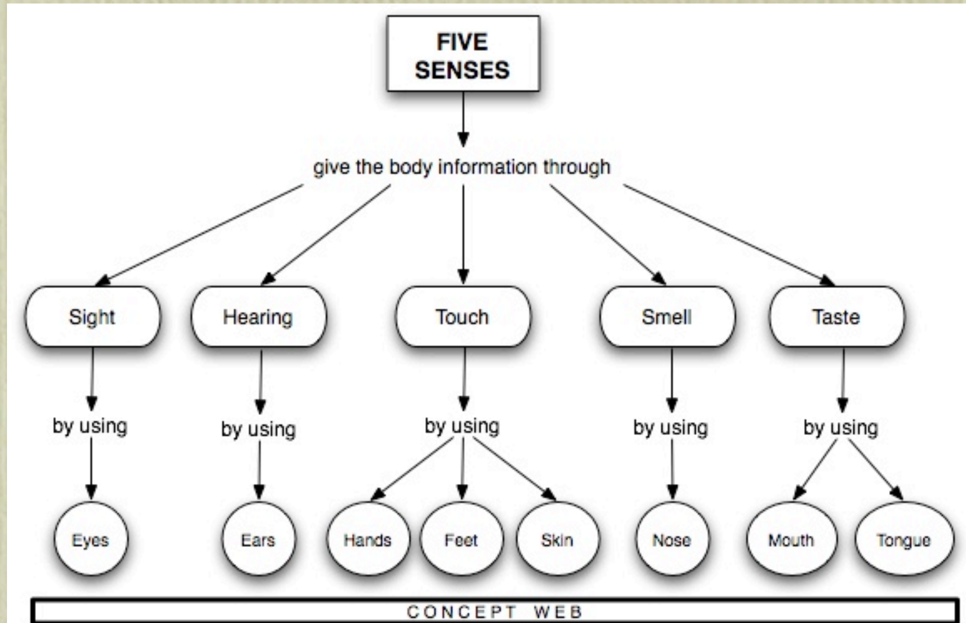
Sensory stimuli:

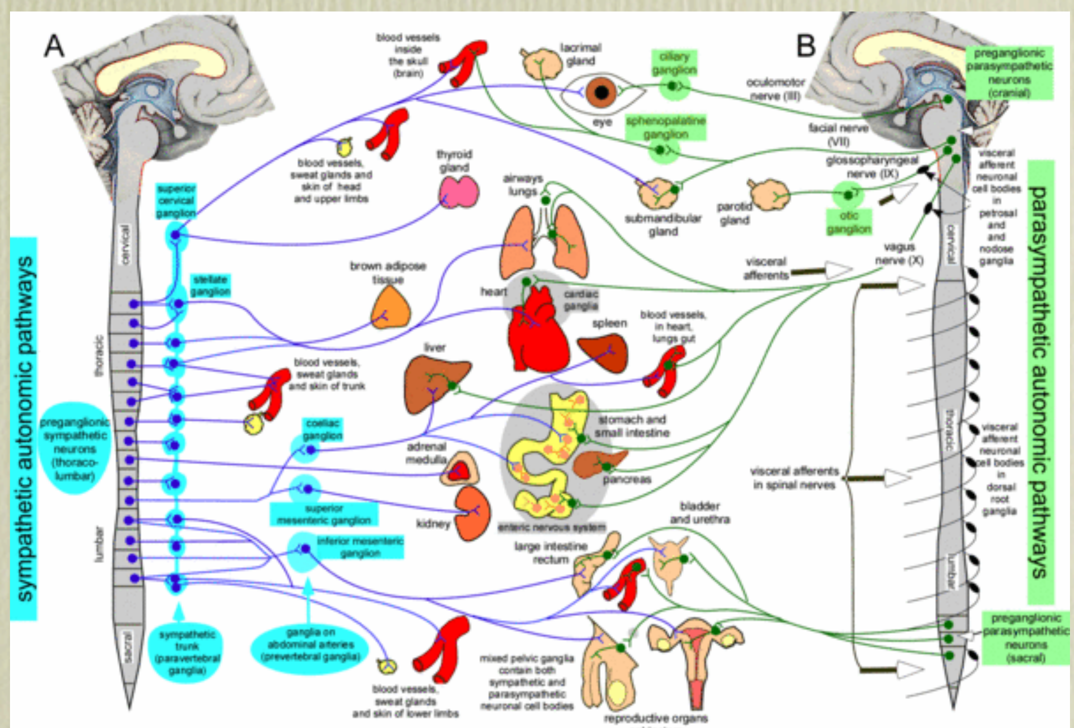
Light
Heat
Mechanical force
Chemical compounds

↔

Sensory cells:

Photo-receptors
Thermo-receptors
Mechano-receptors
Chemo-receptors





<u>Surface</u> sensors

and……

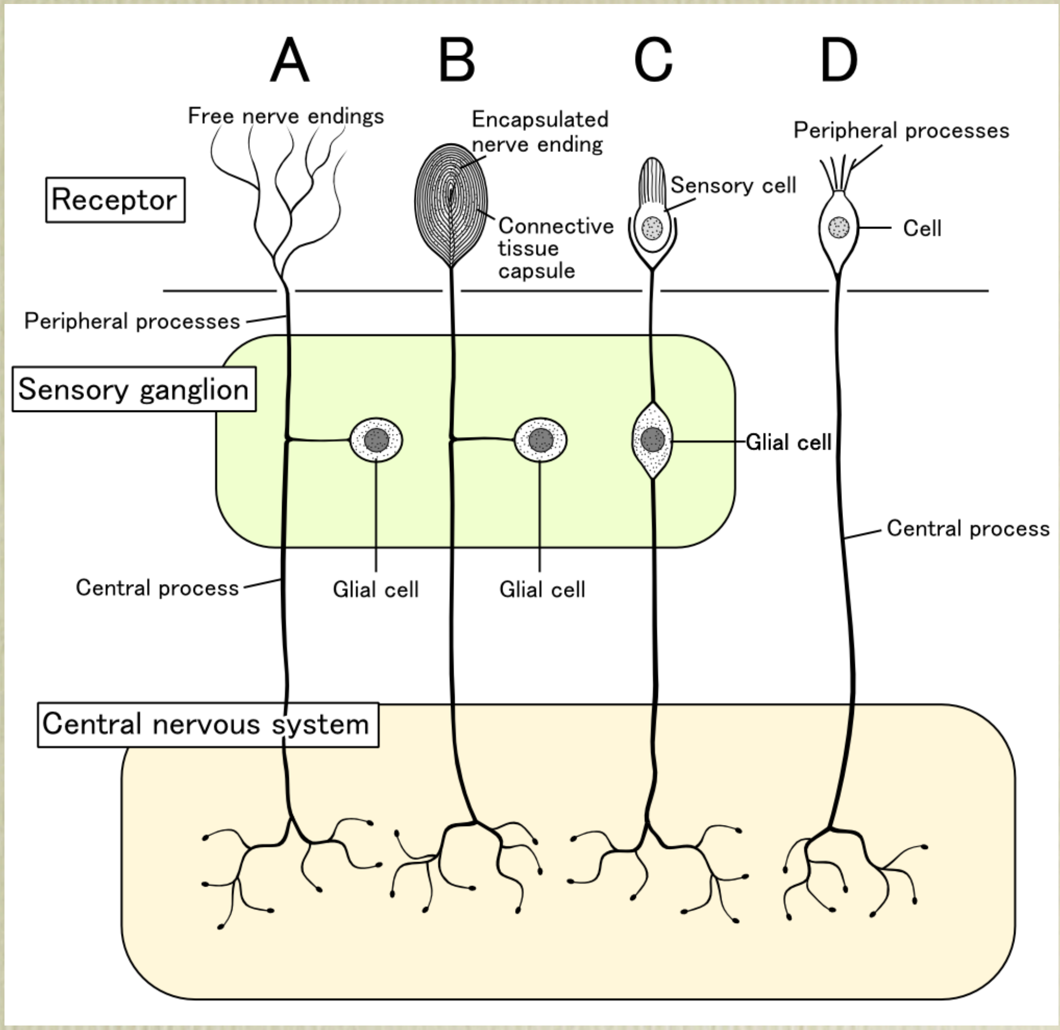
<u>Visceral</u> sensors

<u>External</u> stimuli

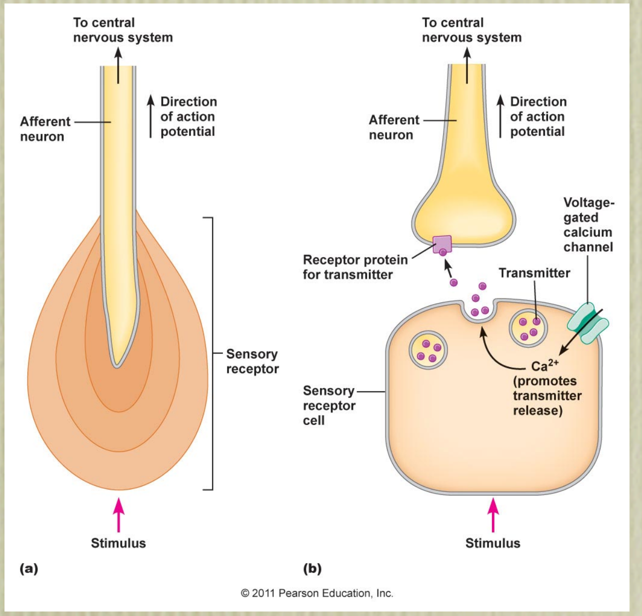
and……

<u>Internal</u> stimuli

SMELL
VISION
HEARING
TASTE
TOUCH
Rod
Cone
Free Nerve Ending
Meissner Corpuscle



A
B
C
D
Free nerve endings
Encapsulated nerve ending
Peripheral processes
Receptor
Sensory cell
Connective tissue capsule
Cell
Peripheral processes
Sensory ganglion
Glial cell
Central process
Central process
Glial cell
Glial cell
Central nervous system



To central nervous system
Afferent neuron
Direction of action potential
Sensory receptor
Stimulus
(a)
To central nervous system
Afferent neuron
Direction of action potential
Voltage-gated calcium channel
Receptor protein for transmitter
Transmitter
Sensory receptor cell
Ca^{2+} (promotes transmitter release)
Stimulus
(b)
© 2011 Pearson Education, Inc.

