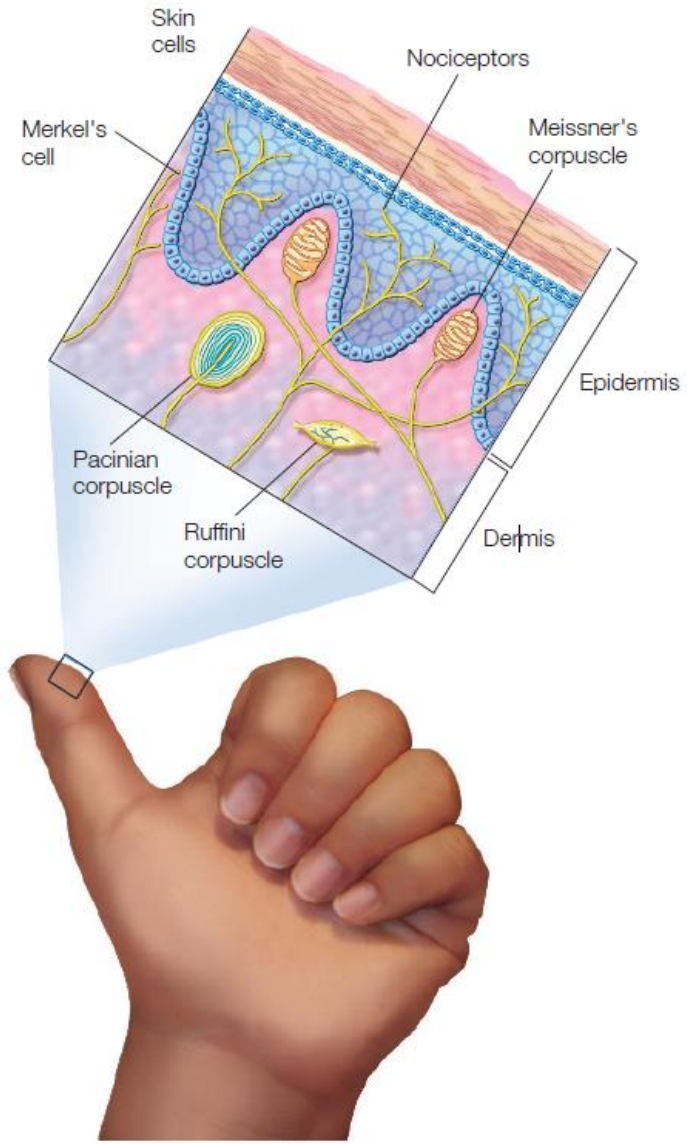
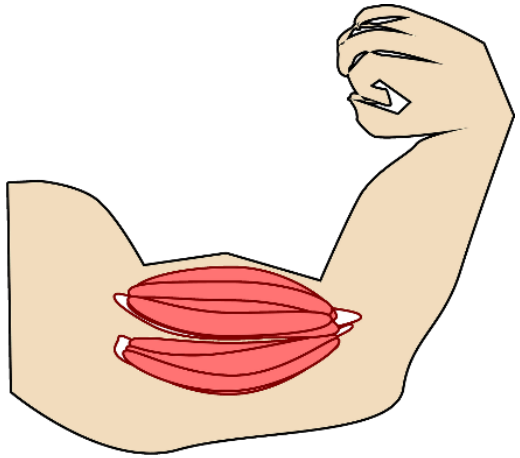
Somatosensation



Somatosensation subgroups

PROPRIOCEPTION

Sensing oneself (proprius → one‘s own).

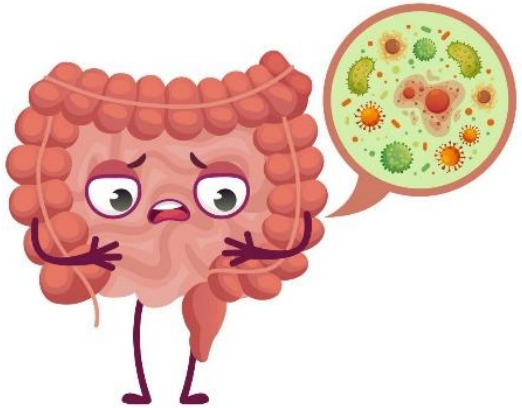


EXTEROCEPTION

Sensing the outside world

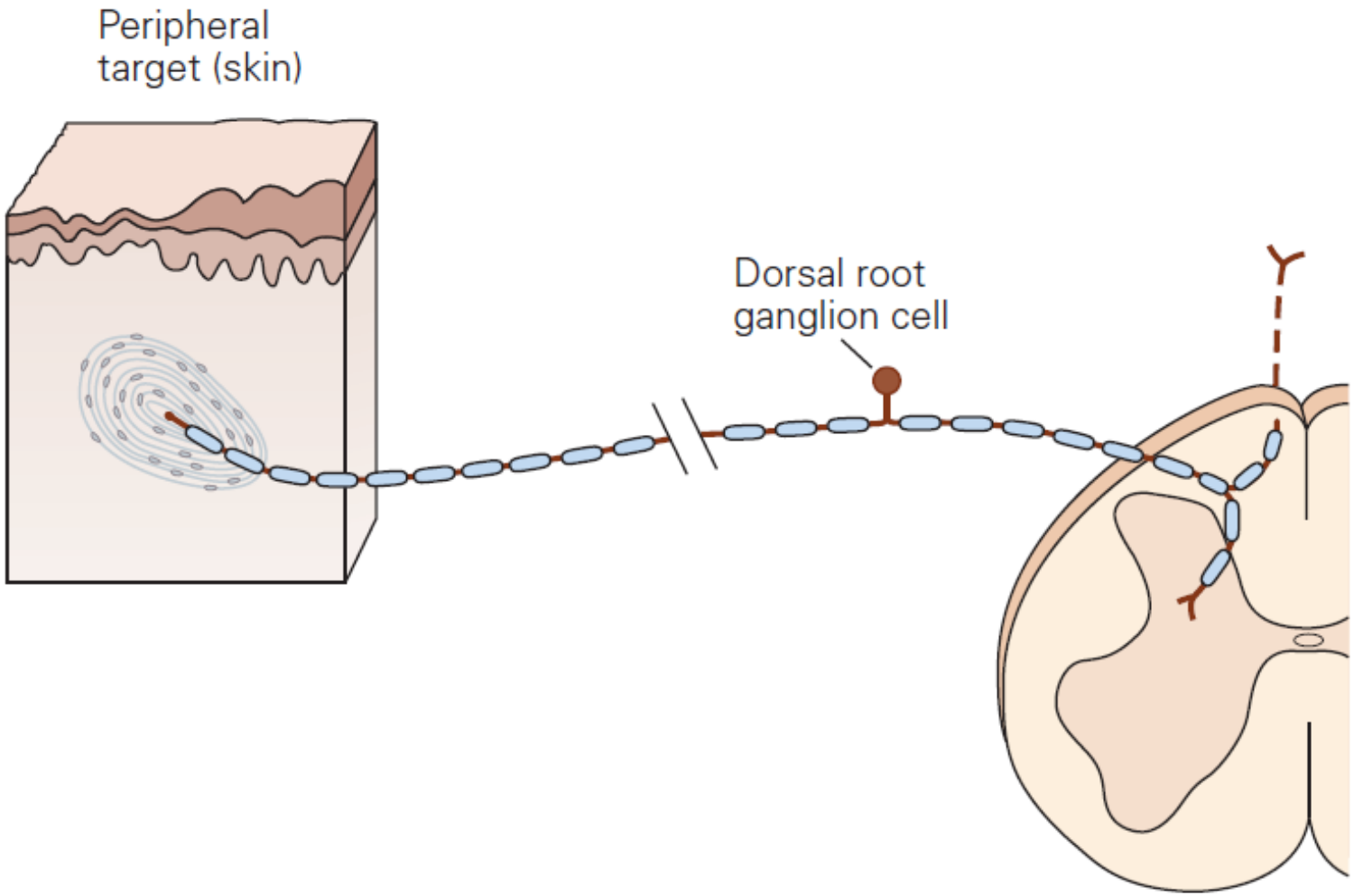
INTEROCEPTION

Sensing the inside world



https://gialliance.com/10-things-to-positively-impact-your-gut-health/

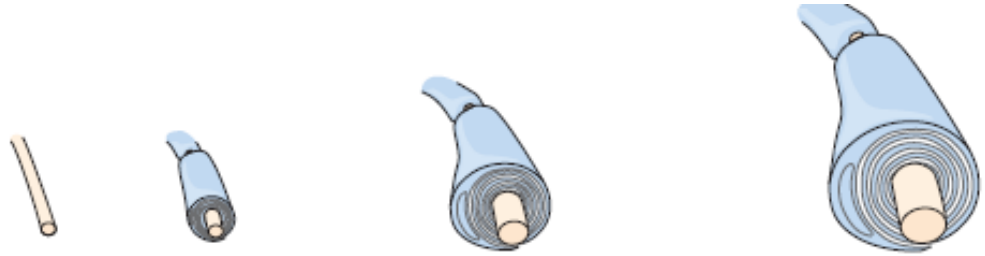
DRGs



Nerve fiber classification

	Muscle nerve	Cutaneous nerve[2]	Fiber diameter (μm)	Conduction velocity (m/s)
Myelinated				
Large diameter	I	Aα	12–20	72–120
Medium diameter	II	Aβ	6–12	36–72
Small diameter	III	Aδ	1–6	4–36
Unmyelinated	IV	C	0.2–1.5	0.4–2.0

[1]Sensory fibers from muscle are classified according to their diameter, whereas those from the skin are classified by conduction velocity.
[2]The types of receptors innervated by each type of fiber are listed in Table 22–2.



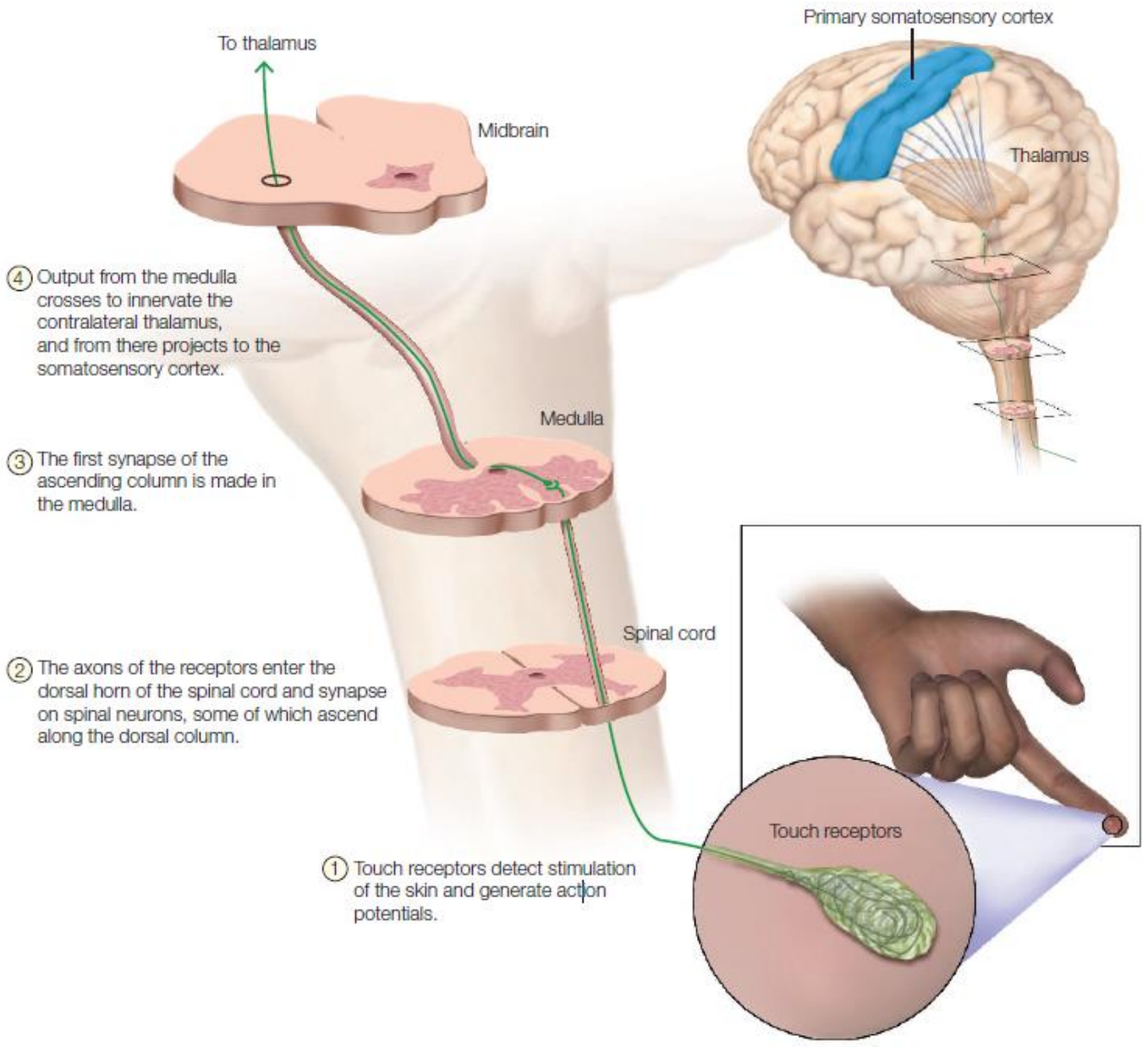
Axon diameter (μm)	1	5	12	20
Conduction velocity (m/s)	1	30	72	120

