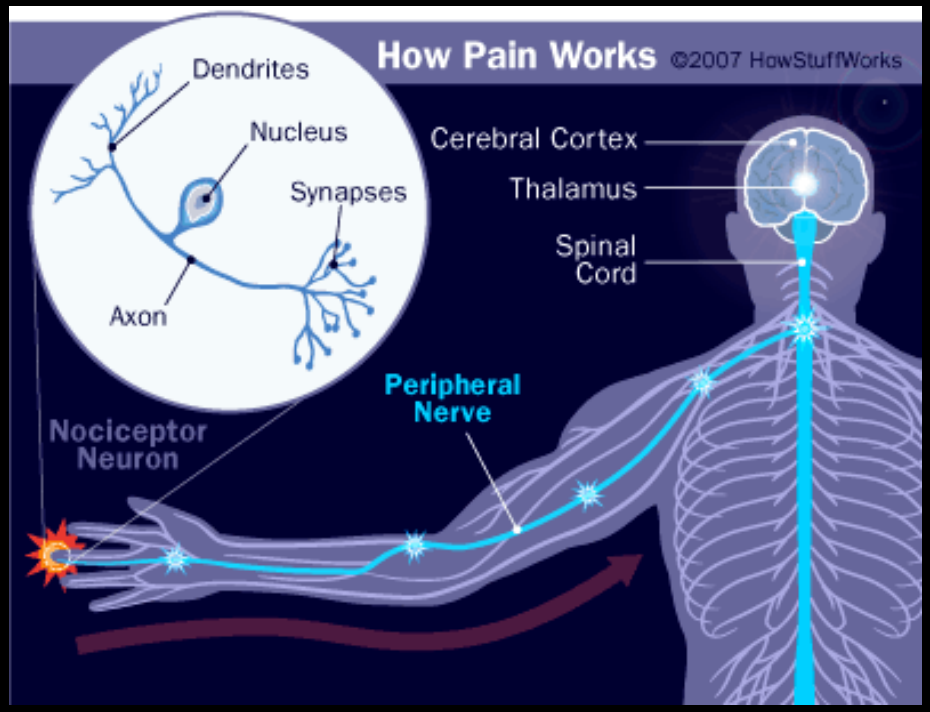
Spinal mechanisms of pain processing

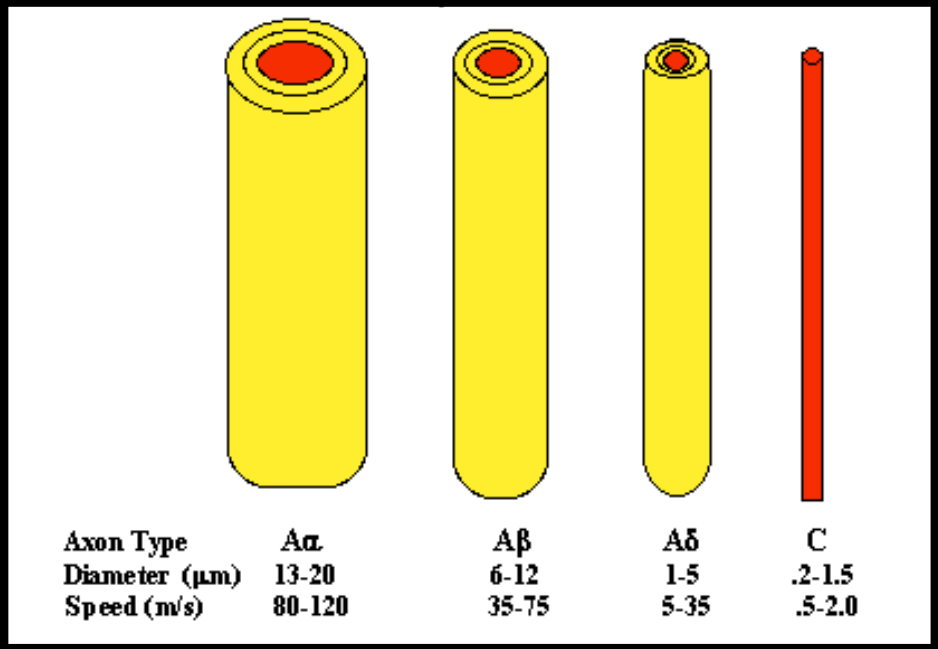
Boris Safronov

Instituto de Biologia Molecular e Celular,
Porto, Portugal

Pain processing pathways