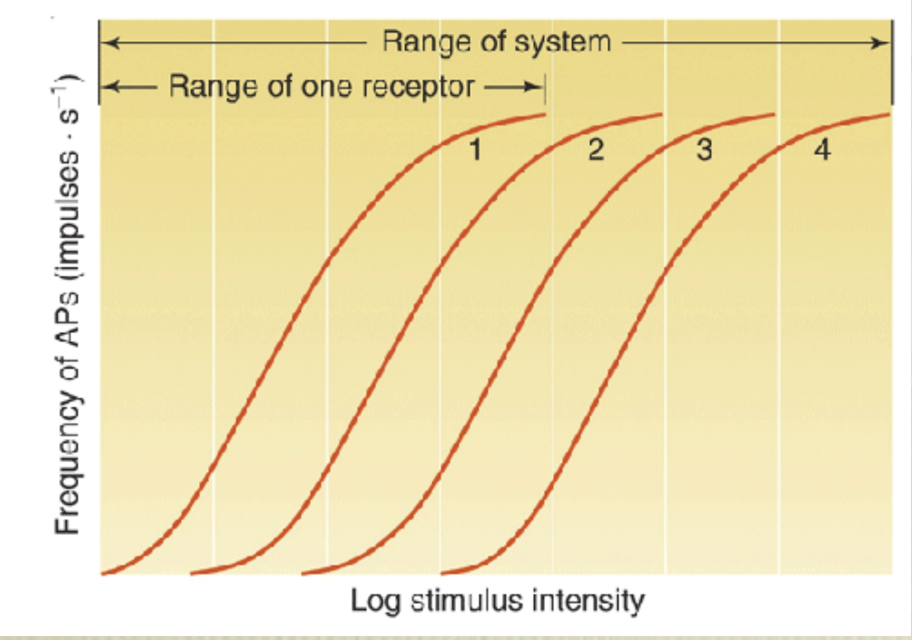
Sensory transduction

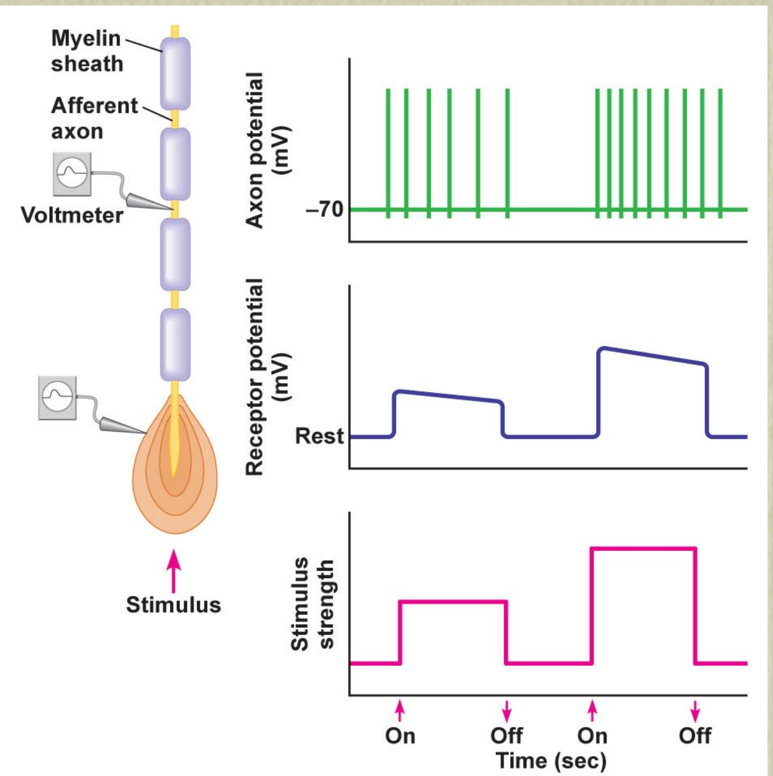
Threshold: the **minimum intensity** of a stimulus that is required to produce a response from a sensory system

Saturation: the **maximal intensity** of a stimulus that produces a response from a sensory system

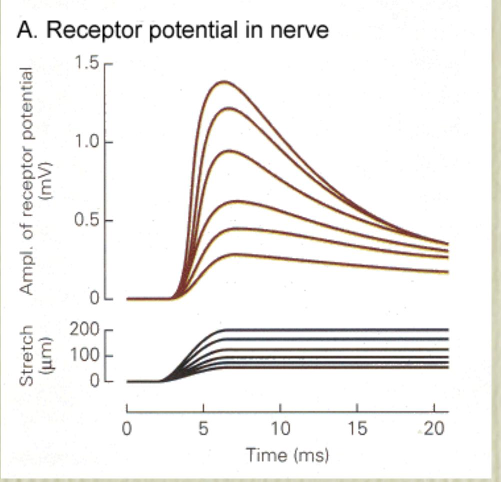
Dynamic Range: the **range of intensities** that will produce a response from a receptor or sensory system (i.e., the difference between threshold and saturation)

LOGARITMIC LAW

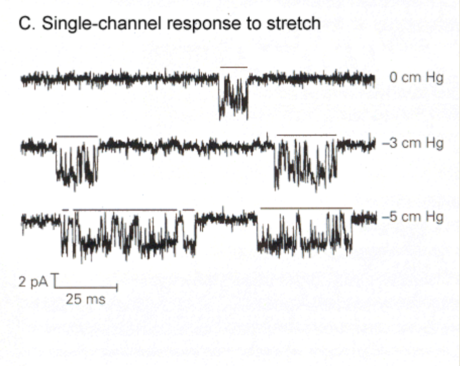




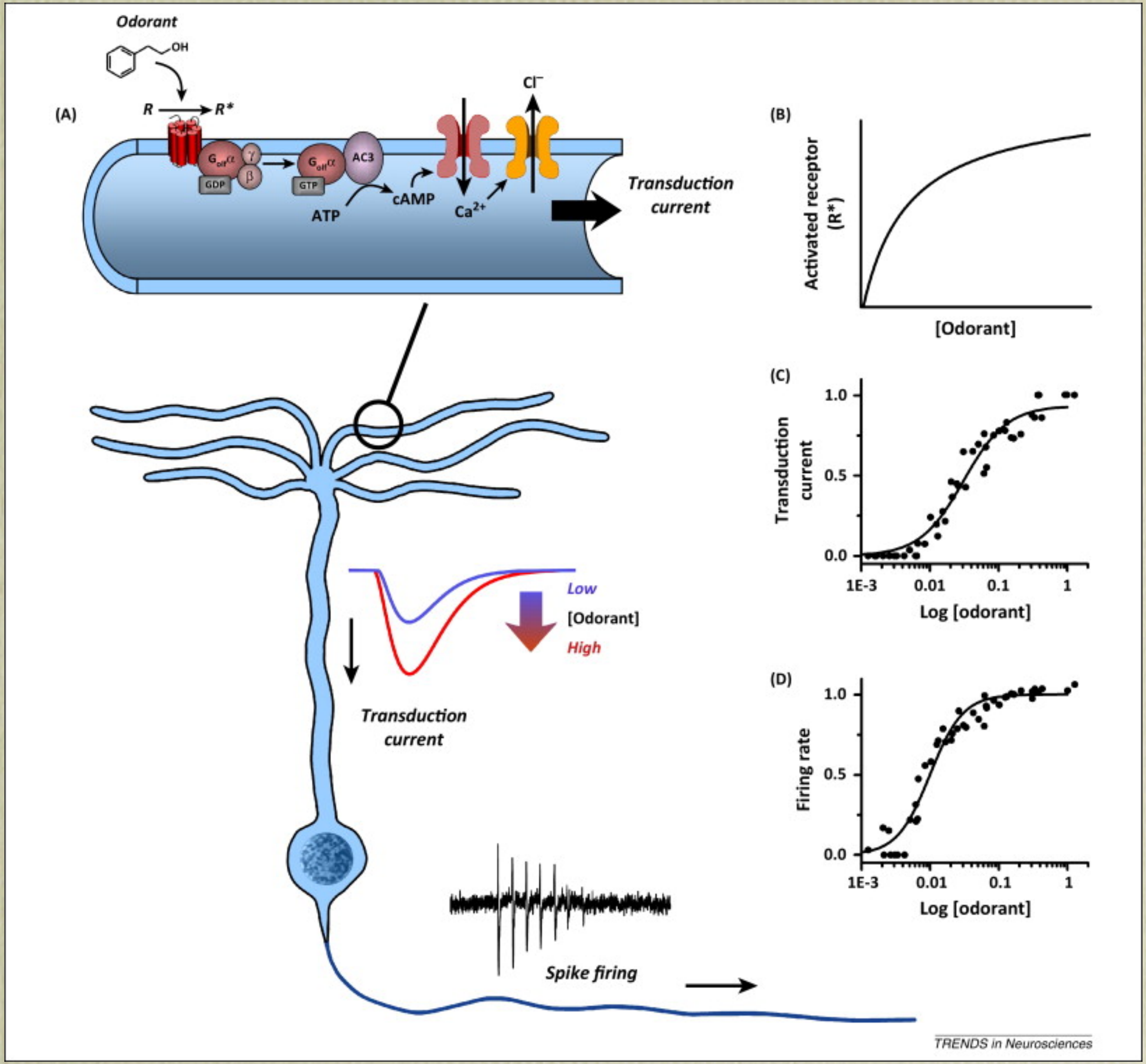
Myelin sheath
Afferent axon
Voltmeter
Stimulus
Axon potential (mV)
–70
Receptor potential (mV)
Rest
Stimulus strength
On
Off
On
Off
Time (sec)



