Lecture 9, 06 Feb 2008

Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2008

Kevin Bonine & Kevin Oh

1. Synapses (Ch12)
2. Sensory Systems (Ch13)

http://eebweb.arizona.edu/eeb_course_websites.htm

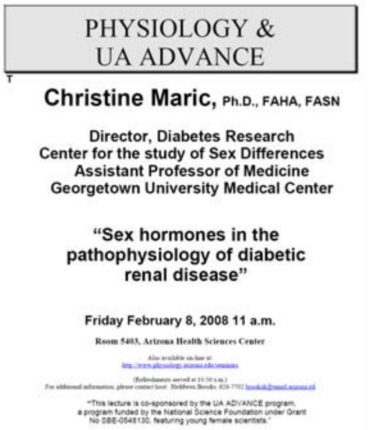
Housekeeping, 06 February 2008

Upcoming Readings
today: Ch13
LAB Wed 06 Feb: Catania 2002, Barinaga 1999, Malakoff 1999
(see website for links to papers; "worksheet" via email)
Fri 08 Feb: Ch13
Mon 11 Feb: Ch13
Wed 13 Feb: Ch13
LAB Wed 13 Feb: none
Fri 15 Feb: Exam 1, through Ch13

Lab discussion leaders: 20 Feb
1pm – Virsheena, Mathew S. Arturo
3pm – Kat, Clif, Amber

Lab discussion leaders: 06 Feb
1pm – Rittner, Whitney
3pm – Roxanne, Maria

Upcoming Physiology Seminar



PHYSIOLOGY &
UA ADVANCE

Christine Maric, Ph.D., FAHA, FASN

Director, Diabetes Research
Center for the study of Sex Differences
Assistant Professor of Medicine
Georgetown University Medical Center

"Sex hormones in the pathophysiology of diabetic renal disease"

Friday February 8, 2008 11 a.m.

Room 5403, Arizona Health Sciences Center

"This lecture is co-sponsored by the UA ADVANCE program, a program funded by the National Science Foundation under Grant No SBE-0548130, featuring young female scientists."

The Edges of Life

Wednesday, February 6
Life's Final Edge? The Origin and Extinction of Species in a Human-Dominated Earth
Michael Rosenzweig, Professor, Ecology and Evolutionary Biology
Today, Earth's treasury of species, its biodiversity, faces an existential challenge and its outcome depends on man. Science now knows we've taken away enough land from nature to precipitate a mass extinction like the one that exterminated the dinosaurs 65 million years ago. Using reconciliation ecology, we can prevent this - and preserve life.

Wednesday, February 13
Life's Cognitive Edge: The Role of the Mind and What it Means to be Human
Anna Dornhaus, Assistant Professor, Ecology and Evolutionary Biology
Our human mind distinguishes us from other animal life-or does it? Recent research has revealed culture and social learning, tool use, complex communication, self-recognition, and planning for the future are not unique to the human experience. With these new findings, science is finally getting closer to understanding exactly what makes us human.

Wednesday, February 20
Life's Human Edge: Changing Perspectives on the End of Life
Michael Gill, Associate Professor, Philosophy
Nothing looms with more certainty than the final edge of one's own life. But in fact, the edge between life and death is anything but clear. This lecture will address the attempts that have been made to define the line between life and death and will explore the biological, legal, ethical, and spiritual debates that have raged around that line.

Wednesday, March 5
Life's Technological Edge: The Singularity is Near: When Humans Transcend Biology
Ray Kurzweil, *via Teleportec Teleporter*
Founder, Chairman and Chief Executive Officer, Kurzweil Technologies
Humanity is on the edge of a vast transformation, when what it means to be human will be both enriched and challenged. Inventor and futurist Ray Kurzweil will introduce this radically optimistic singularity, an era when we break our genetic shackles to create a nonbiological intelligence trillions of times more powerful than today. In this new world, humans will transcend biological limitations to achieve entirely new levels of progress and longevity.
This lecture co-sponsored by: UA College of Engineering and UA College of Science

These do not count as physiology lectures.