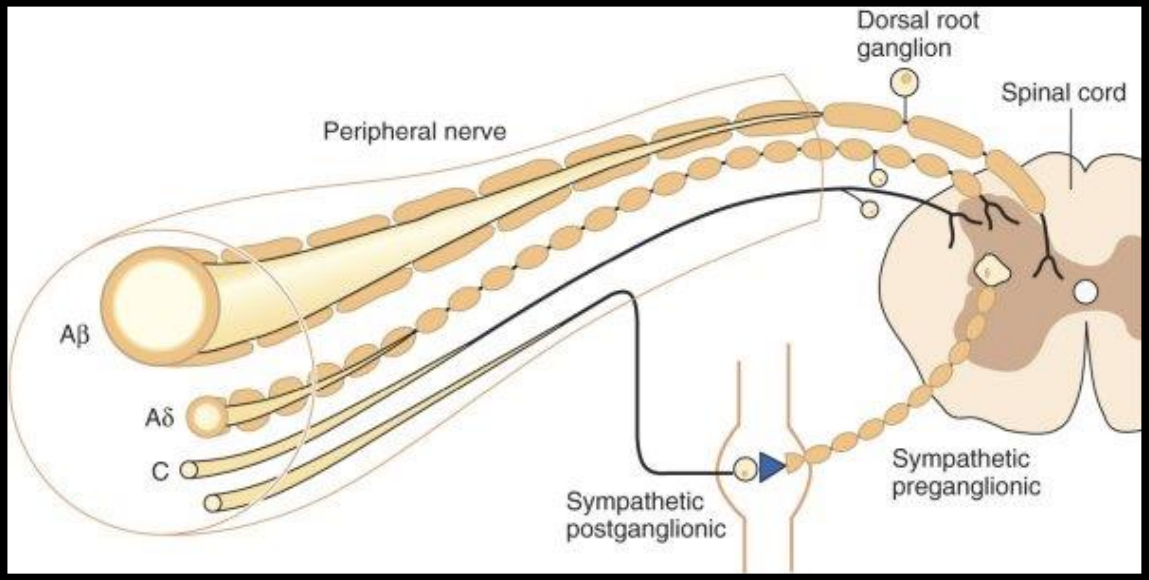


Primary afferent fibers

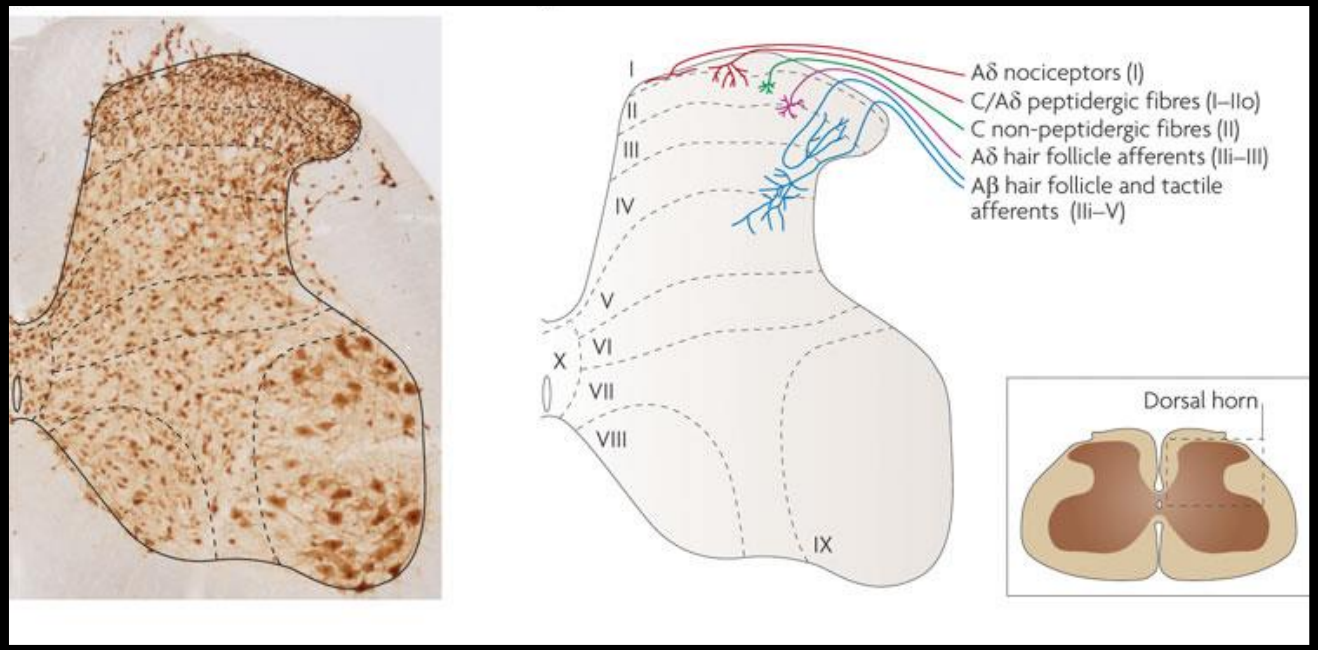


Axon Type	Aα	Aβ	Aδ	C
Diameter (μm)	13-20	6-12	1-5	.2-1.5
Speed (m/s)	80-120	35-75	5-35	.5-2.0