Receptors, Fibers and Modalities

Receptor type	Fiber group[1]	Fiber name	Modality
Cutaneous and subcutaneous mechanoreceptors			Touch
Meissner corpuscle	Aα,β	RA1	Stroking, flutter
Merkel disk receptor	Aα,β	SA1	Pressure, texture
Pacinian corpuscle[2]	Aα,β	RA2	Vibration
Ruffini ending	Aα,β	SA2	Skin stretch
Hair-tylotrich, hair-guard	Aα,β	G1, G2	Stroking, fluttering
Hair-down	Aδ	D	Light stroking
Field	Aα,β	F	Skin stretch
C mechanoreceptor	C		Stroking, erotic touch
Thermal receptors			Temperature
Cool receptors	Aδ	III	Skin cooling (<25°C [77°F])
Warm receptors	C	IV	Skin warming (>35°C [95°F])
Heat nociceptors	Aδ	III	Hot temperature (>45°C [113°F])
Cold nociceptors	C	IV	Cold temperature (<5°C [41°F])
Nociceptors			Pain
Mechanical	Aδ	III	Sharp, pricking pain
Thermal-mechanical (heat)	Aδ	III	Burning pain
Thermal-mechanical (cold)	C	IV	Freezing pain
Polymodal	C	IV	Slow, burning pain
Muscle and skeletal mechanoreceptors			Limb proprioception
Muscle spindle primary	Aα	Ia	Muscle length and speed
Muscle spindle secondary	Aβ	II	Muscle stretch
Golgi tendon organ	Aα	Ib	Muscle contraction
Joint capsule receptors	Aβ	II	Joint angle
Stretch-sensitive free endings	Aδ	III	Excess stretch or force

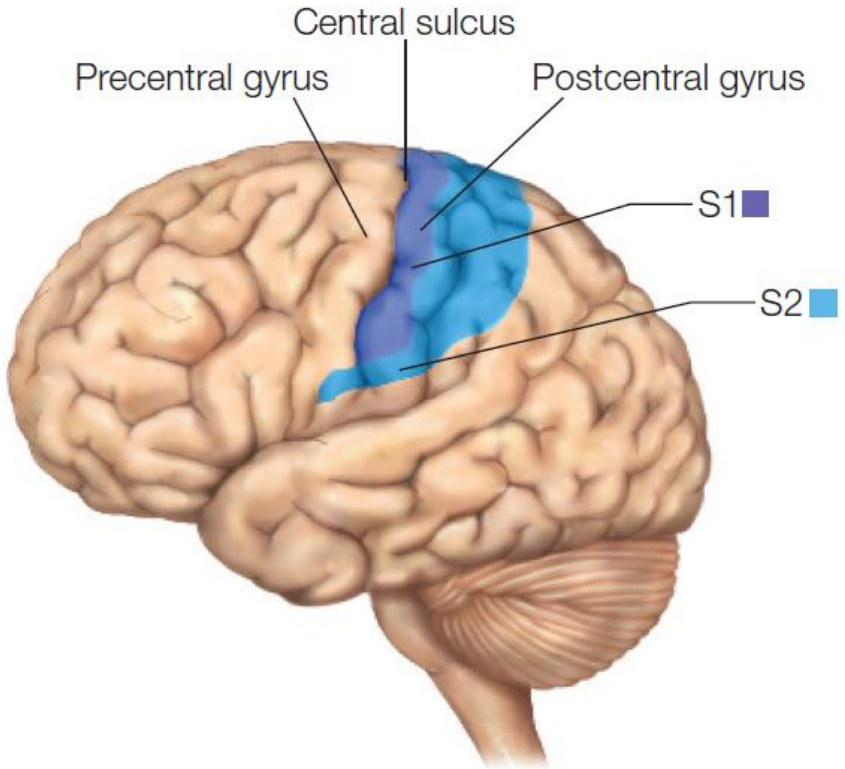
[1]See Table 22–1

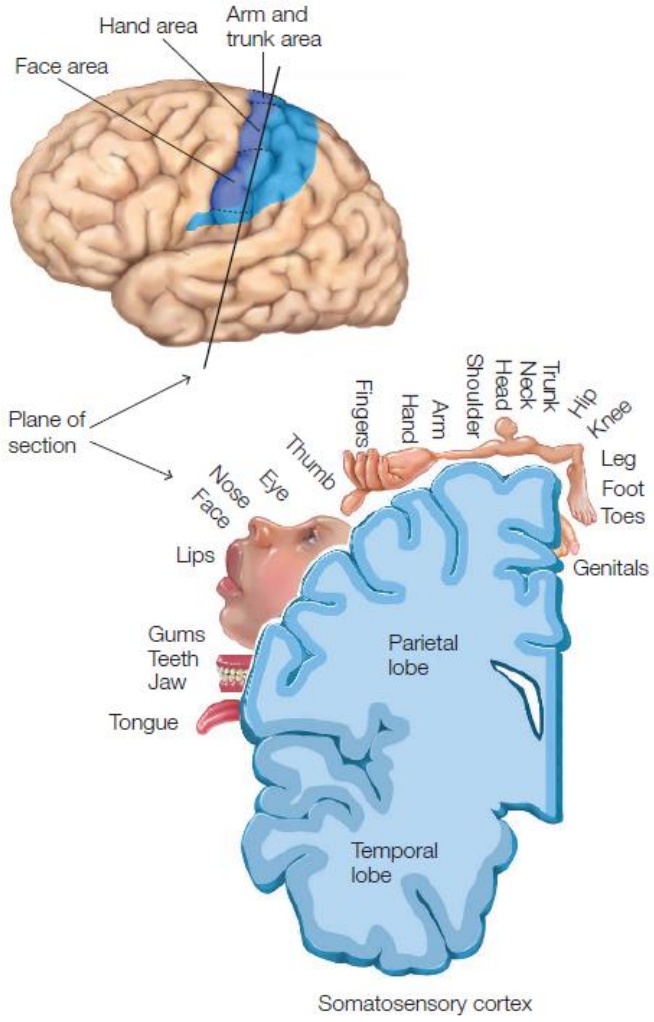
From periphery to brain



Thalamus:
Door to conciousness

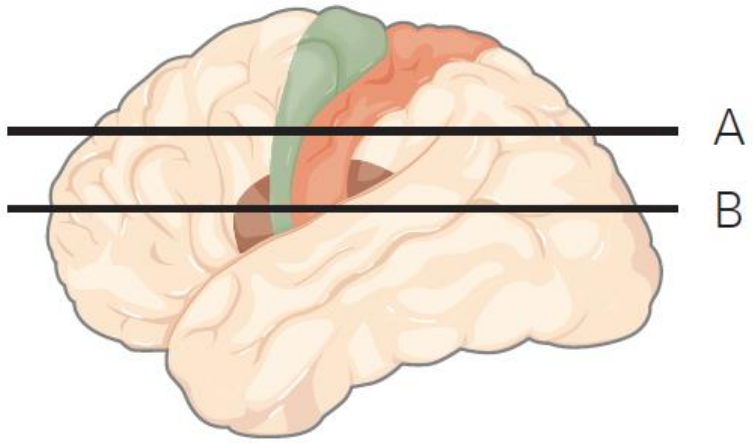
The primary somatosensory cortex

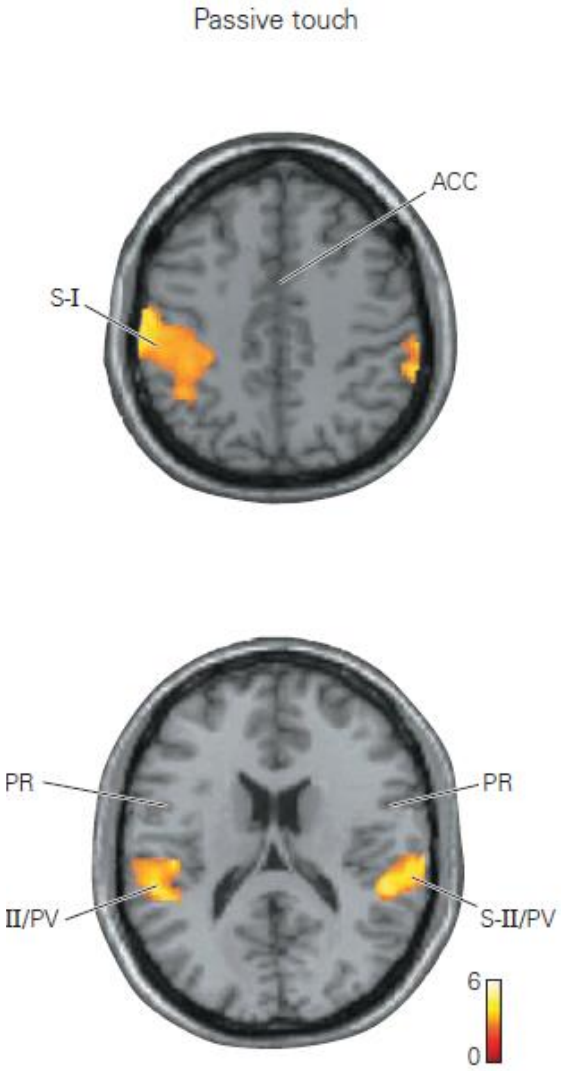




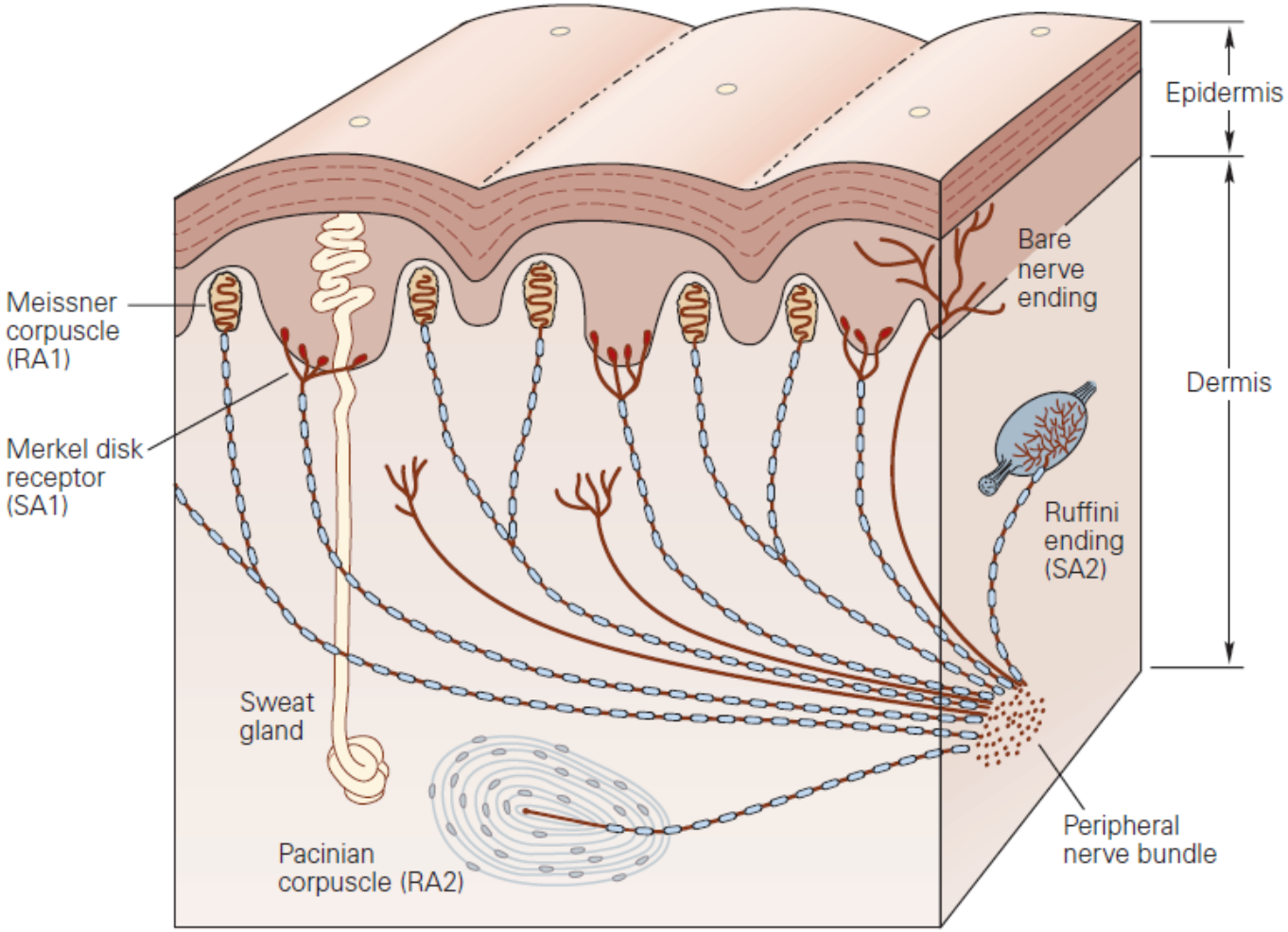
Homunculus

Touch





How does „touch“ work?