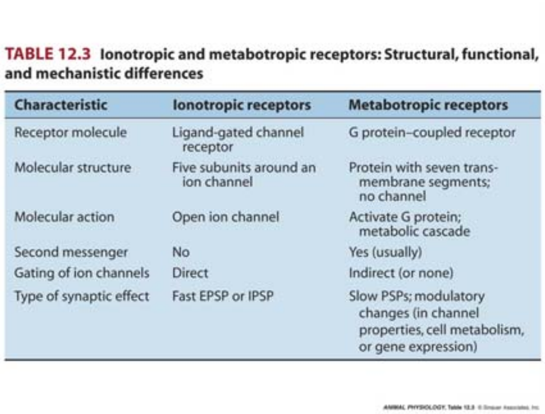


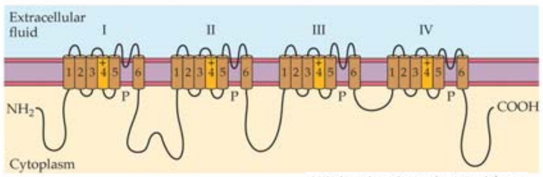
TABLE 12.3 Ionotropic and metabotropic receptors: Structural, functional, and mechanistic differences

Characteristic	Ionotropic receptors	Metabotropic receptors
Receptor molecule	Ligand-gated channel receptor	G protein–coupled receptor
Molecular structure	Five subunits around an ion channel	Protein with seven trans-membrane segments; no channel
Molecular action	Open ion channel	Activate G protein; metabolic cascade
Second messenger	No	Yes (usually)
Gating of ion channels	Direct	Indirect (or none)
Type of synaptic effect	Fast EPSP or IPSP	Slow PSPs; modulatory changes (in channel properties, cell metabolism, or gene expression)

ANIMAL PHYSIOLOGY, Table 12.3 © Sinauer Associates, Inc.

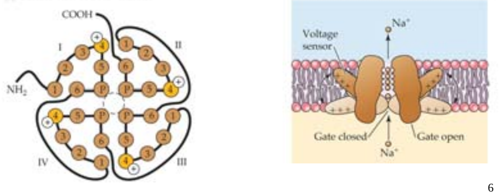
(a) Topology of voltage-gated Na⁺ channels

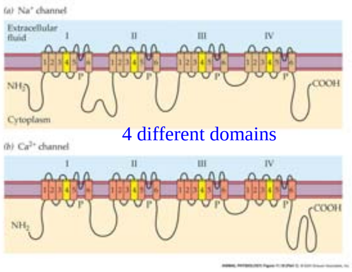
Hill et al. 2004, Fig. 11.17



(b) Surface view of a Na⁺ channel

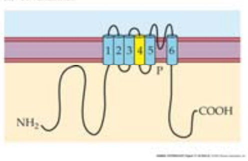
(c) Voltage-dependent conformational change





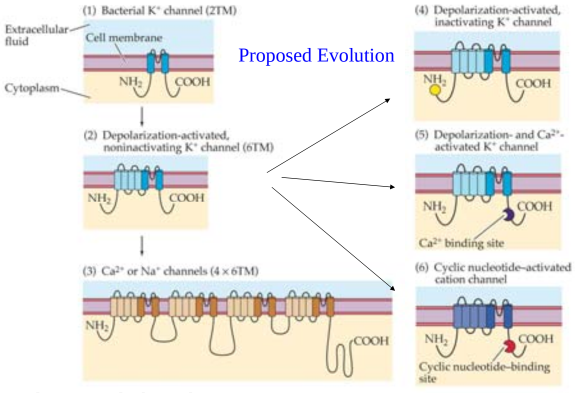
4 different domains

Hill et al. 2004, Fig. 11.18



4 identical subunits

Voltage-gated channel superfamily



Proposed Evolution

Voltage-gated Channels

Hill et al. 2004, pg. 301

Neurotransmitters:

1. small-molecule neurotransmitters
   (often made in axon terminals; common)
2. neuroactive peptides
   (often made in soma and shipped down axon)

Nematodes use a lot of the same neurotransmitters.