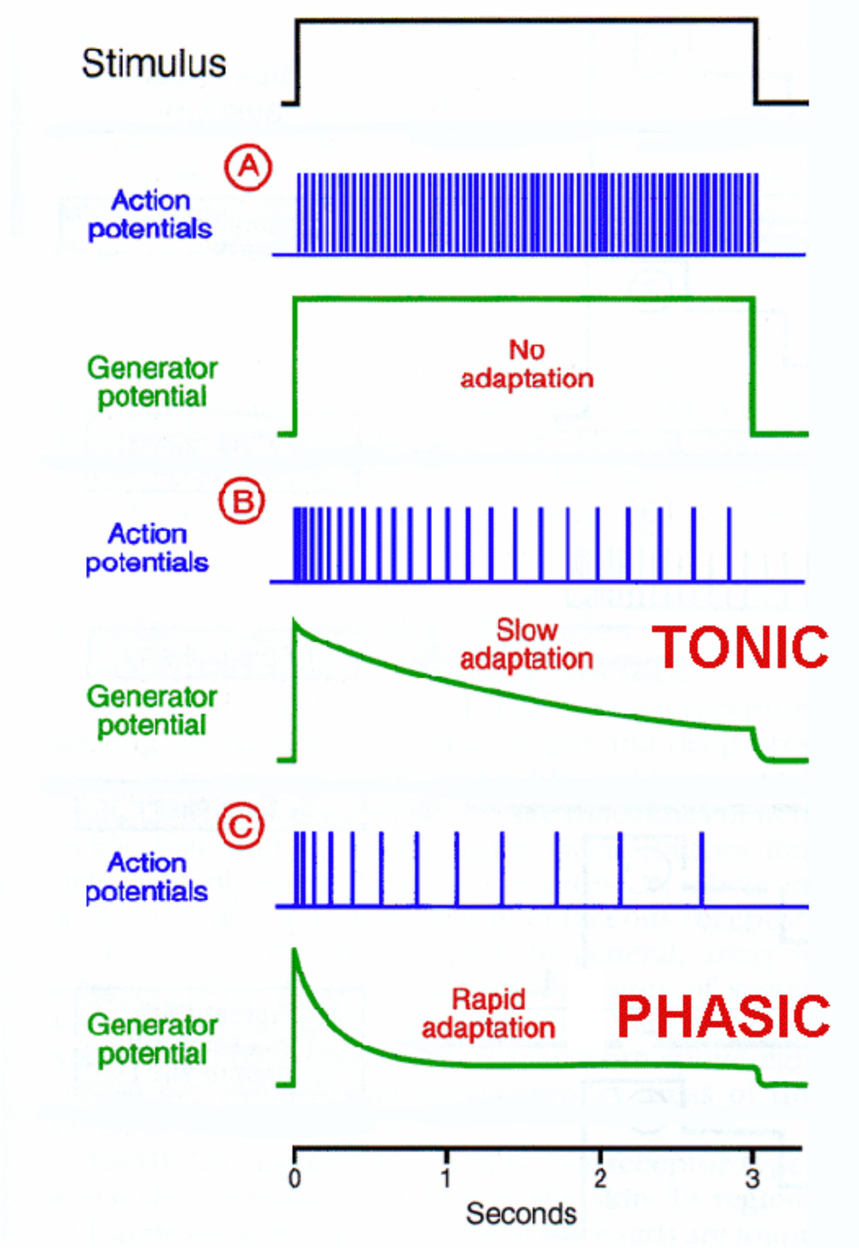
A. Receptor potential in nerve
Ampl. of receptor potential (mV)
1.5
1.0
0.5
0
Stretch (µm)
200
100
0
0
5
10
15
20
Time (ms)



C. Single-channel response to stretch
0 cm Hg
–3 cm Hg
–5 cm Hg
2 pA
25 ms



Odorant
OH
(A)
R
R*
AC3
GDP
GTP
Cl⁻
cAMP
ATP
Ca2+
Transduction current
Low
[Odorant]
High
Transduction current
Spike firing
(B)
Activated receptor (R*)
[Odorant]
(C)
Transduction current
1.0
0.5
0.0
1E-3
0.01
0.1
1
Log [odorant]
(D)
Firing rate
1.0
0.5
0.0
1E-3
0.01
0.1
1
Log [odorant]
TRENDS in Neurosciences



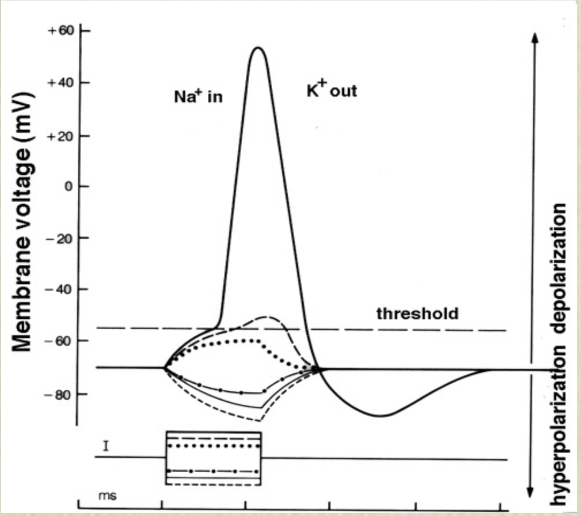
Stimulus
A
Action potentials
Generator potential
No adaptation
B
Action potentials
Slow adaptation
TONIC
Generator potential
C
Action potentials
Rapid adaptation
PHASIC
Generator potential
0
1
2
3
Seconds

Electrotonic potential

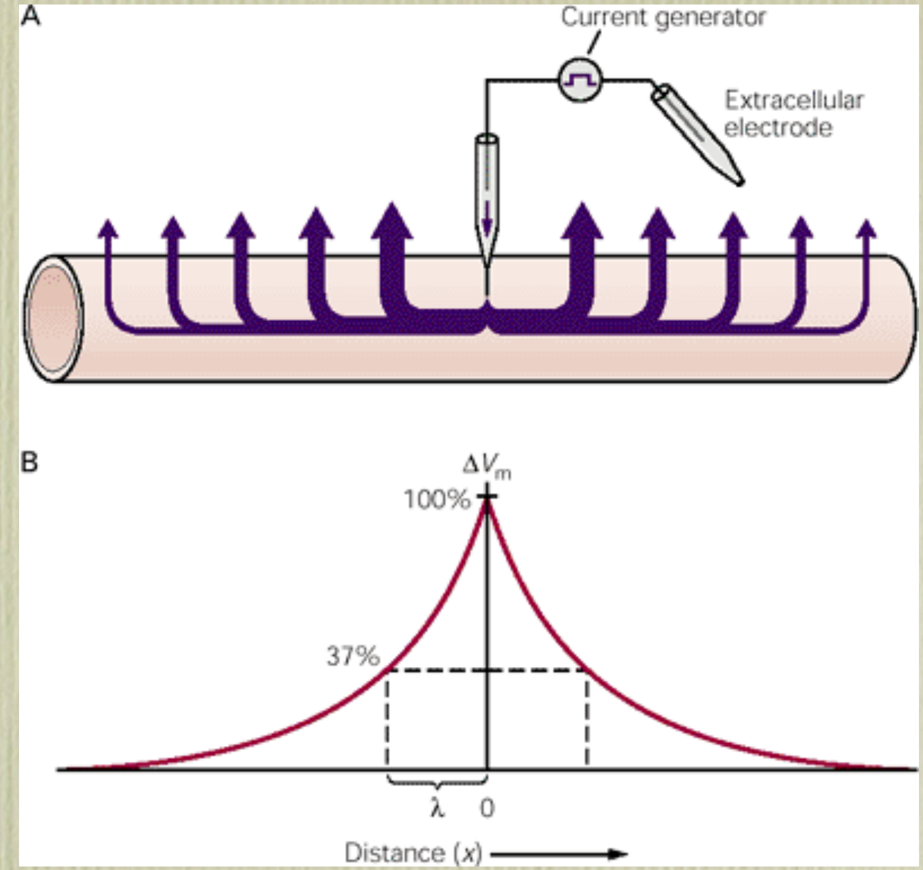
- graduated
- local (propagation with exponential decay)
- integration
- depolarization/hyperpolarization