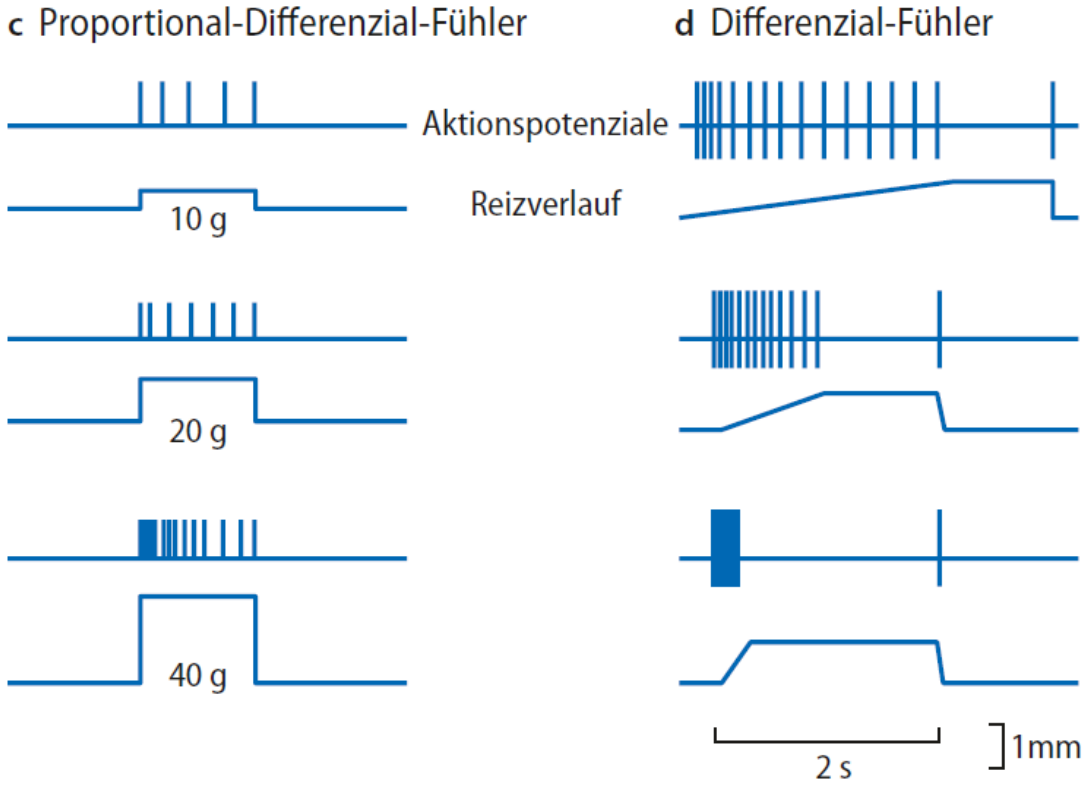
Cutaneous mechanoreceptor systems

	Type 1		Type 2	
	SA1	RA1[1]	SA2	RA2[2]
Receptor	Merkel cell	Meissner corpuscle	Ruffini ending	Pacinian corpuscle
Location	Tip of epidermal sweat ridges	Dermal papillae (close to skin surface)	Dermis	Dermis (deep tissue)
Axon diameter (μm)	7–11	6–12	6–12	6–12
Conduction velocity (ms)	40–65	35–70	35–70	35–70
Best stimulus	Edges, points	Lateral motion	Skin stretch	Vibration
Response to sustained indentation	Sustained with slow adaptation	None	Sustained with slow adaptation	None
Frequency range (Hz)	0–100	1–300		5–1,000
Best frequency (Hz)	5	50		200
Threshold for rapid indentation or vibration (best) (μm)	8	2	40	0.01

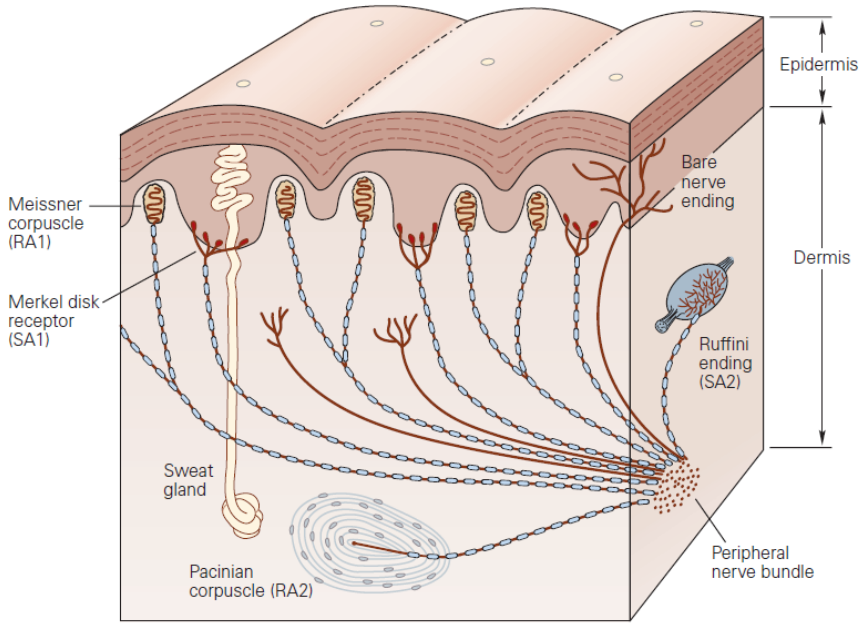
[1]Also called RA, QA, or FA1.
[2]Also called PC or FA2.
RA1, rapidly adapting type 1; **RA2**, rapidly adapting type 2; **SA1**, slowly adapting type 1; **SA2**, slowly adapting type 2.