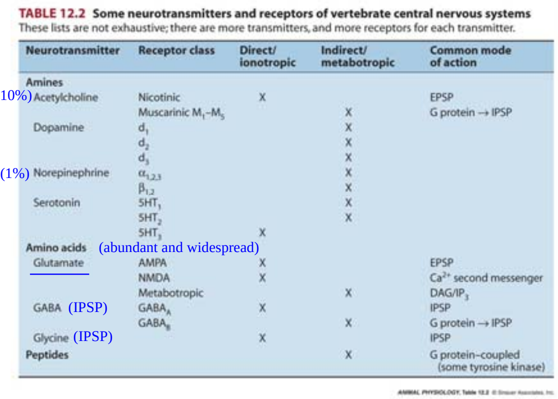


TABLE 12.2 Some neurotransmitters and receptors of vertebrate central nervous systems
These lists are not exhaustive; there are more transmitters, and more receptors for each transmitter.

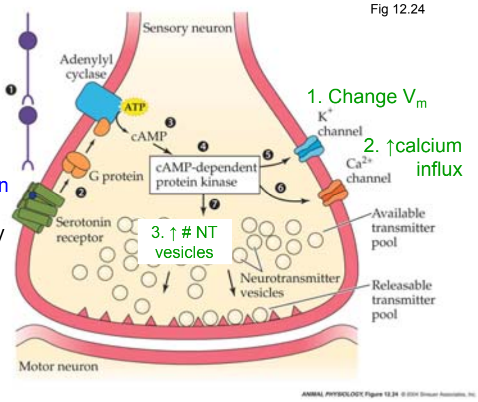
Neurotransmitter	Receptor class	Direct/ ionotropic	Indirect/ metabotropic	Common mode of action
Amines				
(10%) Acetylcholine	Nicotinic	X		EPSP
	Muscarinic M_1–M_5		X	G protein → IPSP
Dopamine	d_1		X	
	d_2		X	
	d_3		X	
(1%) Norepinephrine	$\alpha_{1,2,3}$		X	
	$\beta_{1,2}$		X	
Serotonin	$5HT_1$		X	
	$5HT_2$		X	
	$5HT_3$	X		
Amino acids (abundant and widespread)				
Glutamate	AMPA	X		EPSP
	NMDA	X		Ca^{2+} second messenger
	Metabotropic		X	DAG/IP_3
GABA (IPSP)	$GABA_A$	X		IPSP
	$GABA_B$		X	G protein → IPSP
Glycine (IPSP)		X		IPSP
Peptides			X	G protein–coupled (some tyrosine kinase)

ANIMAL PHYSIOLOGY, Table 12.2 © Sinauer Associates, Inc.

Synaptic Plasticity

- •Change synaptic efficacy
- •Alter rate of NT production and release
- •Learning and Memory
- •Facilitation vs. antifacilitation/depression
- •Retrograde messengers (i.e., NO)
- •Calcium-dependent
  -Research on-going

Hill et al. 2004
Fig 12.24



1. Change V_m

2. ↑calcium influx

3. ↑ # NT vesicles

Sensitization (facilitation) mediated by serotonin

Long-term Potentation

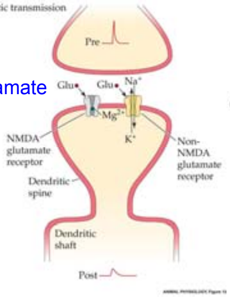
- Often in Hippocampus
  - -Site of Learning and Memory
- “Neurons that fire together wire together”
- NMDA glutamate receptors…

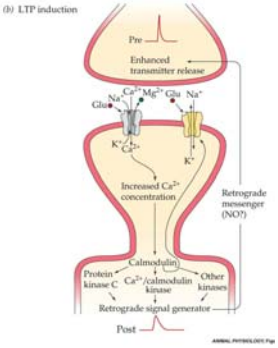
NMDA = N-methyl-D-aspartic acid

Hill et al. 2004, Fig 12.27

Long term potentiation (LTP)

glutamate





- NMDA glutamate receptors
  - role of Mg2+
  - voltage-dependent

Doogie Mice?

