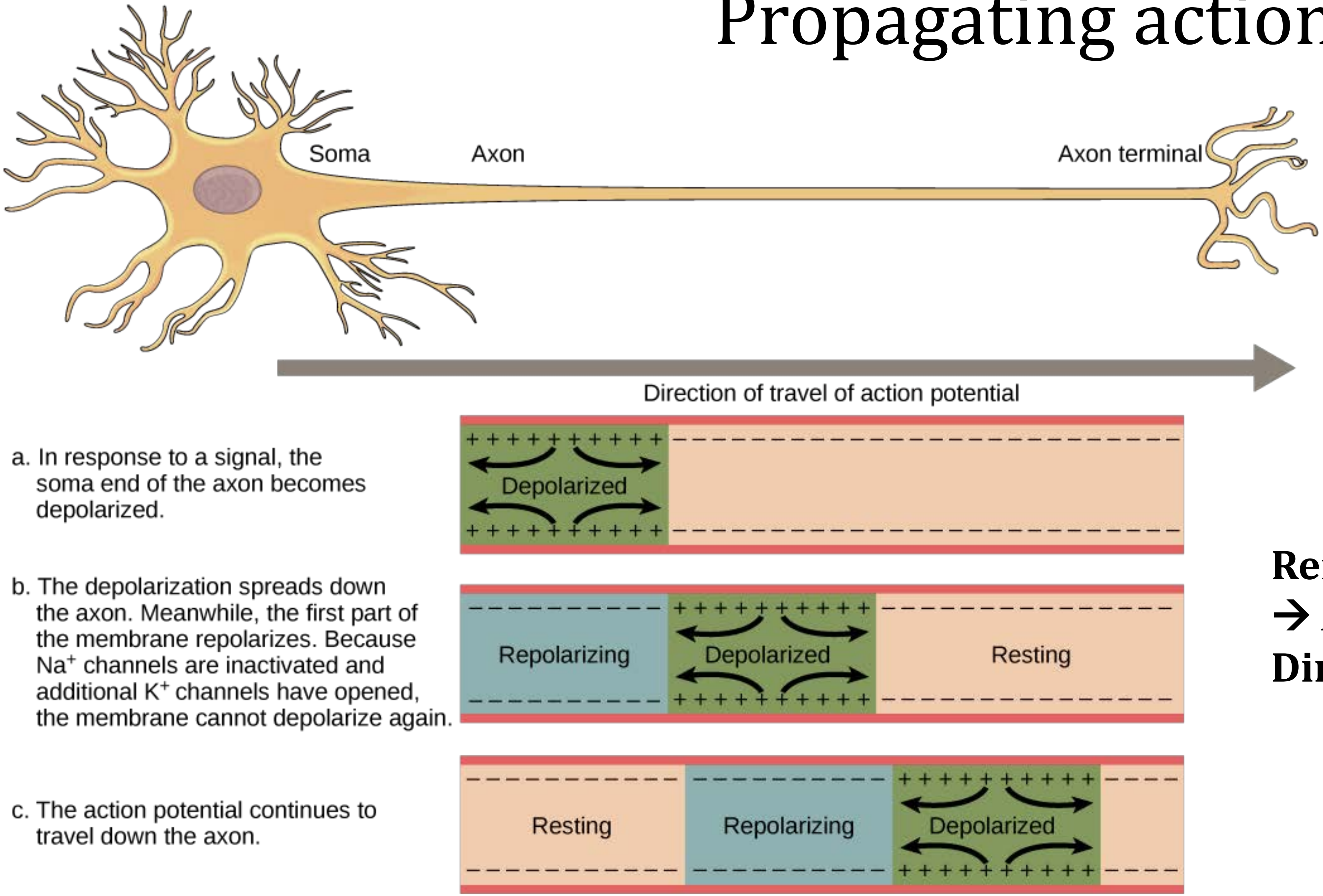
Refractory periods



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

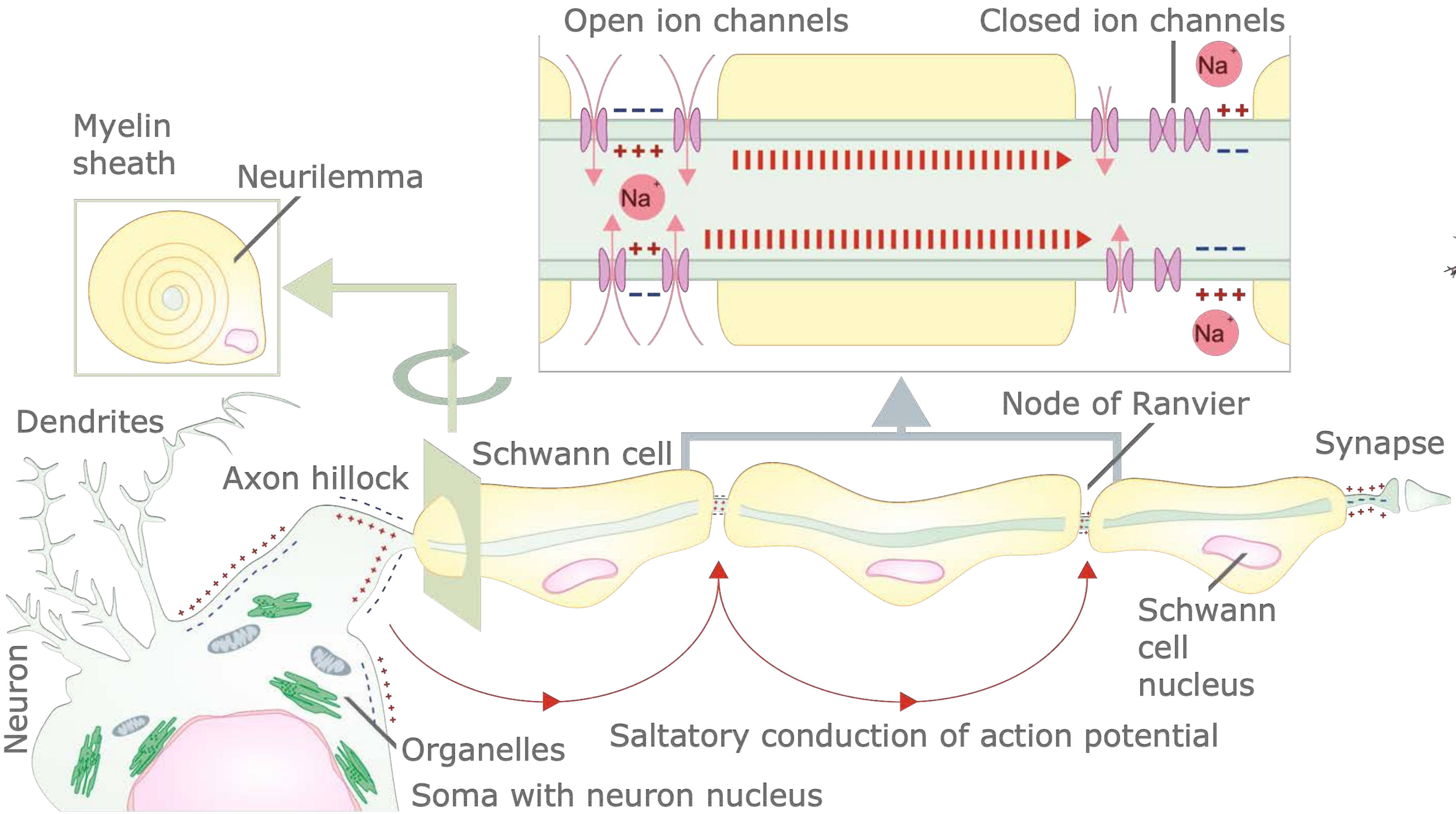
Relative refractory period: time during which a stronger than normal stimulus is needed to elicit neuronal excitation.

Propagating action potential

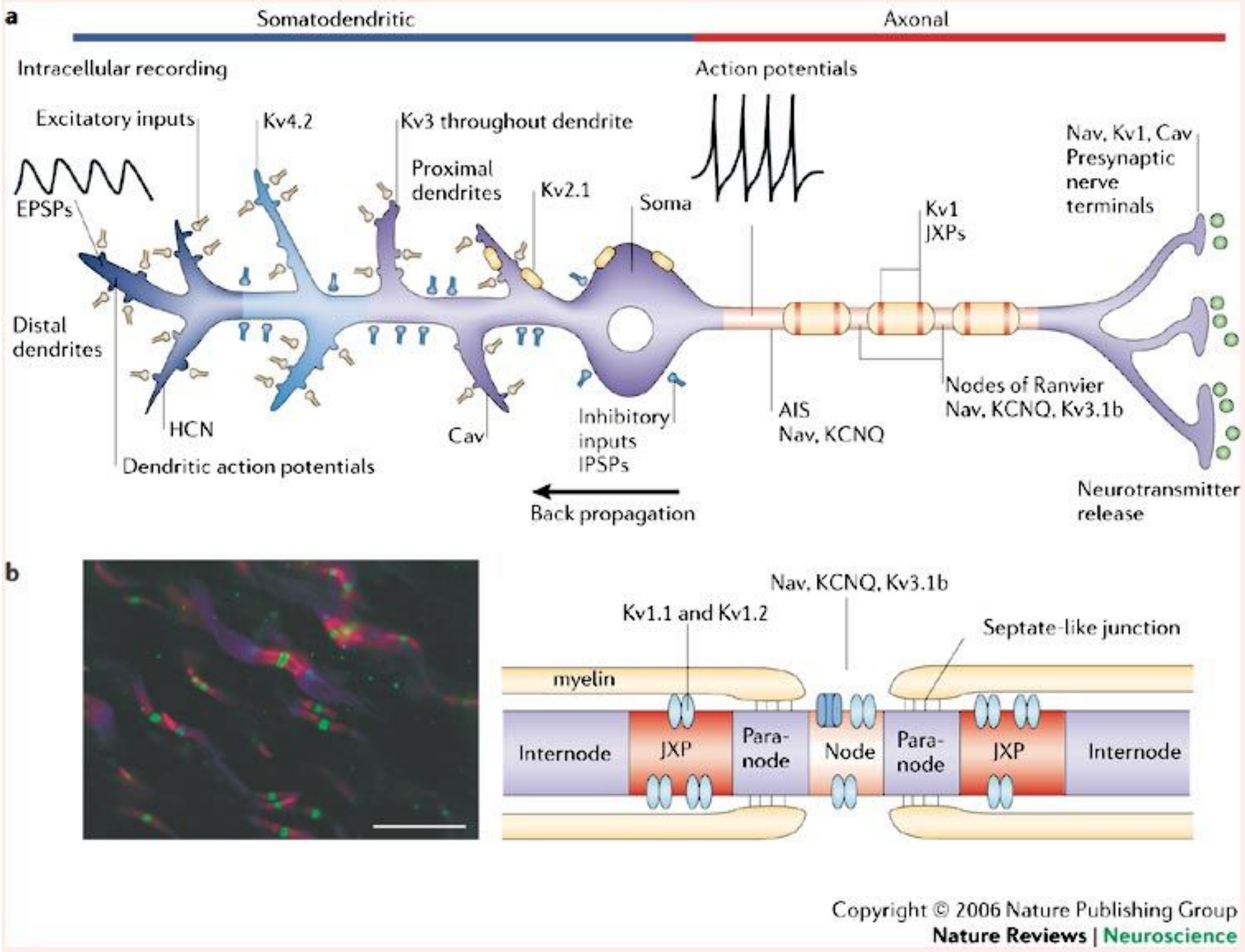


Refractory period
→ AP propagation
Directionality!

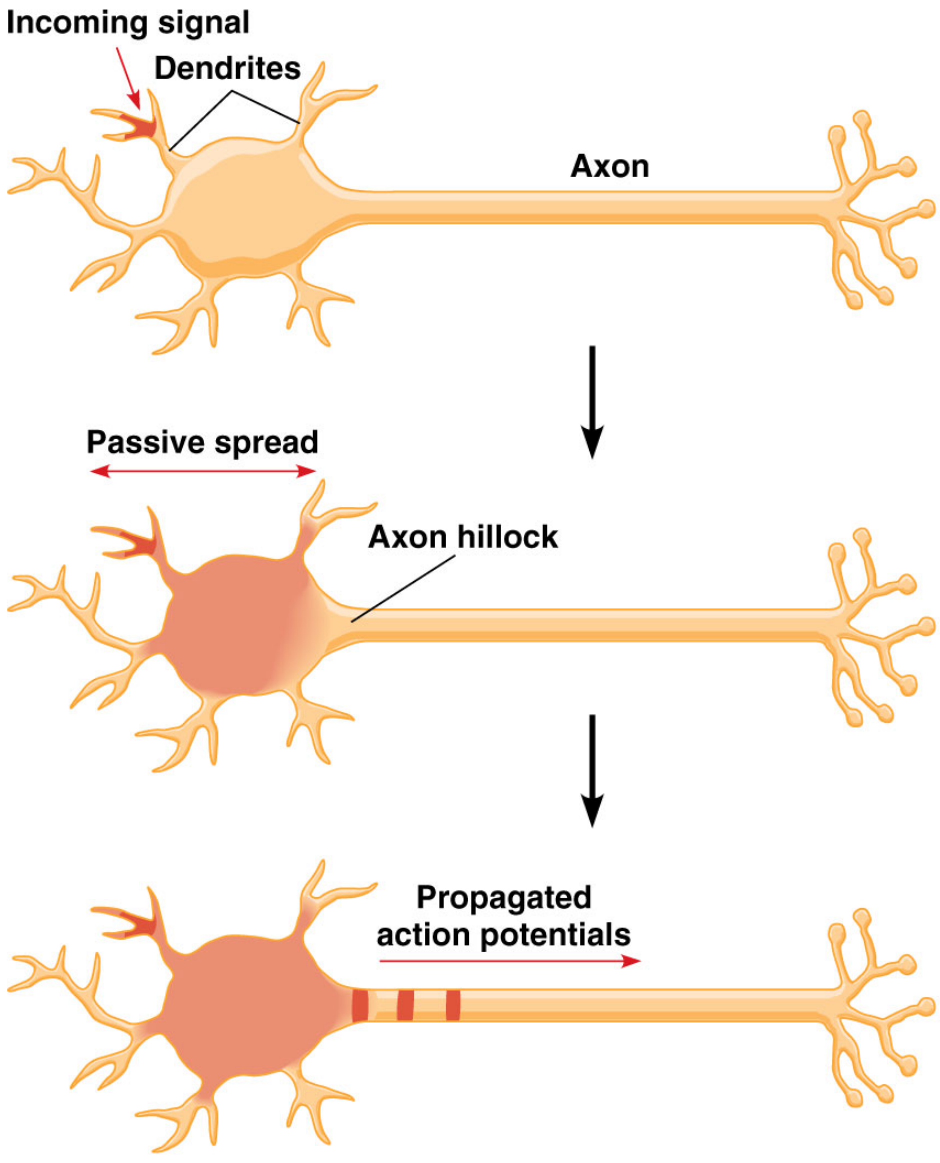
Saltatory conduction



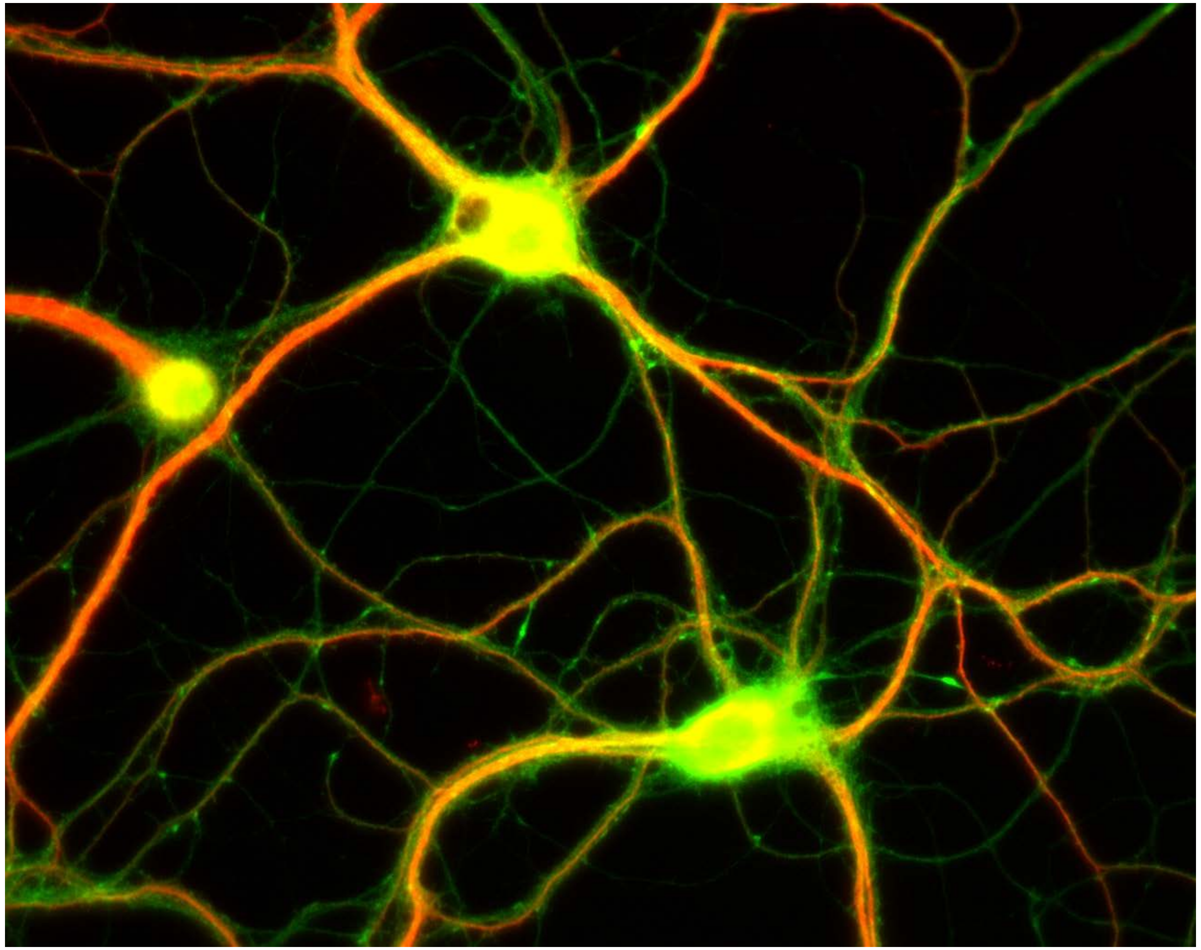
Functional properties of neurons

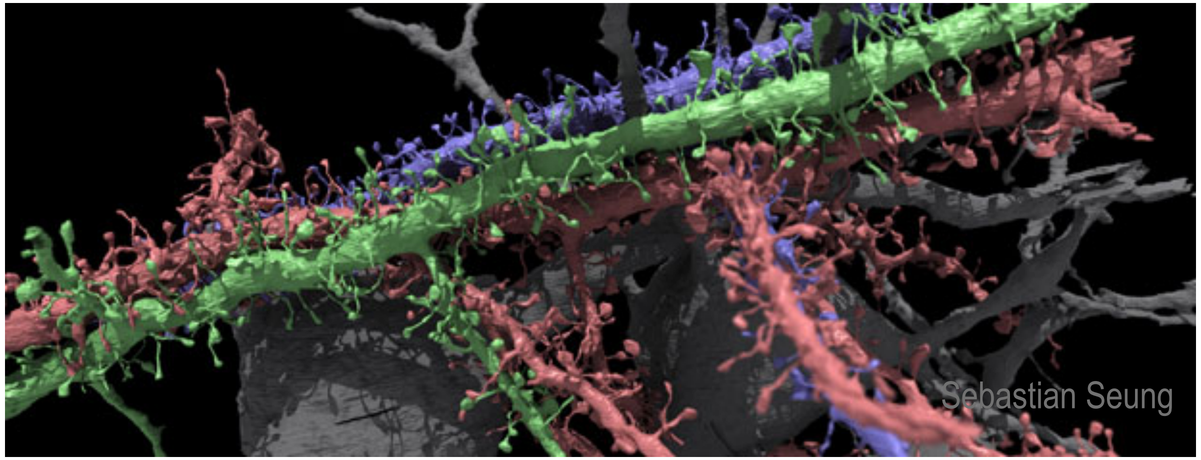


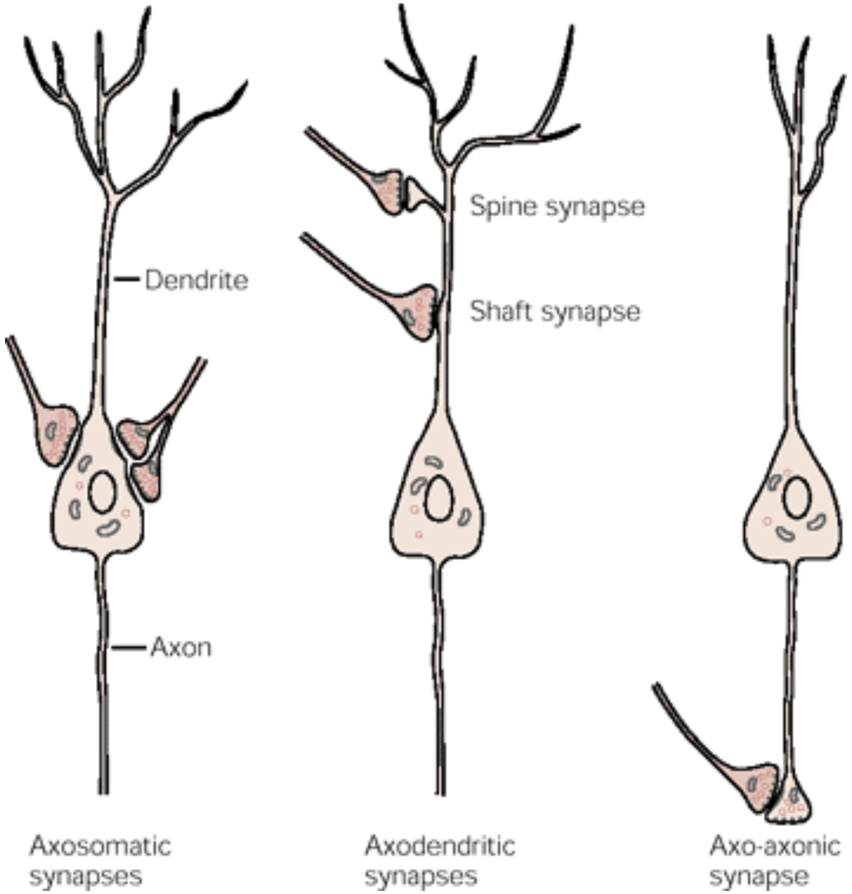
Nature Reviews | Neuroscience



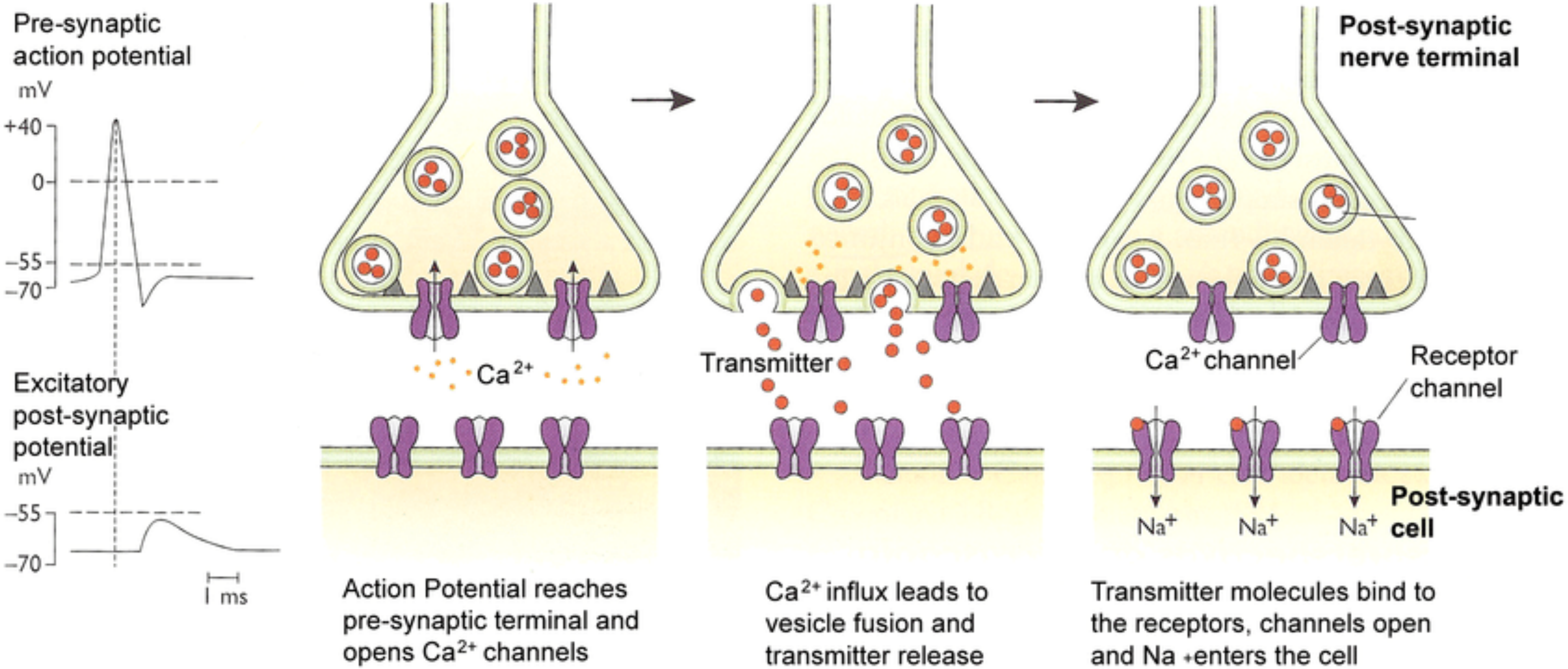
Neuron communication
Synapses/Neurotransmitters







Chemical Synapse



Squire and Kandel (2002)