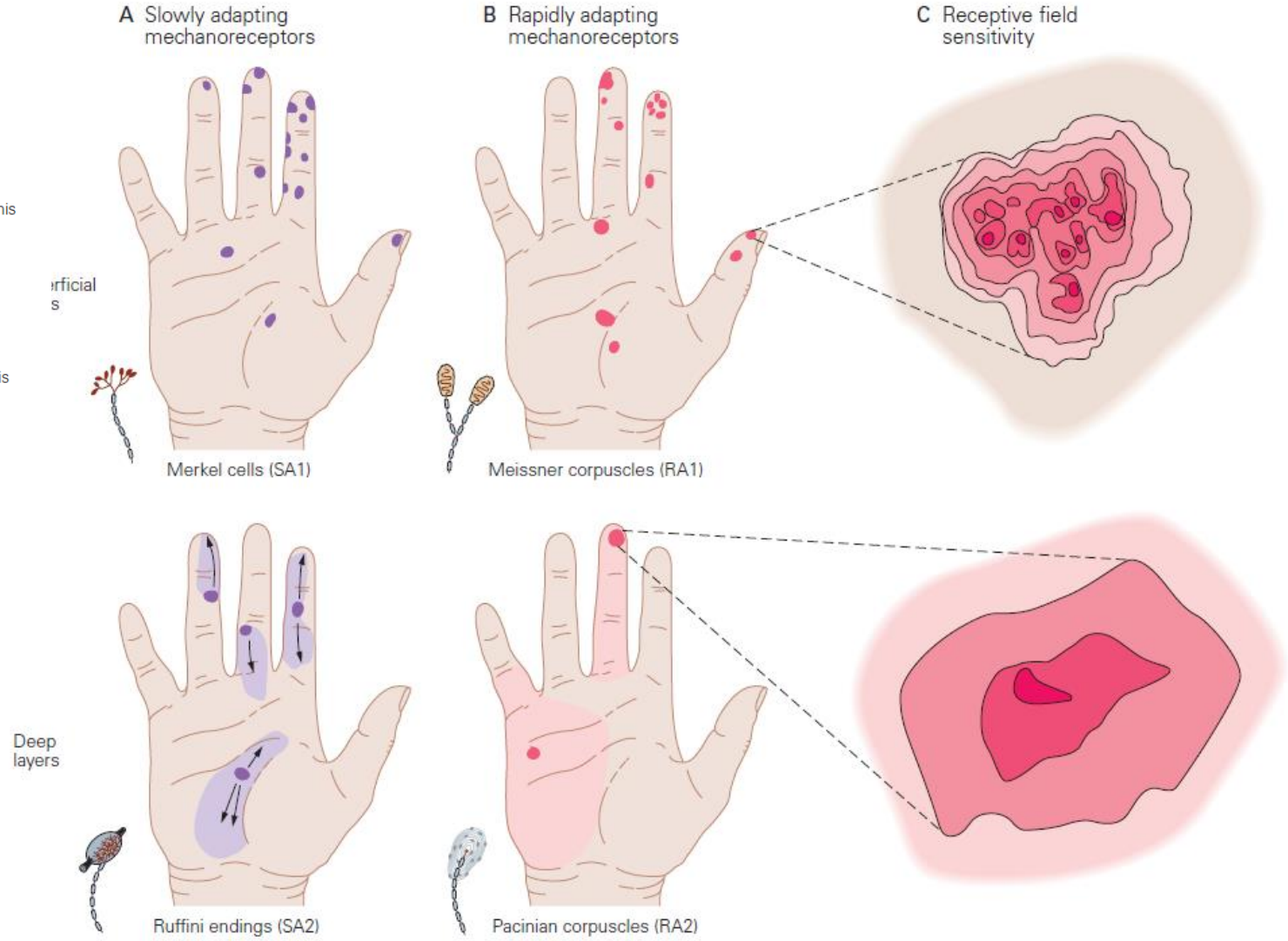
Slow adapting
Proportional-Differential

Rapid adaption
Differential

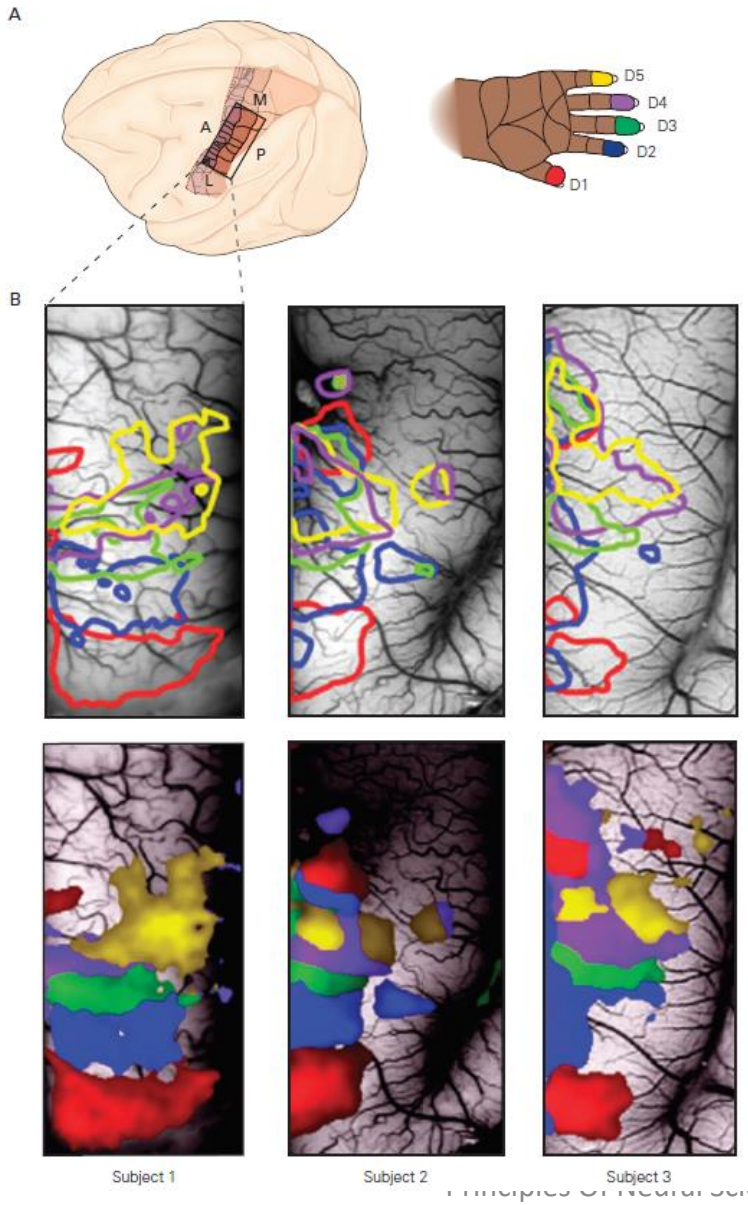


Receptive fields in the skin

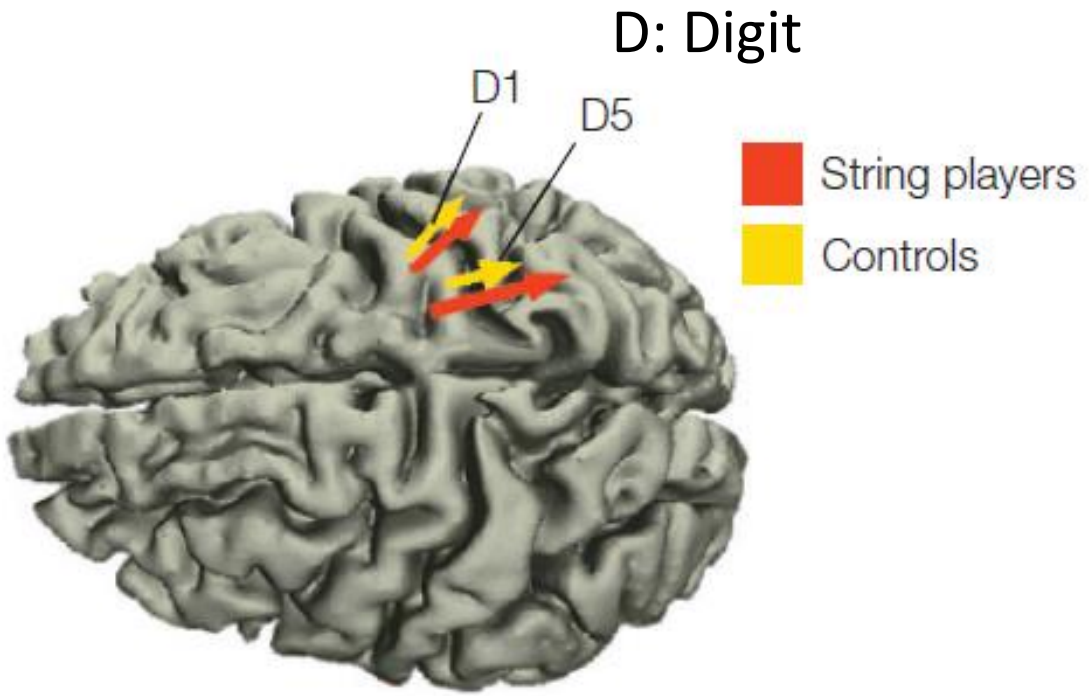


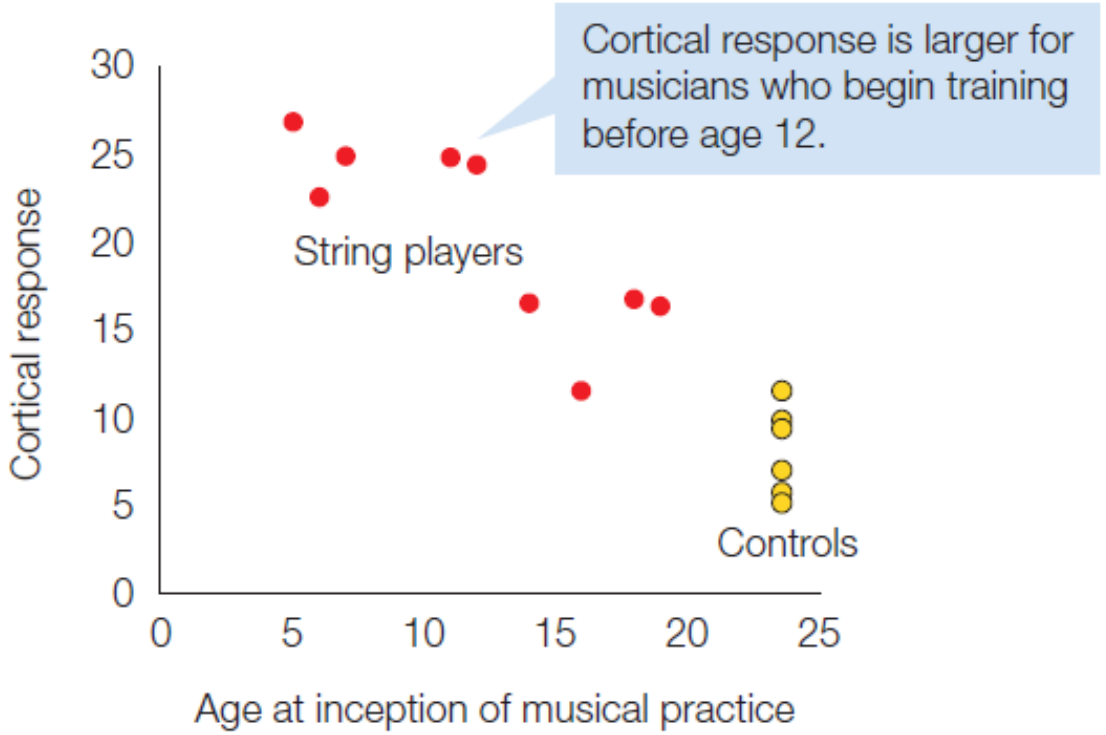


Digit representation follows a common plan



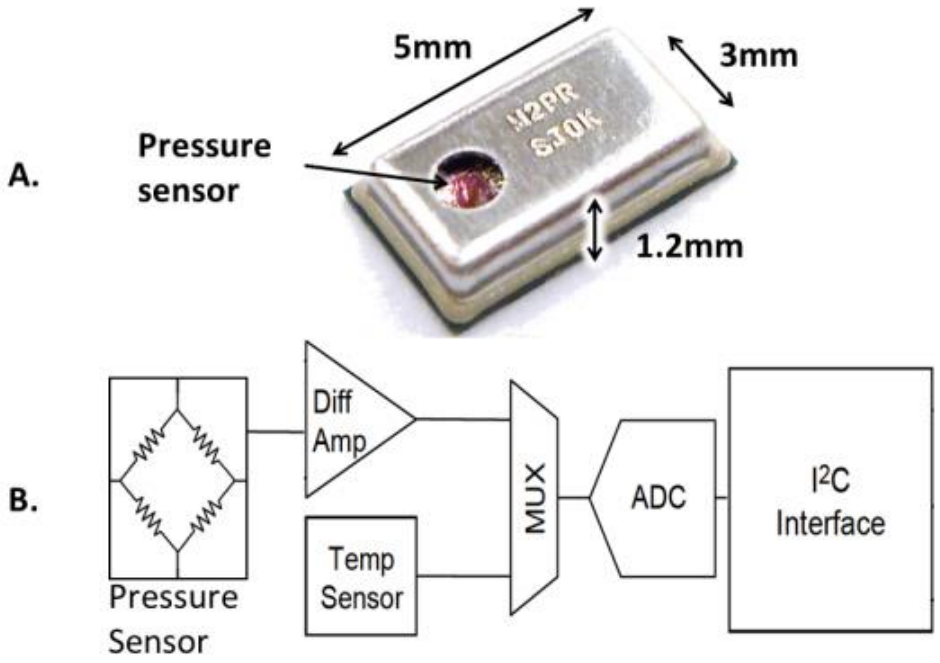
Plasticity in the somatosensory cortex





Elbert et al., 1995

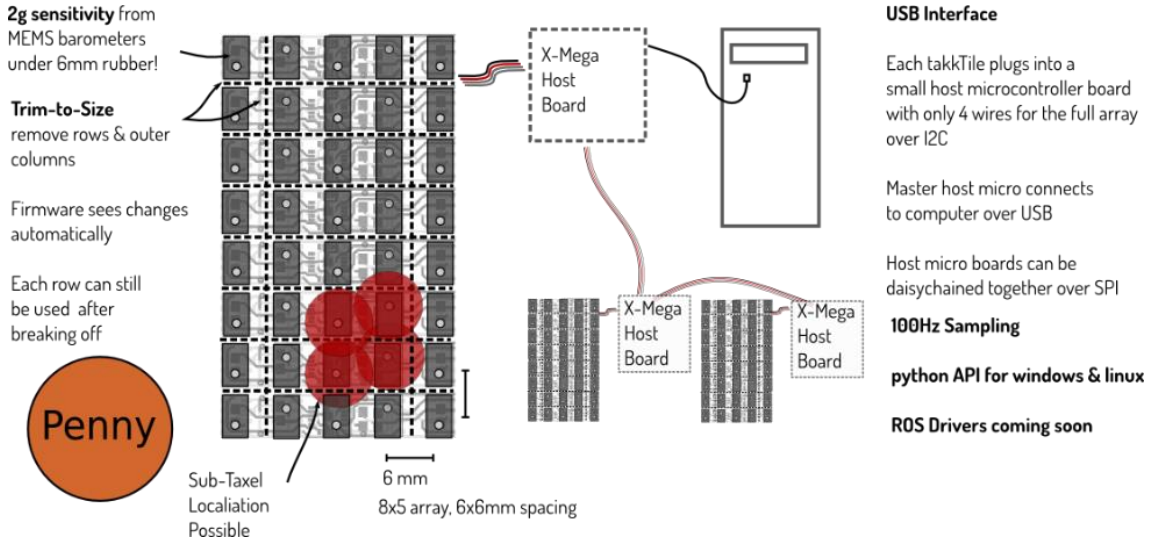
Tactile sensing in robots



MEMS barometer

Inexpensive and Easily Customized Tactile Array Sensors using MEMS Barometers Chips

Yaroslav Tenzer, Leif P. Jentoft, Robert D. Howe
Harvard School of Engineering and Applied Sciences



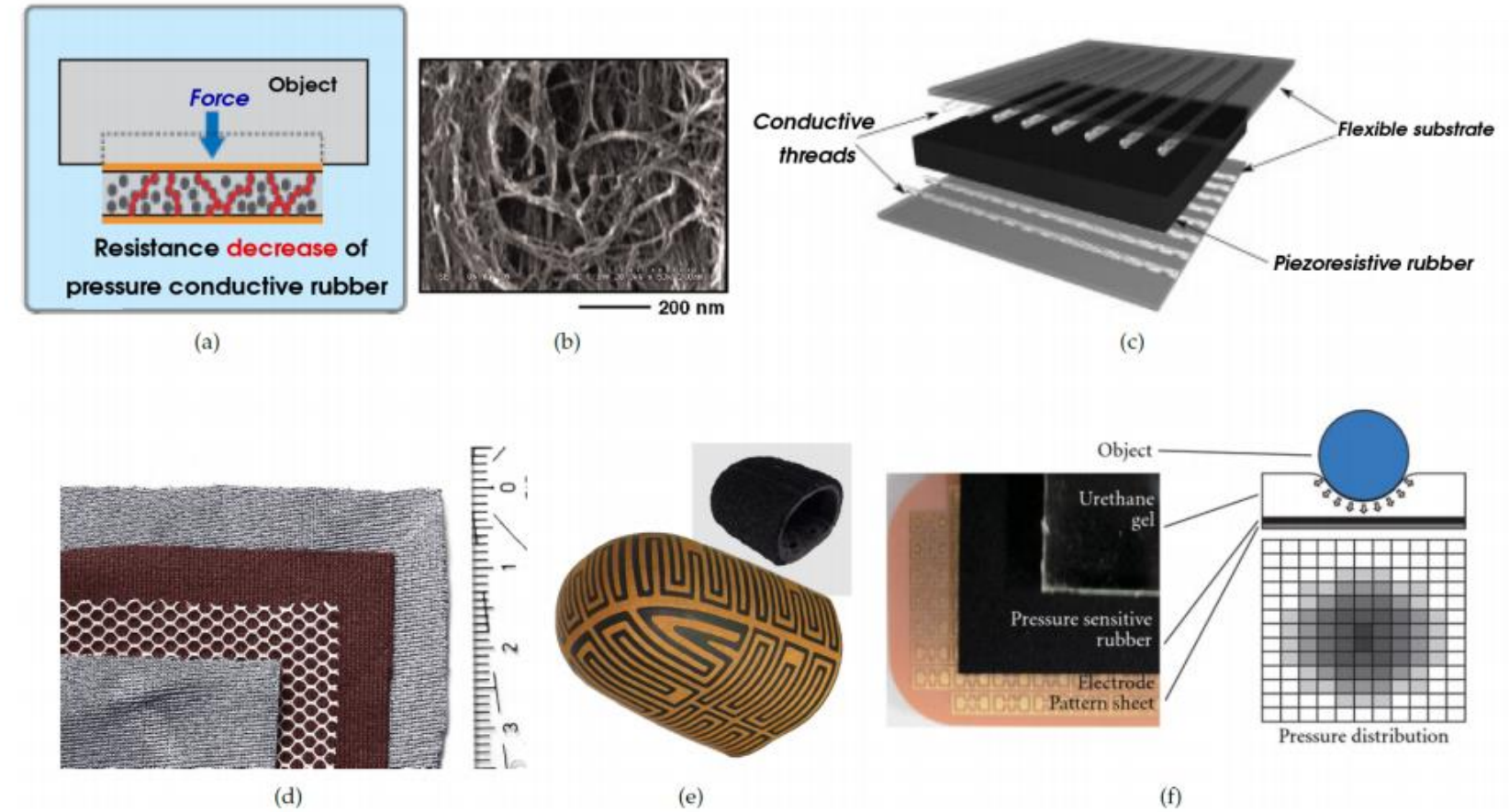
http://www.takktile.com/main:plans

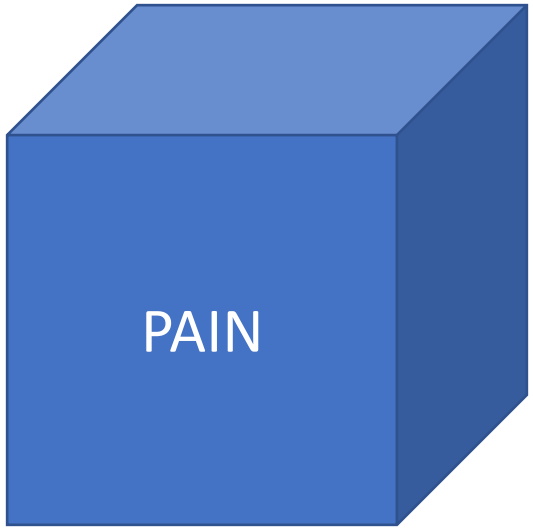
Tactile sensing in robots

Tactile sensing in dexterous robot hands – review

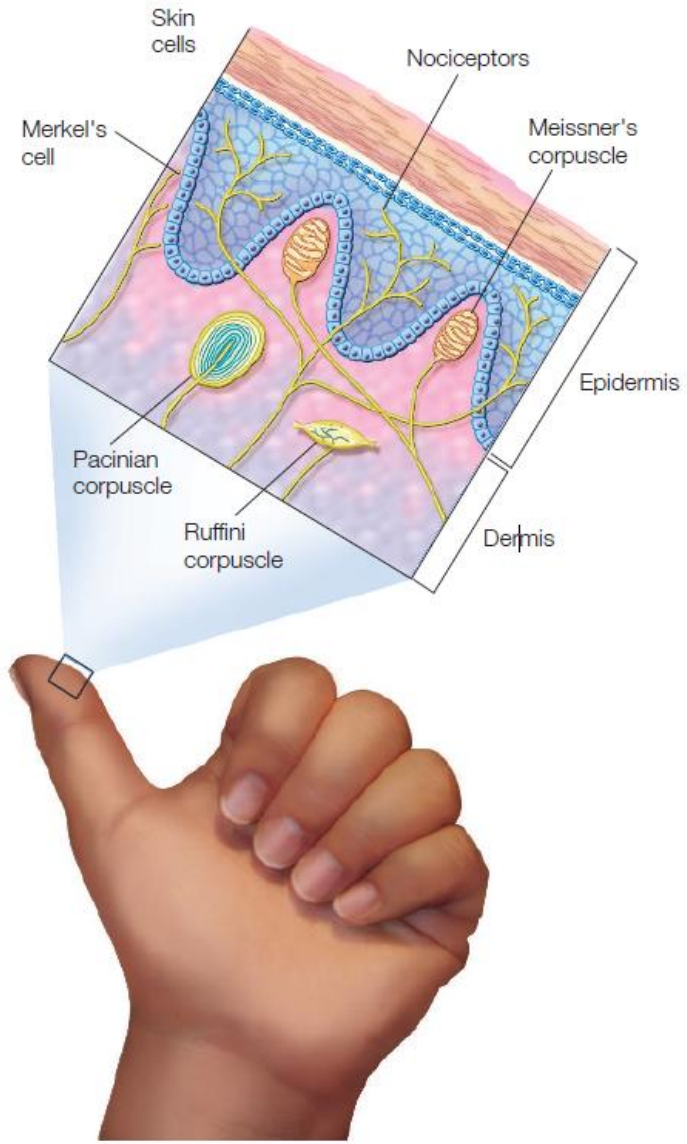
Zhanat Kappassov[a,*], Juan-Antonio Corrales[b], Véronique Perdereau[a]