Action potential

- all or none
- long distance propagation
- always a depolarization

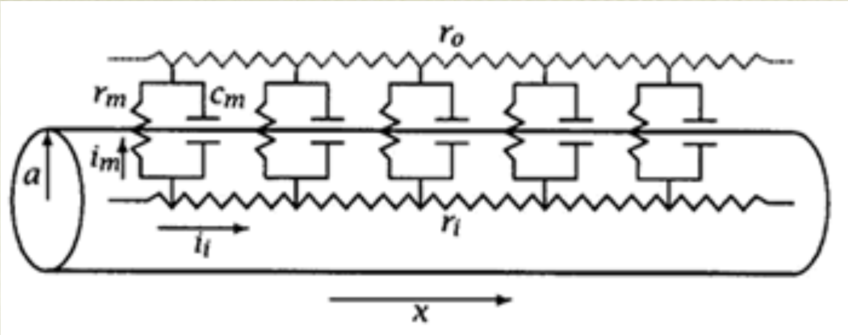


Spatial decay

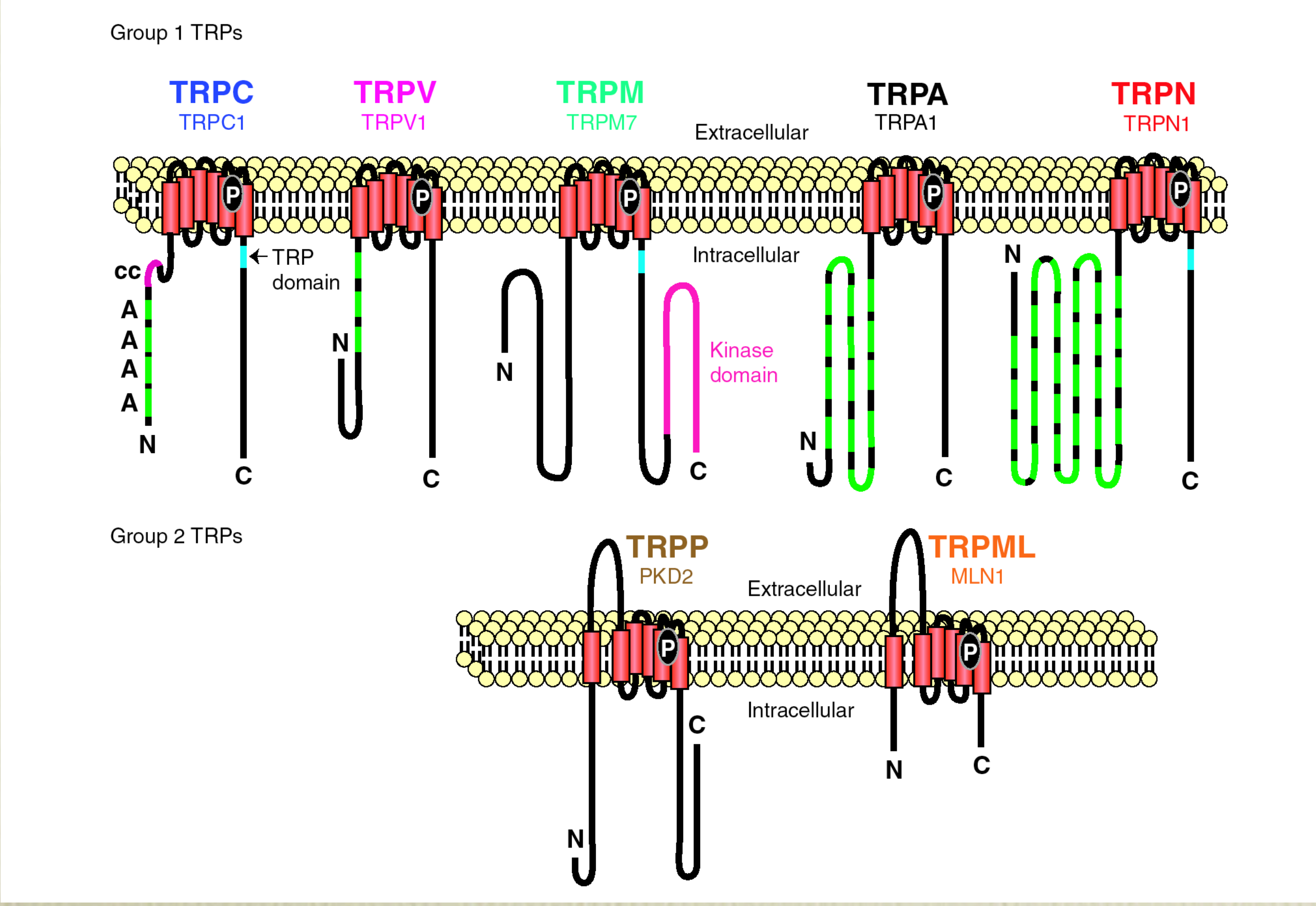


$$V_x = V_0 e^{\frac{-x}{\lambda}}$$

$$\lambda = \sqrt{\frac{r_m}{r_i}}$$



TRP channels and senses



TRP Channels

Kartik Venkatachalam and Craig Montell

Annu. Rev. Biochem. 2007. 76:387–417

Within the six kingdoms of life, bacteria, protozoa, chromista, plantae, fungi and animalia, TRP-related genes seem to be found only in fungi and animalia.

Despite extensive genomic studies, no single TRP-encoding gene has been identified in land plants so far, but the genome of chlorophyte algae seems to contain several types of putative TRP-like genes. In the green alga Ostreococcus tauri, at least one of the putative genes might encode a potential TRP channel involved in a Ca2+ signaling pathway. Therefore, land plants might have lost TRP channels after their divergence from the chlorophyte algae .

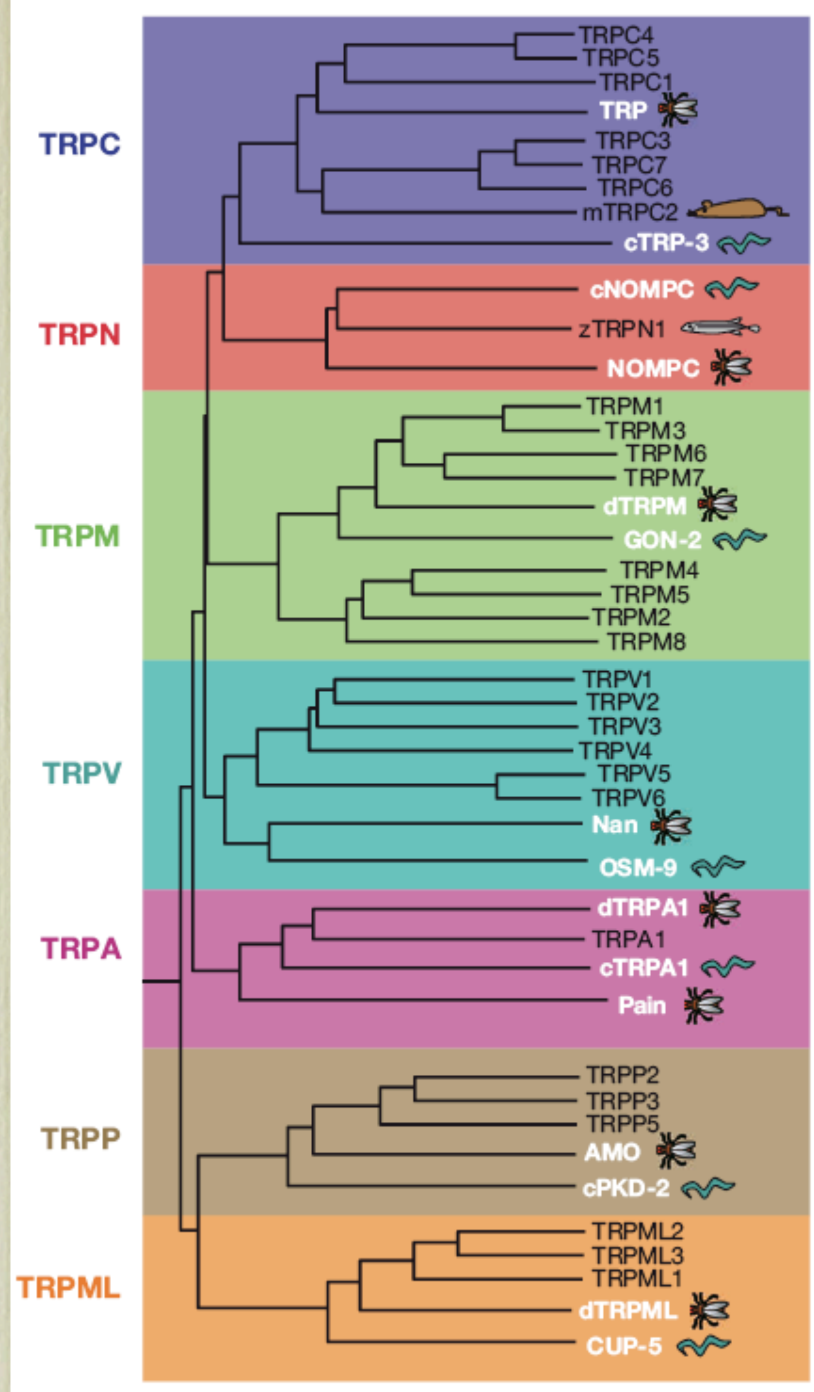


Table 1. The TRP channel families.

	Drosophila melanogaster	*Caenorhabditis elegans*	*Ciona intestinalis*	*Fugu rubripes*	*Danio rerio*	*Mus musculus*	*Homo sapiens*
TRPC	3	3	8	8	8	7	6
TRPV	2	5	2	4	4	6	6
TRPM	1	4	2	6	6	8	8
TRPA	4	2	4	1	2	1	1
TRPN	1	1	1	–	1	–	–
TRPML	1	1	9	2	2	3	3
TRPP	1	1	1	4	4	3	3
Total	13	17	27	25	27	28	27

TRP channels in *Drosophila melanogaster*, *Caenorhabditis elegans*, the sea squirt *Ciona intestinalis*, the puffer fish (*Fugu rubripes*), the zebrafish (*Danio rerio*), mouse and human. Other estimates report that there are nearly 60 TRPs in zebrafish, 30 in sea squirt, and 24 in nematodes [24,99]. The number of channels denoted in the table refers to those that have known functions.

Current Biology 18, R880–R889, September 23, 2008

TRPs in Our Senses

Nils Damann[1], Thomas Voets[1], and Bernd Nilius[1,*]