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	● (orange)	↑	↑	↑			
	Muscarinic:							
	M_1,	● (green)						↑
	M_2, M_3	● (green)		↑			↓	
ADH (= vasopressin)	V_1	● (green)						↑
	V_2	● (green)					↑	
Dopamine	D_1, D_5	● (green)					↑	
	D_2	● (green)		↑	↓		↓	
GABA (= gamma-aminobutyric acid)	$GABA_A$,	● (orange)				↑		
	$GABA_B$	● (green)		↑	↓		↓	
Glutamate (aspartate)	AMPA	● (orange)	↑	↑				
	Kainic acid	● (orange)	↑	↑				
	NMDA	● (orange)	↑	↑	↑			
	mGlu	● (green)					↓	↑
Glycine	–	● (orange)				↑		
Histamine	H_1	● (green)						↑
	H_2	● (green)					↑	
Norepinephrine, epinephrine	α_1 (A–D)	● (green)		↑				↑
	α_2 (A–C)	● (green)		↑	↓		↓	
	β_{1-3}	● (green)					↑	
Opioid peptides	μ, δ, κ	● (green)		↑	↓		↓	
Oxytocin	–	● (green)						↑
Serotonin (5-hydroxytryptamine)	5-HT_1	● (green)		↓			↓	
	5-HT_2	● (green)						↑
	5-HT_3	● (orange)	↑	↑				
	5-HT_{4-7}	● (green)					↑	
Somatostatin (GHIH)	SRIF	● (green)		↑	↓		↓	
Tachykinin	NK1–3	● (green)						↑

Amino acids

Catecholamines

Peptides

Others

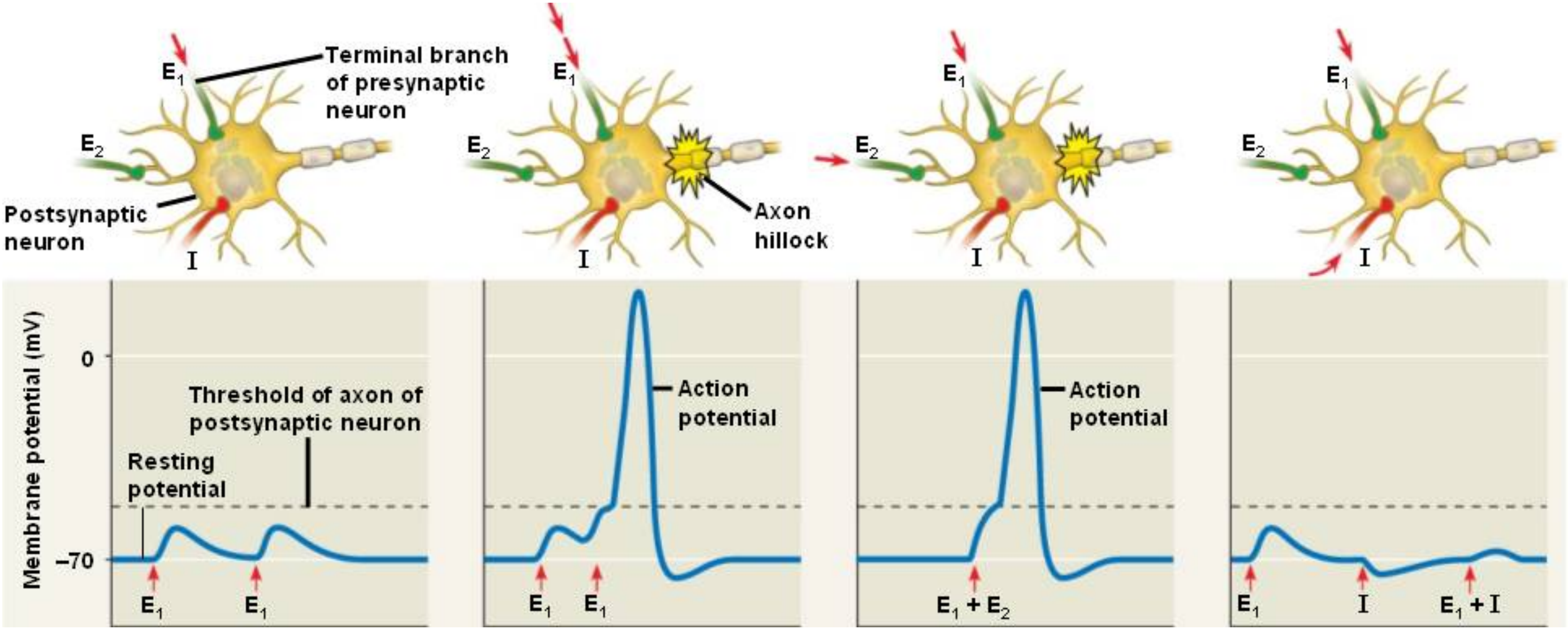
● (orange) = ligand-gated ion channel (ionotropic) receptor

● (green) = G-protein coupled (metabotropic) receptor

↓ = inhibits

↑ = promotes

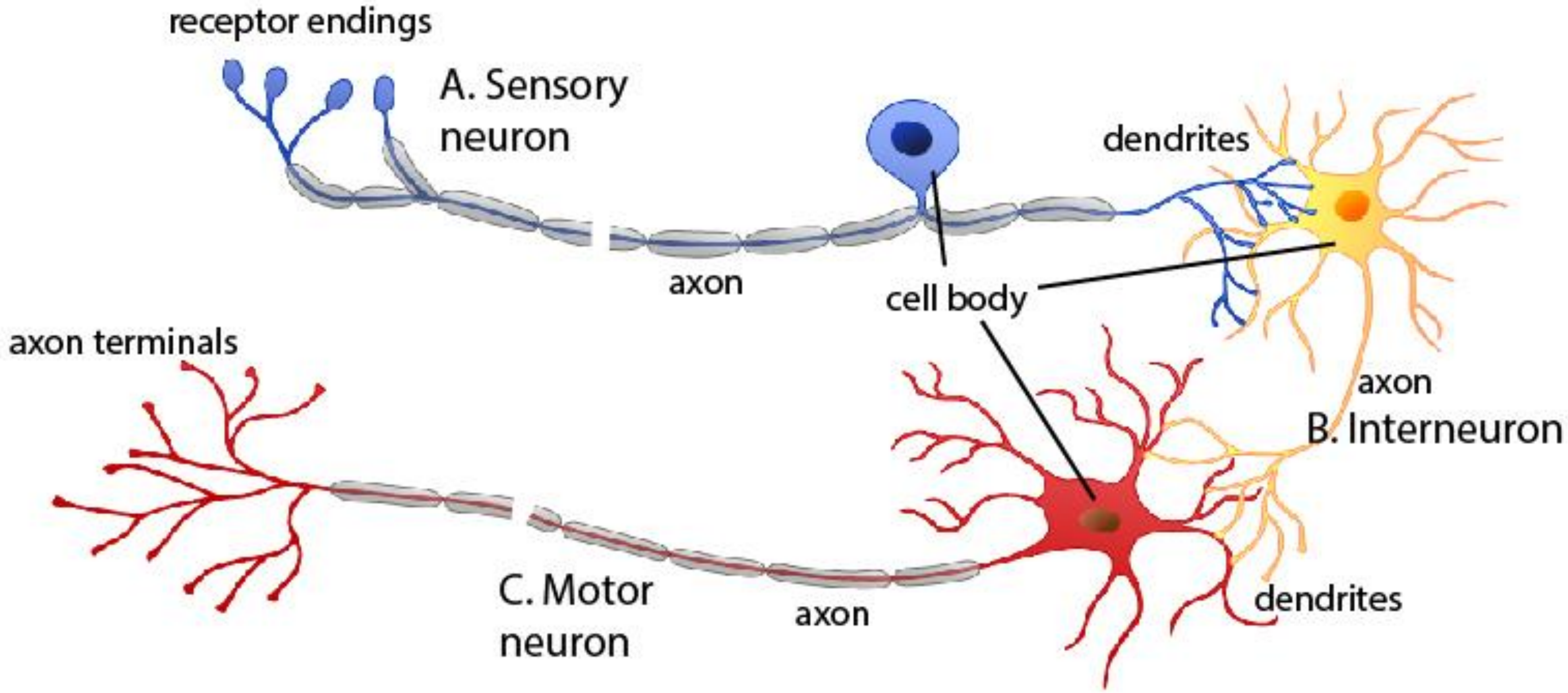
Spatial and temporal summation

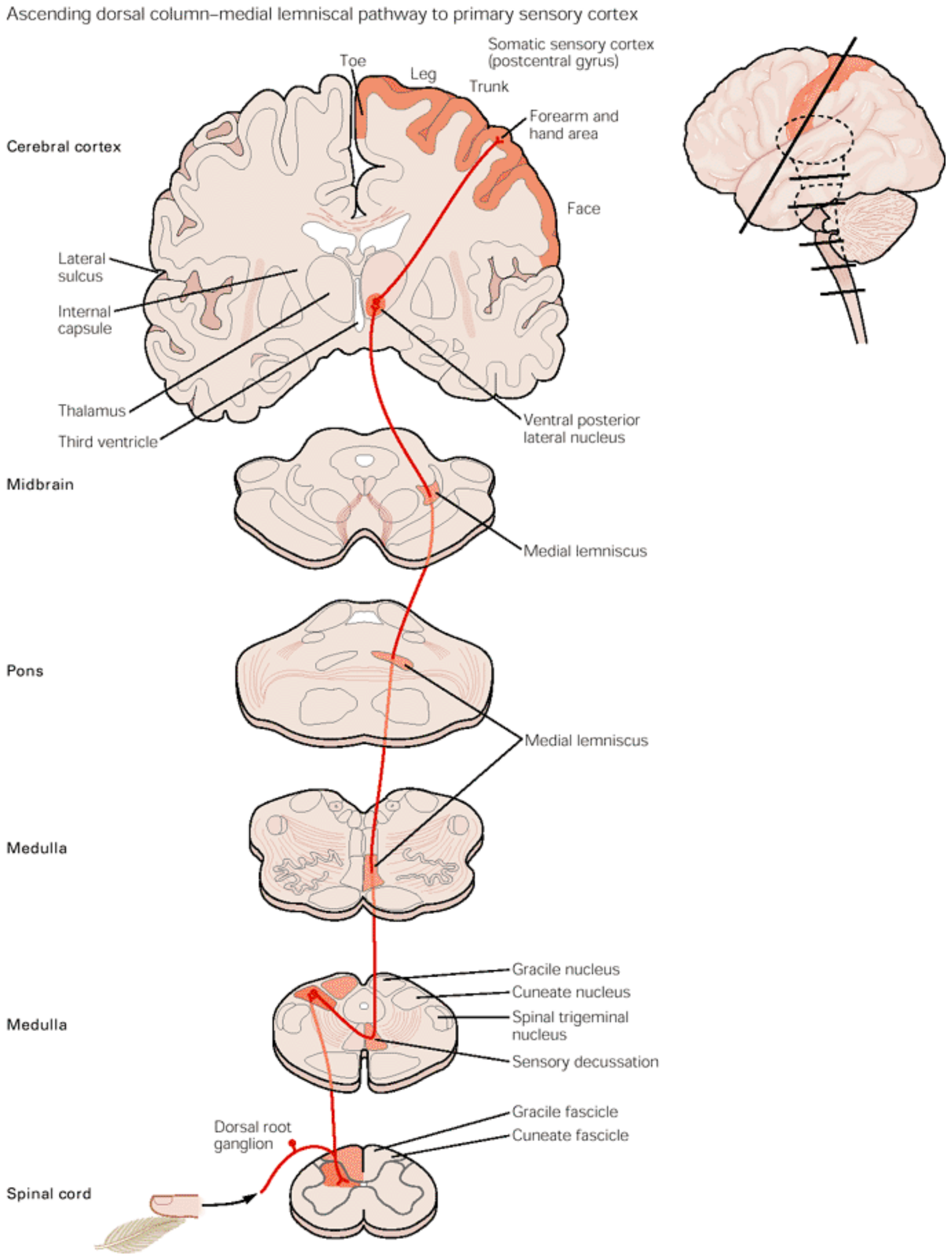


Functional classification of neurons

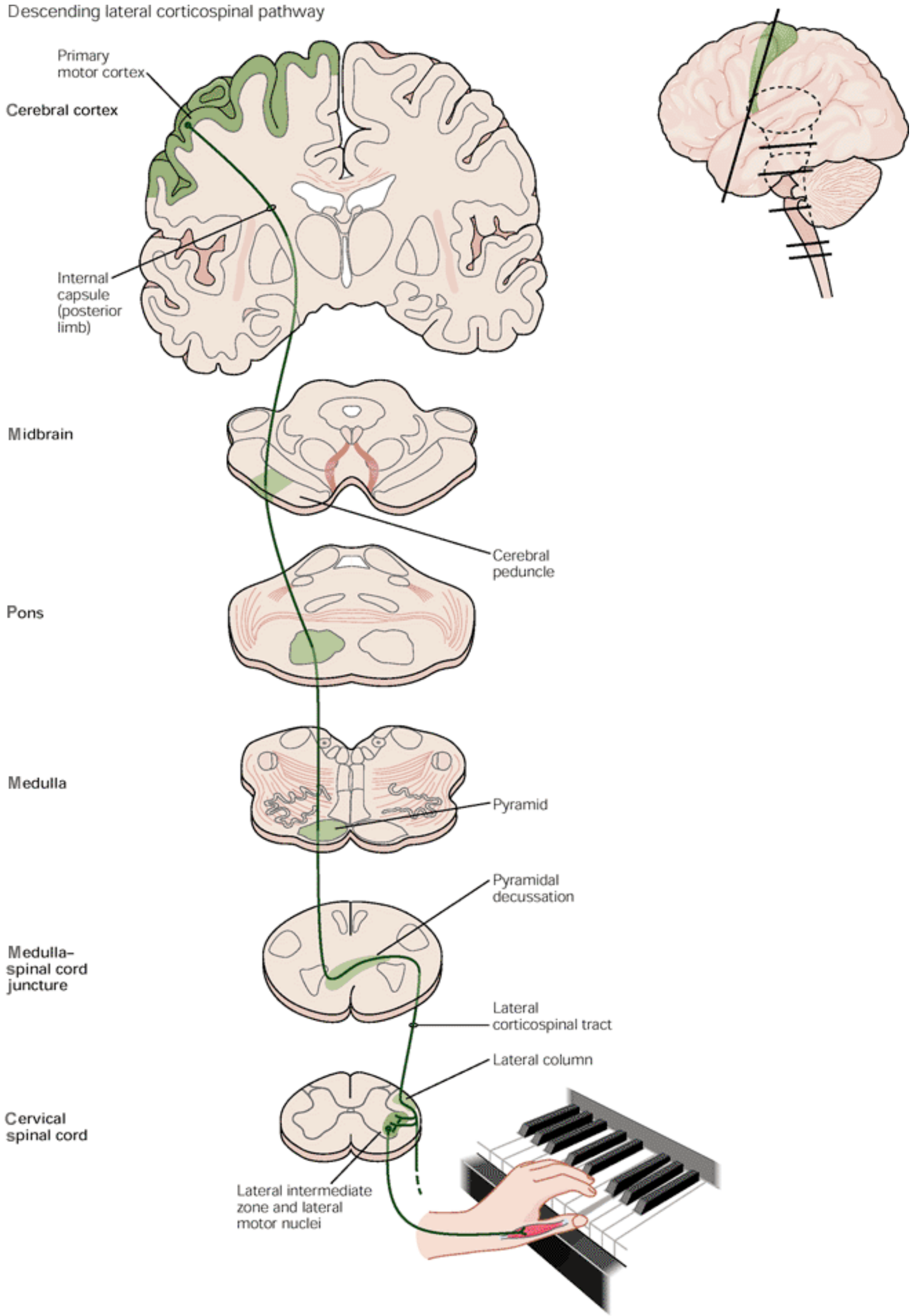
- Action on other neurons (Excitatory – Inhibitory)
- Discharge patterns (Regular spiking, Fast spiking, Bursting)
- Neurotransmitter (GABAergic, Glutamatergic, Dopaminergic, …)
- Direction of signal propagation relative to CNS (Sensory, Motor, Interneuron).

Networks of neurons





Ascending dorsal column–medial lemniscal pathway to primary sensory cortex
Somatic sensory cortex (postcentral gyrus)
Toe
Leg
Trunk
Forearm and hand area
Face
Cerebral cortex
Lateral sulcus
Internal capsule
Thalamus
Third ventricle
Ventral posterior lateral nucleus
Midbrain
Medial lemniscus
Pons
Medial lemniscus
Medulla
Medulla
Gracile nucleus
Cuneate nucleus
Spinal trigeminal nucleus
Sensory decussation
Dorsal root ganglion
Gracile fascicle
Cuneate fascicle
Spinal cord



Descending lateral corticospinal pathway
Primary motor cortex
Cerebral cortex
Internal capsule (posterior limb)
Midbrain
Cerebral peduncle
Pons
Medulla
Pyramid
Pyramidal decussation
Medulla–spinal cord juncture
Lateral corticospinal tract
Lateral column
Cervical spinal cord
Lateral intermediate zone and lateral motor nuclei

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

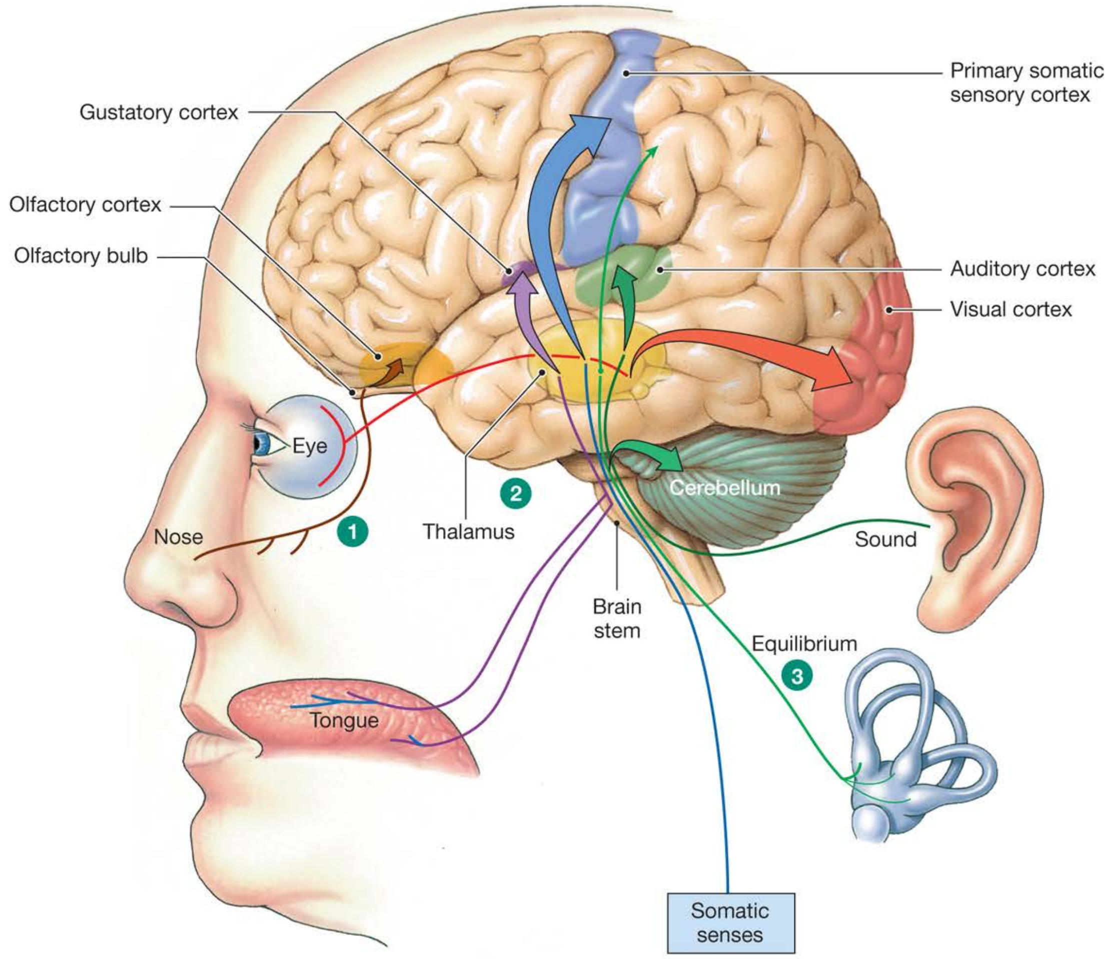
Sensory receptors – Each type is optimized to respond to different kind of stimuli:

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

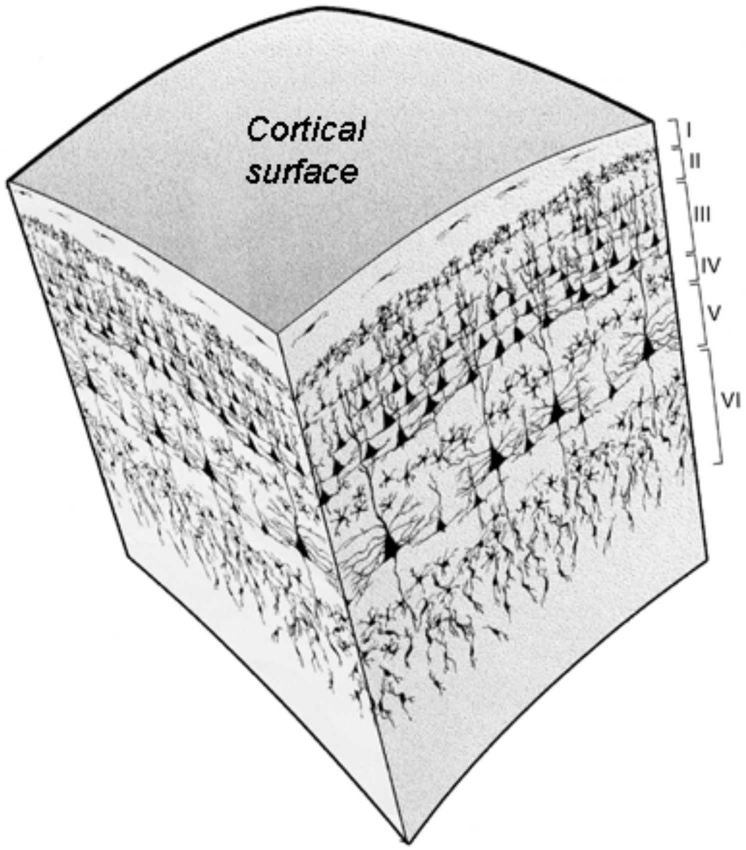
Sensory modalities & primary sensory areas

Labelled line theory

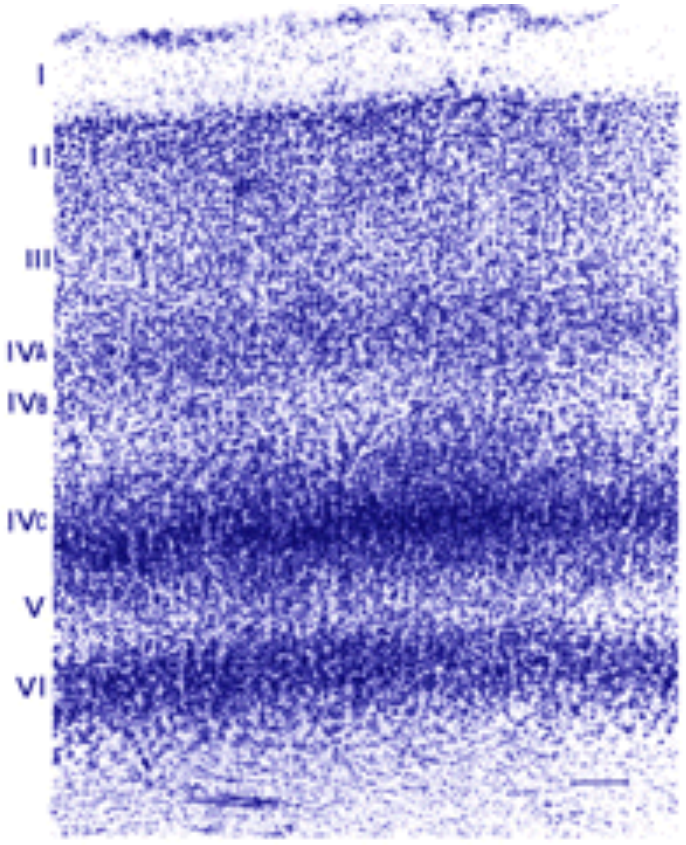
- Individual receptors preferentially transduce information about an adequate stimulus
- Individual primary afferent fibers carry information from a single type of receptor
- The area of the cortex that receives the signal determines the mode of the consequent perception