[a]Institute of Intelligent Systems and Robotics, University of Pierre and Marie Curie, CC 173 - 4 Place Jussieu 75005, Paris, France
[b]Institut Francais de Mecanique Avancee, Campus de Clermont-Ferrand les Cezeaux BP265 63175 AUBIERE Cedex, France




PAIN

Somatosensation



Pain

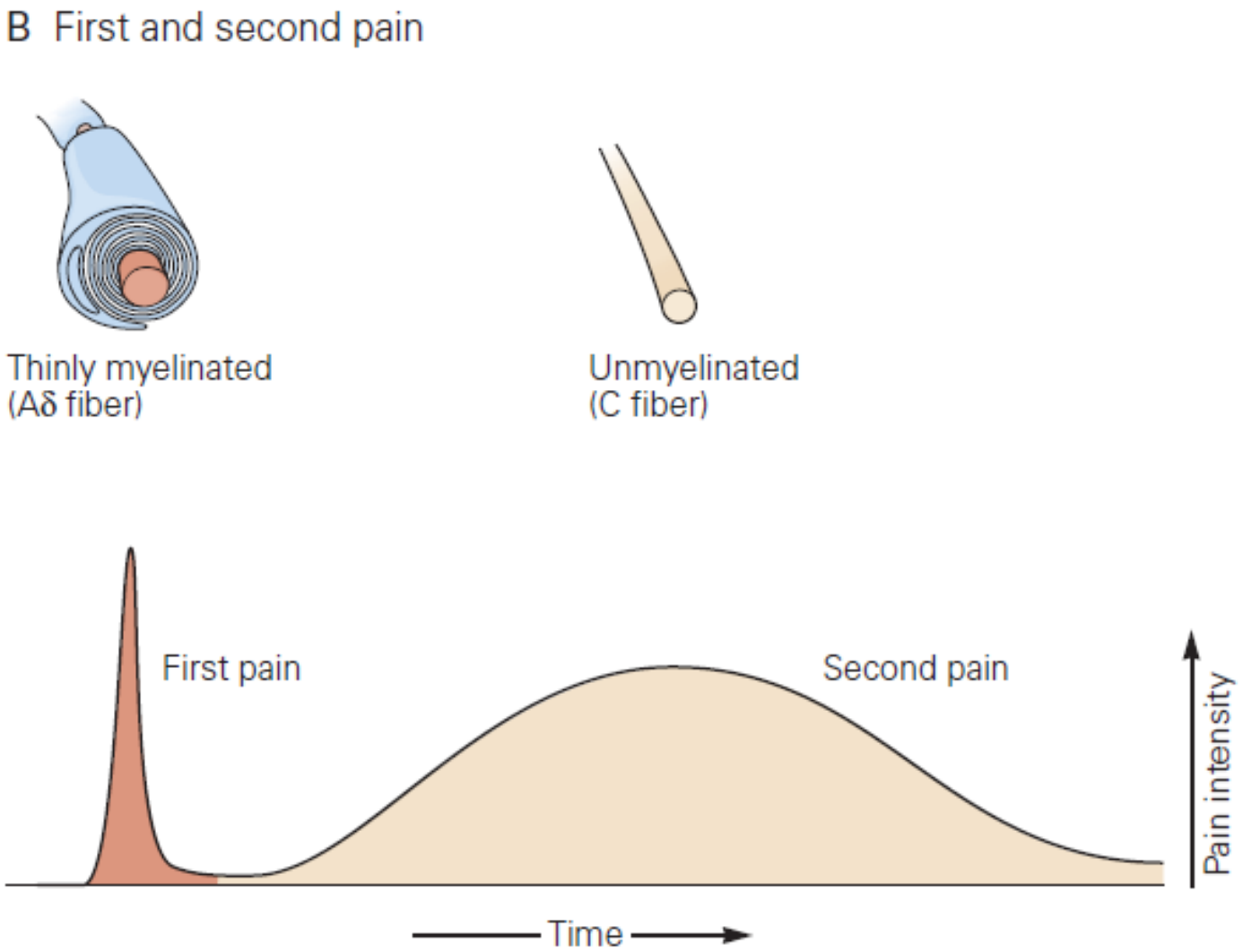
PAIN PERCEPTION IS CONTEXT AND INDIVIDUAL DEPENDENT

ACUTE

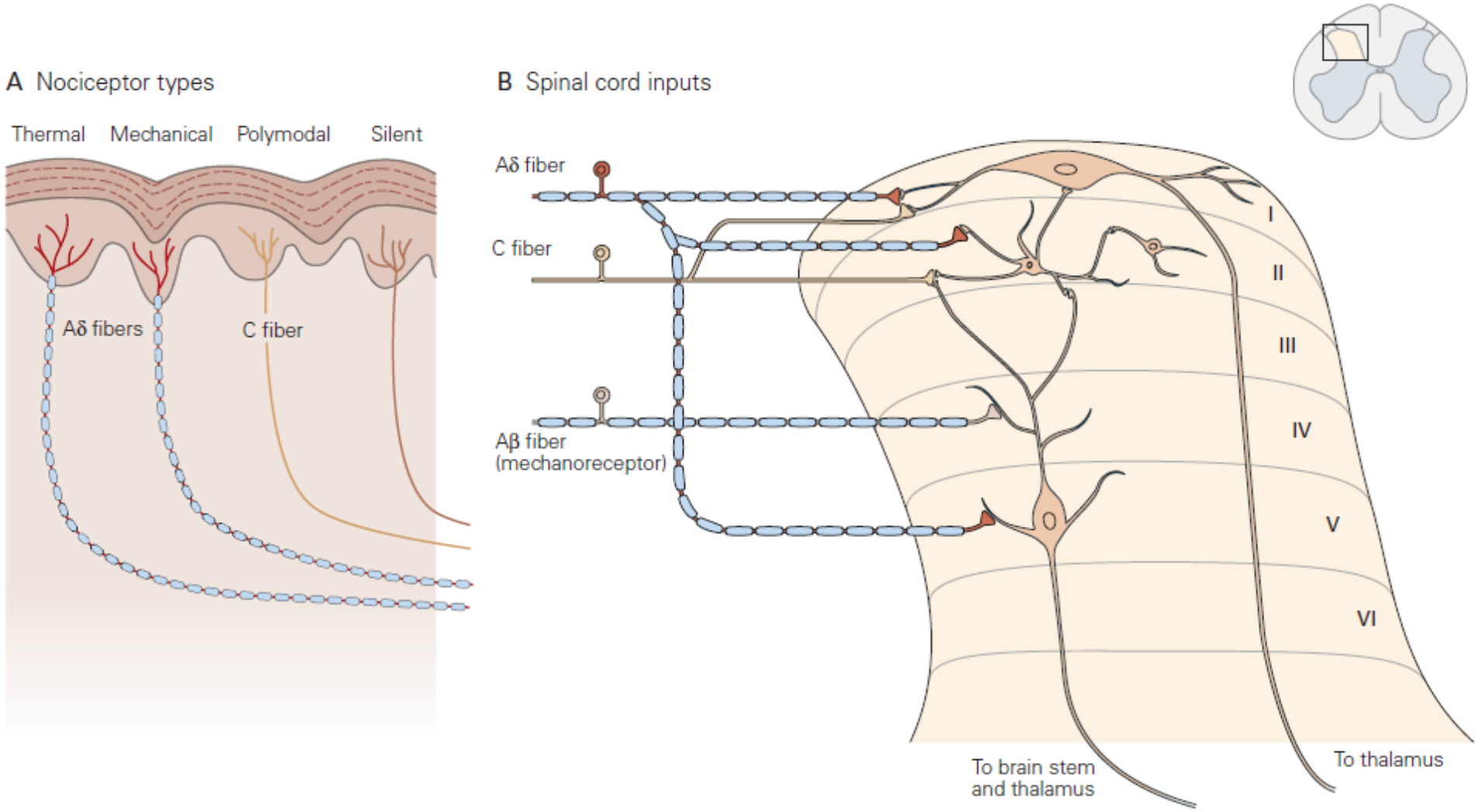
PERSISTANT

CHRONIC

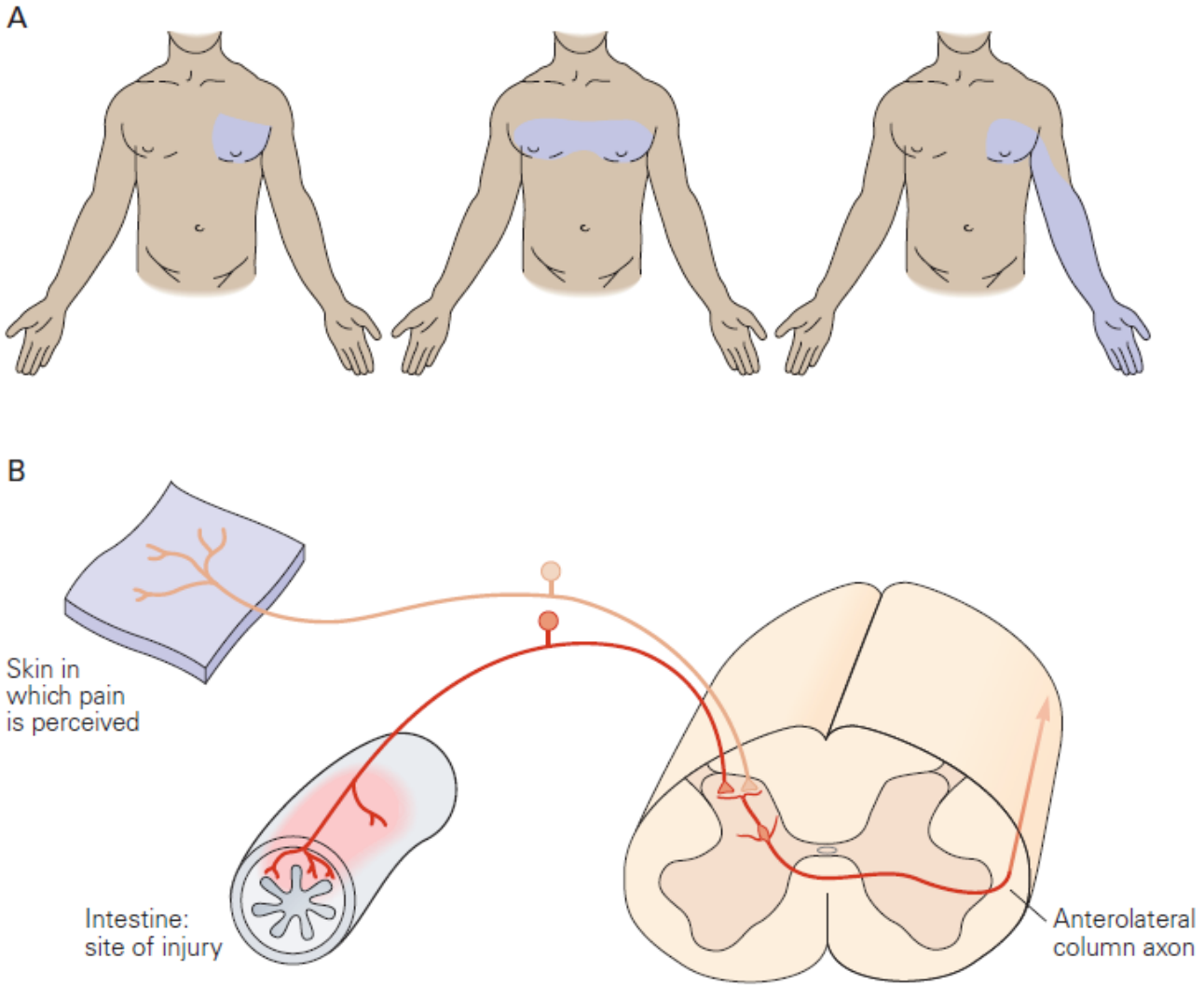
How pain is elicited