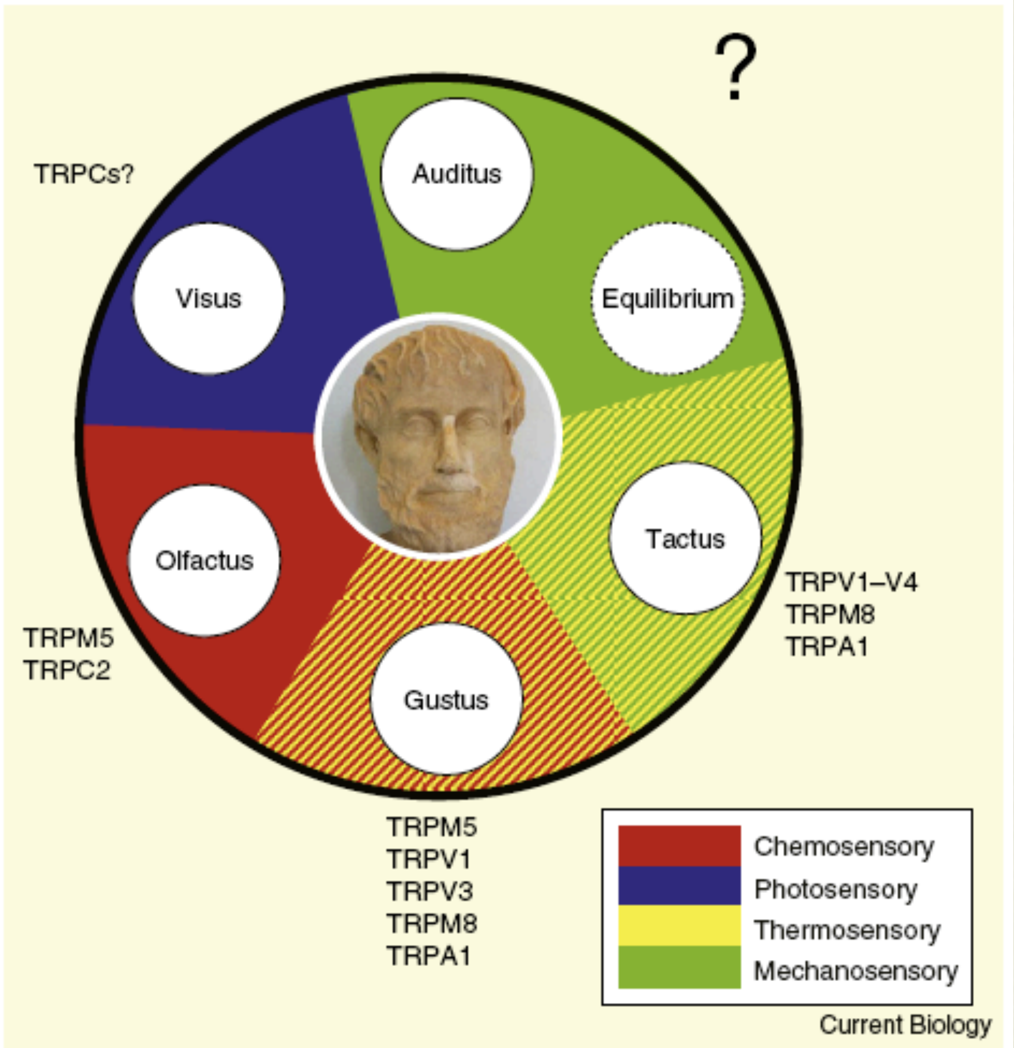
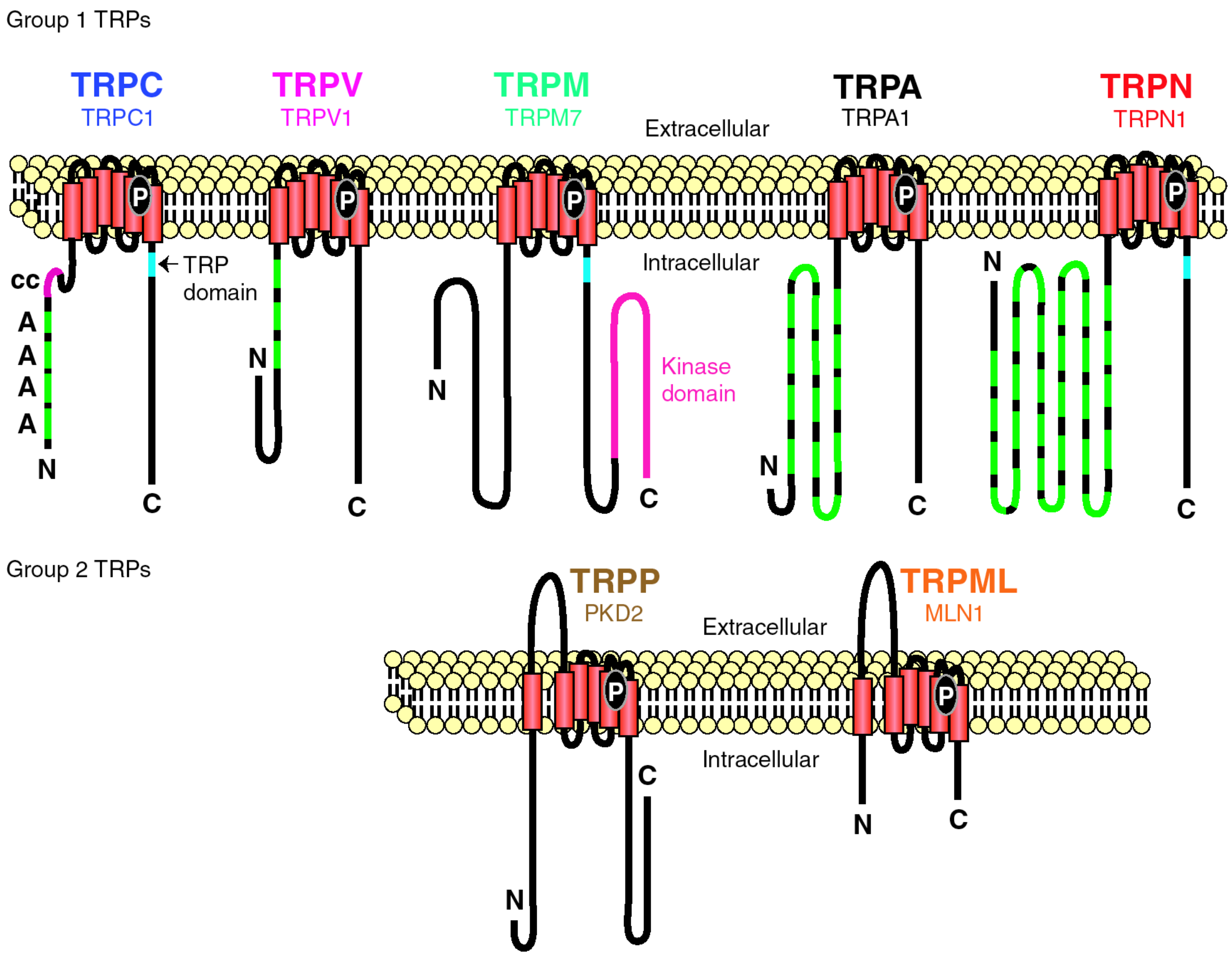


Figure 1. Aristotle's five senses + the sixth sense (equilibrium). Colors and color combinations indicate the type of sensory receptors involved. TRP channels closely involved in the sensory process are also indicated.

Aristotele
'De Anima'


Group 1 TRPs
TRPC
TRPC1
TRPV
TRPV1
TRPM
TRPM7
Extracellular
TRPA
TRPA1
TRPN
TRPN1
P
cc
TRP
domain
Intracellular
A
A
A
A
N
C
Kinase
domain
Group 2 TRPs
TRPP
PKD2
Extracellular
TRPML
MLN1
Intracellular

Gene name	Chromosomal localization	Selectivity $P_{Ca}:P_{Na}$	Modulation of activity	Highest expression
TRPC subfamily				
TRPC1	3q22–q24	Nonselective	Store depletion, conformational coupling, mechanical stretch[b]	Heart, brain, testis, ovary, liver, spleen
TRPC2[a]	7, 50.0 cM	2.7	Diacylglycerol (DAG)	VNO, testis
TRPC3	4q27	1.6	Store depletion, conformational coupling, DAG, exocytosis	Brain
TRPC4	13q13.1–q13.2	7	Store depletion (?), exocytosis	Brain, endothelia, adrenal gland, retina, testis
TRPC5	Xq23	9.5	Store depletion (?), sphingosine-1-phosphate, exocytosis	Brain
TRPC6	11q21–q22	5	Conformational coupling, DAG, PIP_3	Lung, brain, placenta, ovary
TRPC7	5q31.2	1.9[c], 5[d]	Store depletion, DAG	Eye, heart, lung

TRPV subfamily

TRPV1	17p13.3	3.8 (heat), 9.6 (vanilloids)	Heat (43°C), vanilloids, anandamide, camphor, piperine (black pepper), allicin (garlic), ethanol, nicotine, proinflammatory cytokines, protons, PIP_2, phosphorylation exocytosis	TG, DRG, neurons, urinary bladder, testis
TRPV2	17p11.2	3	Heat (52°C), osmotic cell swelling, exocytosis	DRG, spinal cord, brain, spleen, intestine
TRPV3	17p13.3	2.6	Warm (33–39°C); PUFAs; menthol; compounds from oregano, cloves, and thymes	TG, DRG, spinal cord, brain, keratinocytes, tongue
TRPV4	12q24.1	6	Warm (27–34°C), osmotic cell swelling, 5′6′-EET, exocytosis	DRG, kidney, lung, spleen, testis, heart, keratinocytes, heart, liver, endothelia
TRPV5	7q35	>100	Low intracellular Ca^{2+}, hyperpolarization, exocytosis	Kidney, intestine, pancreas, placenta
TRPV6	7q33–q34	>100	Store depletion, exocytosis	Small intestine, pancreas, placenta

Gene name	Chromosomal localization[a]	Selectivity $P_{Ca}:P_{Na}$	Modulation of activity	Highest expression
TRPM subfamily				
TRPM1	15q13–q14	Nonselective	Translocation (?)[b]	Brain, melanosomes
TRPM2	21q22.3	~0.3	ADP-ribose, cADP-ribose, pyrimidine nucleotides, arachidonic acid, NAD, H_2O_2, Ca^{2+}	Brain, bone marrow, spleen
TRPM3	9q21.11	1.6	Osmotic cell swelling, store depletion (?)	Kidney, brain, pituitary
TRPM4	19q13.33	Monovalent cation selective	Ca^{2+}, voltage modulated, PIP_2	Prostate, colon, heart, kidney, testis
TRPM5	11p15.5	Monovalent cation selective	Ca^{2+}, voltage modulated, PIP_2, heat (15–35°C)	Intestine, liver, lung, taste cells
TRPM6	9q21.13	Divalent cation selective (Mg^{2+} and Ca^{2+})	Mg^{2+} inhibited, translocation	Kidney, small intestines
TRPM7	15q21	Divalent cation selective (Mg^{2+} and Ca^{2+})	Mg^{2+} inhibited, ATP, protons, phosphorylation, PIP_2	Kidney, heart, pituitary, bone, adipose
TRPM8	2q37.2	3.3	Cool (23–28°C), menthol, icilin, pH modulated, PIP_2	DRG, TG, prostate, liver

TRPA and TRPN

TRPA1	8q13	0.8	Cold (17°C) (?), icilin, isothiocyanates (mustard oil, horseradish, and wasabi), allicin (garlic), cinnamaldehyde (cinnamon oil), acrolein (tear gas), cannabinoids, bradykinin, DAG, PUFAs, mechanically gated (?)	DRG, hair cells, ovary, spleen, testis
zTRPN	–	?	Mechanically gated (?)	Ear, eye