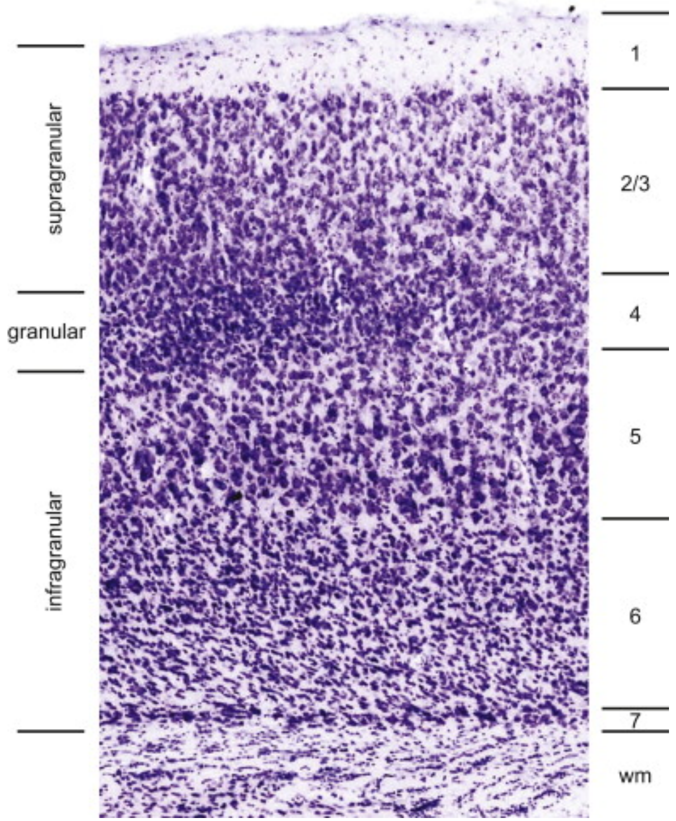
The layered structure of neocortex



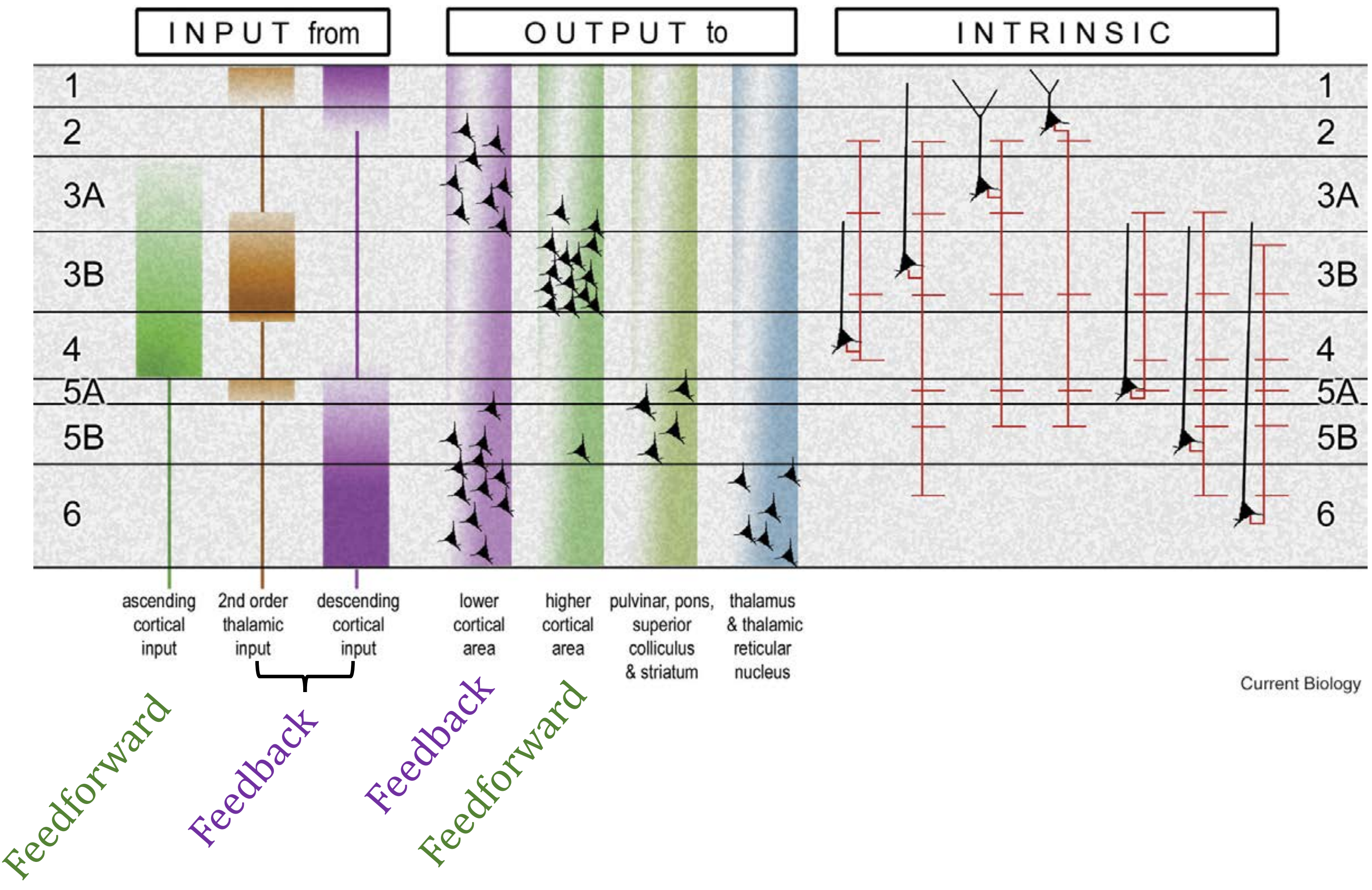
Monkey



Mouse



Canonical connectivity of neocortex



- Feedforward input (from thalamus or from 'lower' cortical areas), comes dominantly into layer 4

L4

- projects strongly to layers 2/3

L2/3

- L5
- L4 of 'higher' cortical areas

L5

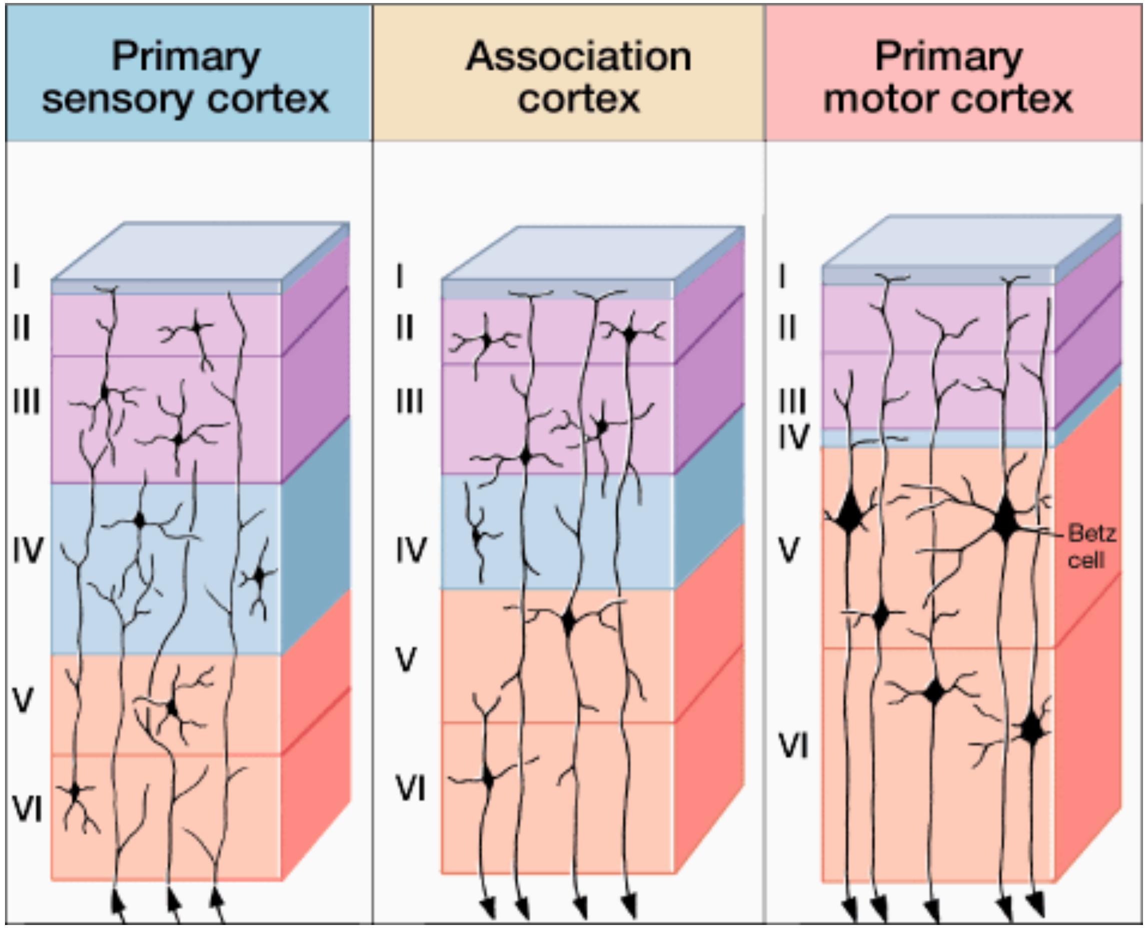
- L6
- Provides the only output from cortex

L6

- L1-L4, completing a loop
- Thalamus & lower cortical areas

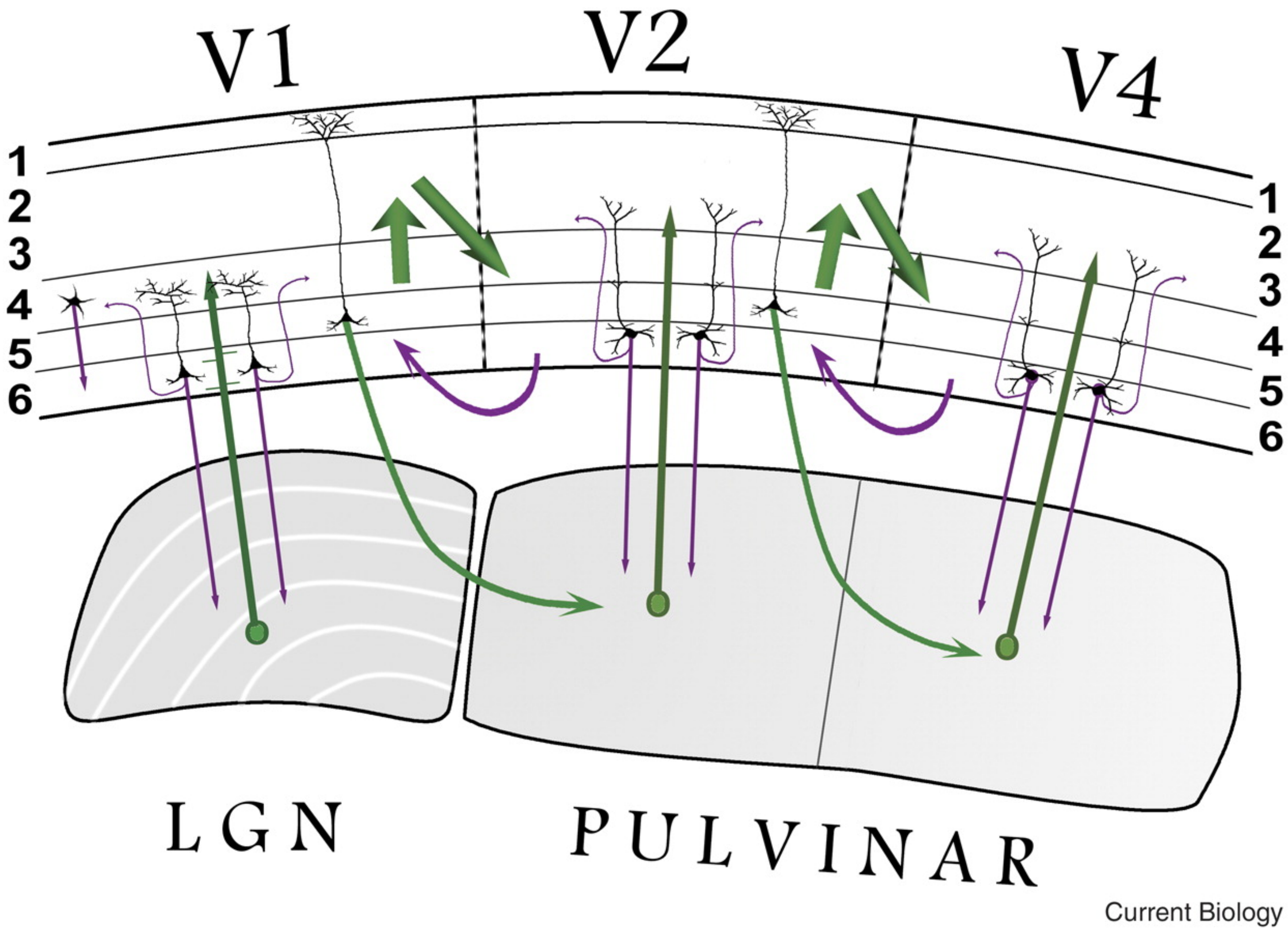
The extent of each cell layer of the neocortex varies throughout the cortex

INPUT



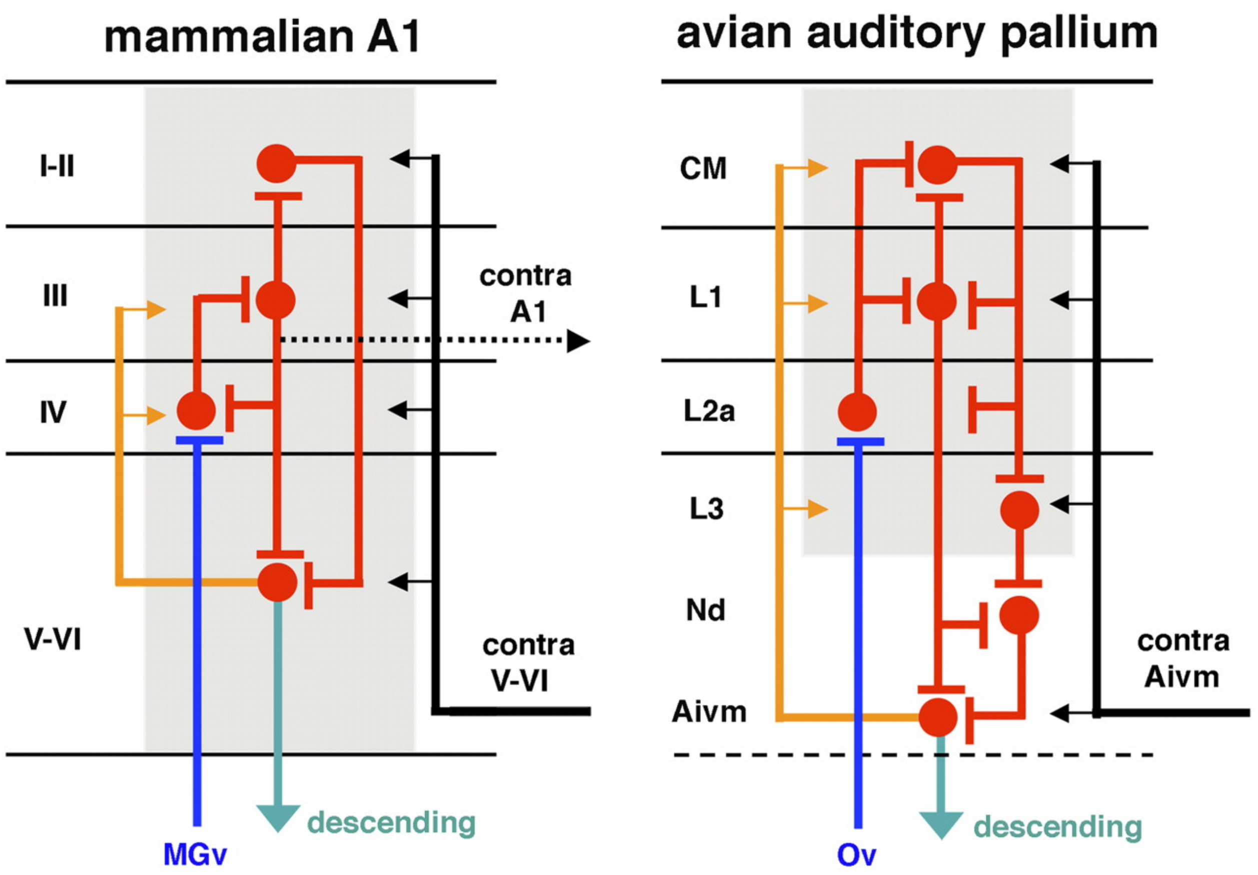
OUTPUT

Connectivity between neocortical layers in sensory areas (excitatory)



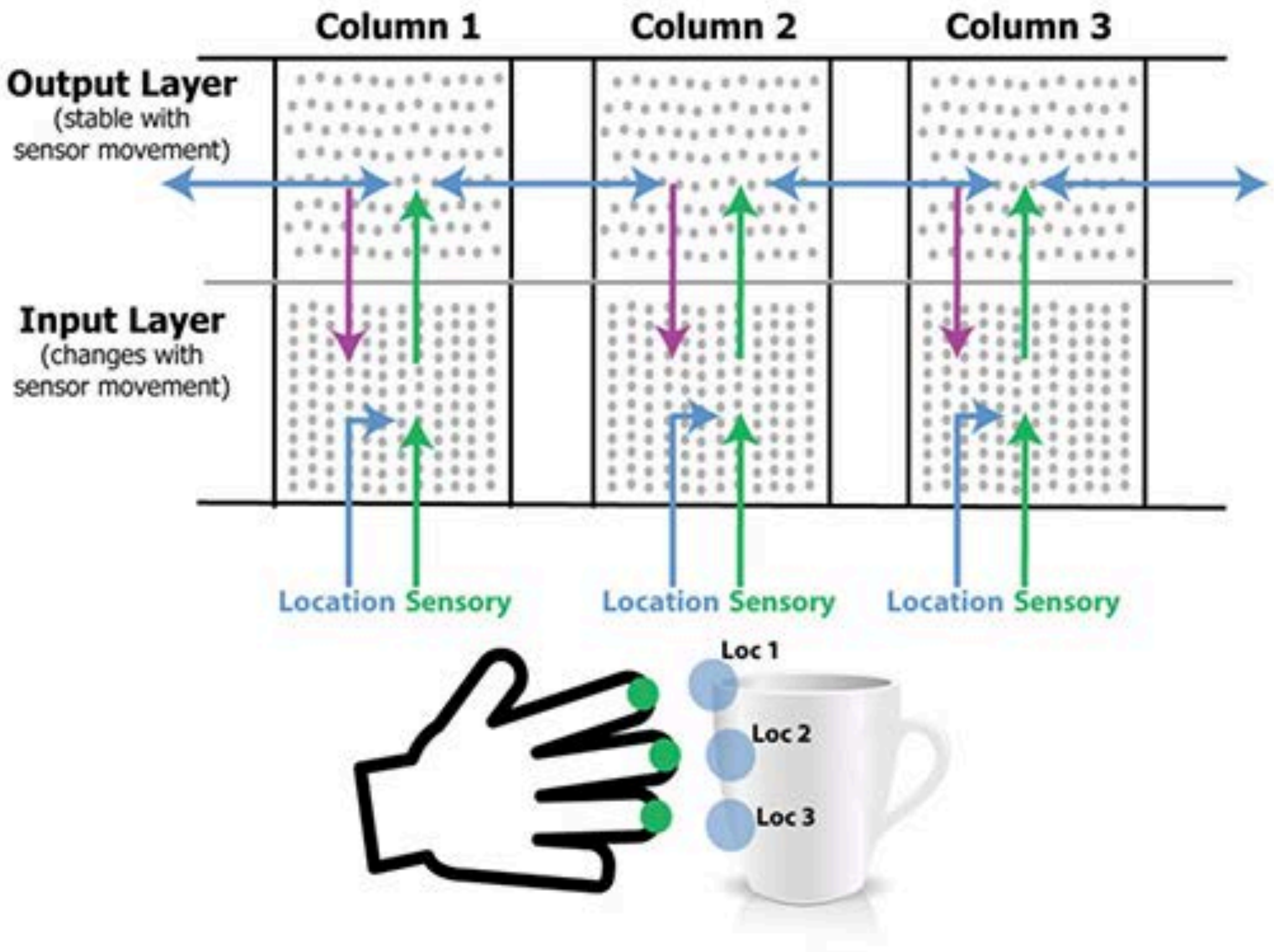
Shipp (2007)

Comparable laminar and columnar organization across species



Yuan Wang et al. 2010

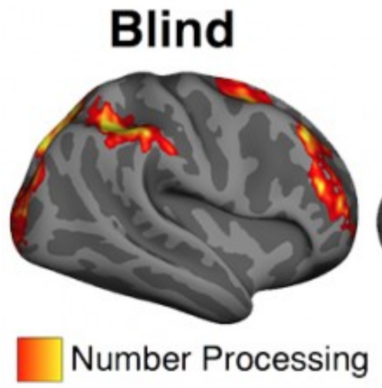
Columnar functional organization: Cortical columns as canonical computations



Each cortical column runs the same algorithm!

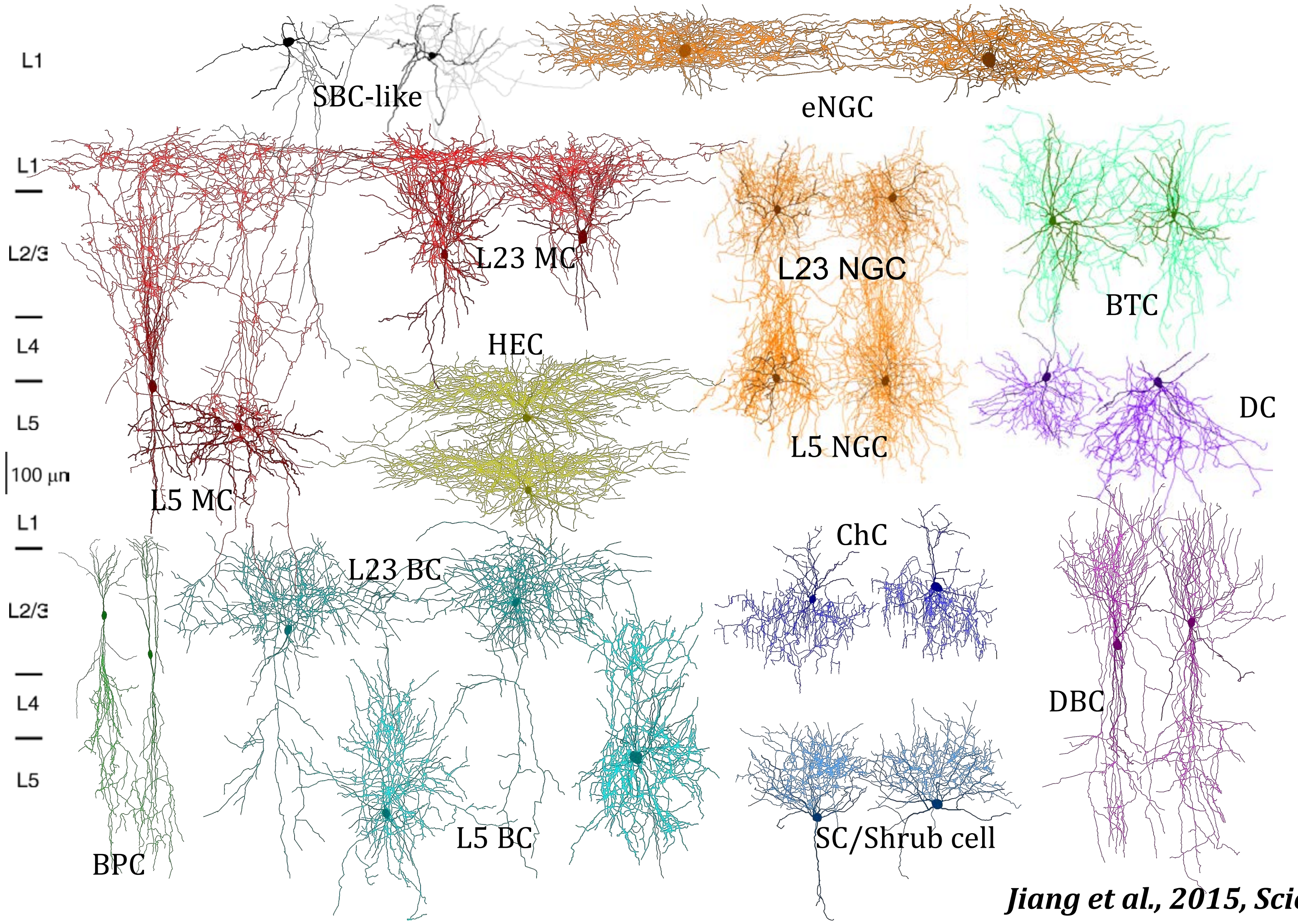
The function of a given cortical area is not fixed! Cortical flexibility

- 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



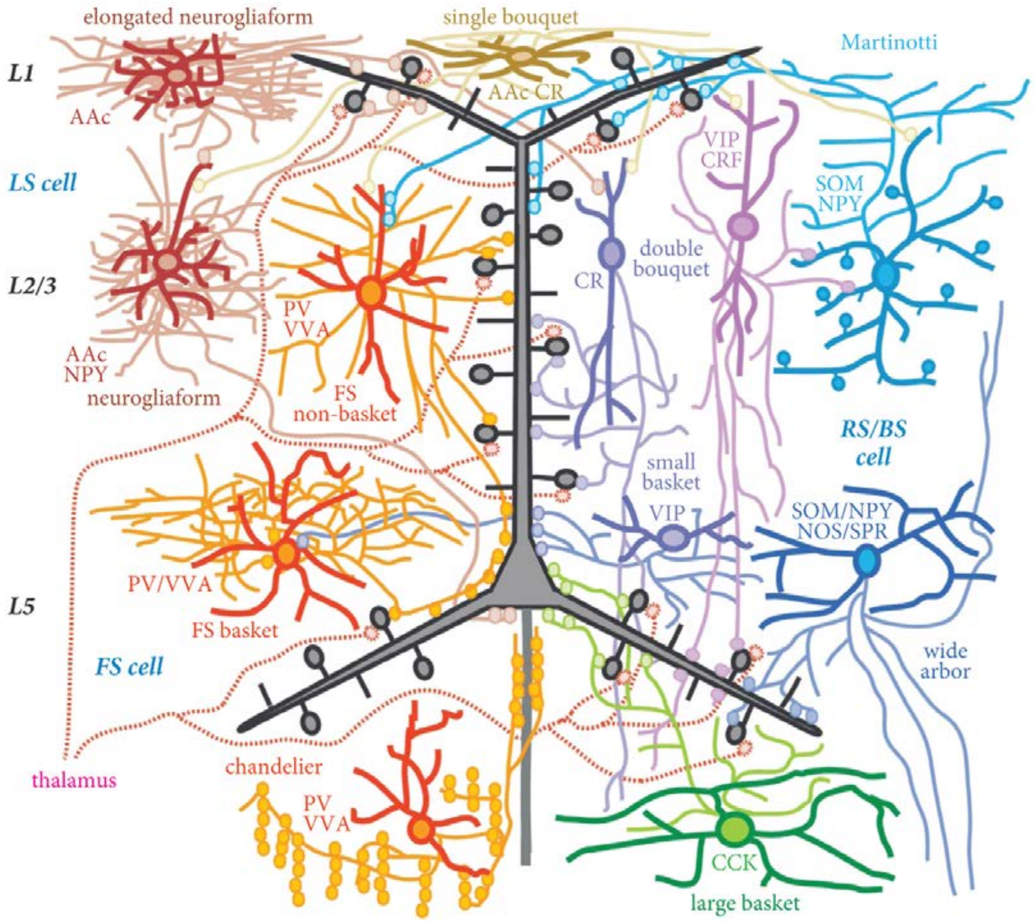
Kanjliaa et al. (2016)