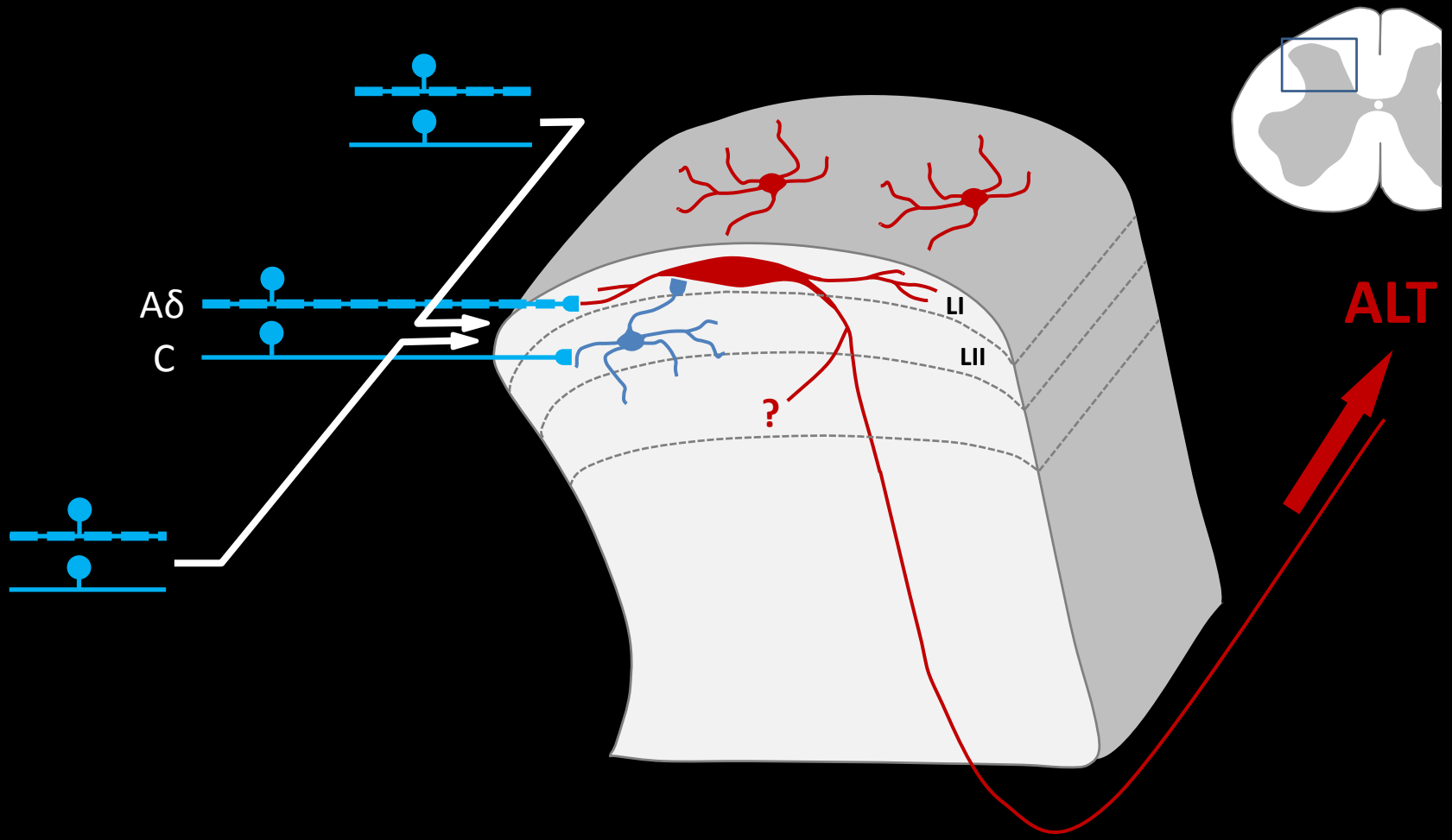
Spinal projections of afferents



Nociceptors project to laminae I-II



The superficial dorsal horn (laminae I-II)



Major topics:

1) Cell imaging and recording in a non-sliced spinal cord

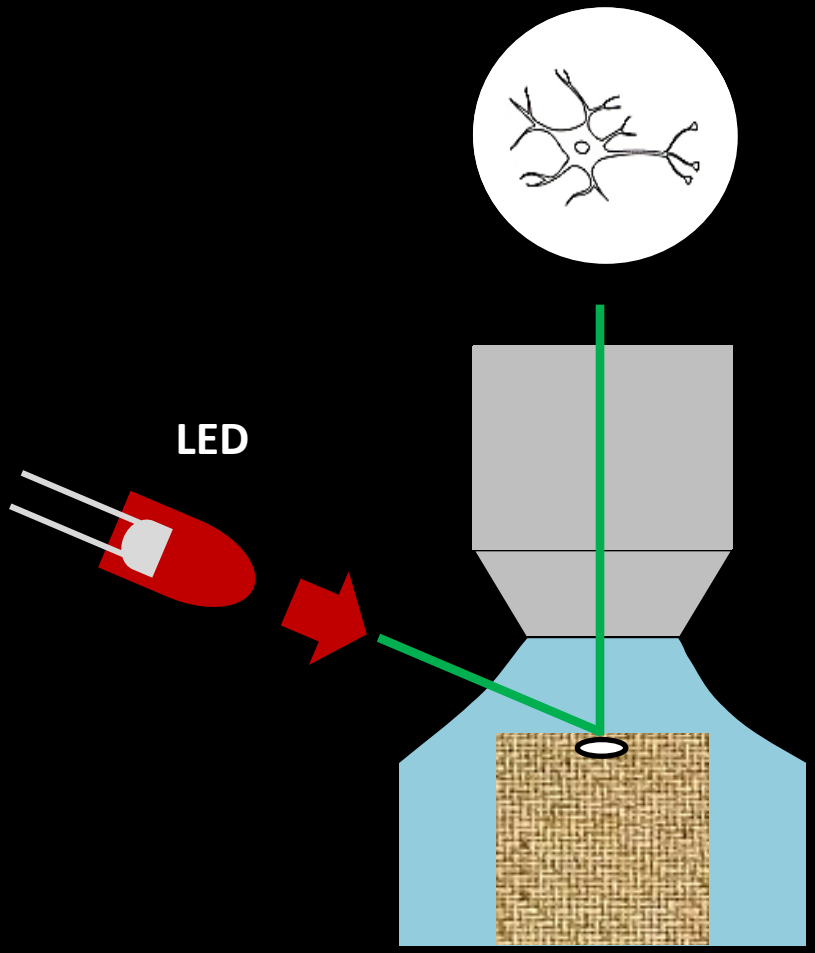
2) Multi-segmental primary afferent input to lamina I and II neurons, and