Gene name	Chromosomal localization[a]	Selectivity $P_{Ca}:P_{Na}$	Modulation of activity	Highest expression
TRPP2	4q21–q23	Nonspecific	Ca^{2+}, translocation, TRPP1, EGF, PIP_2, fluid flow, actin cytoskeleton[b]	Widely expressed, kidney
TRPP3	10q24	4.3	Ca^{2+}	Kidney, heart
TRPP5	5q31	–	–	Testis, heart
TRPML1	19p13.2–p13.3	Monovalent cation selective (?)	pH, Ca^{2+}, proteolytic cleavage	Brain, heart, skeletal muscle
TRPML2	1p22	–	–	–
TRPML3	1p22.3	–	–	Cochlear hair cells[c]

TRP in yeast: TRPY1 in vacuolar membranes

Hypertonic shock– calcium entry

TRPY1 is a mechanosensor and chemosensor sensitive to indols and aromatic compounds

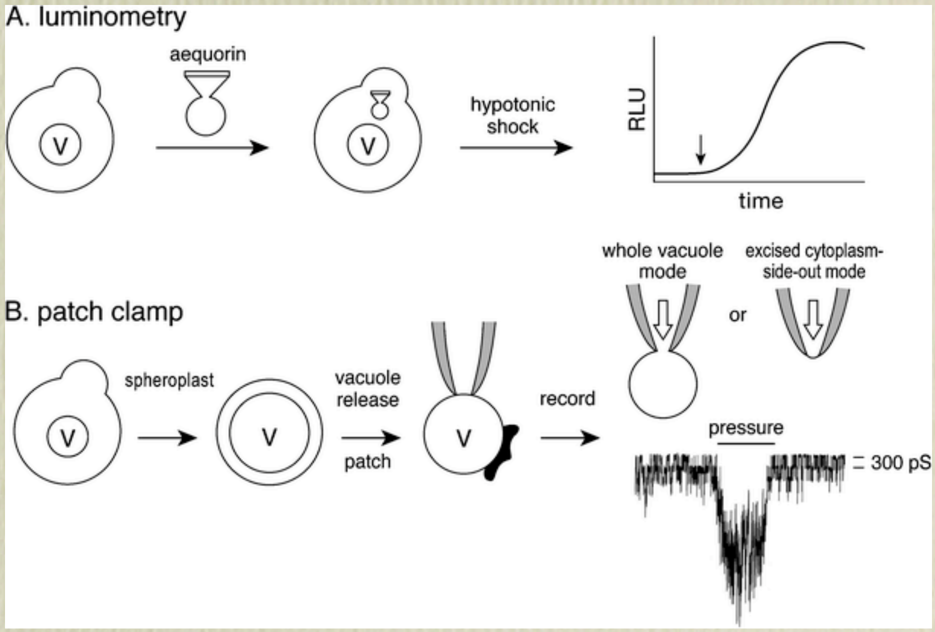
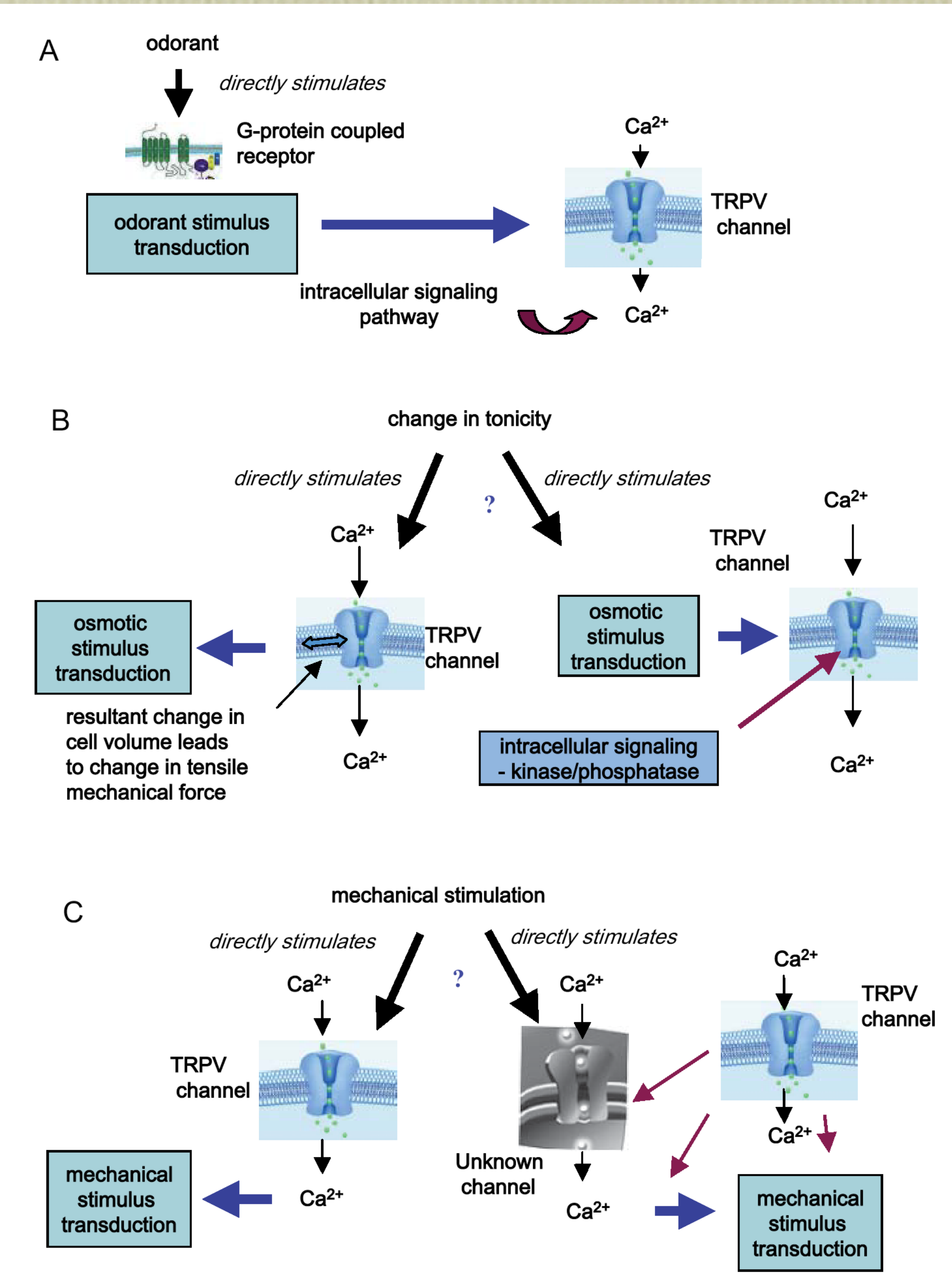


Fig. 1 Experimental procedures to examine TRPY1 activities in vivo and in vitro. a Monitoring of TRPY1's response to hypertonic shock in vivo. As described in [2, 10], yeast cells are transformed with plasmids bearing the apoaequorin gene. Transformed yeast cells are then challenged with hypertonic shocks and the Ca2+ release following TRPY1's activation is gauged by aequorin-Ca2+ relative luminescence units (RLUs). b Recording of TRPY1's current triggered by membrane stretch under patch clamp.

!

Yeast cells are spheroplasted as described before being broken by hypotonic swelling to release vacuoles (V). Released vacuoles are patch clamped in whole-vacuole mode or excised cytoplasmic-side-out mode.

Membrane stretch forces are applied by directly blowing the patches with pressures of tens of millimeter Hg. A representative trace shows TRPY1's response to ~30 mmHg pressure stimulation



J Physiol 567.1 (2005) pp 53–58

SYMPOSIUM REPORT

TRPV4 plays an evolutionary conserved role in the transduction of osmotic and mechanical stimuli in live animals

Wolfgang Liedtke

Cell swelling, heat, and chemical agonists use distinct pathways for the activation of the cation channel TRPV4

J. Vriens, H. Watanabe, A. Janssens, G. Droogmans, T. Voets*, and B. Nilius

396–401 | PNAS | January 6, 2004 | vol. 101 | no. 1

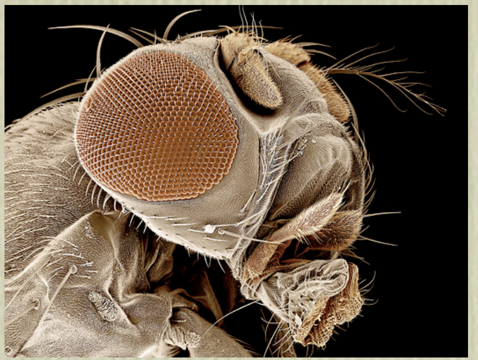
Figure 1. Schematic drawings showing the specifics of signal transduction in sensory (nerve) cells in response to odorant (*A*), osmotic (*B–C*) and mechanical (*D–E*) stimuli
A, the odorant activates the TRPV ion channel via a G protein-coupled receptor mechanism. This happens, e.g. in the ASH sensory neurone of *C. elegans* in response to 8-octanone, an aversive odorant. The TRPV channel, OSM-9 or OCR-2, is down-stream of the G protein-coupled receptor. Calcium influx through the TRPV channel is an amplification mechanism which is necessary for this signalling pathway. *B*, one hypothetical scenario where, analogous to *A*, the TRPV channel functions down-stream of an – as yet unknown – osmotic stimulus transduction apparatus. Intracellular signalling via phosphorylation (dephosphorylation)-dependent pathways activates the channel. For heterologous cellular expression systems, two groups have obtained – contradictory – data that suggest phosphorylation of TRPV4 to be of relevance (Vriens *et al.* 2003; Xu *et al.* 2003). *C*, another hypothetical scenario where the TRPV channel is on top of the signalling cascade. Scenario I and II need not be mutually exclusive. Apart from phosphorylation of the TRPV channel, which could possibly be of relevance *in vivo*, a direct physical linkage of the TRPV channel to the cytoskeleton, to the extracellular matrix and to the lipids of the plasma