Large number of inhibitory subtypes in the cortex

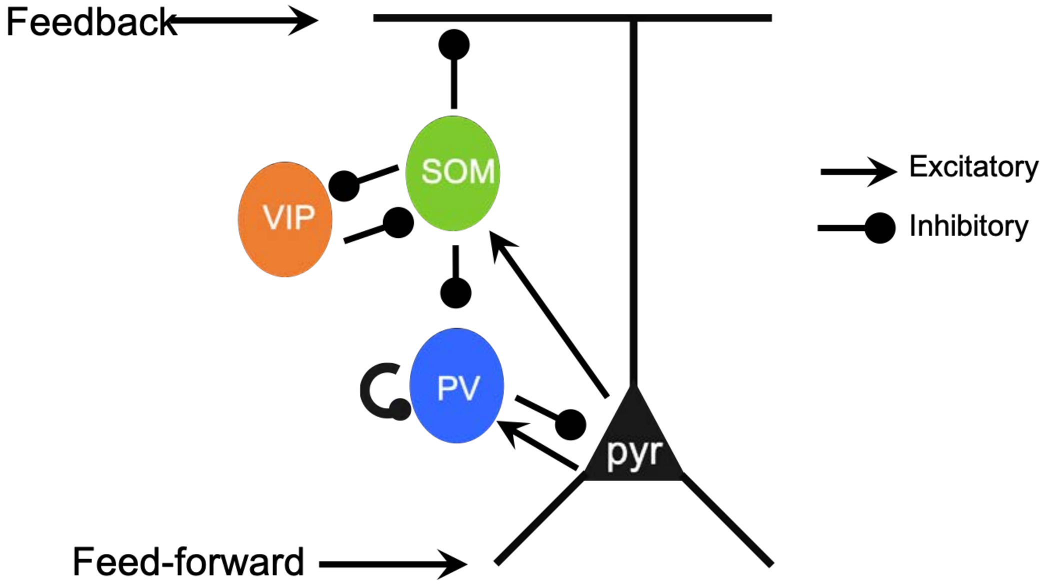


Jiang et al., 2015, Science

Local connectivity with inhibitory neurons neurons—simplified version

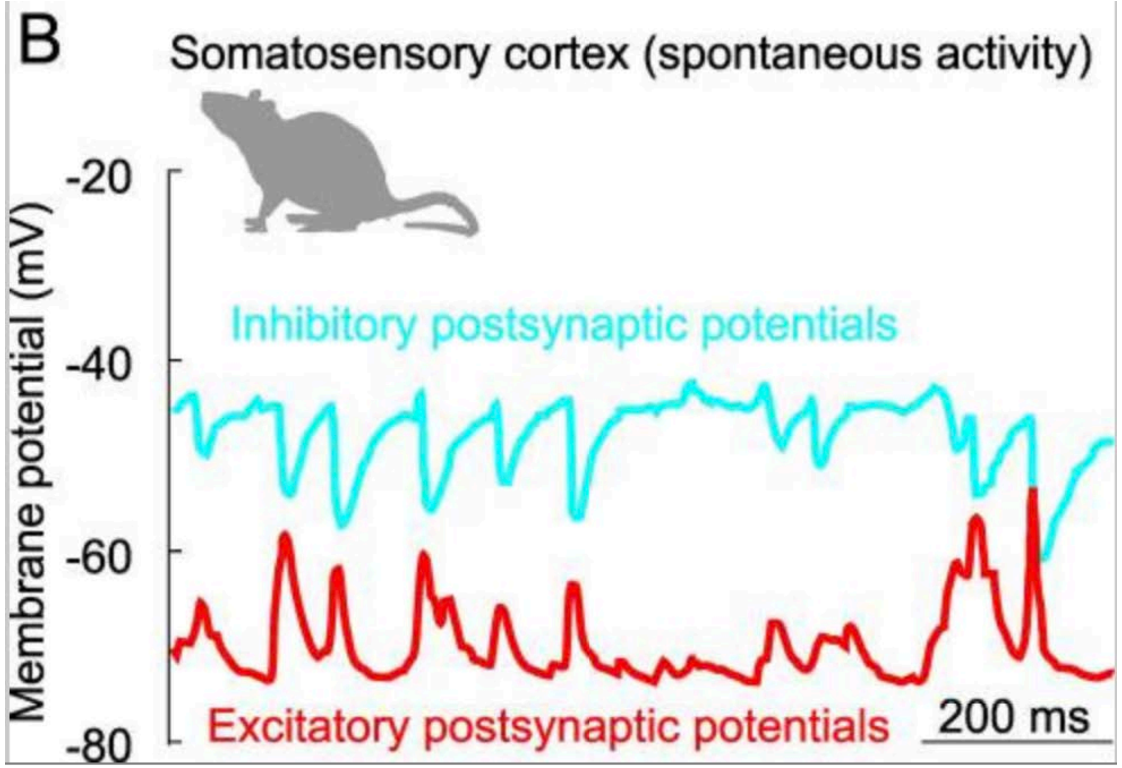


Kubota (2014)

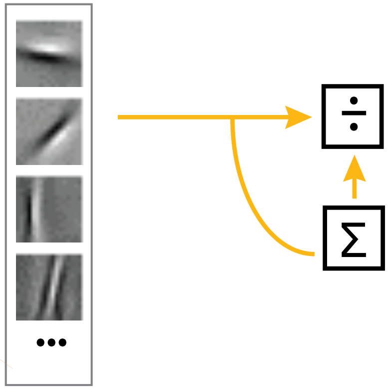


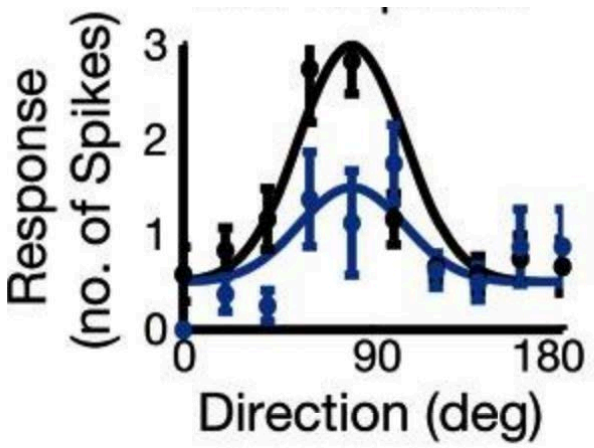
Pfeffer et. al (2013)

Balance of excitation and inhibition

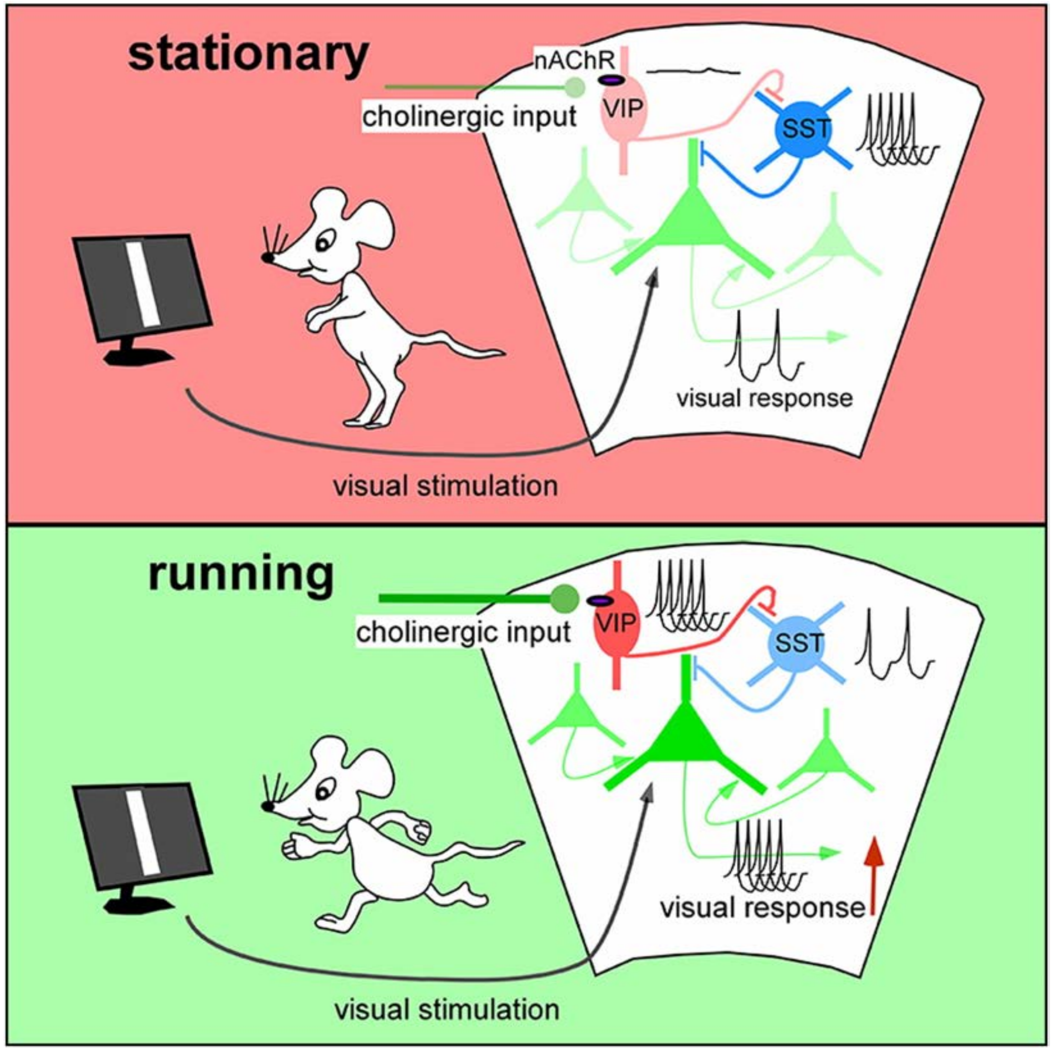


Divisive normalization





Gain Control by Behavioral State

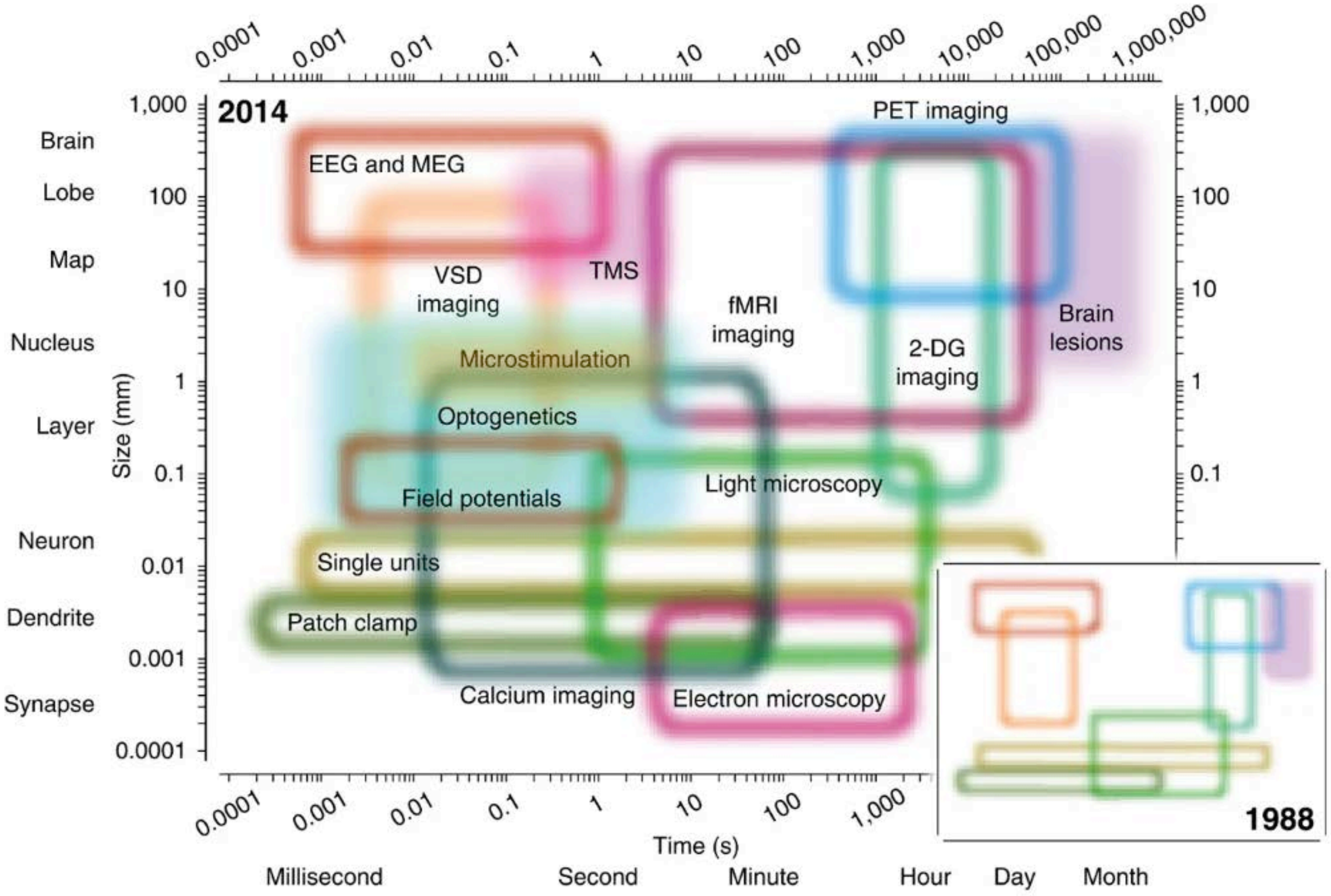


- VIP neurons in mouse V1 are activated during running basal forebrain
- SST neuron activity is decreased, disinhibiting excitatory neurons, during running

Fu et al. 2014

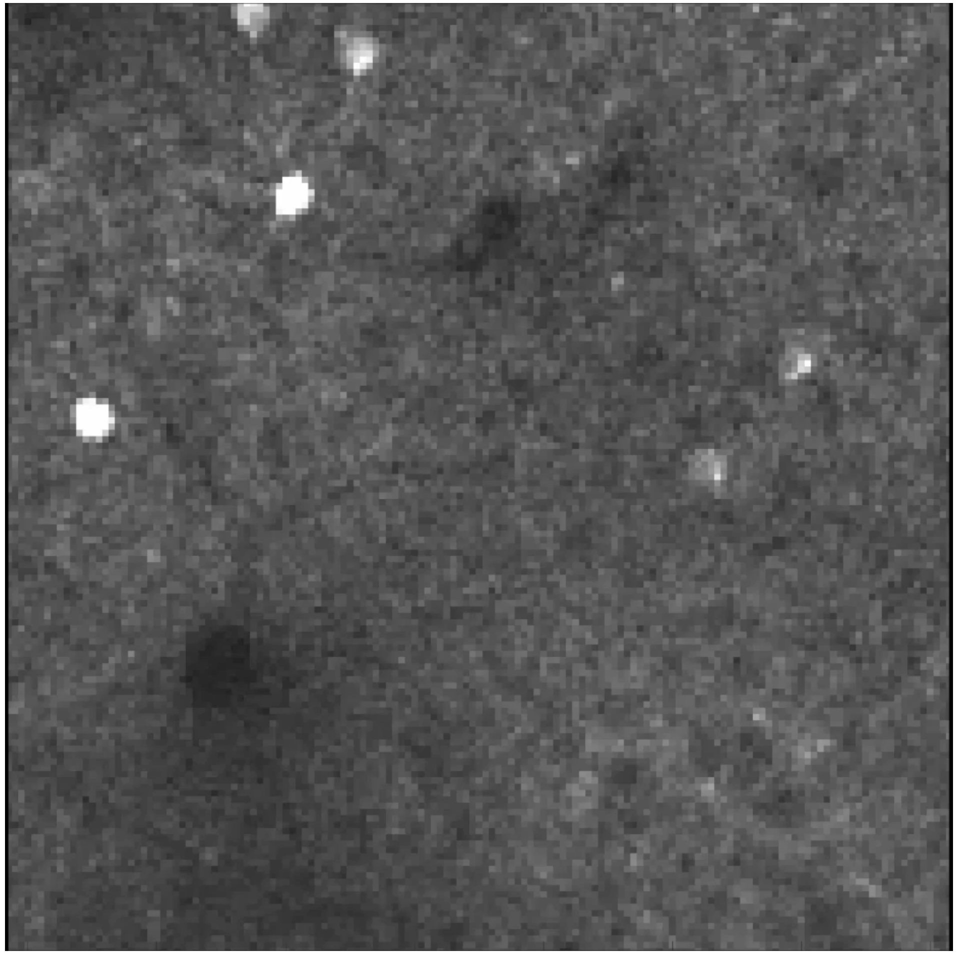
Functional properties of the neocortex

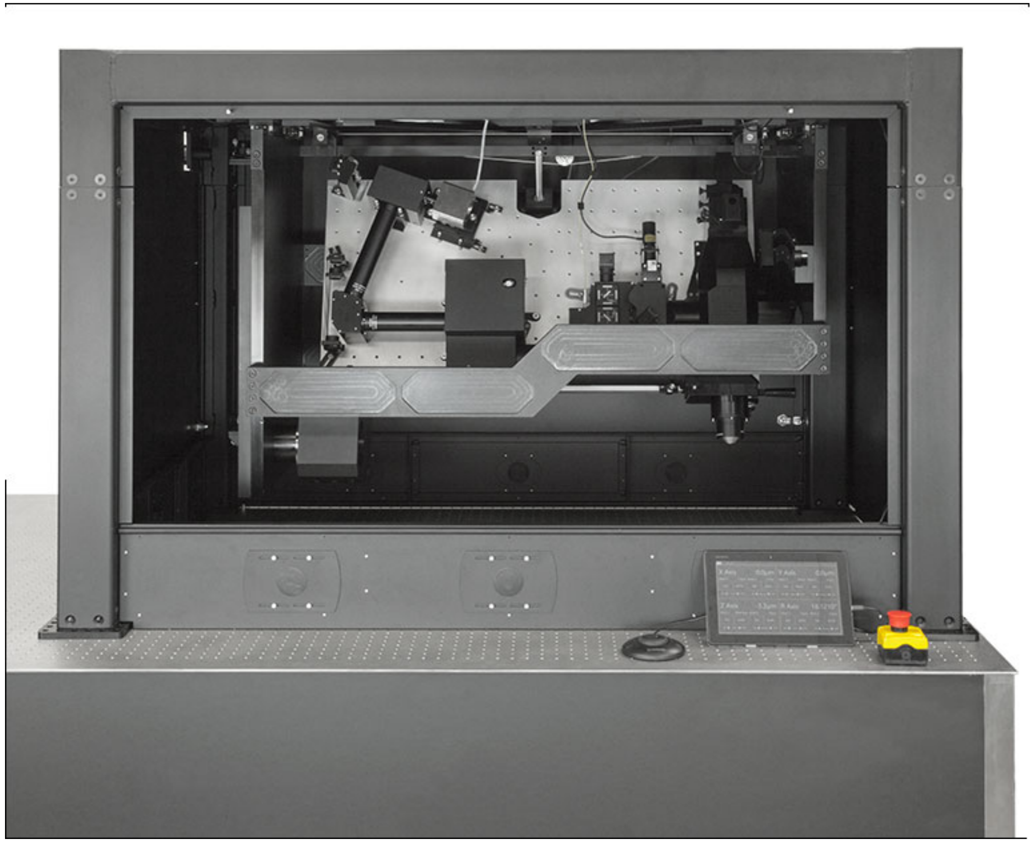
Methods for observing the living brain



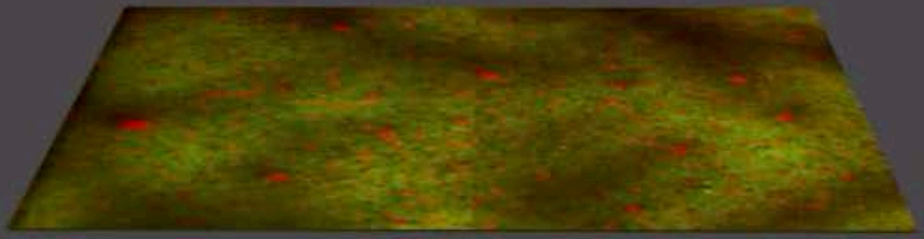
Sejnowski, T.J., Churchland, P.S., and Movshon, J.A. (2014). Nat Neurosci *17*, 1440–1441.

Mesoscope - Large field recordings





Sofroniew et al. 2016

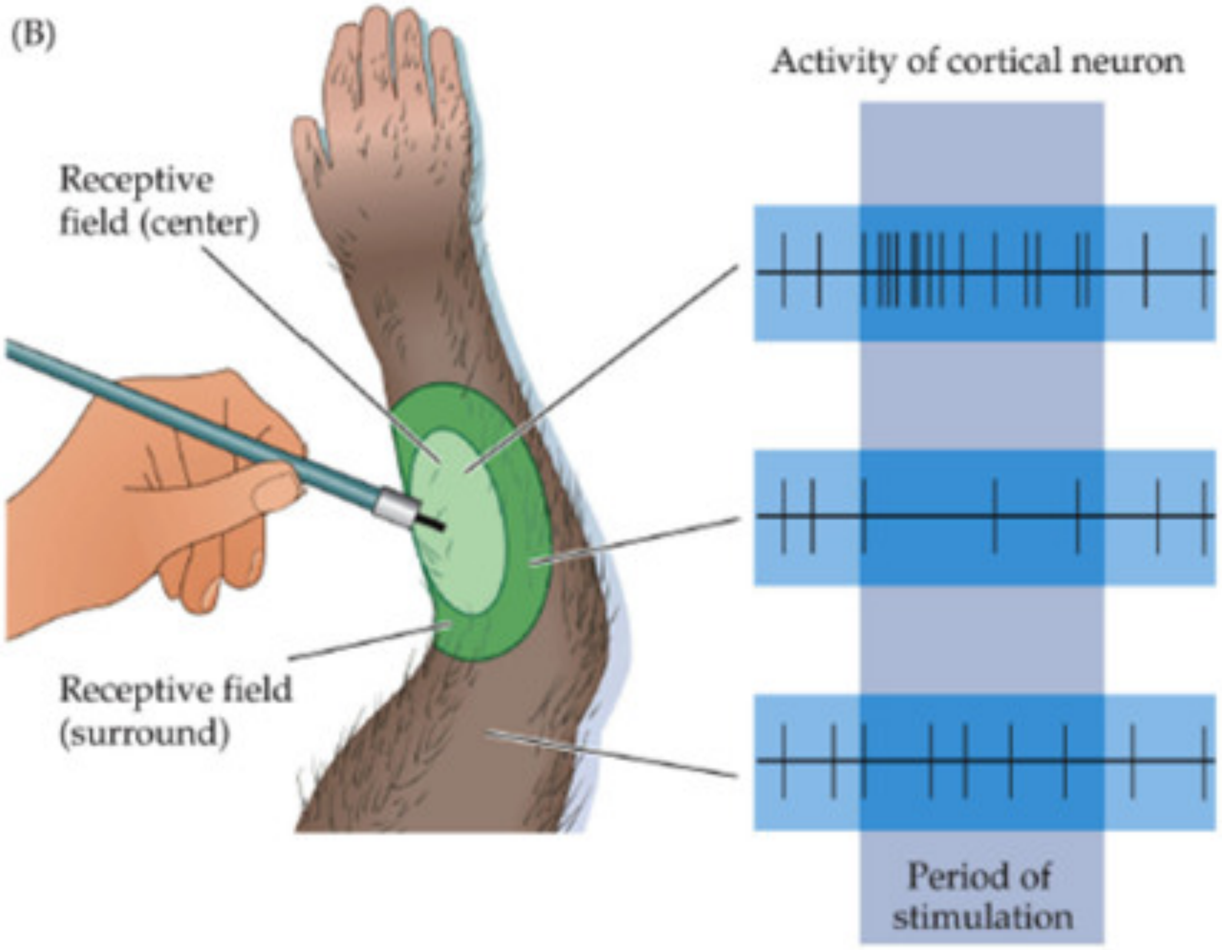


Receptive field

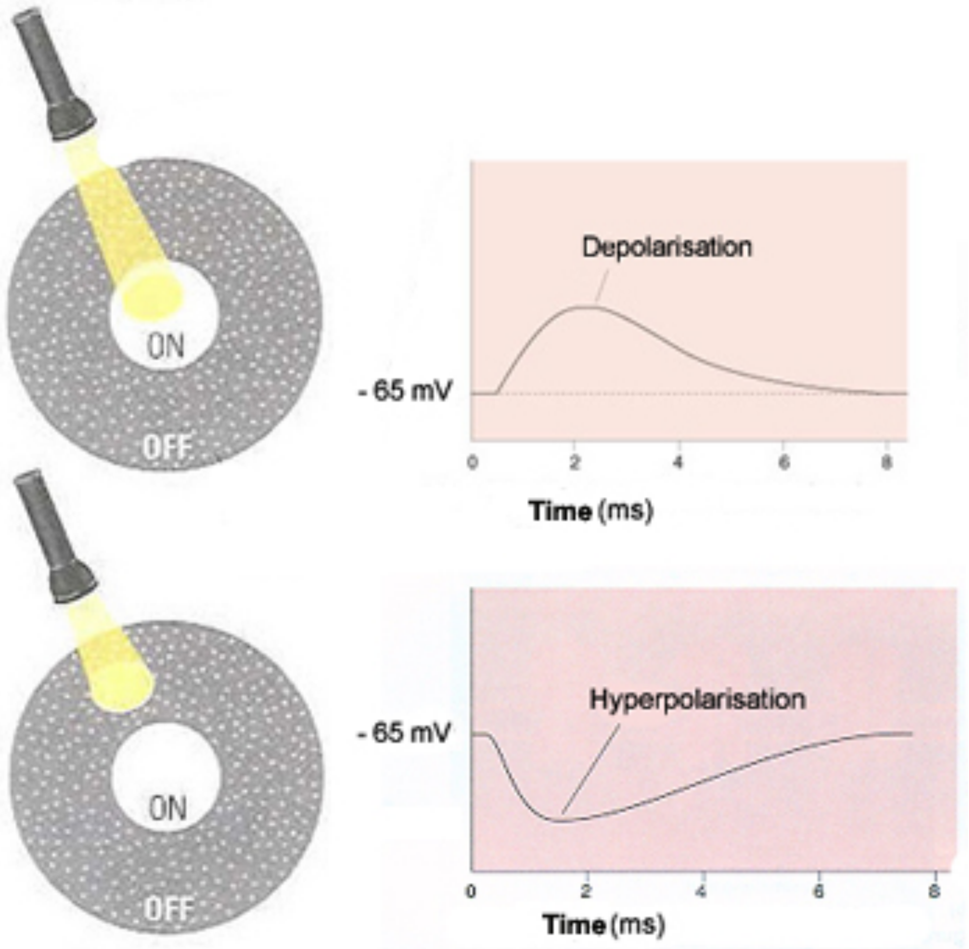
- The **receptive field** of a sensory neuron is the portion of the sensory space in which a stimulus will elicit neuronal response. The amplitude response depends on the intensity of the stimulus.