Genetic engineers upregulated production of juvenile subunit of NMDA receptor in adult mice (Doogie mice).

Ethical?

Should we do this in humans or other animals?

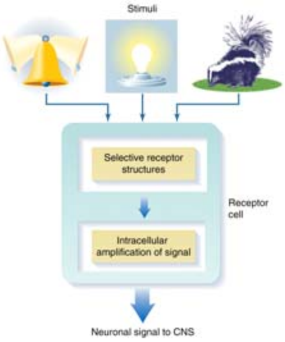
Under what conditions?

Vertebrate Physiology 437

Chapter 13

Sensory Processes/Systems

Sensing the Environment



7-1 Randall et al. 2002

Sensory Reception
- -Environment
- -Within body

Integrated and Processed by NS

Sensory Receptors send signals to brain so perceive sensations

Sensory Receptor cells often organized into organs

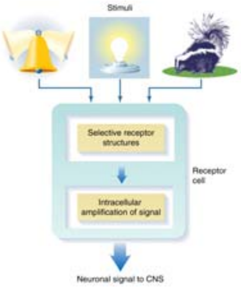
Properties of Receptor Cells

Sensory Modality

Modalities include:
vision, hearing, touch, taste, smell, chemical, thermal, proprioceptors

Qualities within each modality

e.g., Red or yellow;
High or low-pitched



7-1 Randall et al. 2002

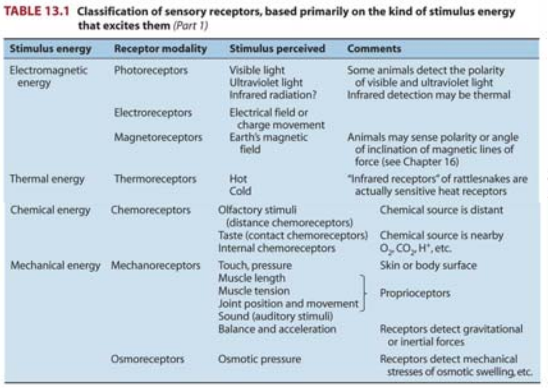
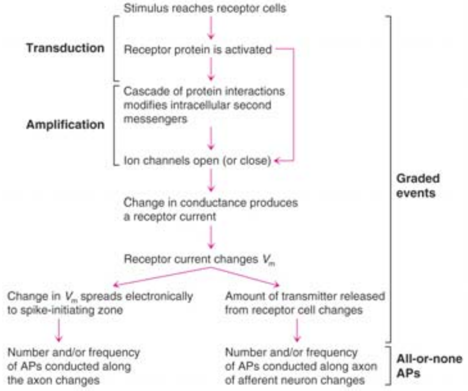


TABLE 13.1 Classification of sensory receptors, based primarily on the kind of stimulus energy that excites them *(Part 1)*

Stimulus energy	Receptor modality	Stimulus perceived	Comments
Electromagnetic energy	Photoreceptors	Visible light Ultraviolet light	Some animals detect the polarity of visible and ultraviolet light
		Infrared radiation?	Infrared detection may be thermal
	Electroreceptors	Electrical field or charge movement	
	Magnetoreceptors	Earth's magnetic field	Animals may sense polarity or angle of inclination of magnetic lines of force (see Chapter 16)
Thermal energy	Thermoreceptors	Hot Cold	"Infrared receptors" of rattlesnakes are actually sensitive heat receptors
Chemical energy	Chemoreceptors	Olfactory stimuli (distance chemoreceptors)	Chemical source is distant
		Taste (contact chemoreceptors)	Chemical source is nearby
		Internal chemoreceptors	O_2, CO_2, H^+, etc.
Mechanical energy	Mechanoreceptors	Touch, pressure	Skin or body surface
		Muscle length Muscle tension Joint position and movement	Proprioceptors
		Sound (auditory stimuli)	
		Balance and acceleration	Receptors detect gravitational or inertial forces
	Osmoreceptors	Osmotic pressure	Receptors detect mechanical stresses of osmotic swelling, etc.