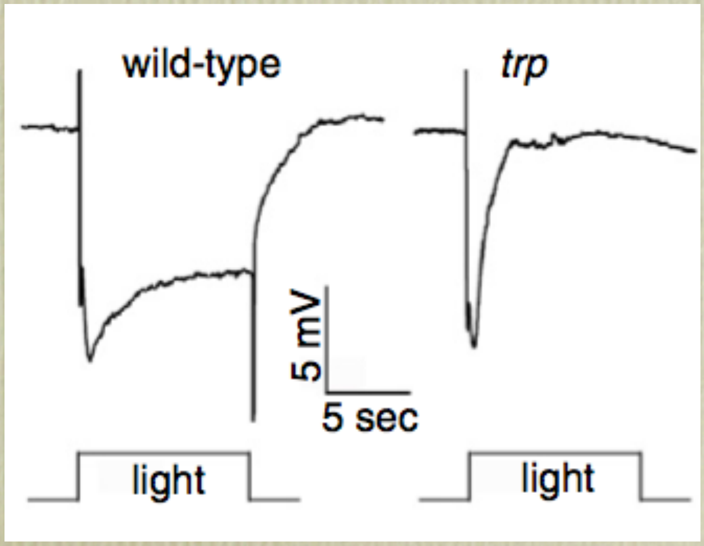
Drosophila visual transduction

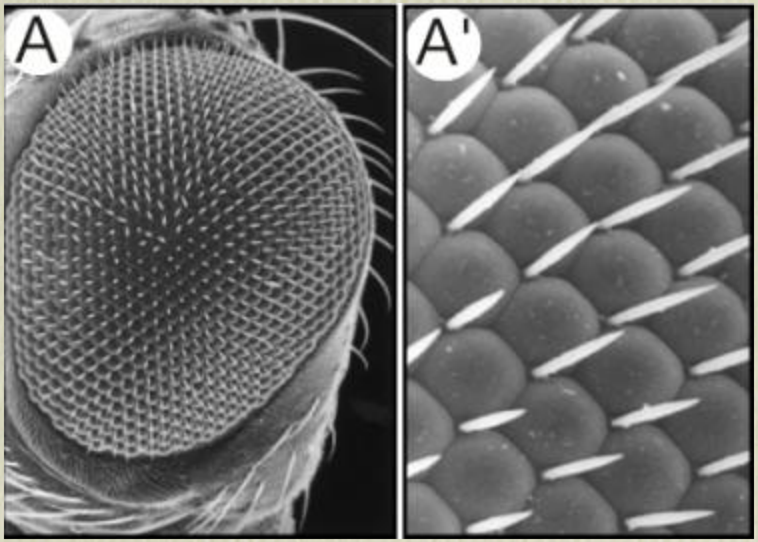
Craig Montell

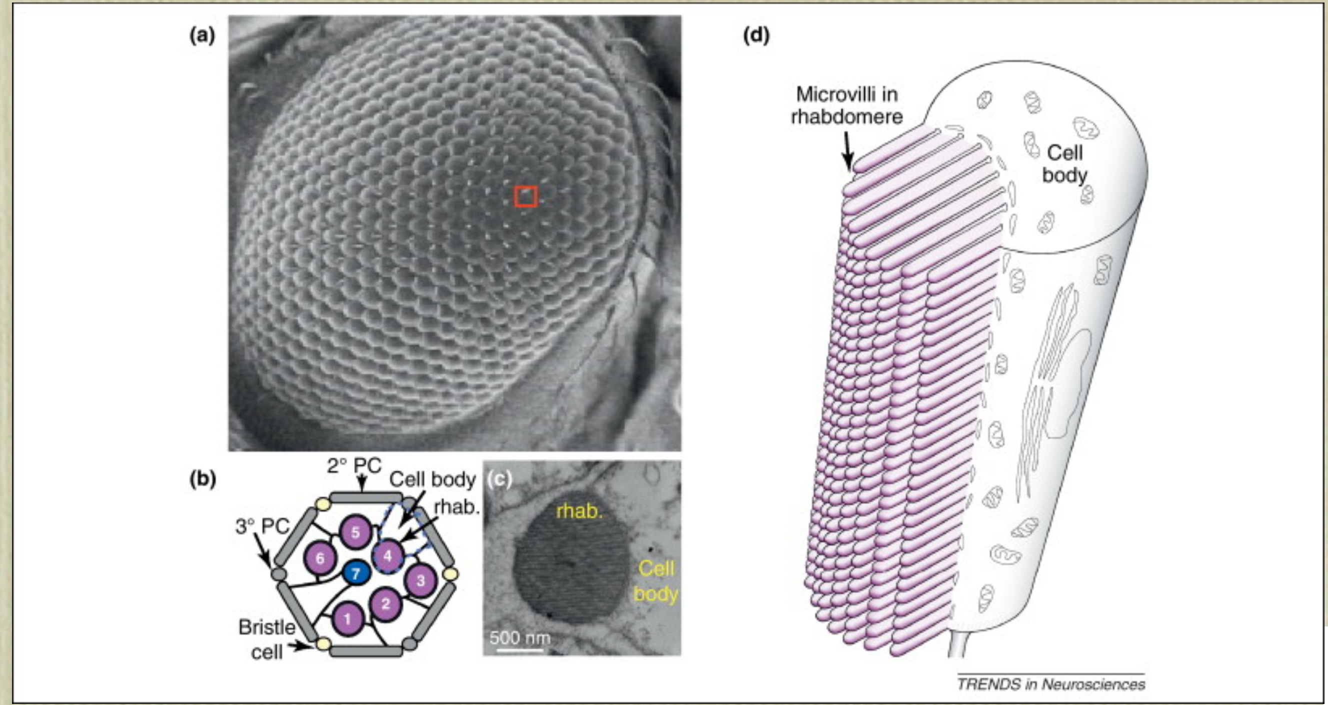
Trends in Neurosciences, June 2012, Vol. 35, No. 6

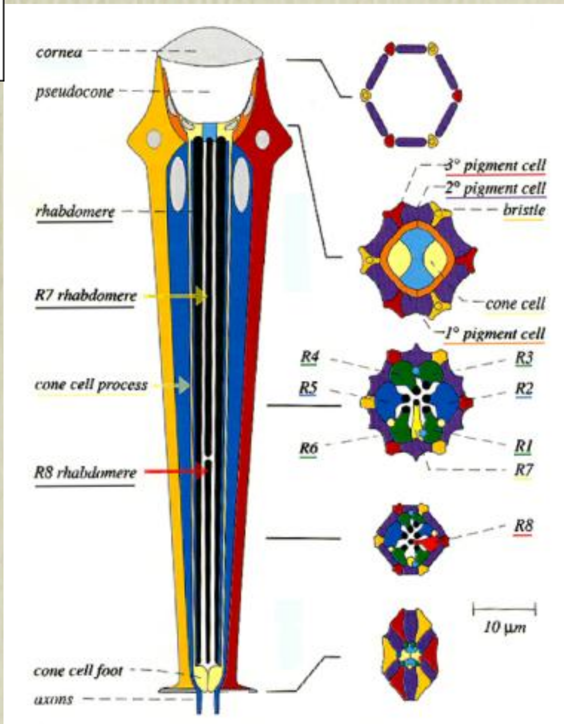
The story began in Drosophila…







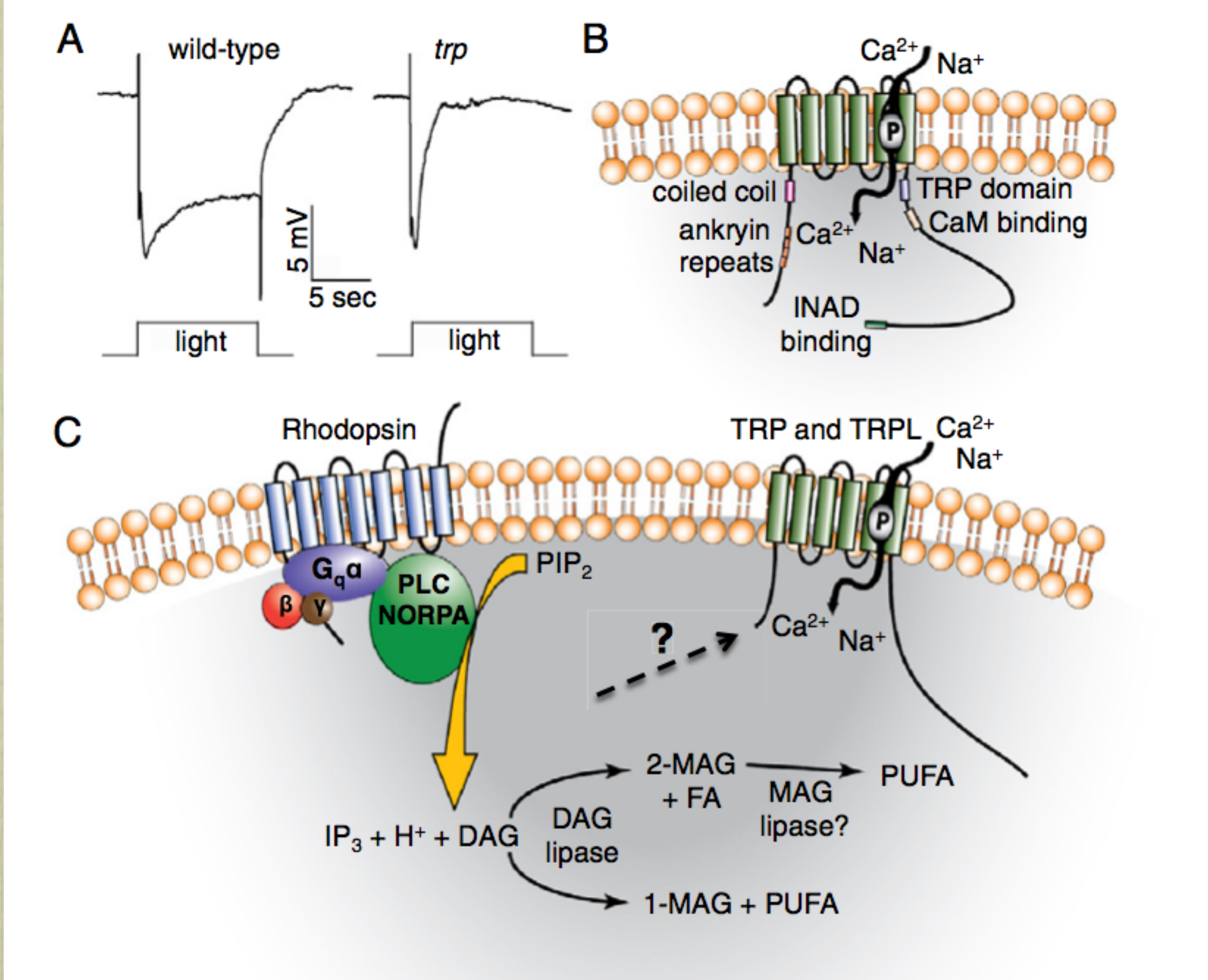

(a)
(b)
2° PC
Cell body
rhab.
3° PC
Bristle cell
(c)
rhab.
Cell body
500 nm
(d)
Microvilli in rhabdomere
Cell body
TRENDS in Neurosciences


cornea
pseudocone
rhabdomere
R7 rhabdomere
cone cell process
R8 rhabdomere
cone cell foot
axons
3° pigment cell
2° pigment cell
bristle
cone cell
1° pigment cell
R4
R3
R5
R2
R6
R1
R7
R8
10 µm