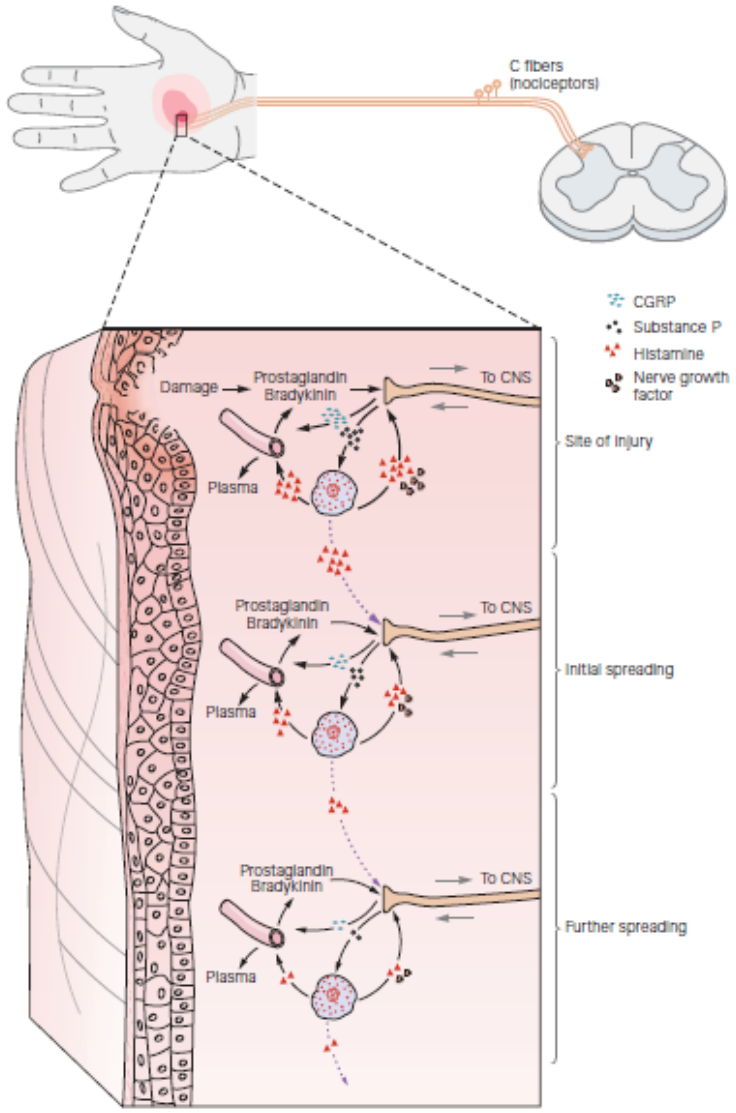
Nociceptor types



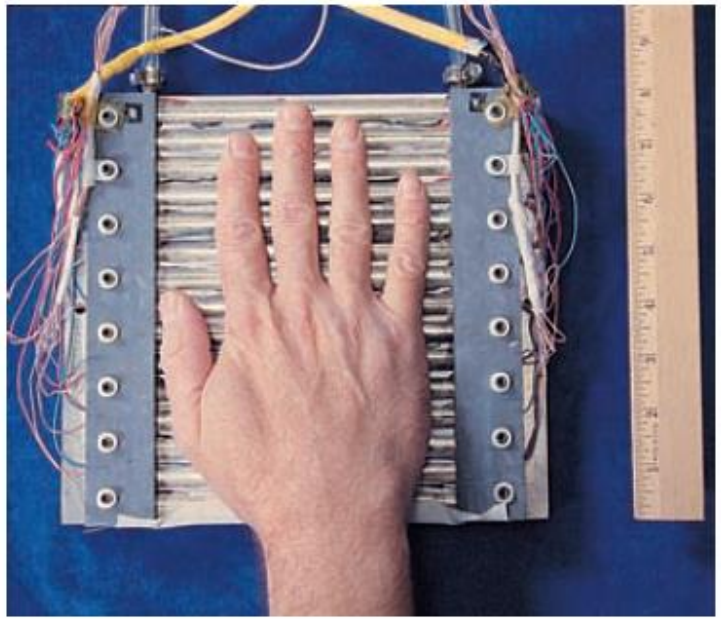
Referred pain

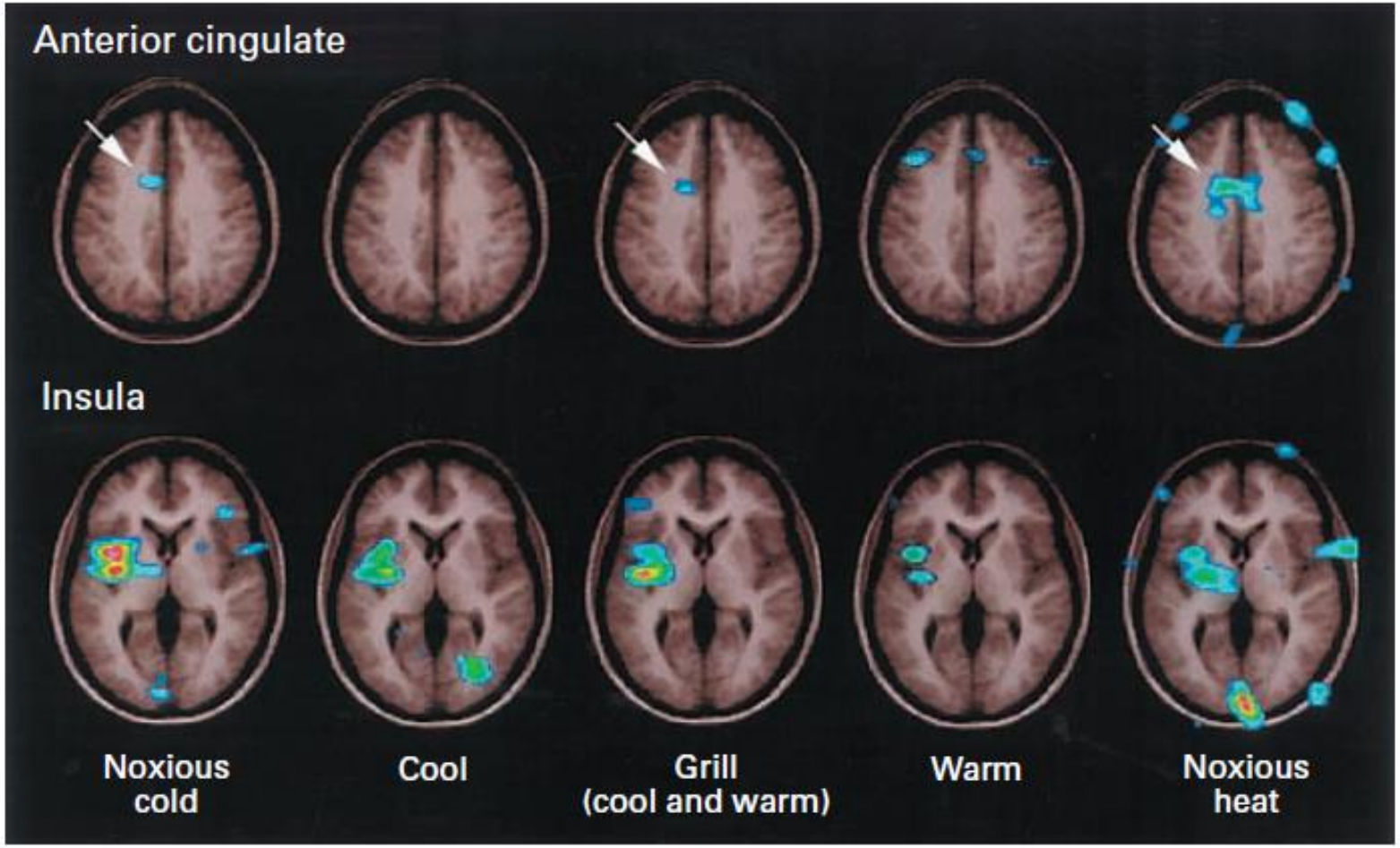


Neurogenic inflammation

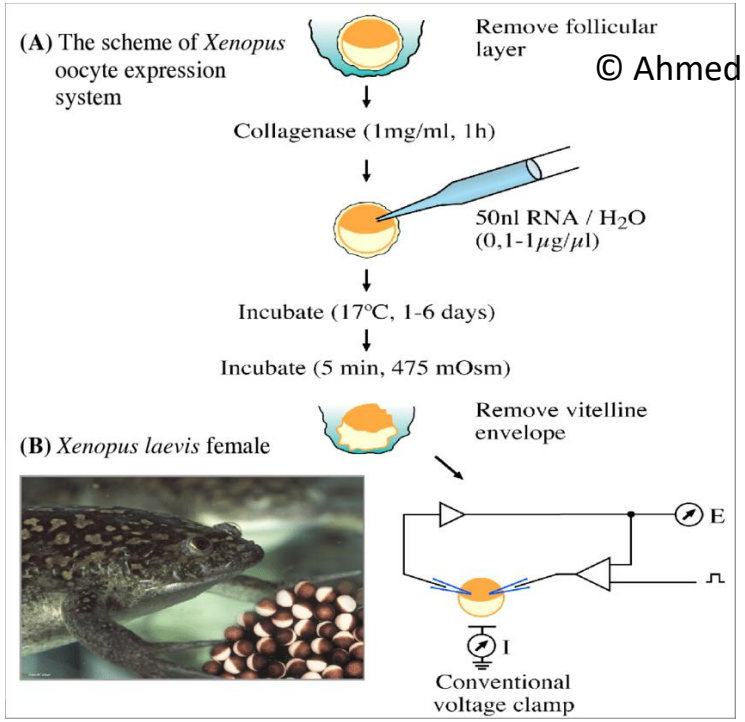


Thunberg‘s illusion



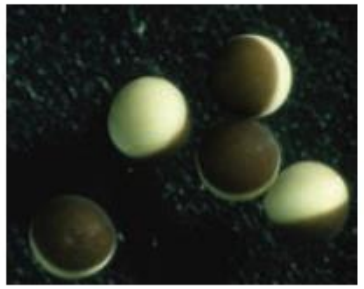


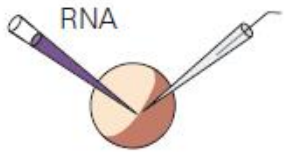
Electrophysiology in Xenopus oocytes

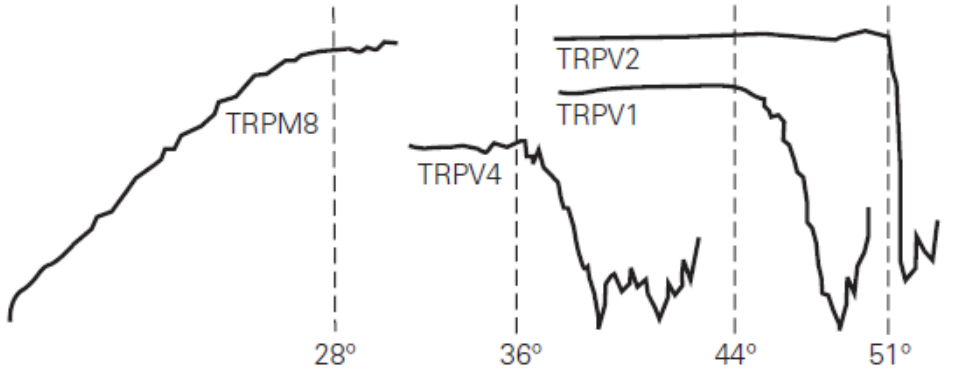


© Ahmed Al-Sabi

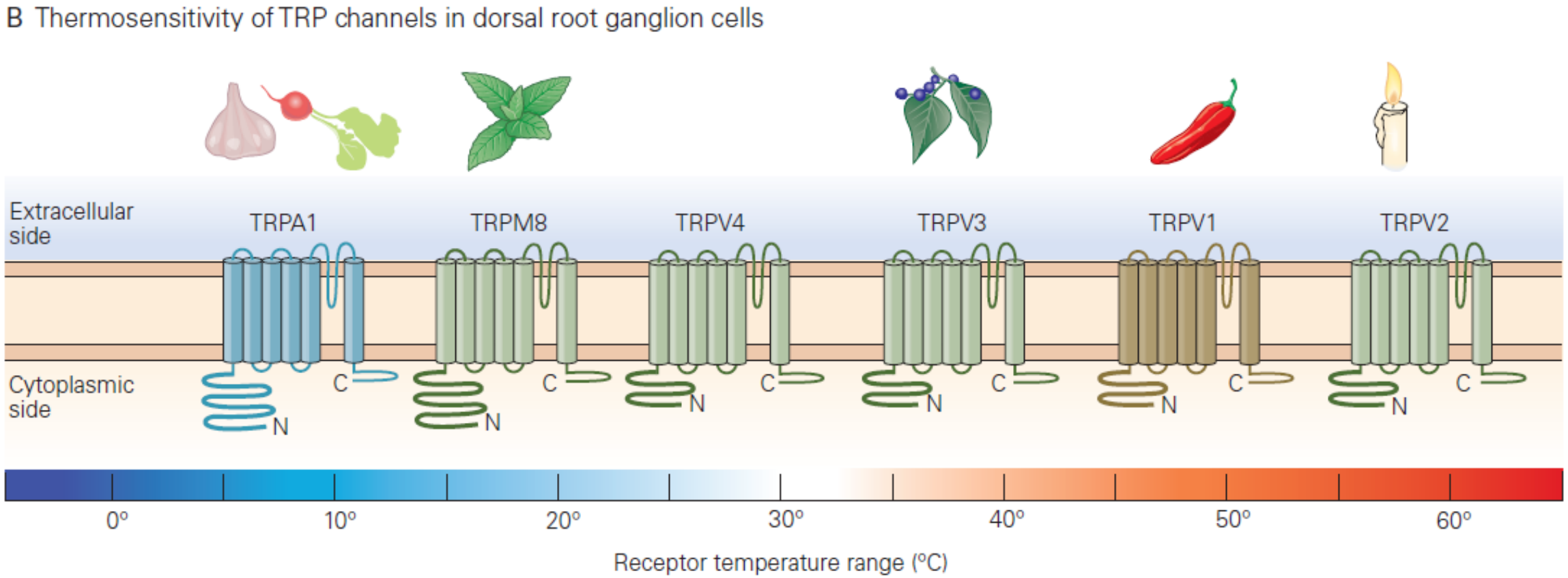
A Thermosensitivity of TRP channels in *Xenopus* oocytes