7-5 Randall et al. 2002



Stimulus reaches receptor cells

Transduction

Receptor protein is activated

Amplification

Cascade of protein interactions modifies intracellular second messengers

Ion channels open (or close)

Change in conductance produces a receptor current

Receptor current changes V_m

Change in V_m spreads electronically to spike-initiating zone

Amount of transmitter released from receptor cell changes

Number and/or frequency of APs conducted along the axon changes

Number and/or frequency of APs conducted along axon of afferent neuron changes

Graded events

All-or-none APs

Mechanisms and Molecules

Enzymatic Cascade to amplify

Threshold of Detection
e.g., 1 photon or hair cell
movement of H diam.

Sour (pH; H+) and salt (Na+)
move directly – no amplification

To measure quality need many receptors grouped into organ; different 'tunage' (e.g, wavelength of light or frequency of sound)

Enhancing Sensitivity

- Efferent Control

e.g., stretch receptors in muscle
control length so can perceive stretch

- Feedback Inhibition

Auto (helps keep in dynamic range)
vs.
Lateral…

Properties of Receptor Cells

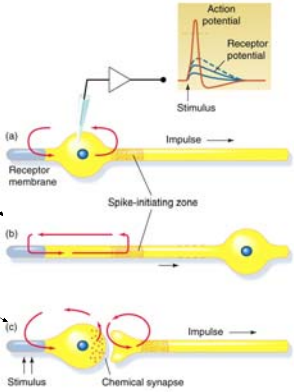
7-2 Randall et al. 2002

Receptor Cells
- Specialized
- Selective for energy type and modality

-either is a neuron or
-Synapses immediately on a neuron

(1° afferent neuron to CNS)

Stimulus modifies conformation of receptor



Properties of Receptor Cells

Transduction=
Stimulus energy
converted to
nerve impulse

Example
Mechanoreceptors (touch)

1- Proteins respond to membrane distortion

2- Ion channels opened directly or indirectly

3- Current flows across membrane (often Na^+)

4-Vm changes (aka receptor potential changes)

5- Signal often amplified

6- AP sent or NT released causing AP

Mechanisms and Molecules

Sensory Adaptation

- orders of magnitude different stimulus strength
- often controlled via Ca++ availability
- local control or feedback from CNS

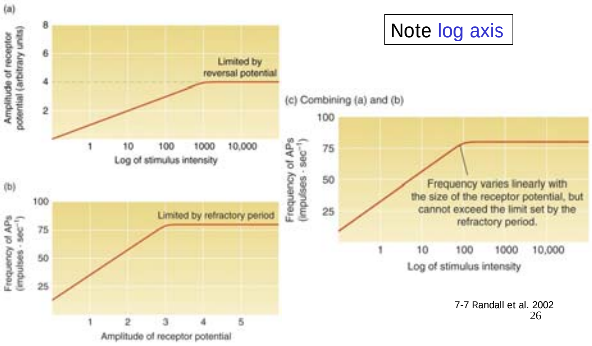
Type of stimulus received depends on where in CNS (~brain) AP arrives (LABELED LINES).

Rub eyes and see light!

Intensity signalled by frequency of APs, but…

Stimulus Intensity and Dynamic Range

From lowest threshold, to upper limit imposed by refractory period:



Note log axis

7-7 Randall et al. 2002

Dynamic Range

Shifting range of appropriate AP frequency

Detectable light intensity varies over 9 orders magnitude

Detectable sound intensity varies over 12 orders magnitude

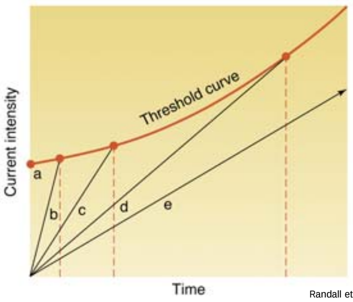
Range Fractionation

- Function of sensory adaptation
- Also recruit receptors with different 'tunage' or sensitivity (e.g., rods and cones in eye)

Sensory Adaptation Possibilities:

1. Receptor cell mechanical properties may filter
2. Receptor cells may be depleted (e.g., visual pigments; need to be regenerated)
3. Enzyme cascade (during amplification) may be inhibited by (intermediate) product
4. Electrical properties change b/c ↑ [Ca⁺⁺]
5. Accommodation of spike initiating zone
6. Sensory adaptation in downstream neurons (CNS)

-Accommodation

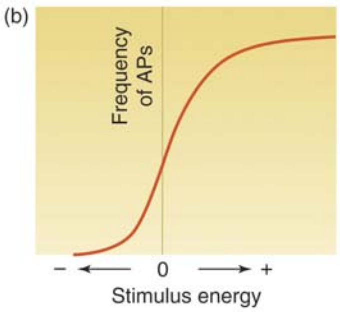


Randall et al. 2002

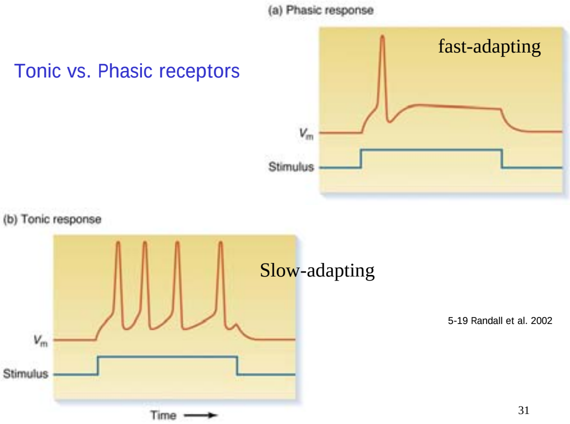
Enhancing Sensitivity

- Spontaneous basal activity
- Constant rate of APs
- Directionality if ↑ or ↓ AP frequency

7-12 Randall et al. 2002



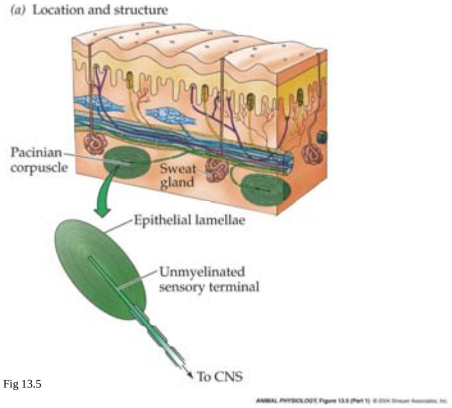
Tonic vs. Phasic receptors



fast-adapting

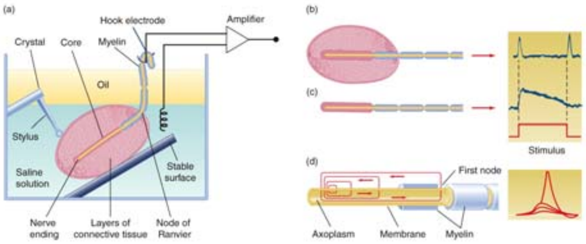
Slow-adapting

5-19 Randall et al. 2002



Hill et al. 2004, Fig 13.5

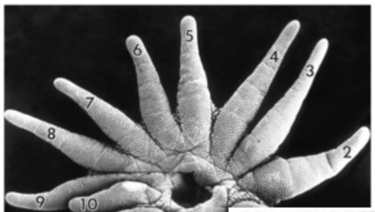
Sensory Adaptation; Pacinian Corpuscle - Touch Example



Movement of Oil between layers is what triggers APs

Signal changes in pressure, not steady pressure

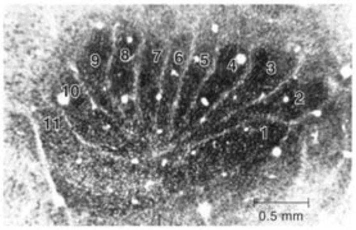
7-10 Randall et al. 2002



Star-Nosed Mole

(↑ # neurons, ↑ subtlety)

(receptor field size?)



External Chemoreception (Taste and Smell)

-Taste
  ~ direct contact

-Smell
  ~ distant signal source

-Chemoreception very sensitive

-*Bombyx* moth antenna example:

Male responds to female pheromone at low [ ] of 1 molecule in 10^{17} !