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

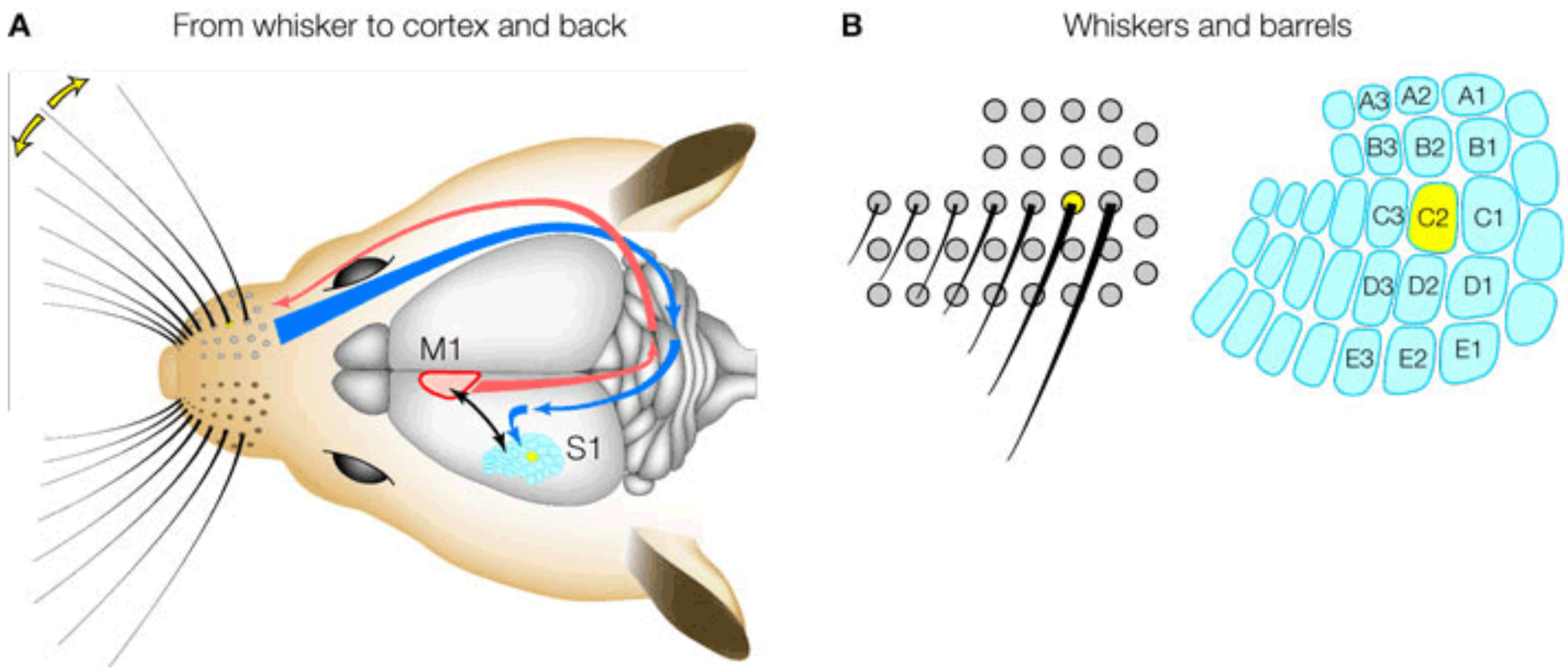
Receptive field examples



NEUROSCIENCE, Fourth Edition, Figure 1.13 (Part 2)



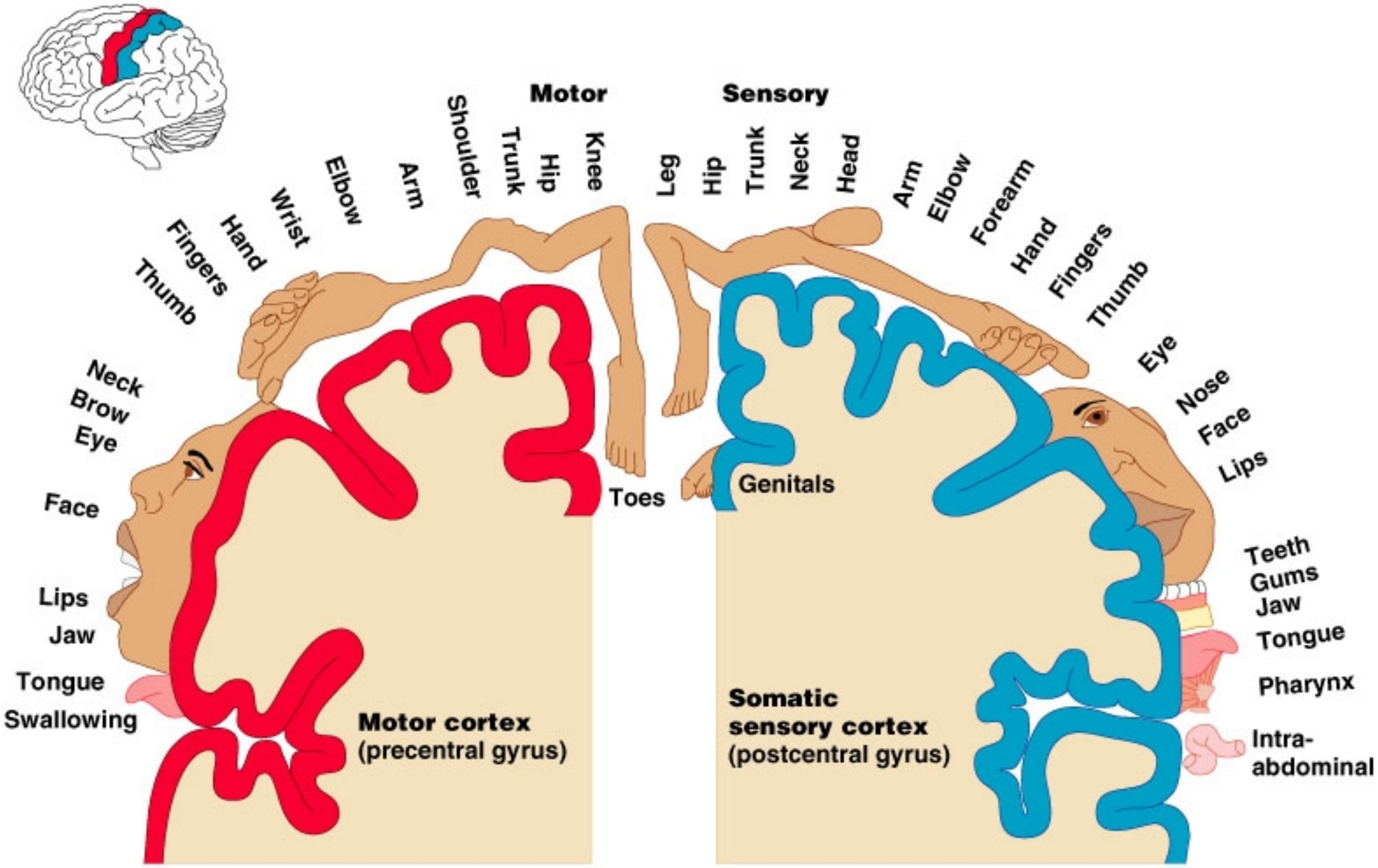
Barrel columns in the mouse somatosensory system



Aronoff and Petersen 2008

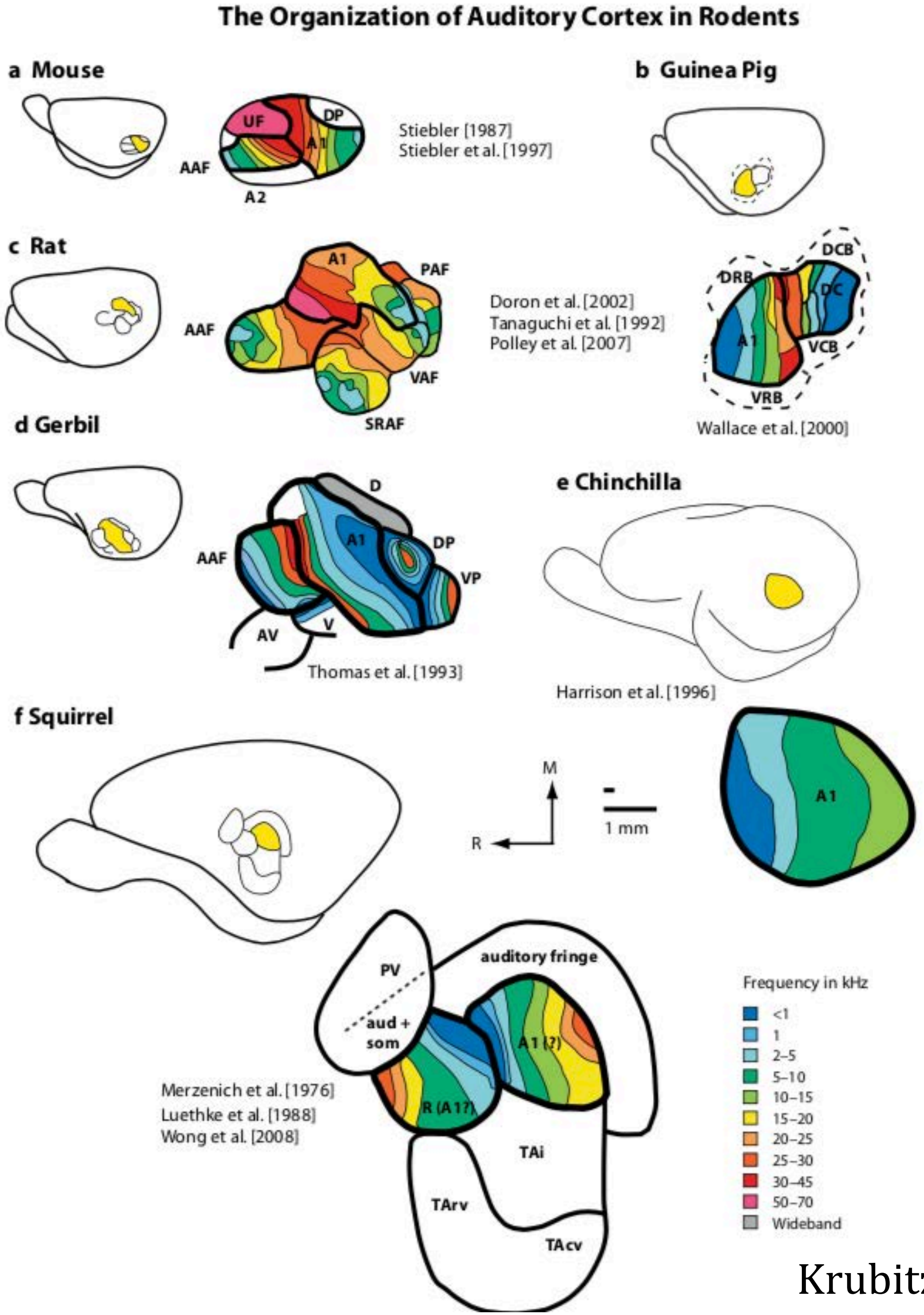
Functional Maps -> The spatial distributions of neural response properties & their interactions

Body maps in somatosensory and motor areas



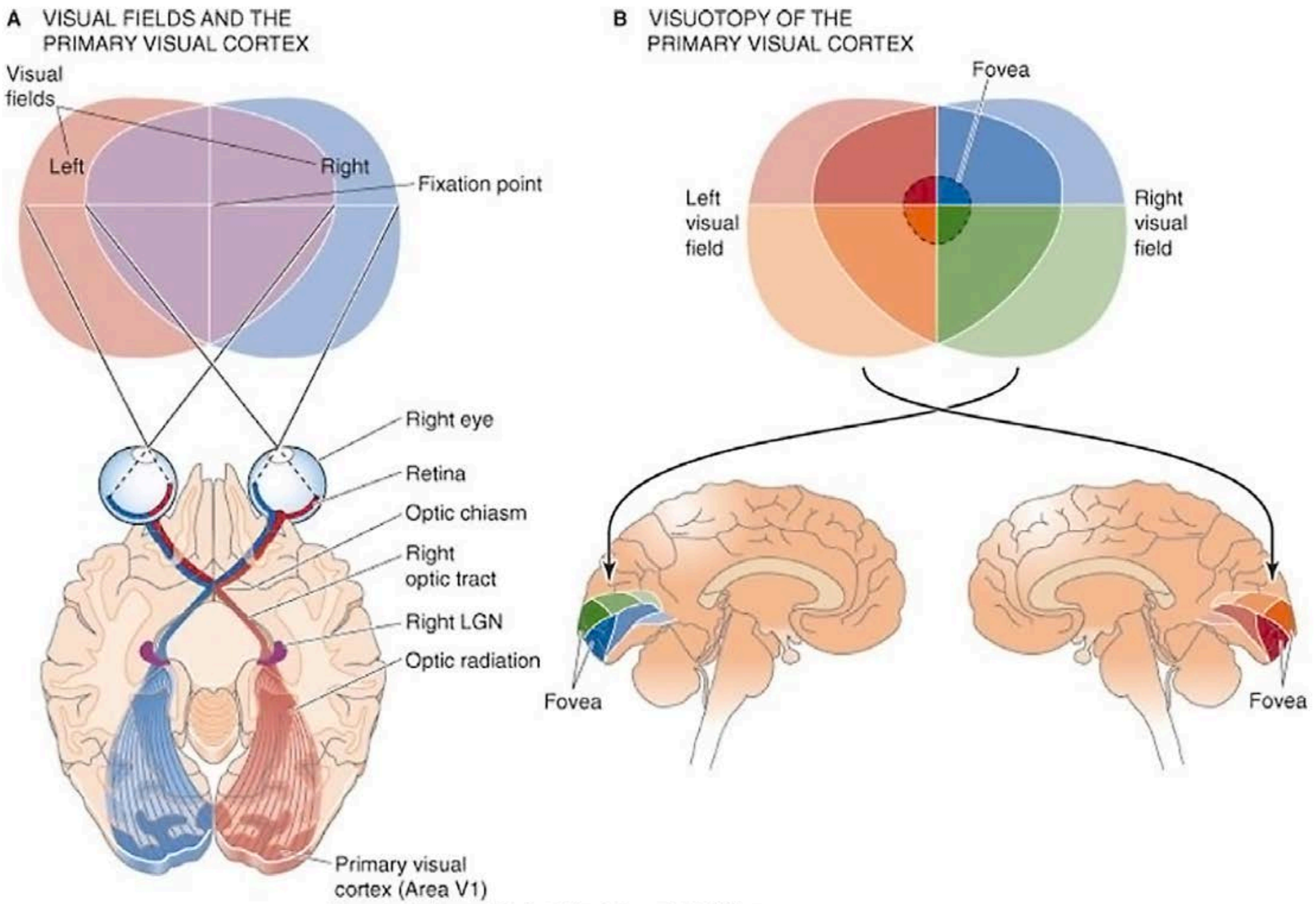
A cortical homunculus is a distorted representation of the human body, based on a neurological "map" of the areas and proportions of cortex dedicated to processing motor functions, or sensory functions, for different parts of the body.

Tonotopic maps in auditory system



Krubitzera et al. 2011

Topographic maps in the visual system



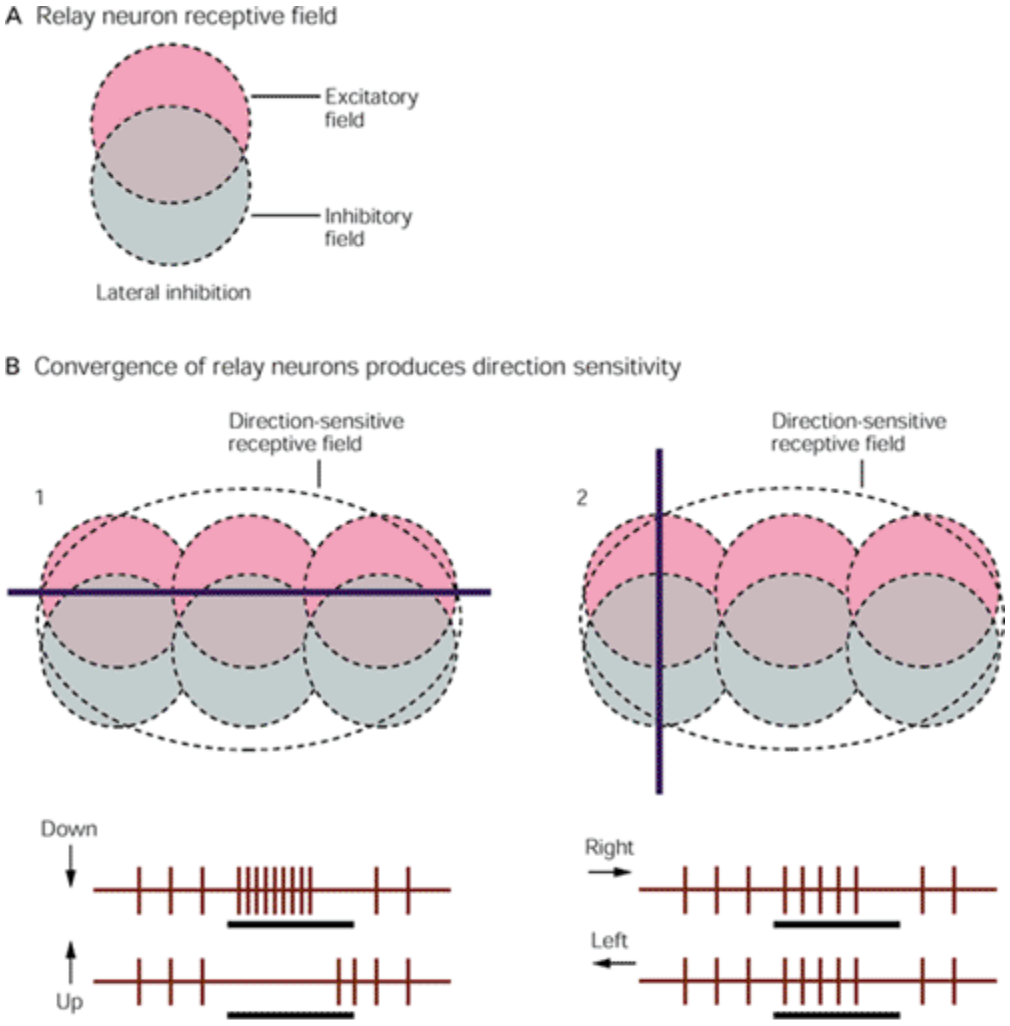
Boron & Boulpaep: Medical Physiology, 2nd Edition.

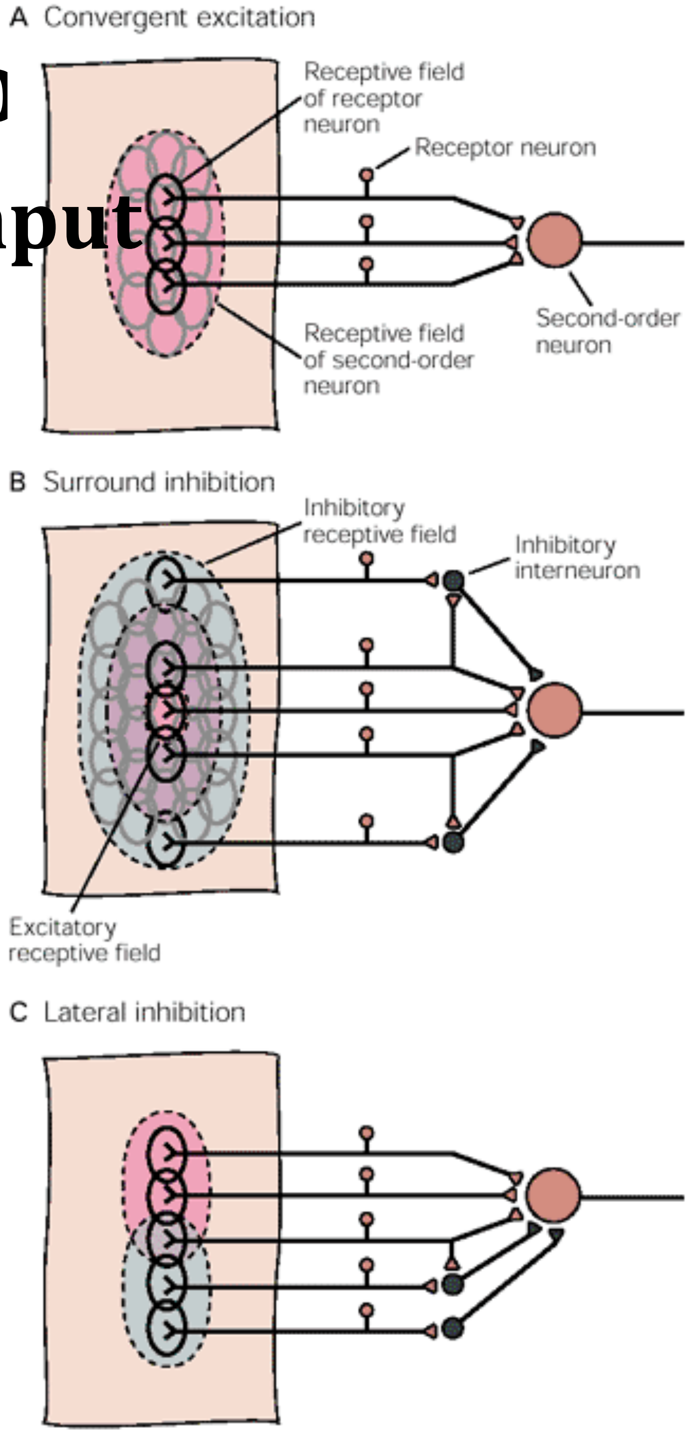
Adjacent points on the sensory surface are represented at adjacent locations in the brain.

Cortical magnification:
The amount of space a brain map dedicates to a stimulus reflects its usefulness rather than its real physical properties.