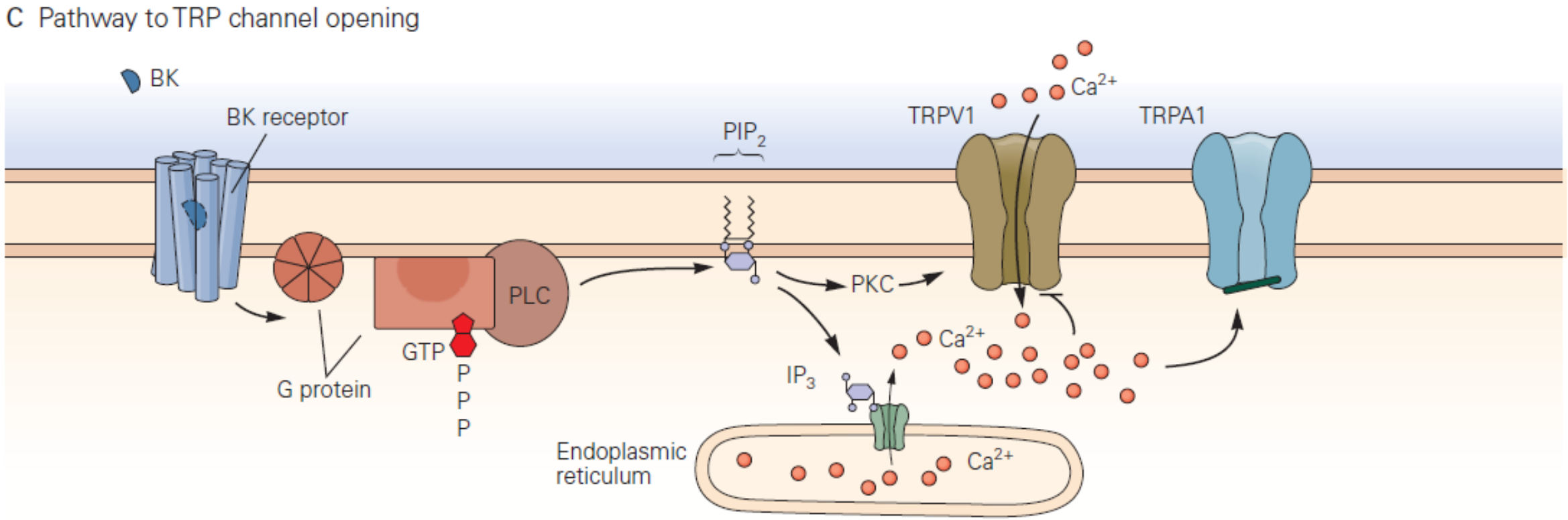
Thermosensitivity of TRP channels



Pathways

Bradykinin

Sensitizing TRP channels



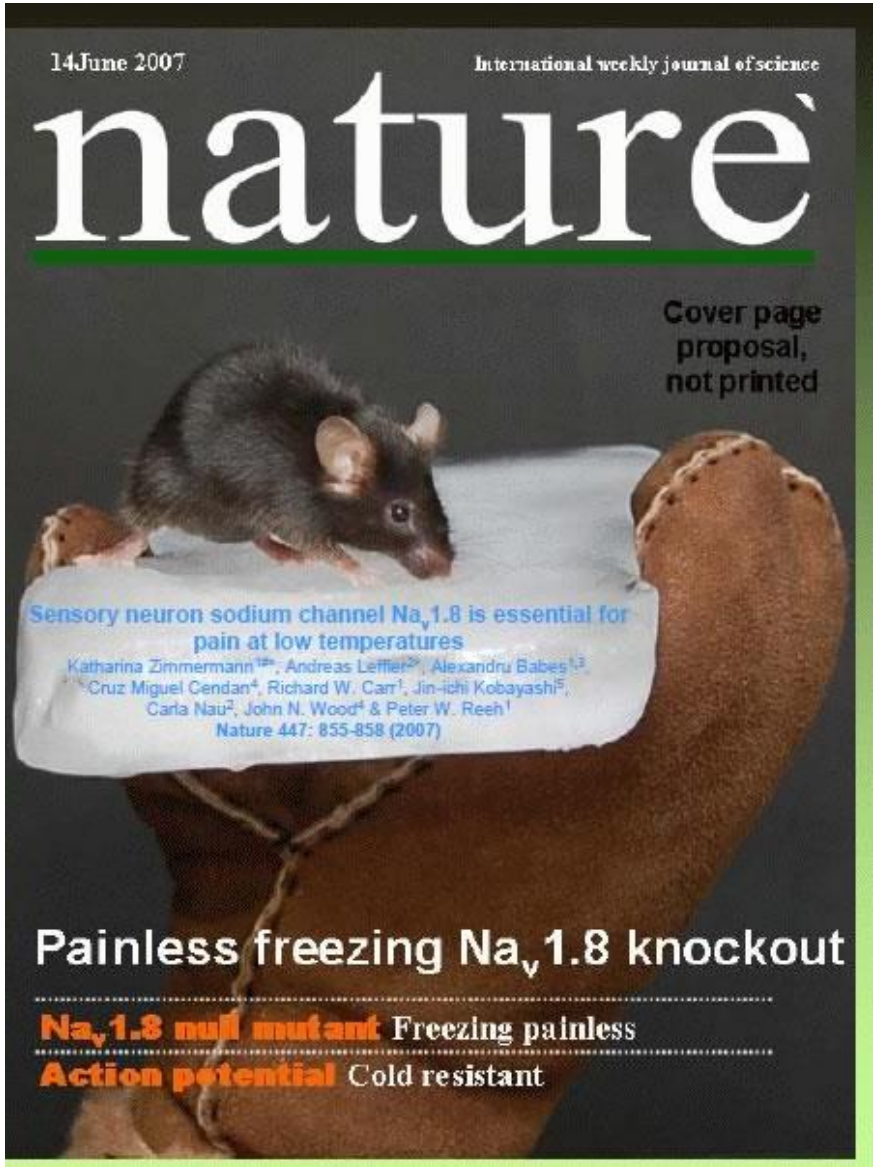
Navs and cold perception

Published: 14 June 2007

Sensory neuron sodium channel $Na_v1.8$ is essential for pain at low temperatures

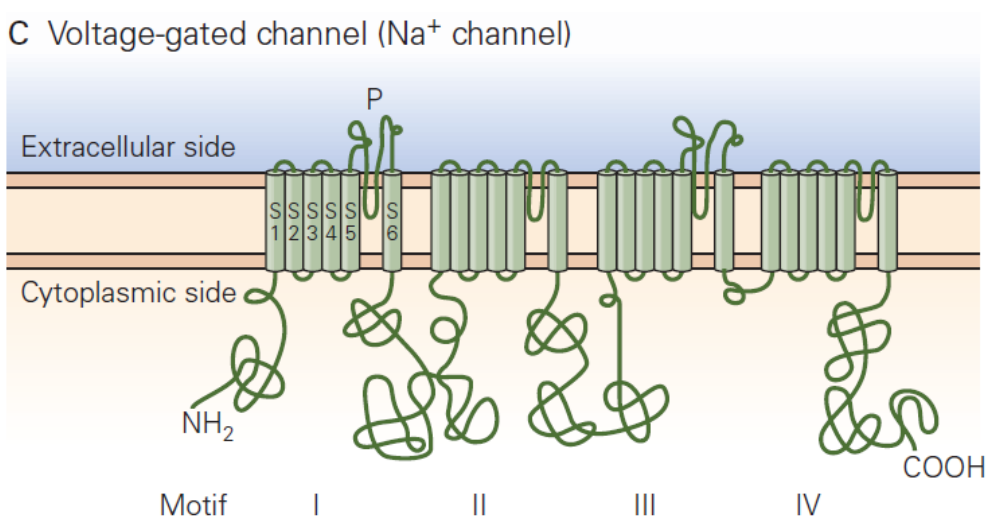
Katharina Zimmermann ✉, Andreas Leffler, Alexandru Babes, Cruz Miguel Cendan, Richard W. Carr, Jin-ichi Kobayashi, Carla Nau, John N. Wood & Peter W. Reeh

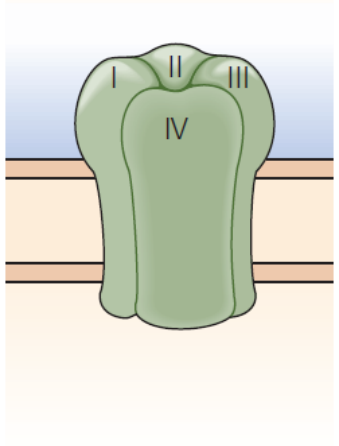
Nature **447**, 856–859 (2007) | Cite this article

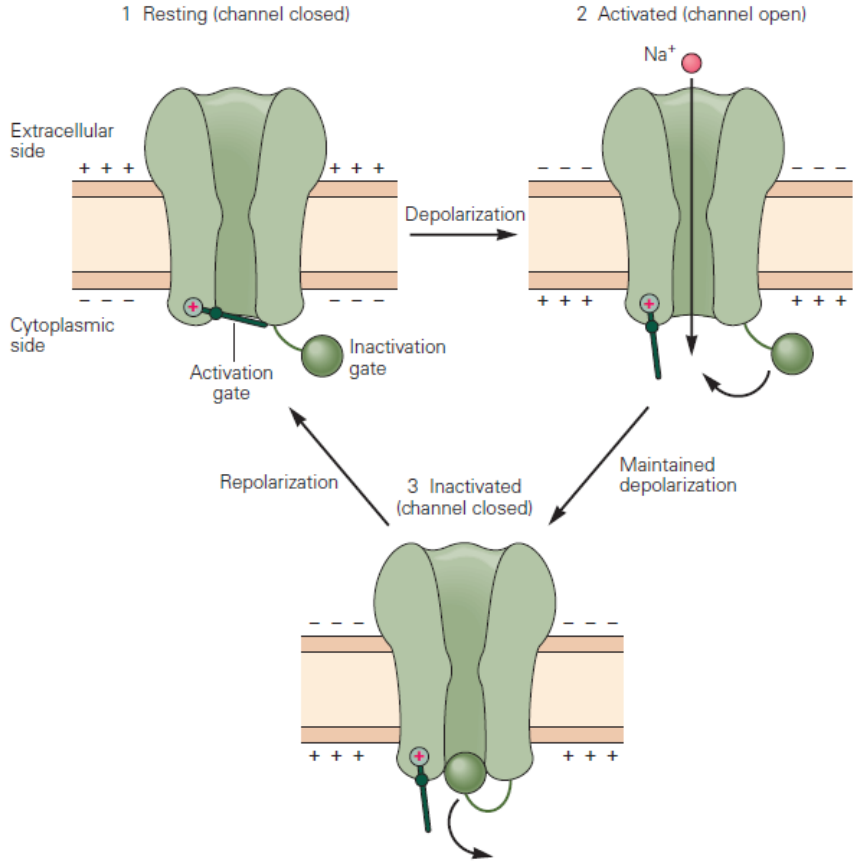


Congenital insensivity to pain (CIP)

Very often defects in SCN9A (Nav1.7)