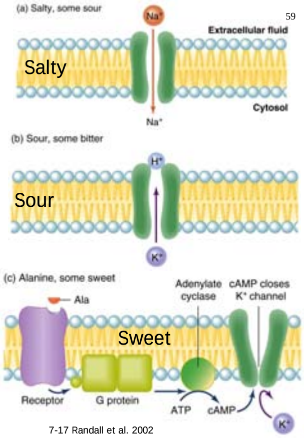
Taste Chemoreception

-Taste

Usually oral cavity
Some fish fins!

4-5 qualities:
1. Salt
2. Sour
3. Sweet
4. Bitter
5. Umami
   ("savory" or "meaty")

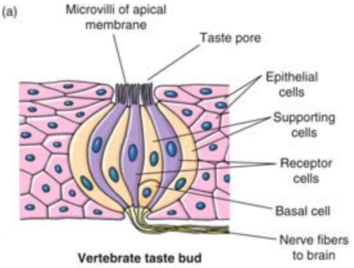
Differing Receptor Properties



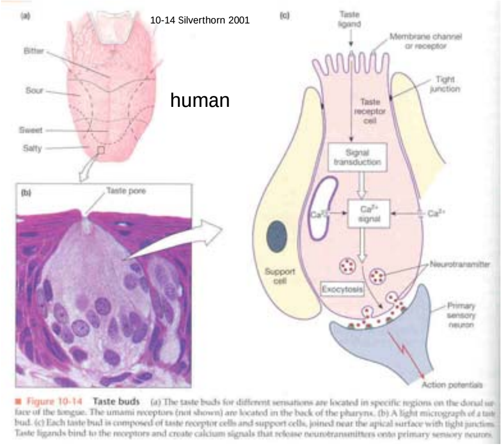
7-17 Randall et al. 2002

Taste

- microvilli
- basal cells give rise to new receptor cells every 10 days



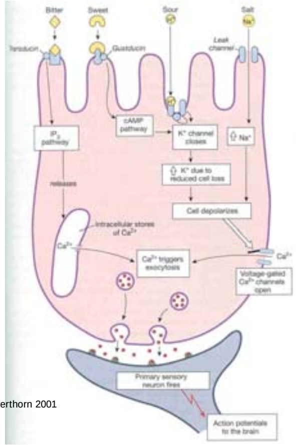
7-16 Randall et al. 2002



10-14 Silverthorn 2001

human

Figure 10-14 Taste buds (a) The taste buds for different sensations are located in specific regions on the dorsal surface of the tongue. The umami receptors (not shown) are located in the back of the pharynx. (b) A light micrograph of a taste bud. (c) Each taste bud is composed of taste receptor cells and support cells, joined near the apical surface with tight junctions. Taste ligands bind to the receptors and create calcium signals that release neurotransmitters onto primary sensory neurons.



10-15 Silverthorn 2001

Figure 10-15 Taste transduction Bitter and sweet ligand signal transduction uses G protein-coupled membrane receptors. Transducin releases Ca^{2+} from intracellular stores. Gustducin activates a cAMP second messenger pathway that closes K^+ channels. Ionic ligands alter ion channels and depolarize the taste receptor, which allows Ca^{2+} entry from the extracellular fluid. For all taste ligands, the Ca^{2+} signal triggers exocytosis of neurotransmitter.