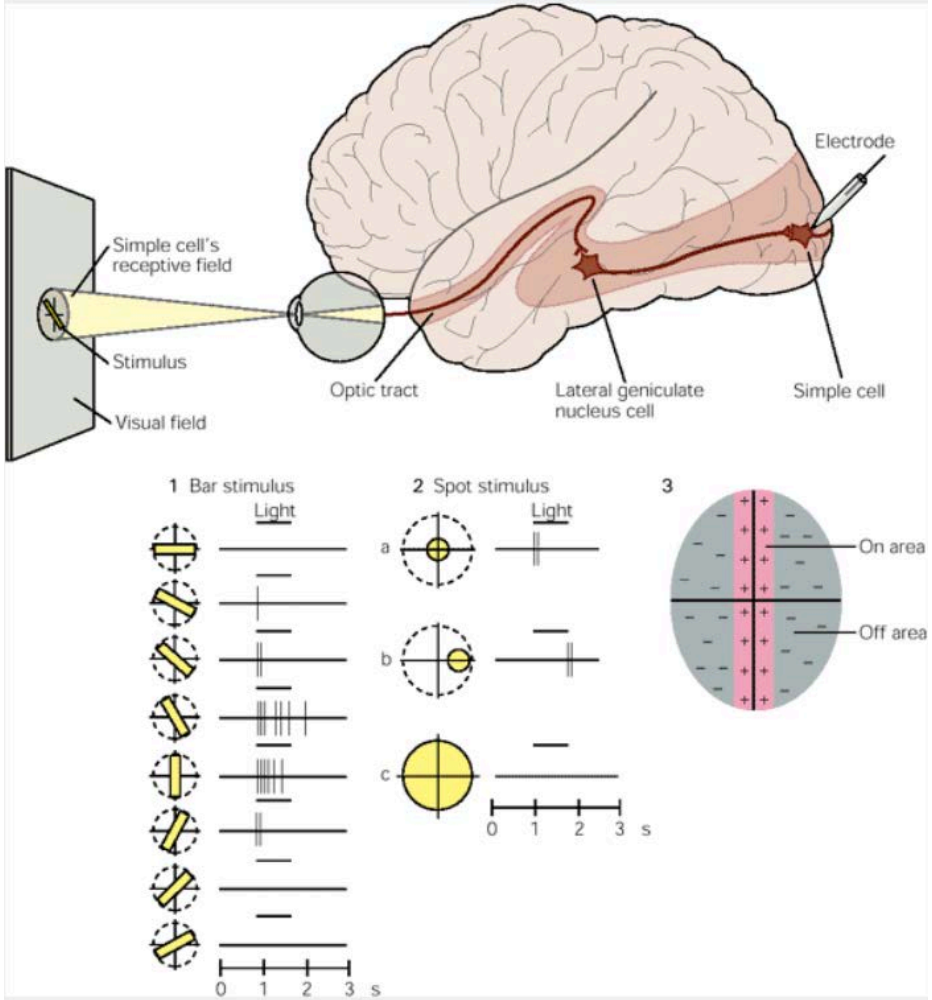
From connections to computatio

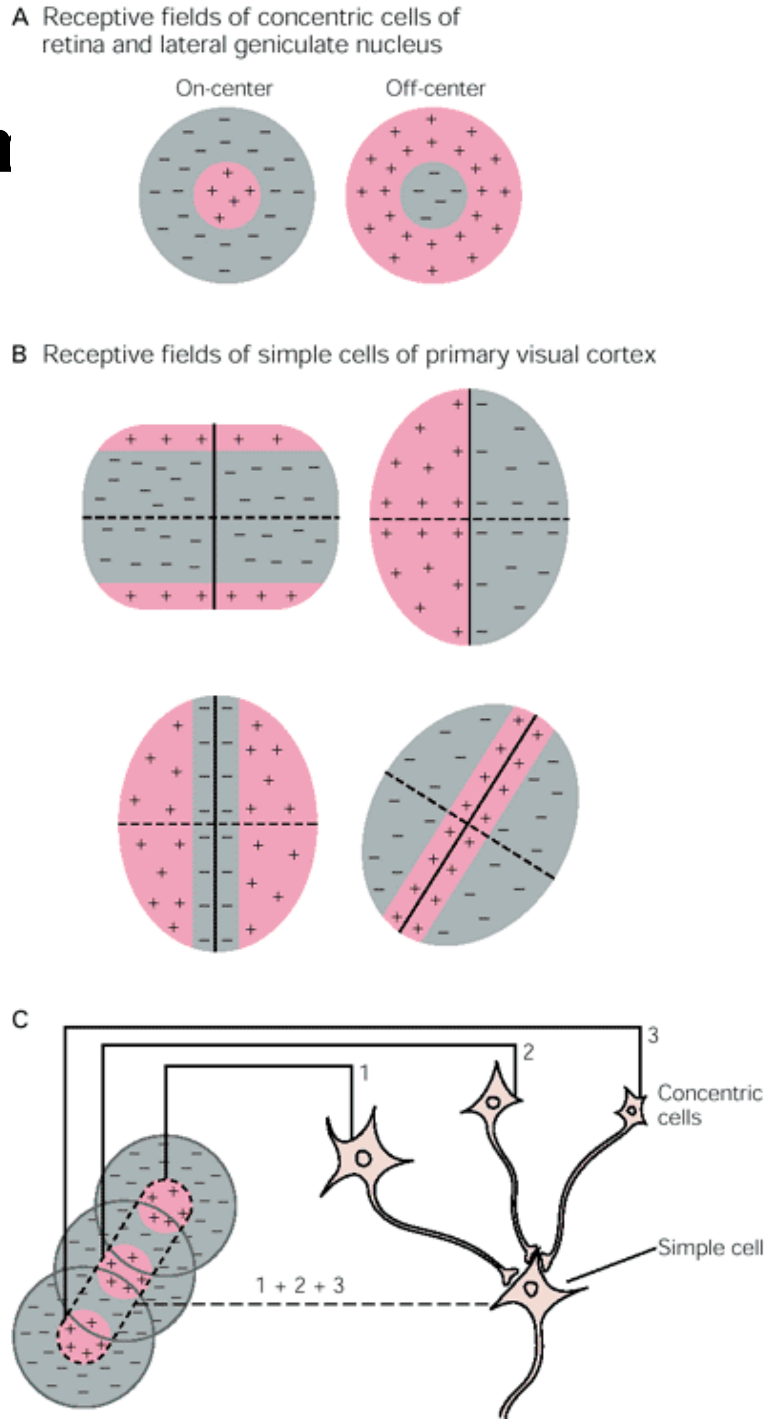
→ Convergence of excitatory input



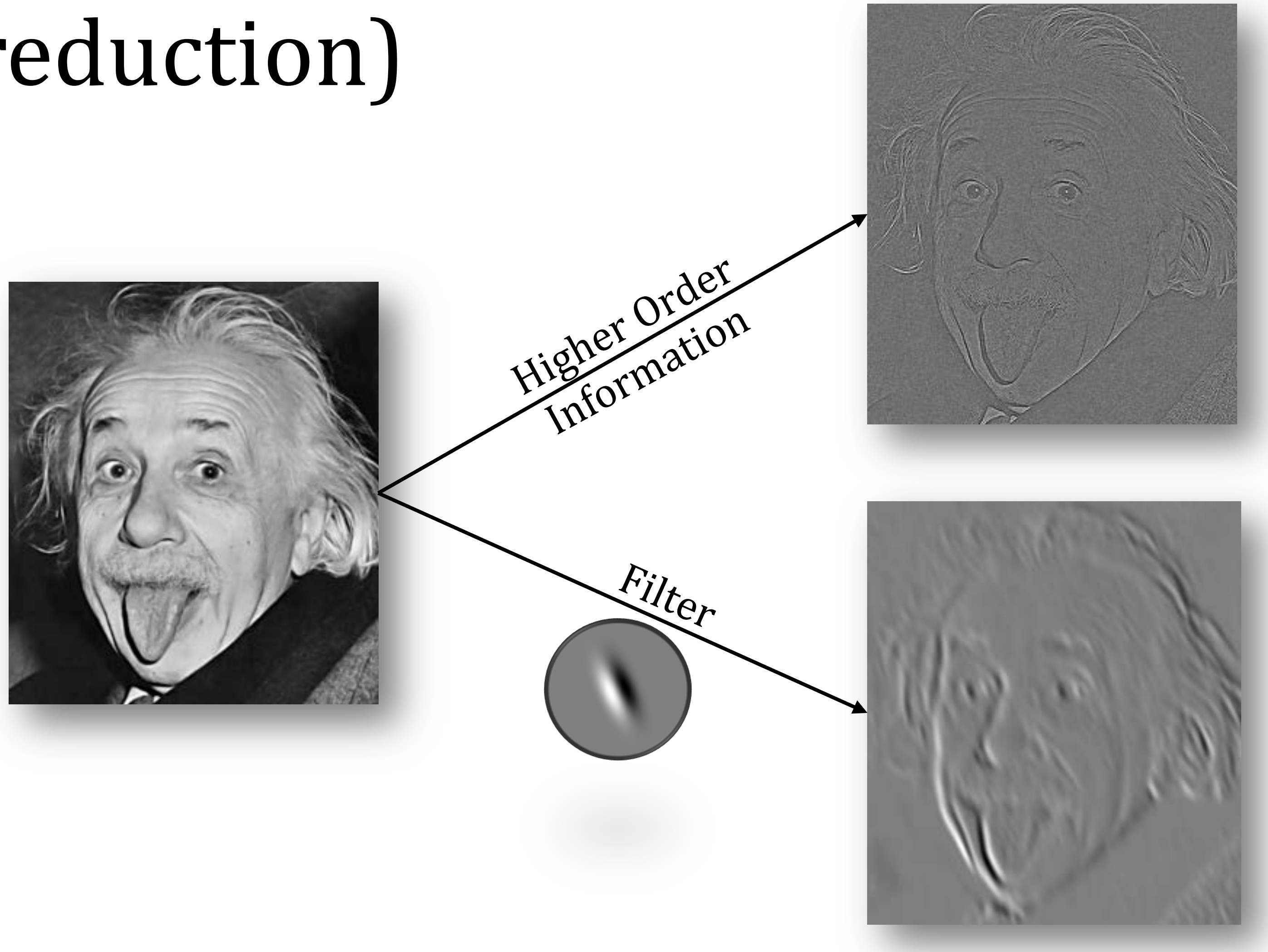


Receptive fields in the visual systen





Primary visual cortex RFs respond to edges (redundancy reduction)



Orientation columns in primary visual cortex

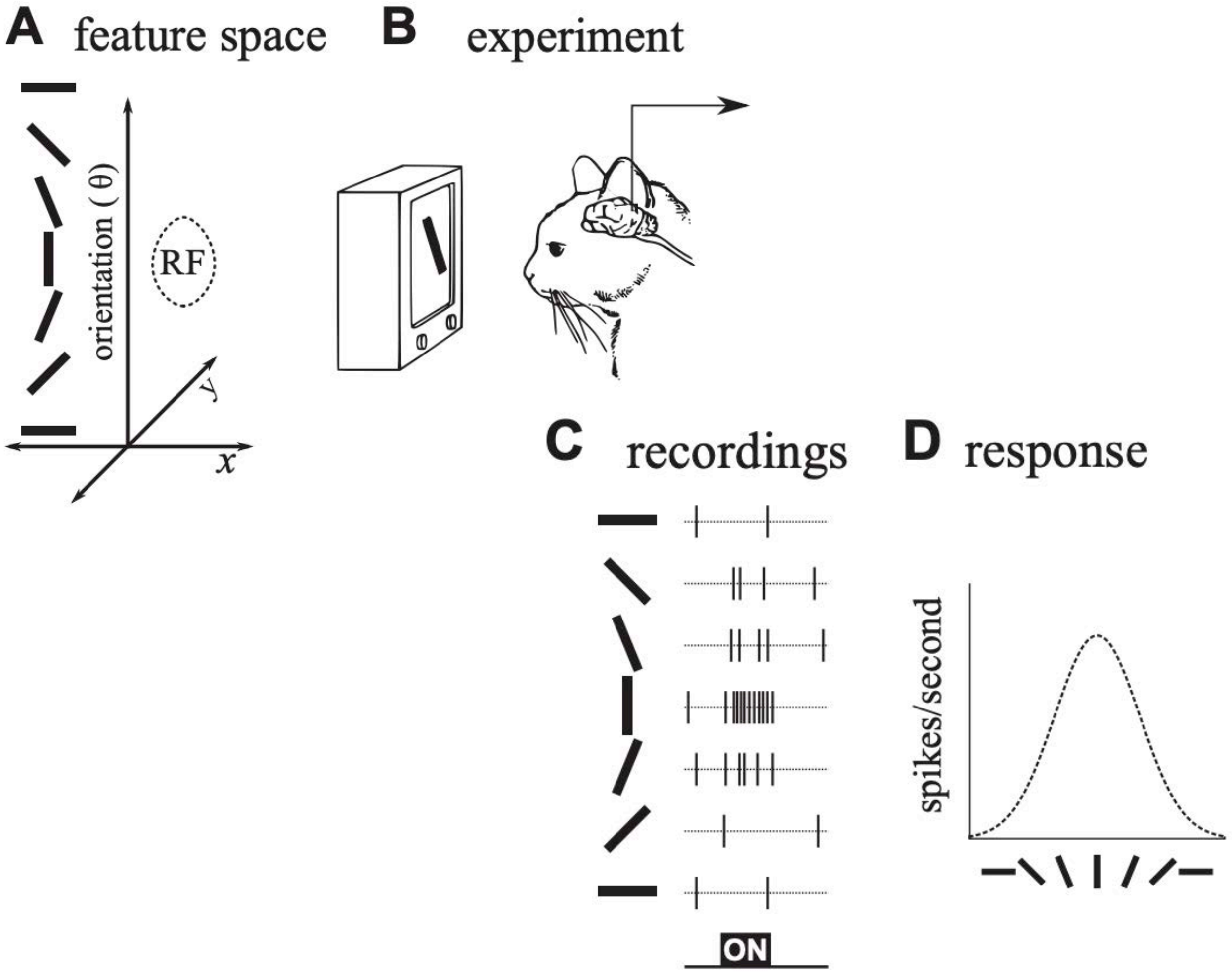
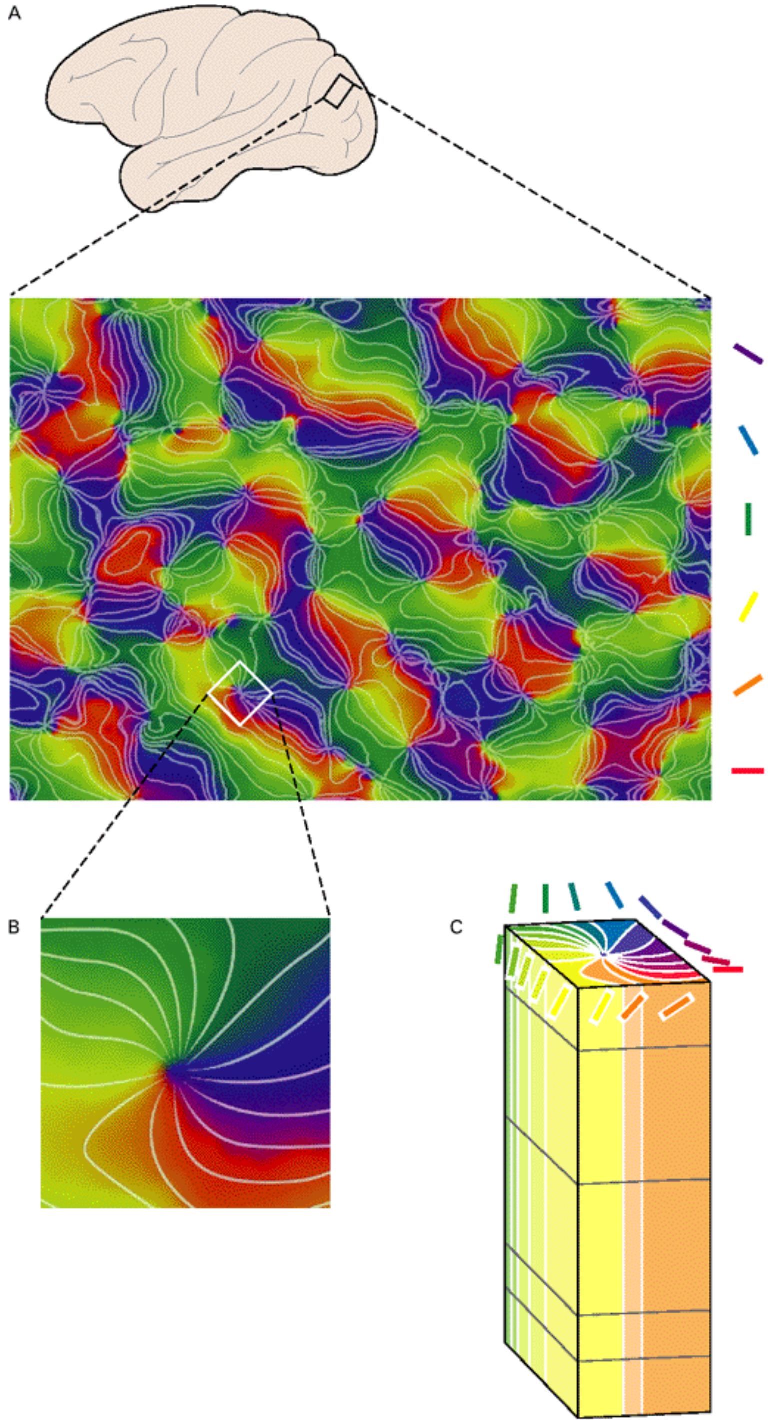
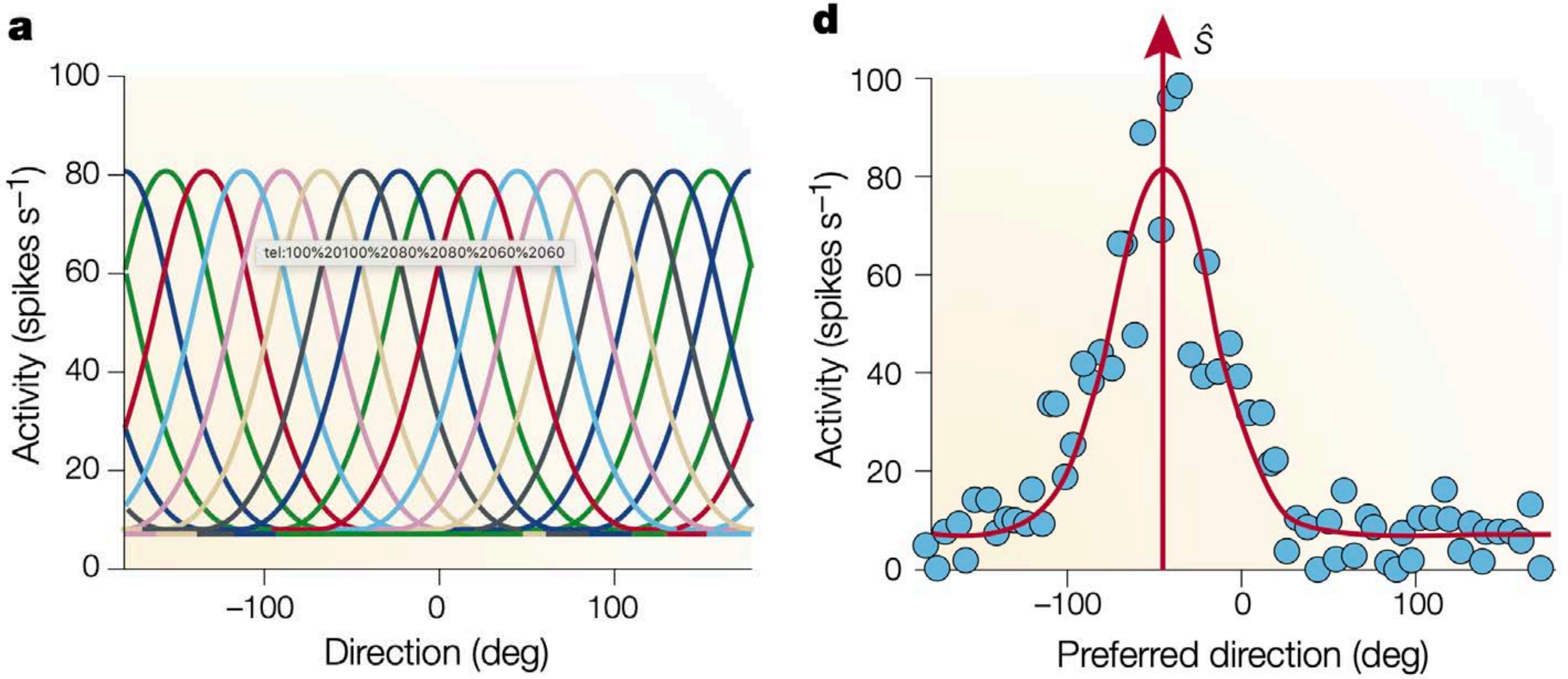


FIGURE 4.8 Response of a single cortical cell to bars presented at various orientations.

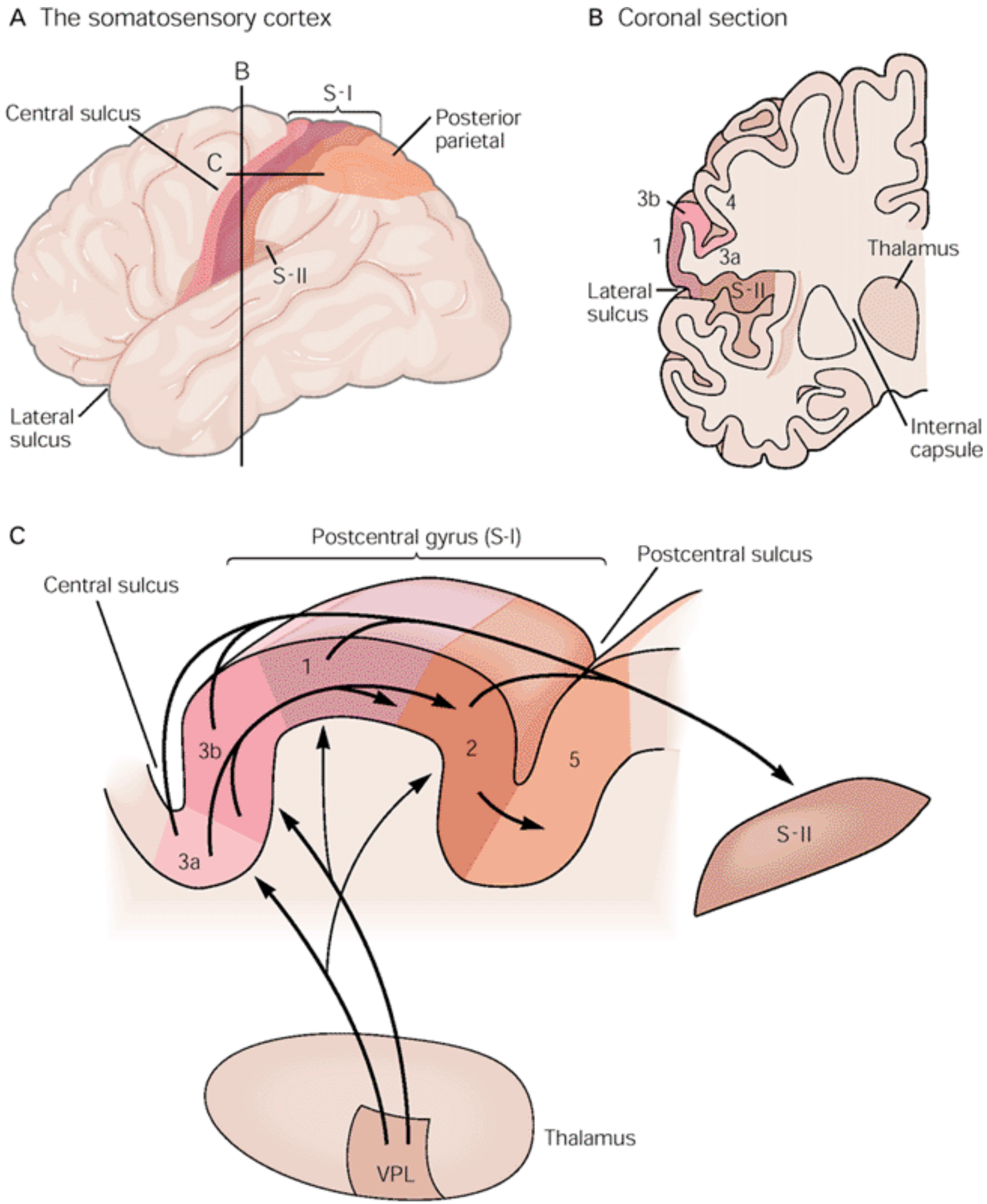


The standard population coding model

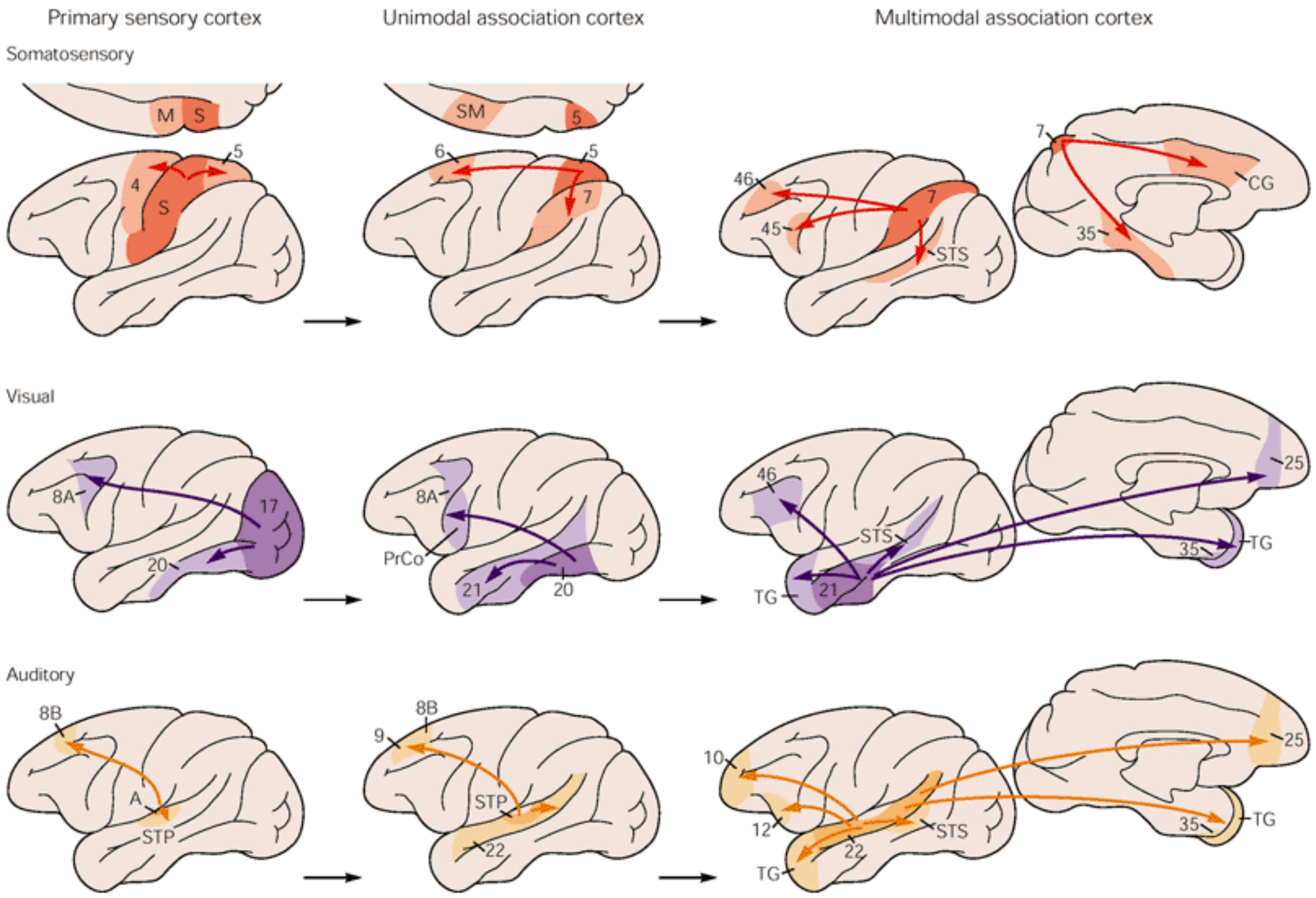


Pouget, A., Dayan, P., and Zemel, R. (2000). Nat Rev Neurosci *1*, 125–132.