Minireview

Drosophila TRP channels and animal behavior

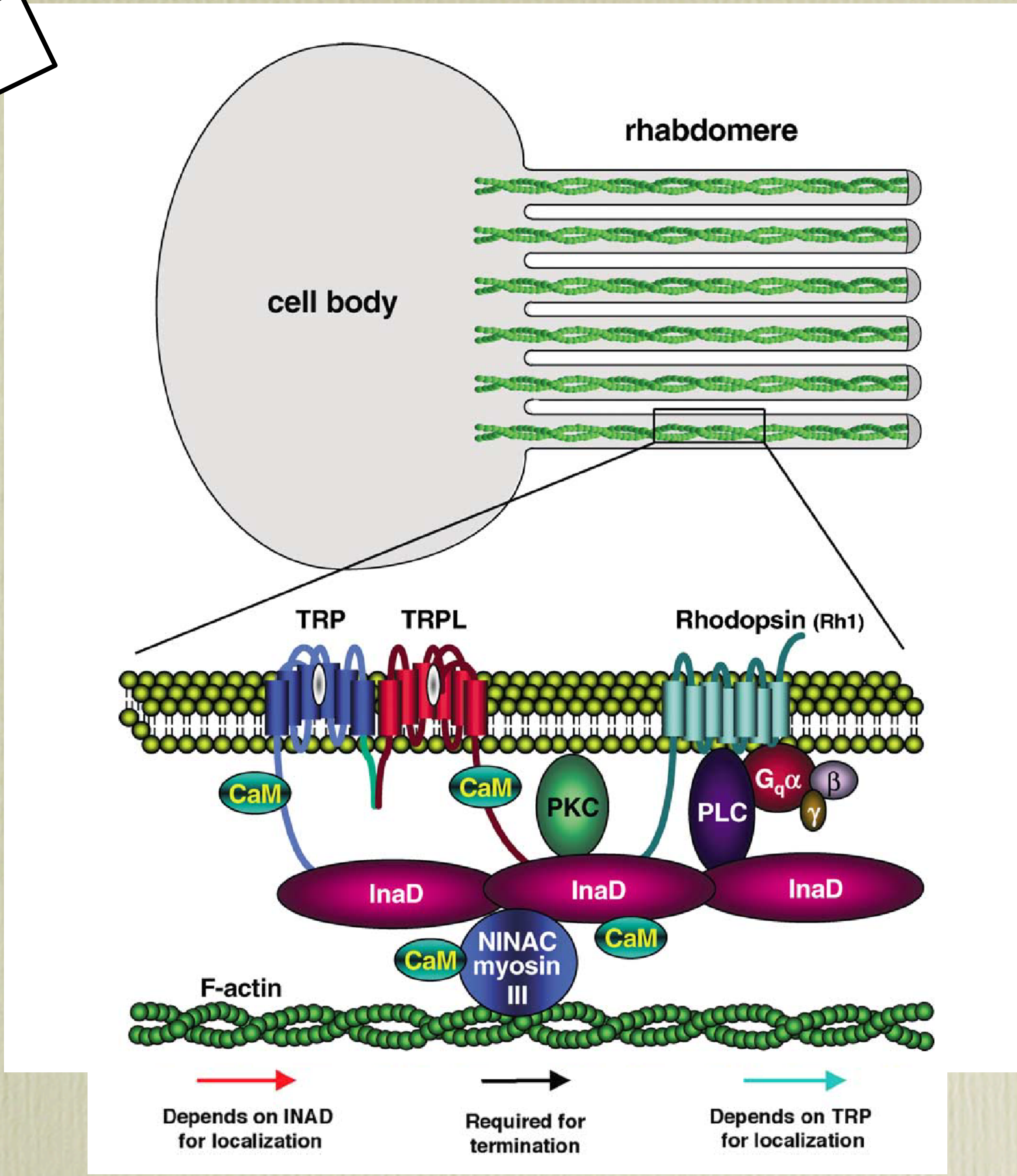
Melissa A. Fowler, Craig Montell *

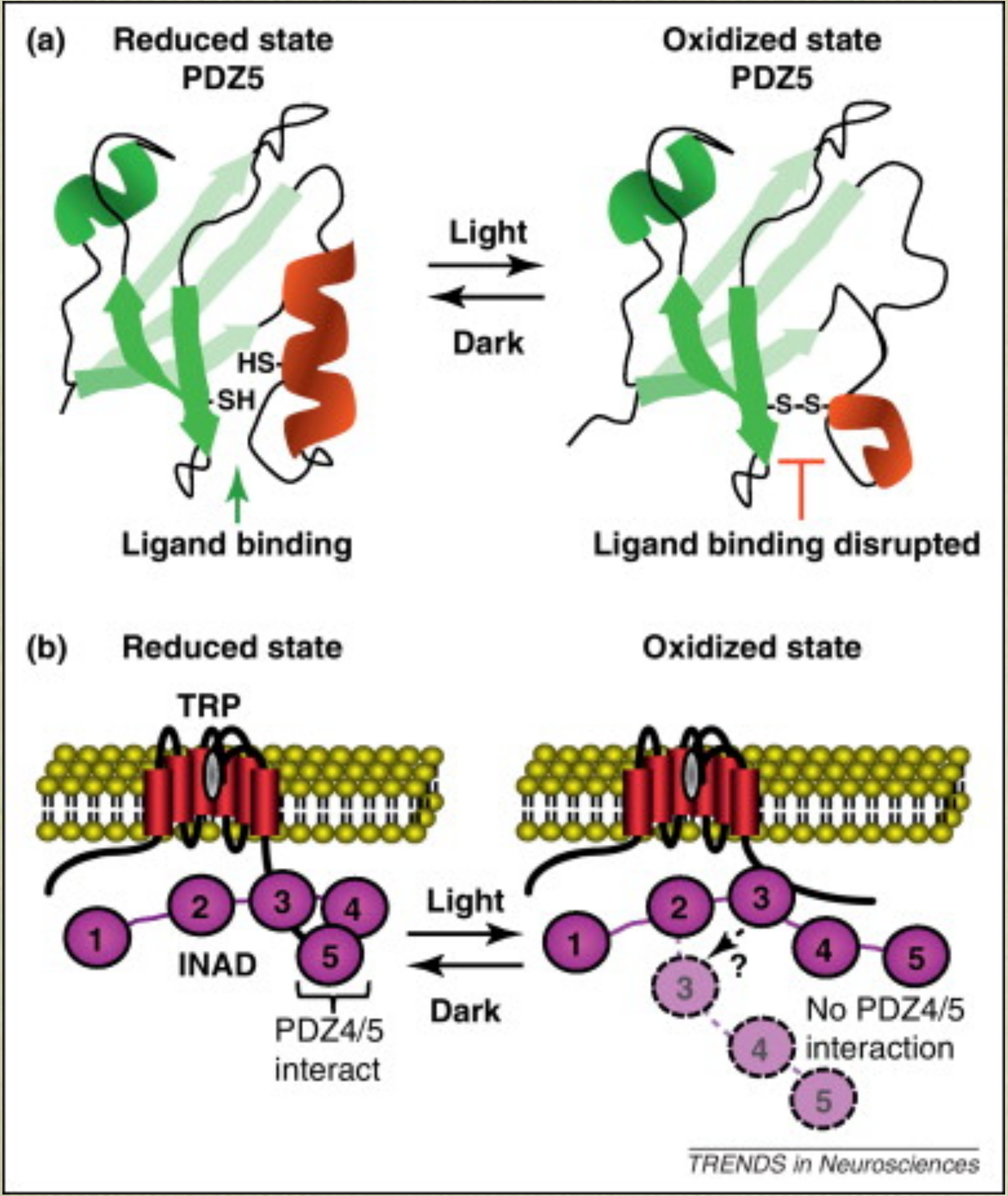


Recall signalplexes !

IMPROVED FEATURES

. Efficiency
. Specificity
. Speed
. Modularity
. Regulation





Dynamic binding of TRP with INAD. (a) The two cysteines lining the surface groove in INAD PDZ5 are reduced in the dark [84] and [98]. As a consequence, PDZ5 can bind to binding proteins, including the C-terminus of TRP [84]. Light results in oxidation of the two key cysteines in PDZ5, which precludes target binding. (b) In the dark, PDZ4 and PDZ5 interact, thereby promoting the reduced state in PDZ5 [85]. Under these conditions TRP binds to PDZ5 through the C terminus, and to PDZ3 via a separate binding site near the C terminus. Following light stimulation, the PDZ4–PDZ5 interaction is disrupted, leading to oxidation of PDZ5 [85]. This prevents binding of the TRP C terminus to PDZ5. Given that the affinity of the internal binding site in TRP to PDZ3 is weak, binding to PDZ3 may dissociate as a secondary consequence of the oxidation of PDZ5. However, the light-induced impairment of the TRP–PDZ3 interaction is speculative, as indicated by a question mark. Abbreviations: INAD, inactivation but no afterpotential D; TRP, transient receptor potential (channel).