Taste

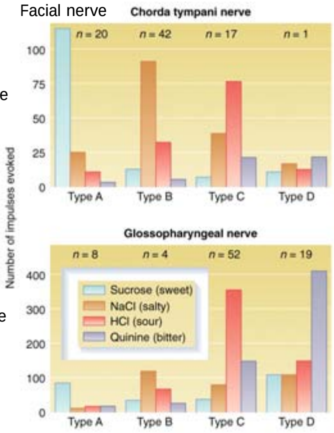
Facial nerve

Outer tongue

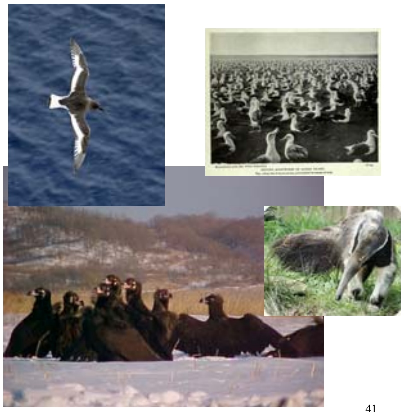
-Quasi Labelled lines

- multiple receptor types/neuron

Inner tongue

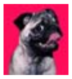


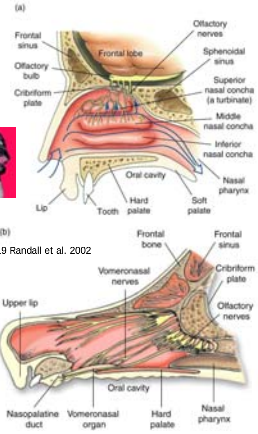
Smell



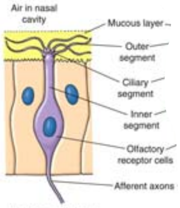
Smell/ Olfaction

- -1 Nasal Cavity
  - -turbinates (↑s.a.)
- -2 Vomeronasal organ
  - -usually conspecific communication





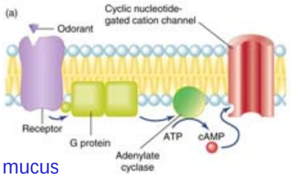
7-19 Randall et al. 2002



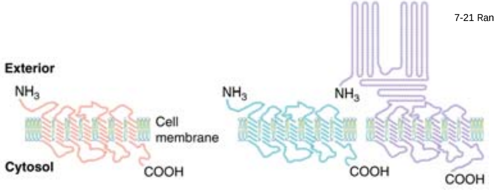
Vertebrate olfactory receptor 7-16 Randall et al. 2002

Smell/ Olfaction

-Nasal and Vomeronasal:



-Epithelial tissue origin
 -Cilia or Microvilli covered in mucus
-Receptor proteins with 7-transmembrane helices
 -Coupled to G-protein cascade

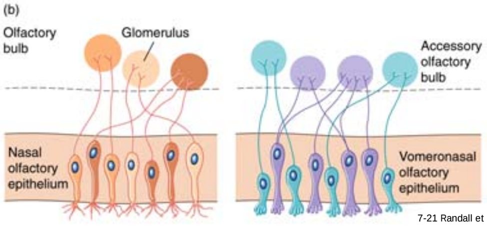


7-21 Randall et al. 2002

Smell/ Olfaction

- Nasal and Vomeronasal:

-Thousands of receptor proteins (general & special)
 -but different for nasal and vomeronasal
-Receptor cells contain axons
 - Glomeruli in olfactory bulb/accessory olfactory bulb



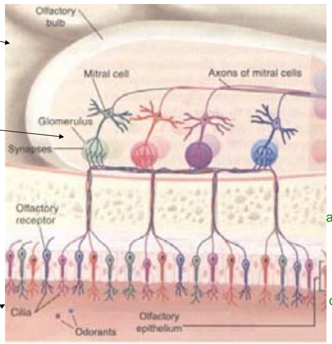
7-21 Randall et al. 2002

Olfactory bulb (info processing in brain)

Glomeruli (similar odor receptor synapses)

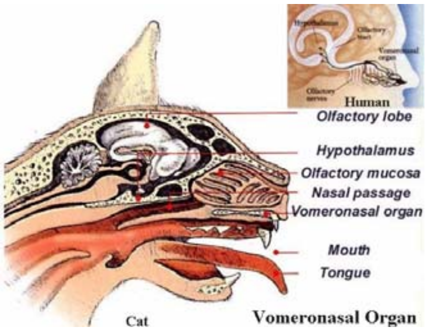
Sensory neurons (~ odor specific)

Mucus from epithelial glands



axons

dendrites



Olfactory Neurons

In humans, 10^7 olfactory receptor neurons

In dogs, $2x10^8$

Human auditory nerve: 10^4
Human optic nerve: 10^5

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end