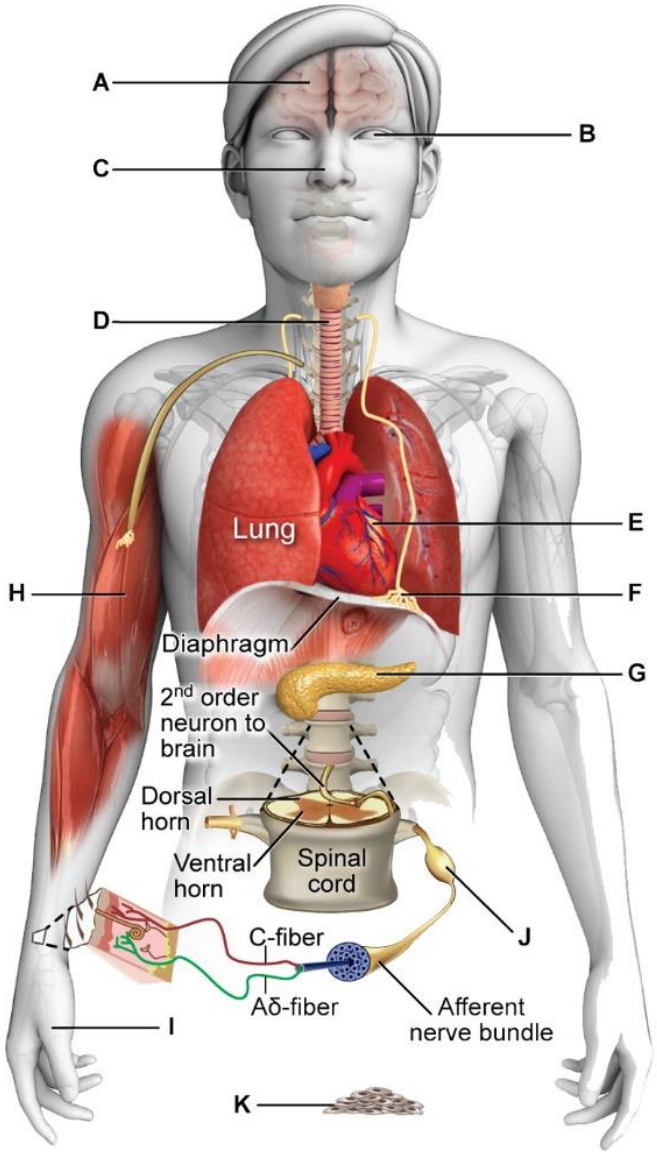






→ Lack of Nav1.7 leads to no pain experience

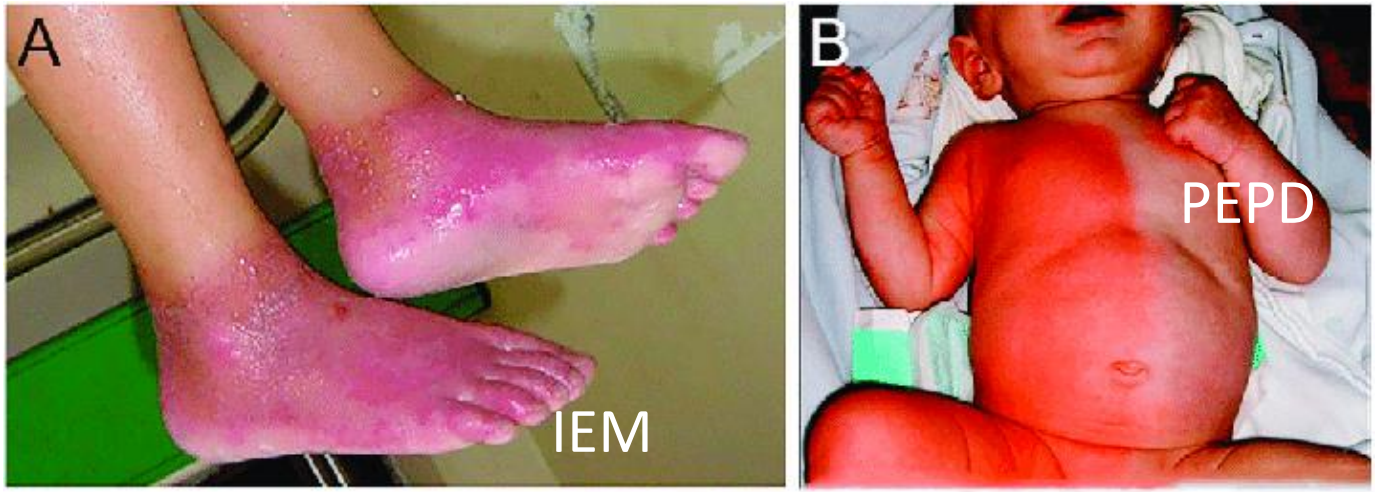
Voltage-gated sodium channels

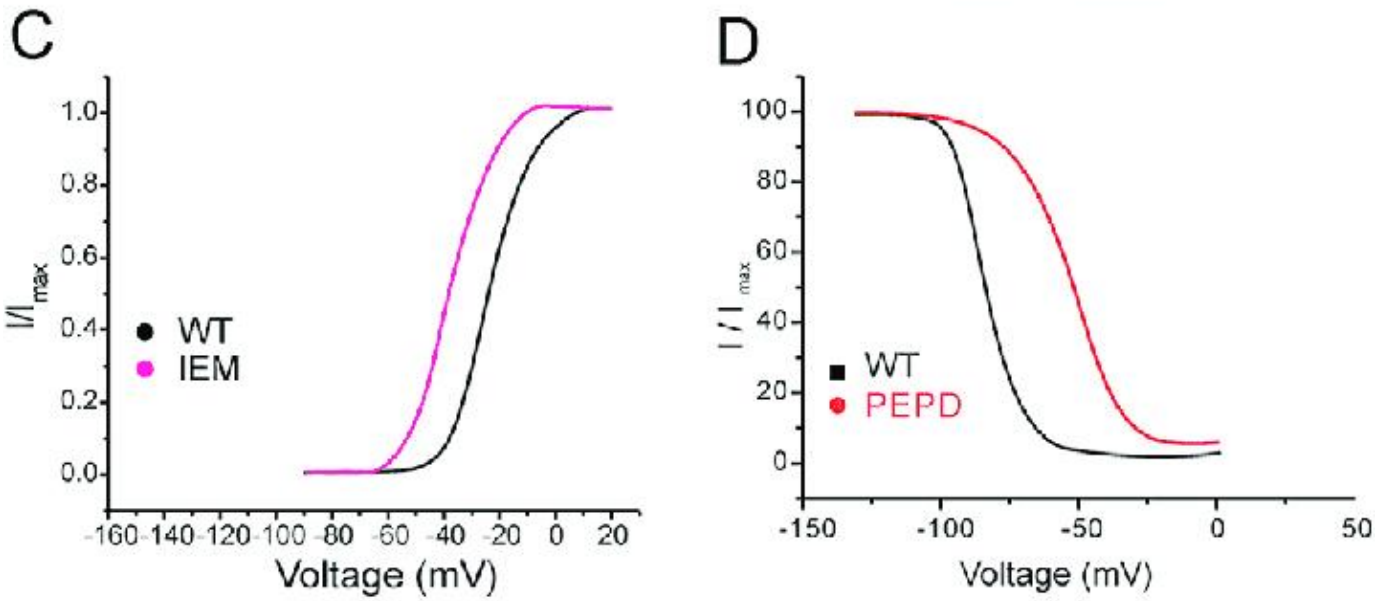


	Tissue	Na_v Subtype	Effect of Na_v Dysfunction on Physiology
A	Central nervous system	1.1, 1.2, 1.3, 1.6	Epilepsy, migraine, autism, ataxia[36]
B	Retina	1.8, 1.9	Altered visual processing[62]
C	Olfactory sensory neurons	1.7	Anosmia[40,42]
D	Sensory neurons and vagal sensory neurons innervating airways	1.7, 1.8, 1.9	Cough[36,68]
E	Heart muscle	1.5, 1.8	Brugada syndrome, QT syndrome, atrial fibrillation[66,67]
F	Nerves, musculature involved in ventilation	TTX-s Na_vs	Respiratory cessation (TTX poisoning)[69]
G	Pancreatic β-cells	1.7	Diabetes[36]
H	Skeletal muscle	1.4	Hyperkalaemic periodic paralysis, paramyotonia congenita, hypokalaemic periodic paralysis[36]
I	Skin	1.7, 1.8	Pain disorders, paroxysmal itch[37,39]
J	DRG neurons	1.6, 1.7, 1.8, 1.9	Pain disorders, paroxysmal itch[37,39,51]
K	Metastatic cancer cells	1.1-1.9 and β-subunits	Ovarian, cervical, prostate, breast, colon, small cell lung cancer, melanoma, lymphoma[35,70,71]

De Lera-Ruiz and Kraus, J Med Chem 2015

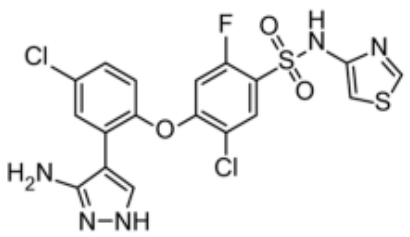
Hyperexcitability of Nav1.7



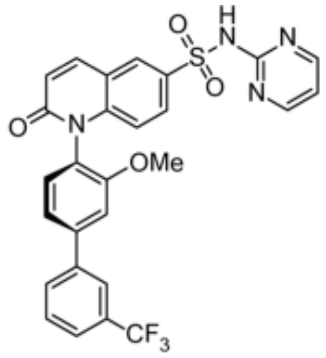


Waxman and Dib-Hajj, 2019

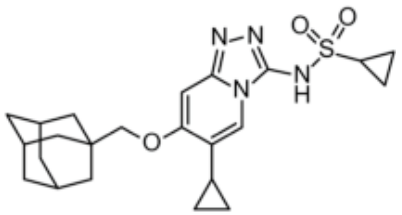
Pain killer development for Nav1.7



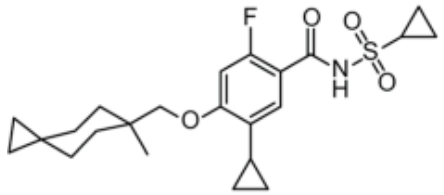
PF-05089771 (1a)
Nav1.7 IC_{50} = 11 nmol/L
Nav1.5 IC_{50} > 10 μmol/L



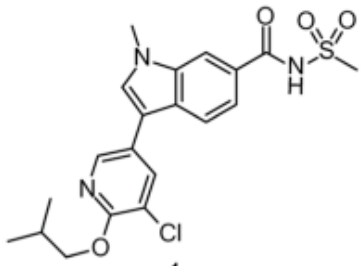
AM-0466 (1b)
Nav1.7 IC_{50} = 21 nmol/L
Nav1.5 IC_{50} > 30 μmol/L



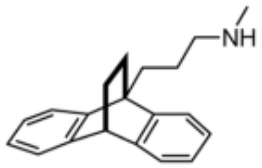
GNE-131 (1c)
Nav1.7 IC_{50} = 3 nmol/L
Nav1.5 IC_{50} = 110 nmol/L



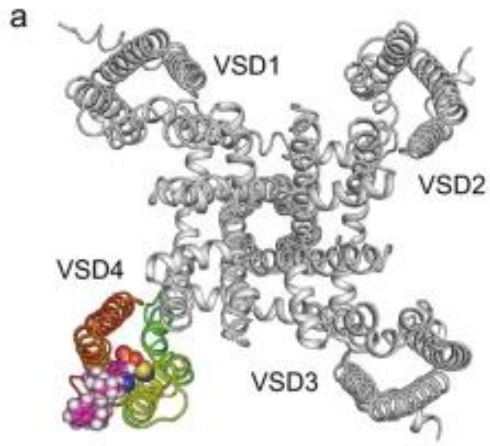
1d
Nav1.7 IC_{50} = 0.6 nmol/L
Nav1.5 IC_{50} = 50 nmol/L

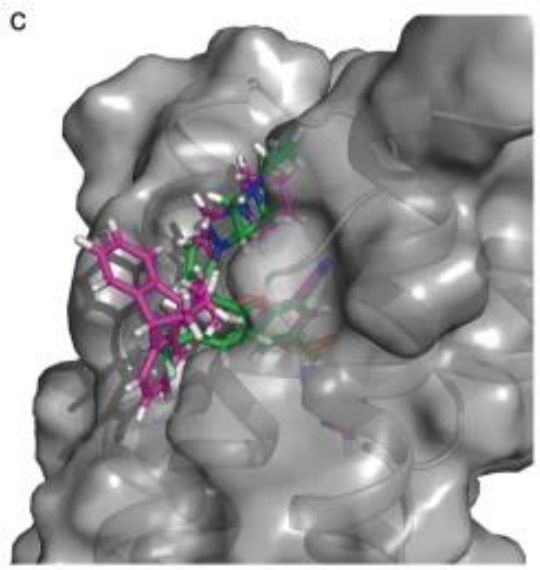


1e
Nav1.7 IC_{50} = 8 nmol/L



Maprotiline
Nav1.7 IC_{50} = 1.51 μmol/L





Article | Published: 17 July 2019

Discovery of aryl sulfonamide-selective Nav1.7 inhibitors with a highly hydrophobic ethanoanthracene core

Jin-tao Wang, Yue-ming Zheng, Yue-ting Chen, Min Gu, Zhao-bing Gao ✉ & Fa-jun Nan ✉

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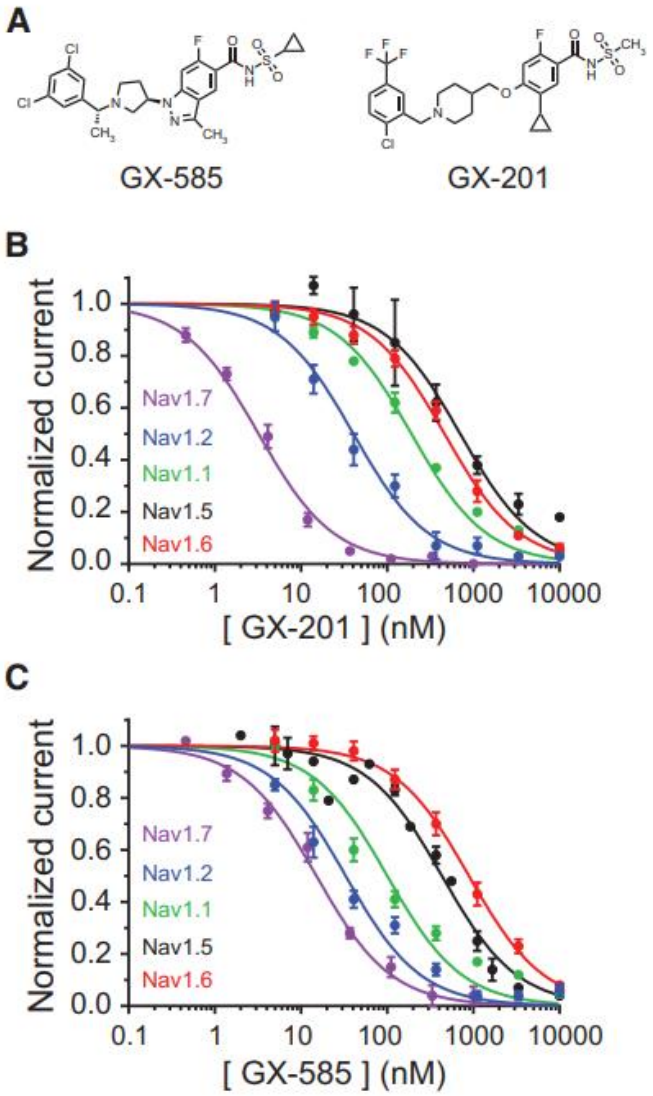
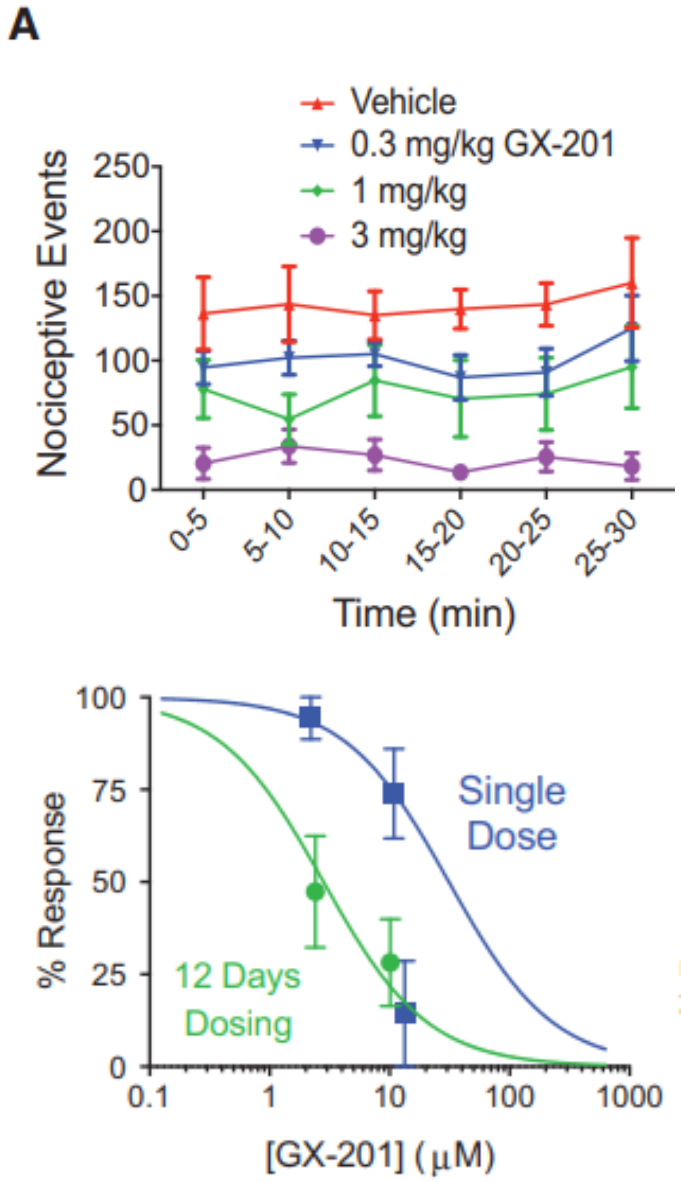
Pain killer II





Cell Reports
Article

Selective $Na_V1.7$ Antagonists with Long Residence Time Show Improved Efficacy against Inflammatory and Neuropathic Pain

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Opioids as pain killer