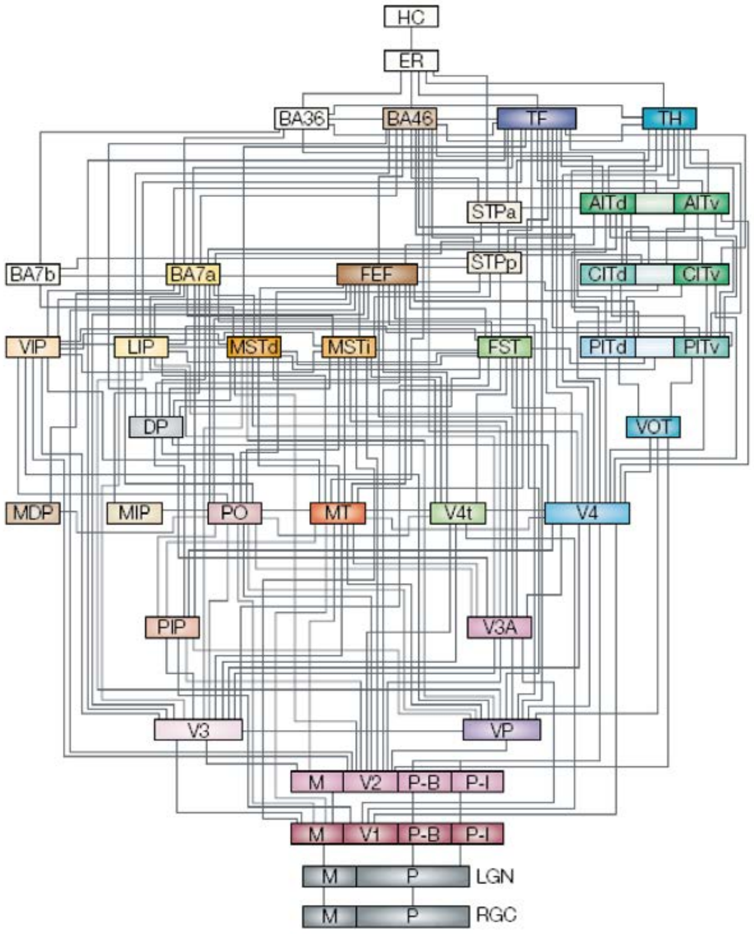
Hierarchical processing in the somatosensory cortex

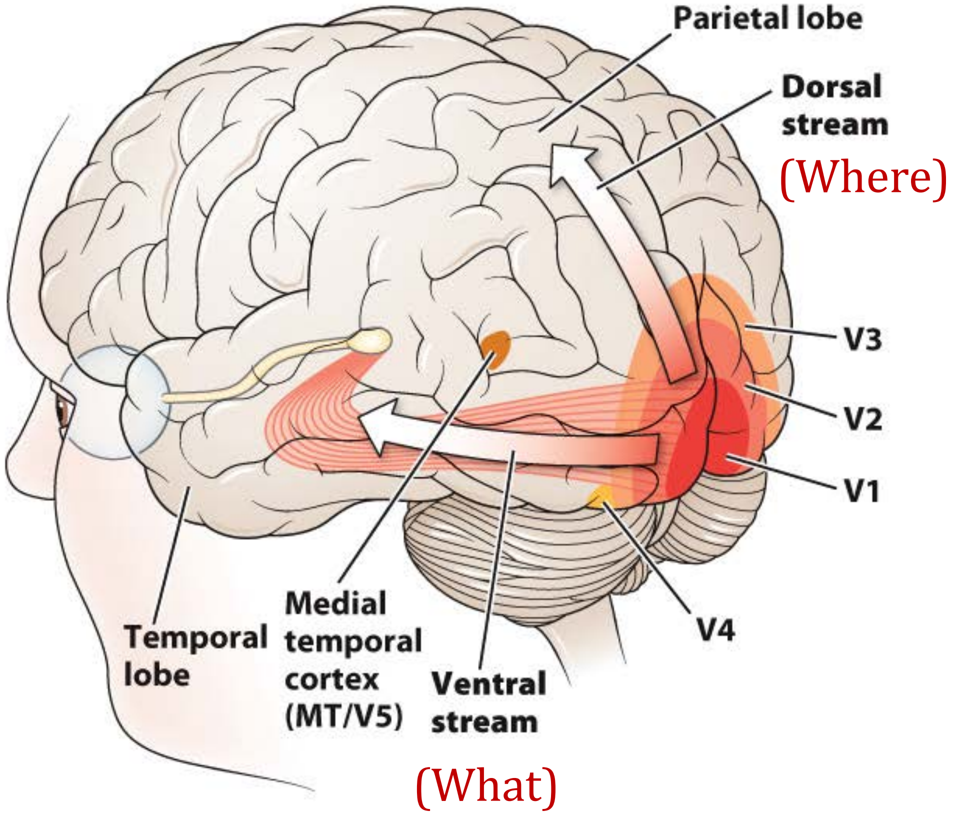


Stages of sensory information processing



Hierarchical processing in the visual system



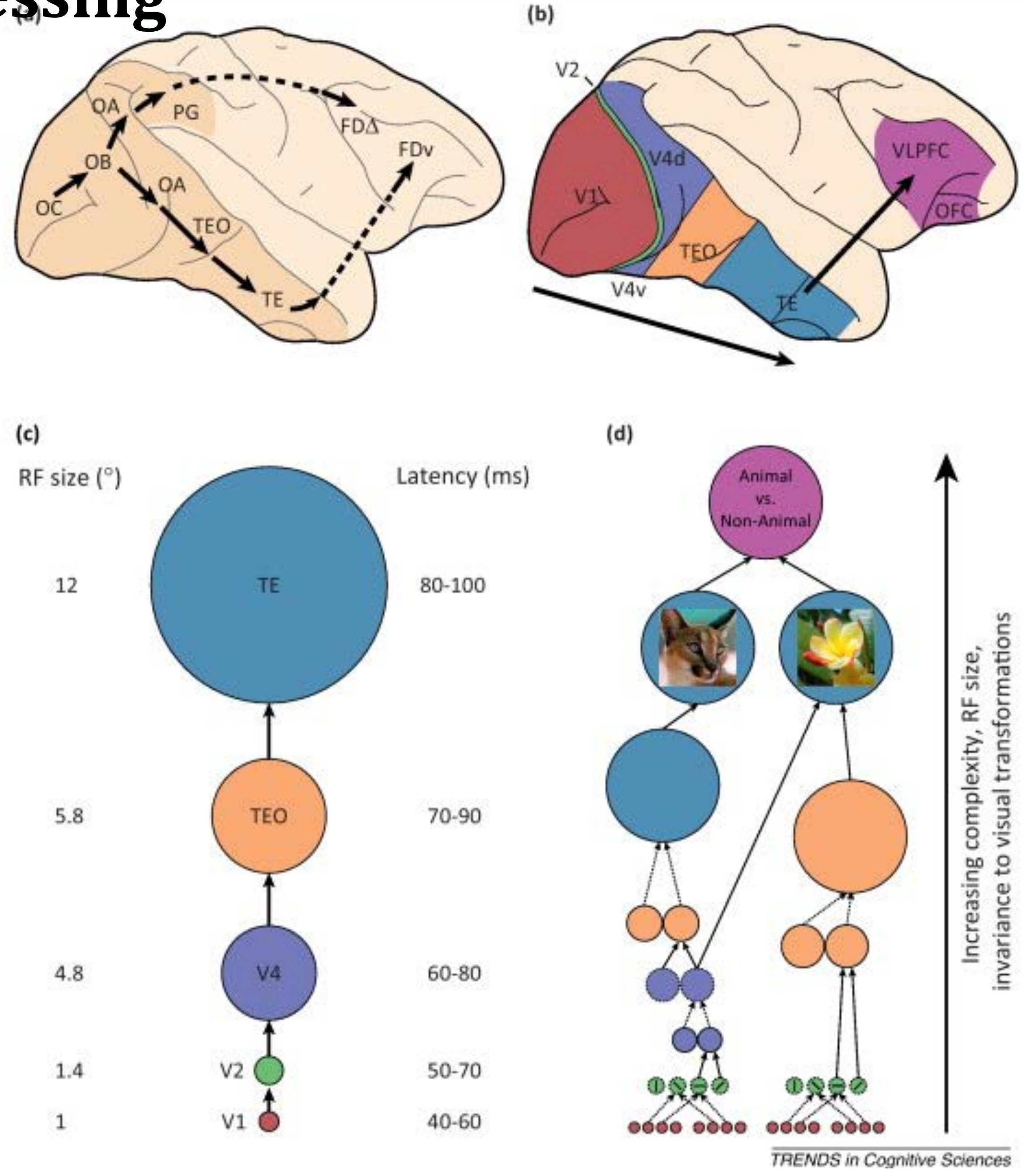


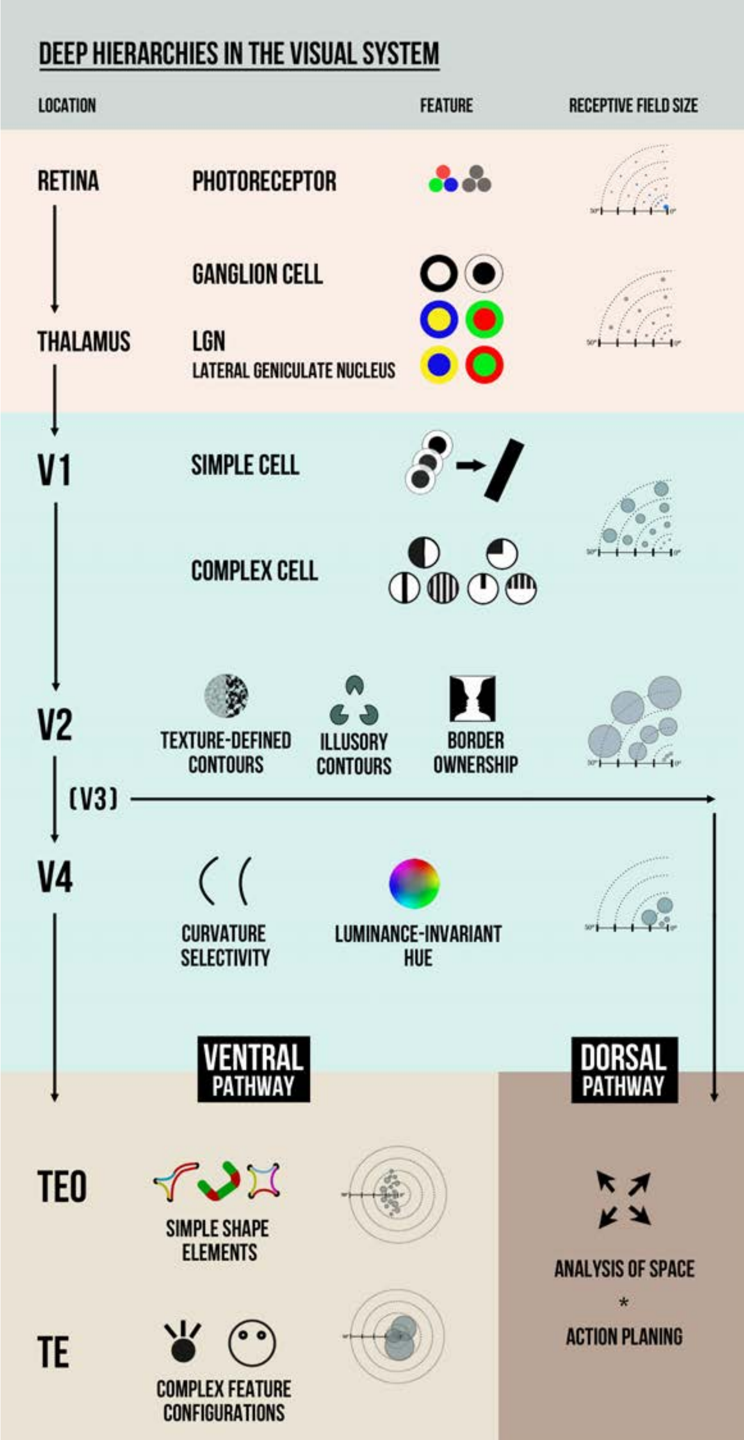
Hierarchical processing

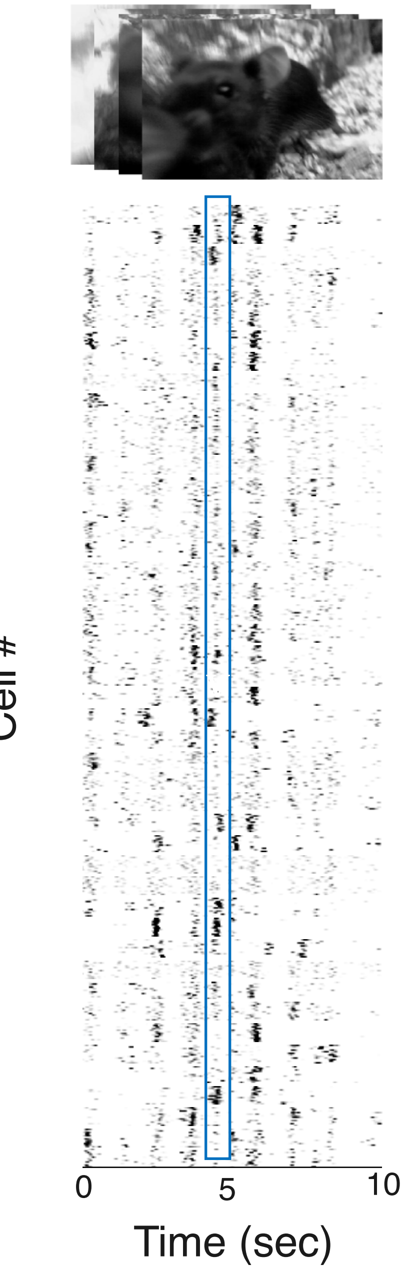
Through selectivity, each neuron responds to a narrow range of stimuli, across time, space, frequency, etc.

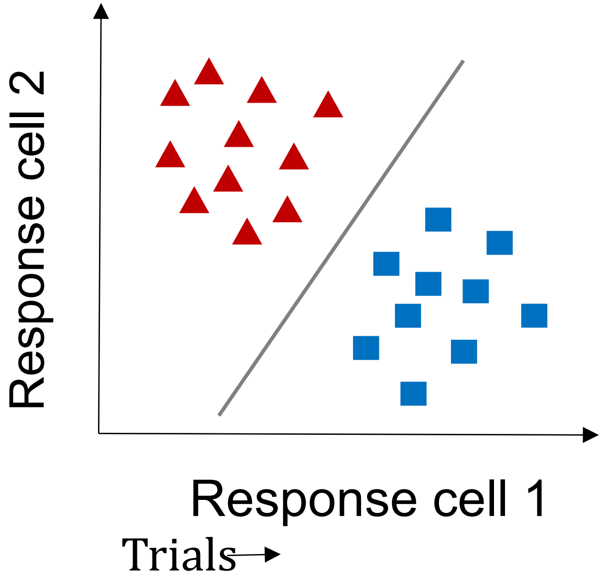
At each processing step, signals from previous neurons converge and activate another neuron.

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

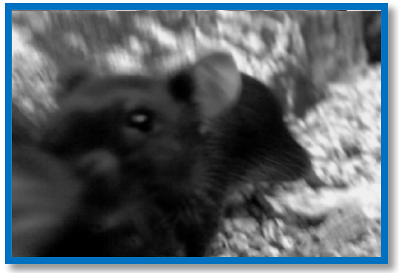




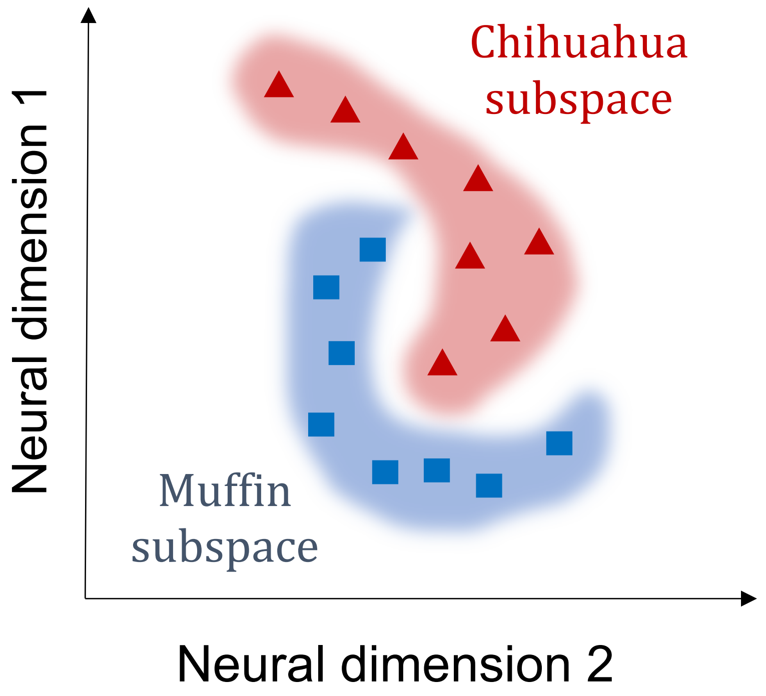




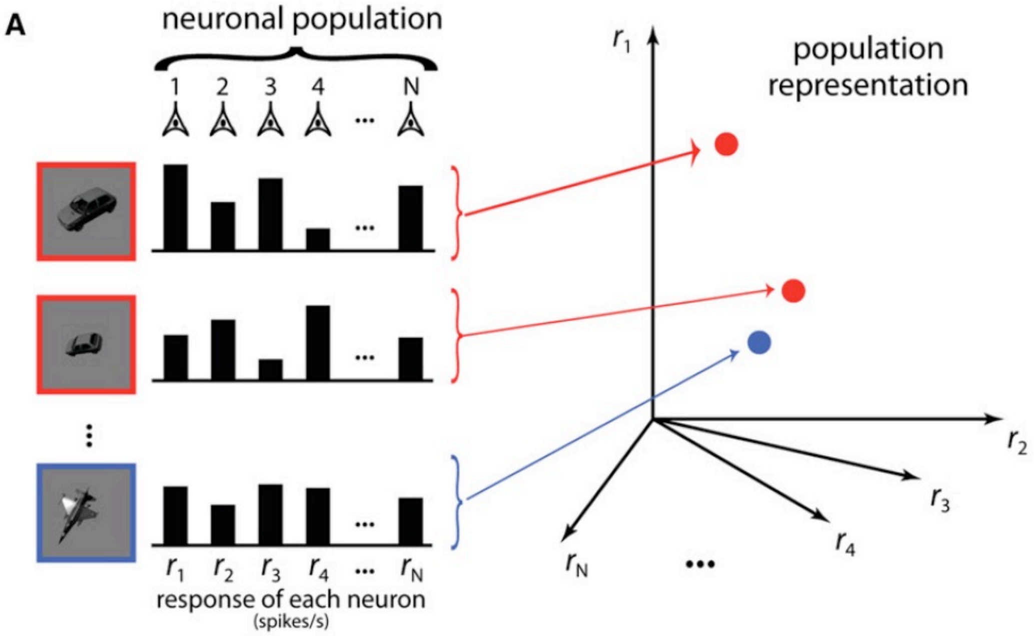
How can we discriminate responses to 2 objects?



Objects & Invariant representation

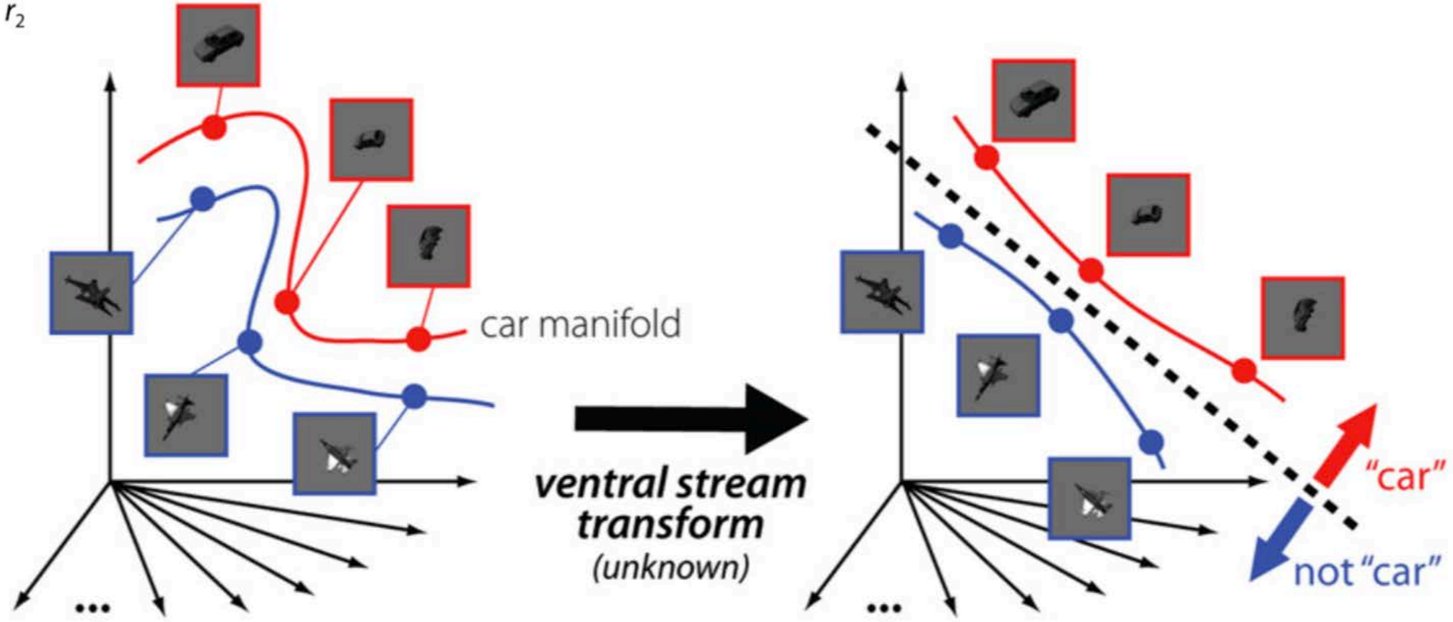


Object recognition as data representation problem



Neuronal populations in early visual areas (retinal ganglion cells, LGN, V1) contain object identity manifolds that are **highly curved and tangled together.**

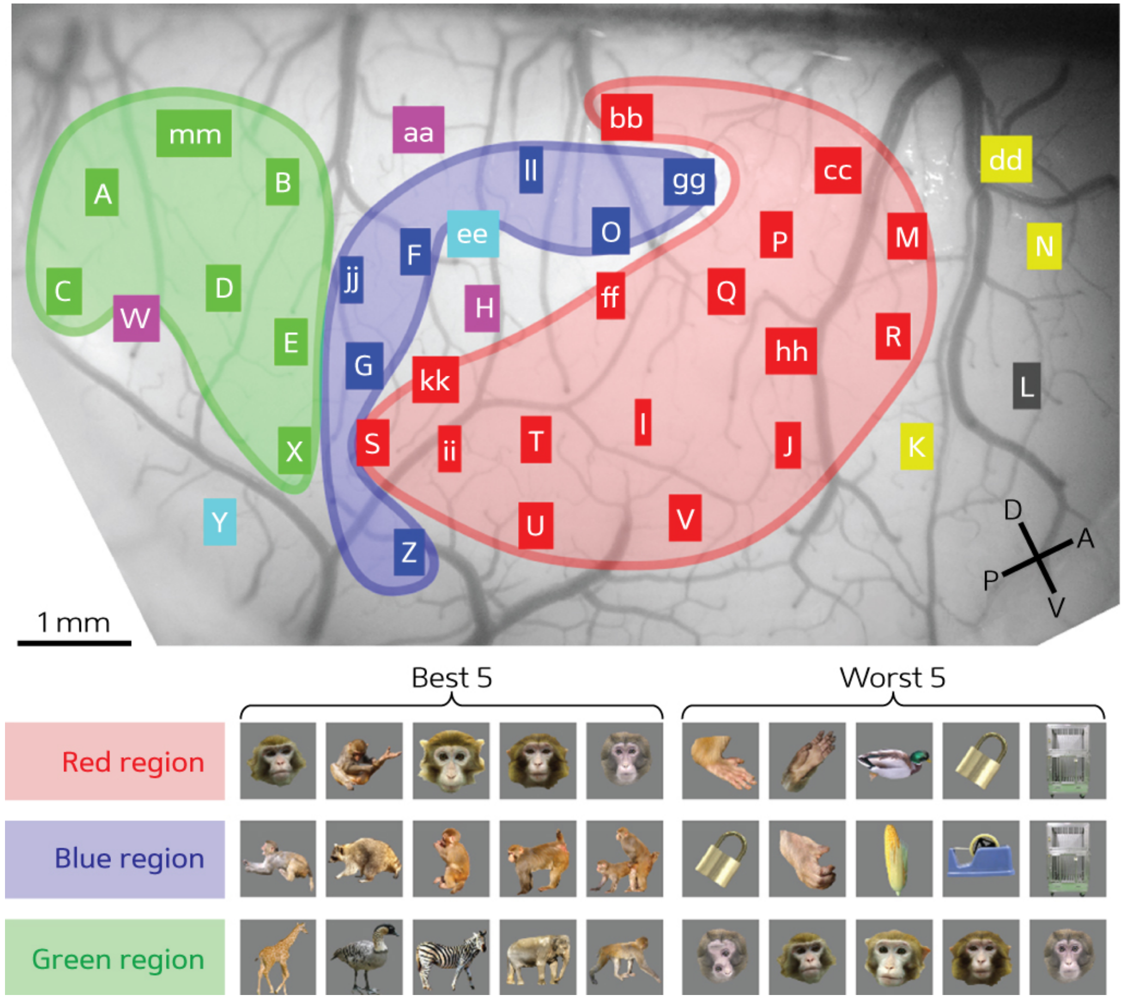
At higher stages of visual processing, neurons tend to maintain their selectivity for objects across changes in view→ manifolds that are more flat and separated (more "**untangled**")