3) Its relevance for the somatovisceral processing and referred pain

4) Spinal control of pain

5) Axon structure of ALT-projection and local-circuit lamina I neurons

Cell imaging in thick tissues: The basic idea

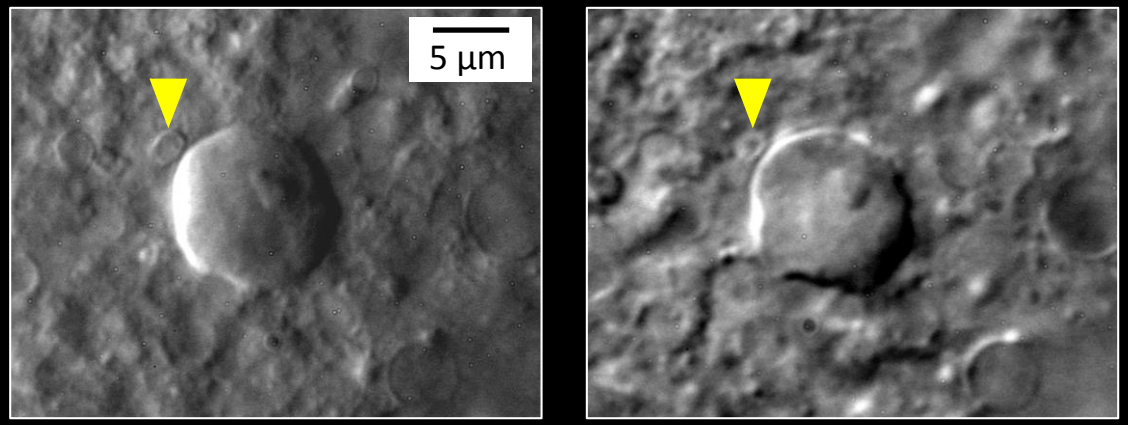