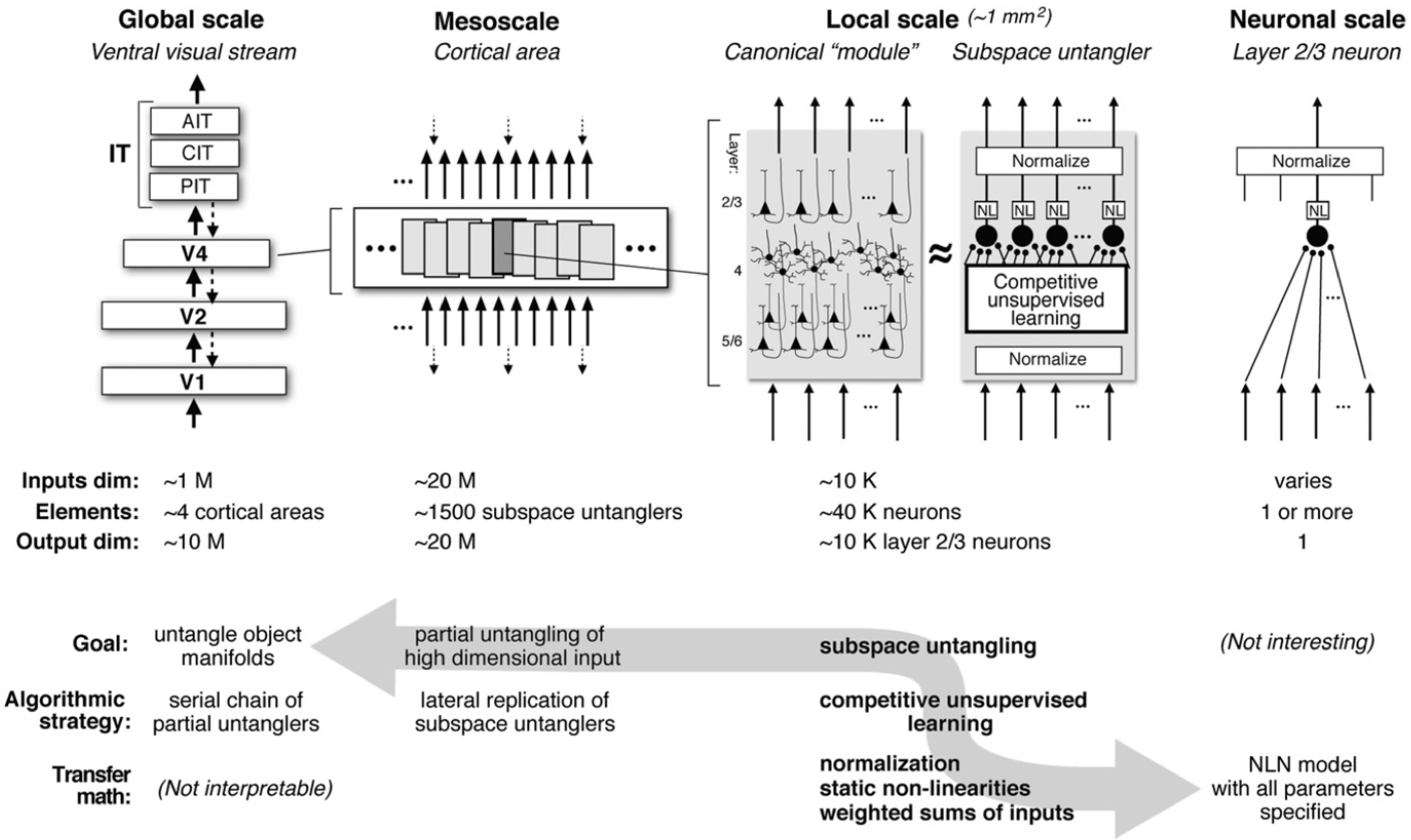
DiCarlo et al. 2012

Functional maps in abstract spaces

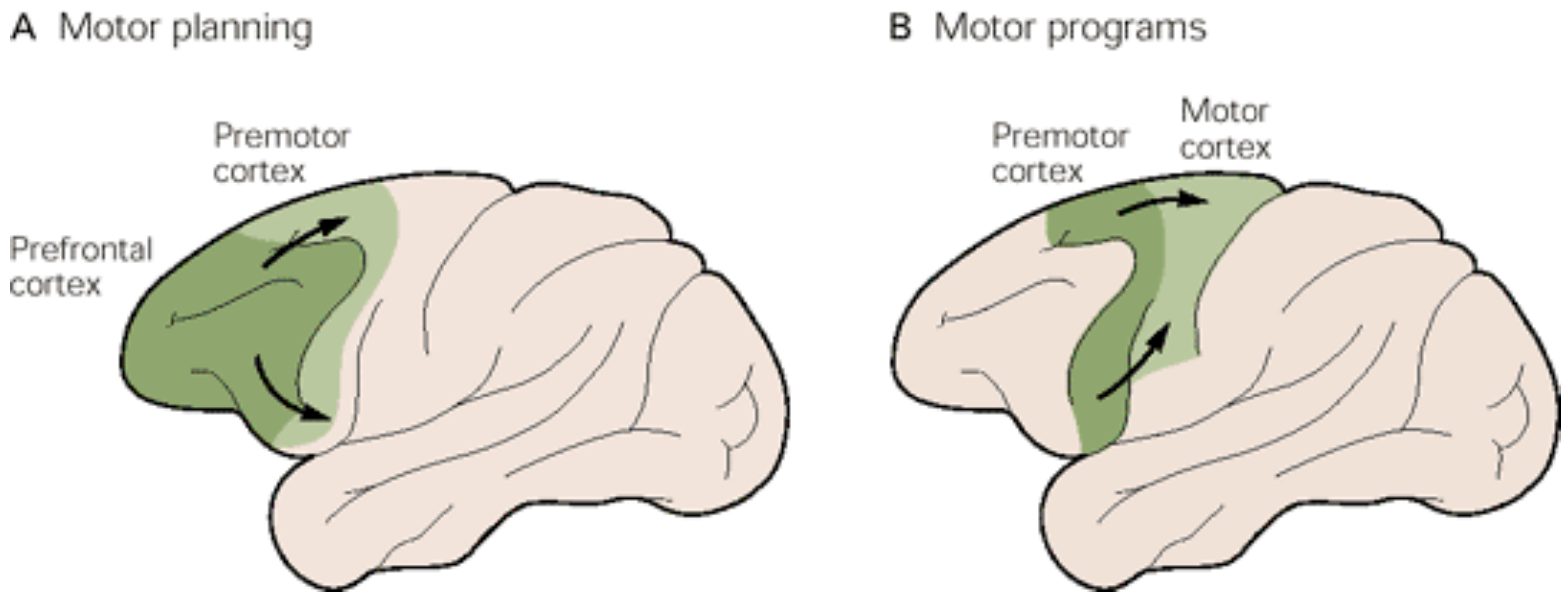
Object representation in inferior temporal cortex is organized hierarchically in a mosaic-like structure



Sato, T., Uchida, G., Lescroart, M.D., Kitazono, J., Okada, M., and Tanifuji, M. (2013). J. Neurosci. *33*, 16642–16656.


Global scale
Ventral visual stream
Mesoscale
Cortical area
Local scale (~1 mm²)
Canonical "module"
Subspace untangler
Neuronal scale
Layer 2/3 neuron
IT
AIT
CIT
PIT
V4
V2
V1
Layer:
2/3
4
5/6
Normalize
NL
Competitive unsupervised learning
Normalize
Normalize
NL
Inputs dim: ~1 M ~20 M ~10 K varies
Elements: ~4 cortical areas ~1500 subspace untanglers ~40 K neurons 1 or more
Output dim: ~10 M ~20 M ~10 K layer 2/3 neurons 1
Goal: untangle object manifolds partial untangling of high dimensional input subspace untangling (Not interesting)
Algorithmic strategy: serial chain of partial untanglers lateral replication of subspace untanglers competitive unsupervised learning
Transfer math: (Not interpretable) normalization static non-linearities weighted sums of inputs NLN model with all parameters specified

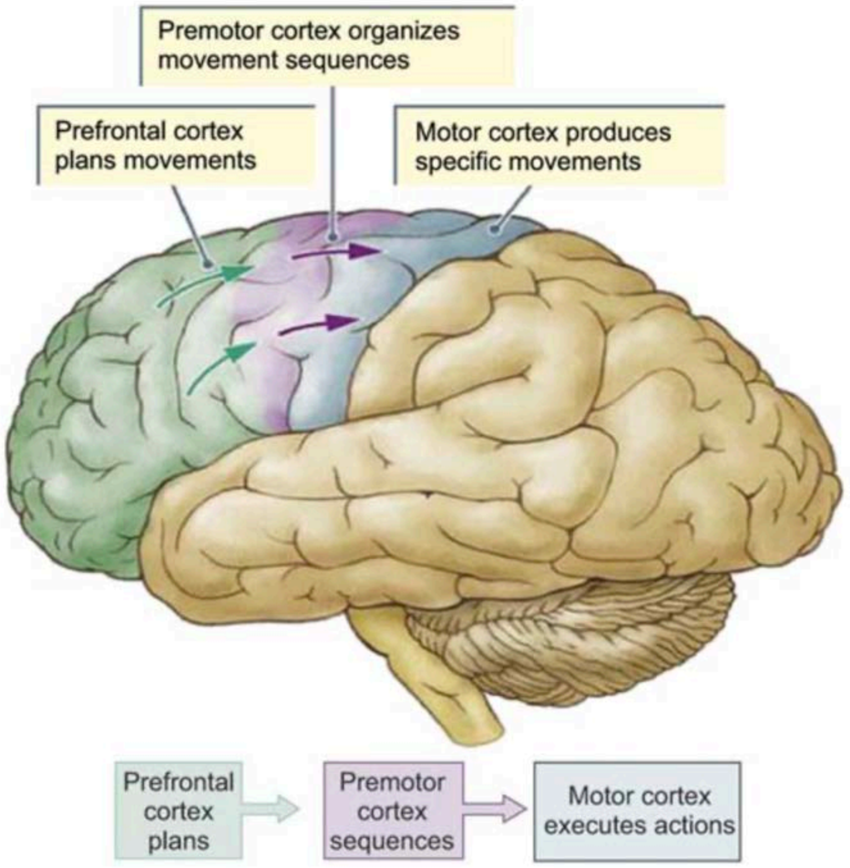
The flow of information in the motor system is the reverse of that in the sensory systems



From abstract representations to specific muscle activations

Prefrontal Cortex
- Abstract representation of intentions/plans

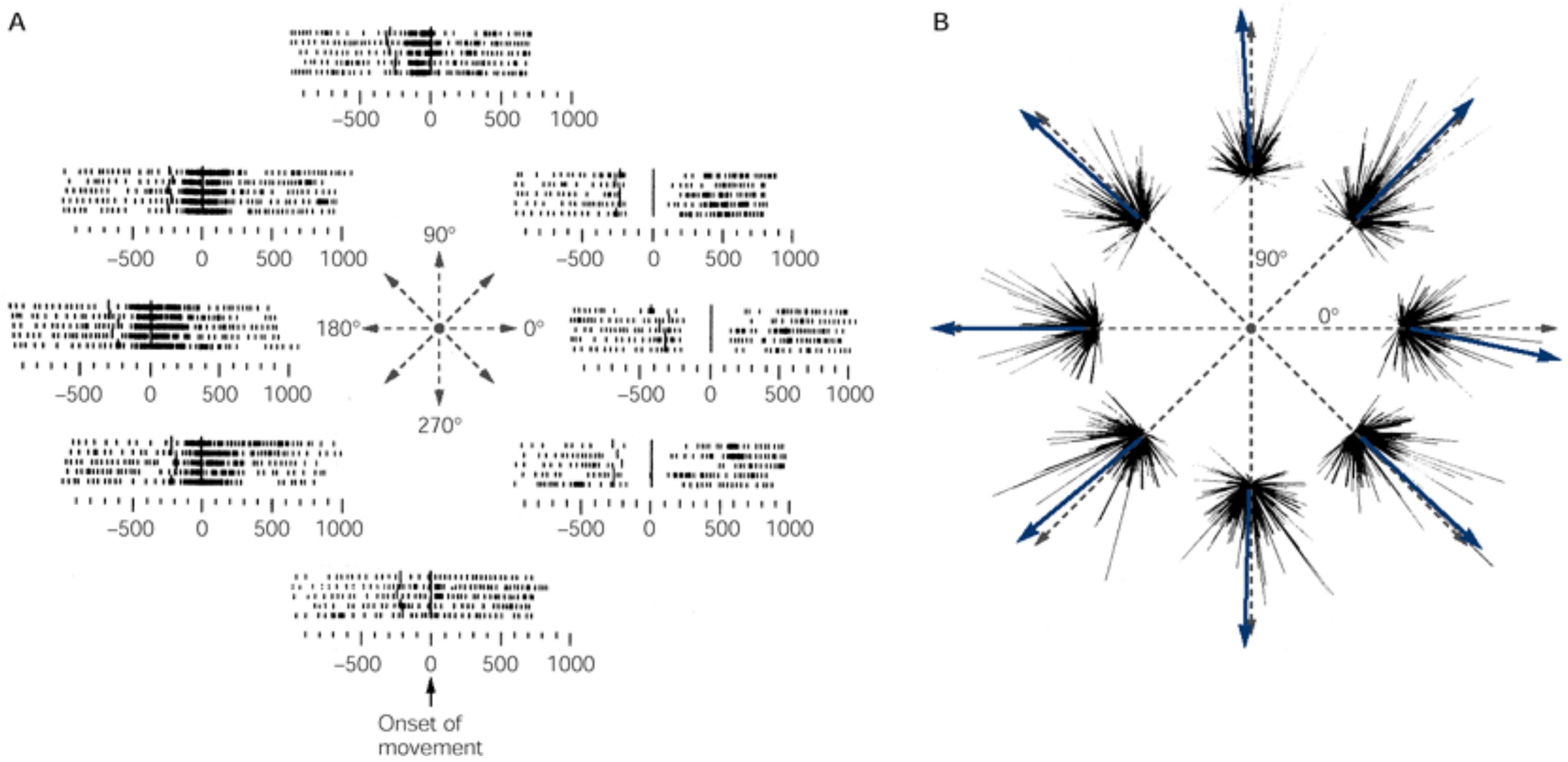
Premotor Cortex & Supplementary Motor Areas
- Abstract representations of intended moves
- SMA is involved in the transformation of **kinematic** to **dynamic representations**



Motor Cortex
- Dynamic representations of intended moves (population vectors)

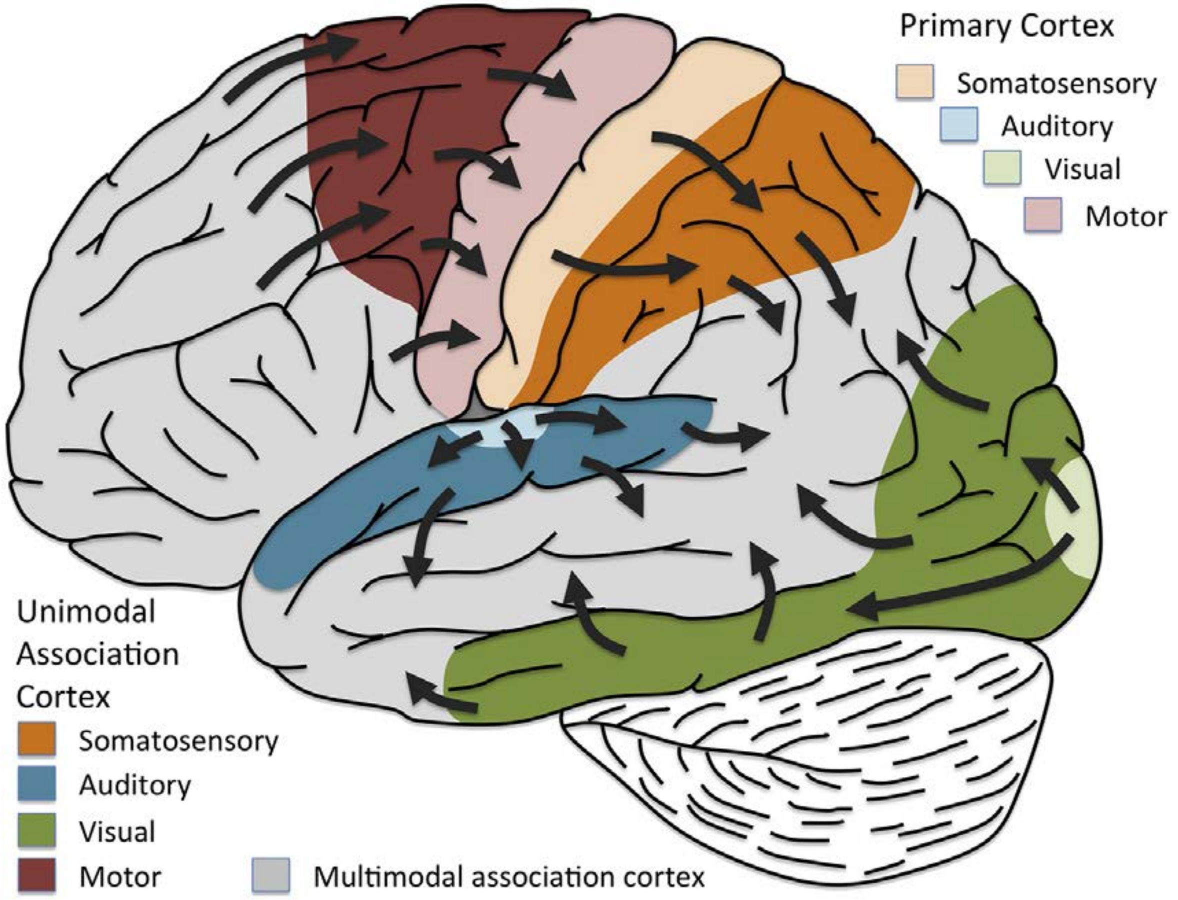
Population vector

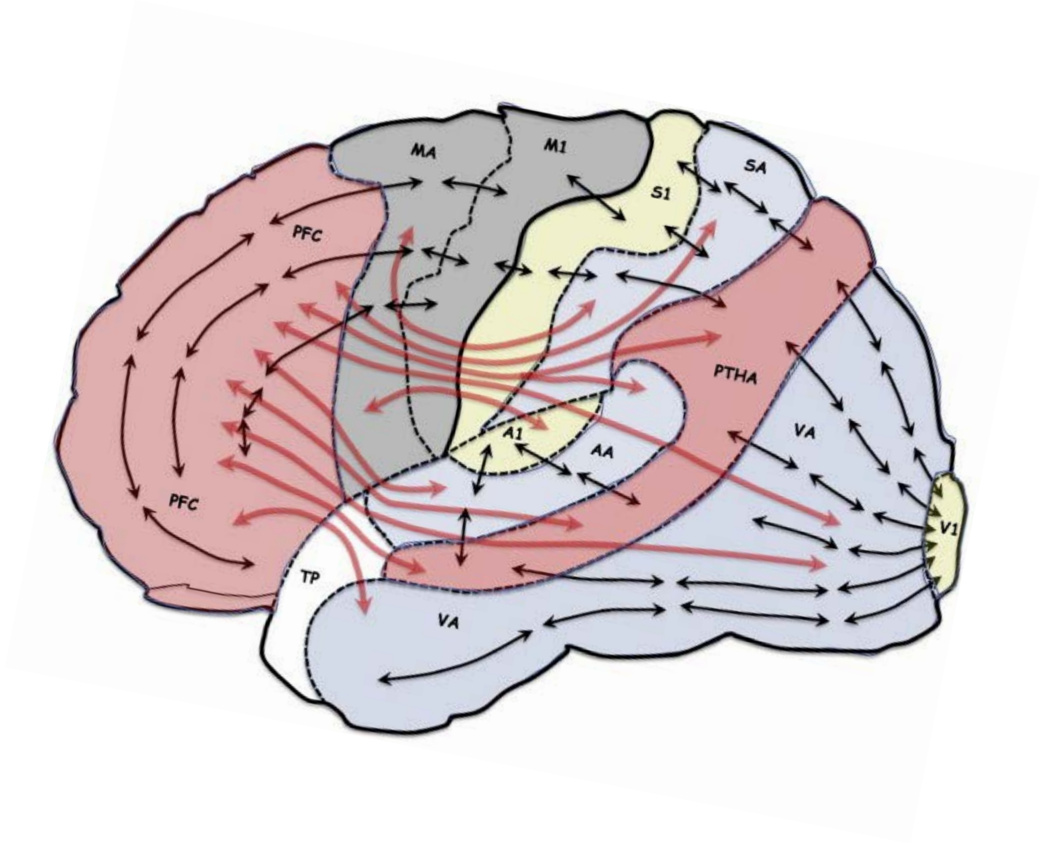
The ***neuronal population vector*** is the outcome of a computation by which weighted neural activities of individual elements in a population yield an estimate of the population’s functional operation.



Georgopoulos, A.P., Kalaska, J.F., Caminiti, R., and Massey, J.T. (1982). J. Neurosci. *2*, 1527–1537.

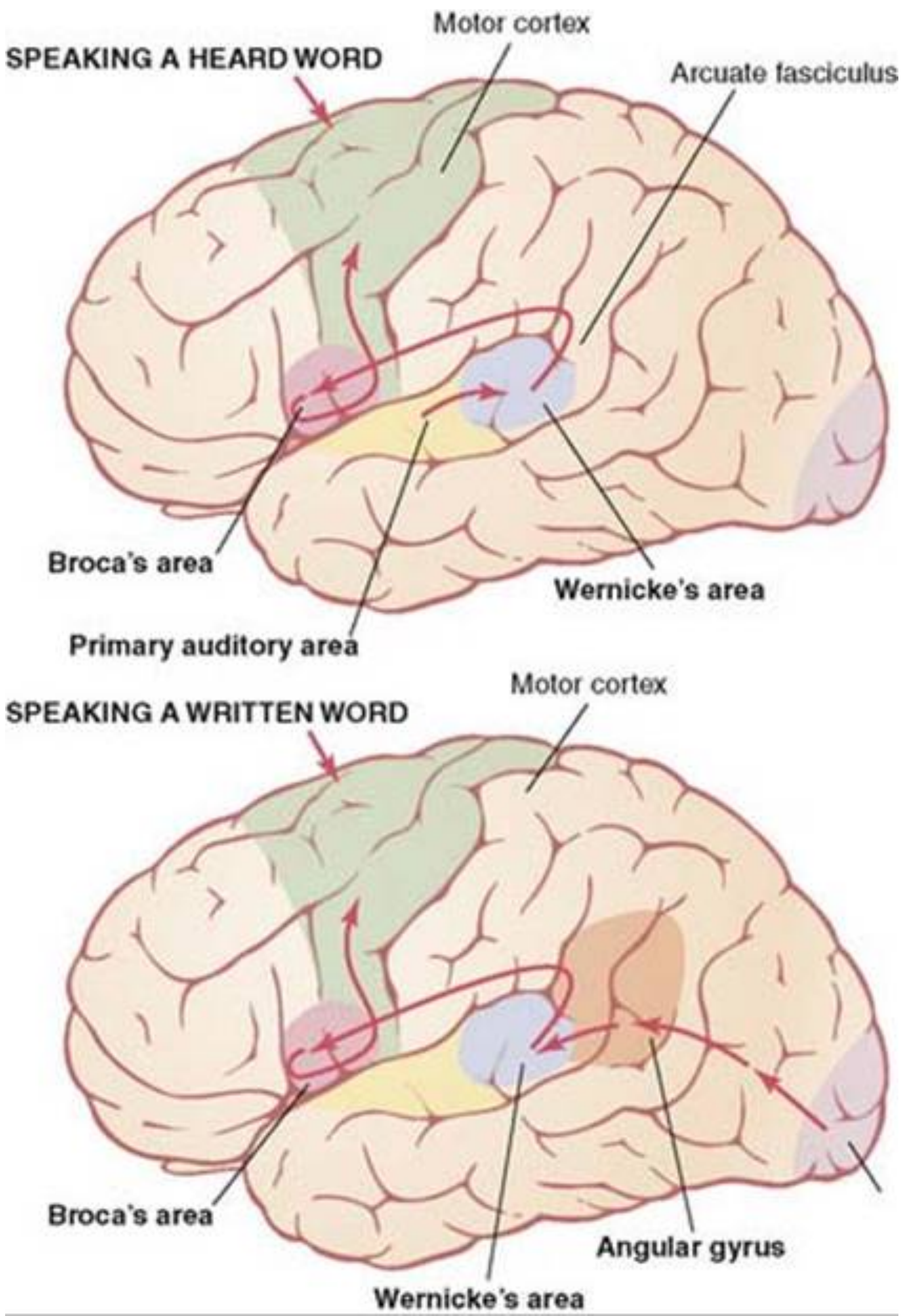
Convergence on multimodal association areas



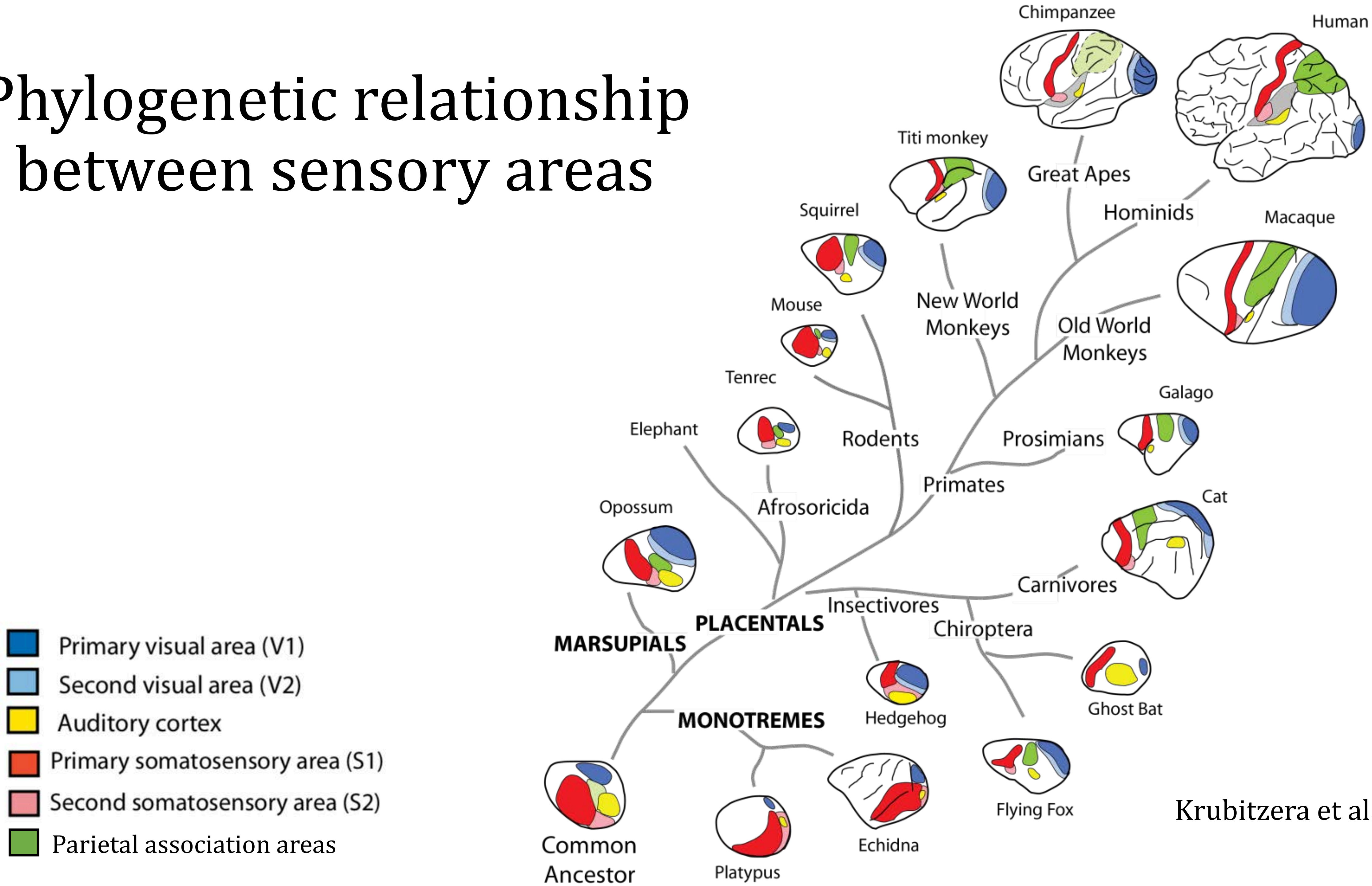


Cortical areas & speech

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



Phylogenetic relationship between sensory areas



Krubitzera et al. 2011

Understanding the function of the neocortex:

- How it processes external information
- How it performs computations
- How it generates motor output

is a universal problem across many species