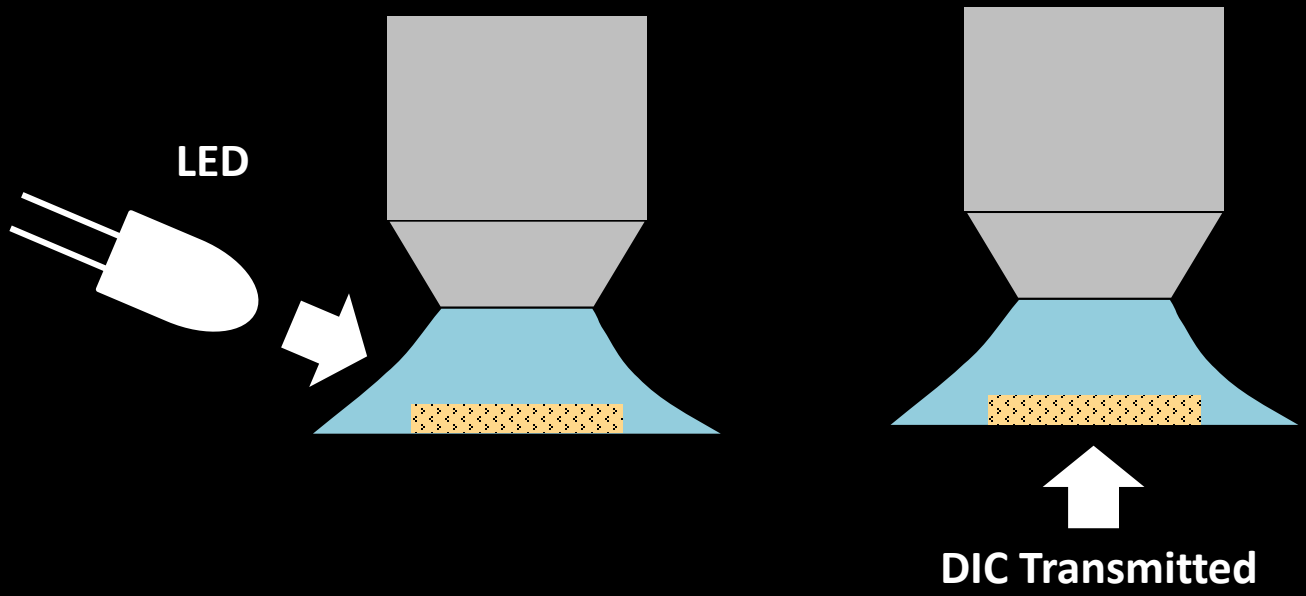
The Fresnel equation

Refractive indices n_1=1.33 n_2=1.35

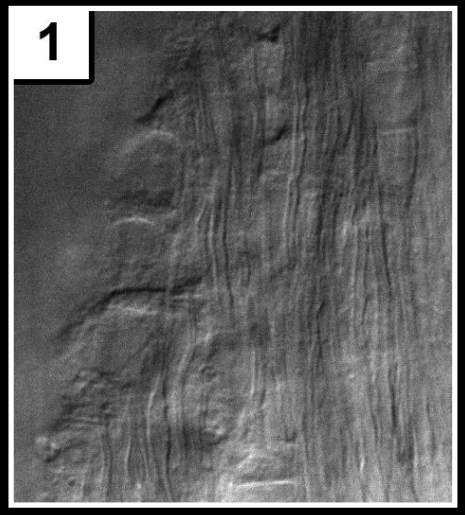
Angle

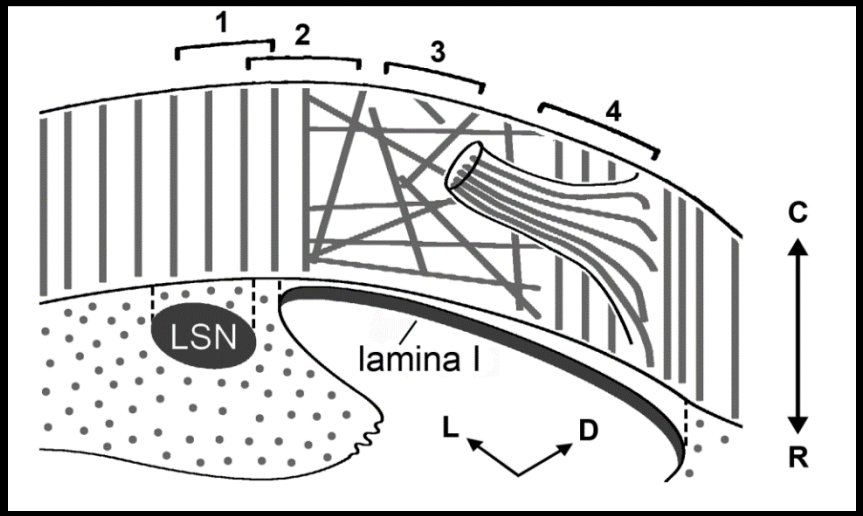
LED *versus* DIC in a 200-µm slice

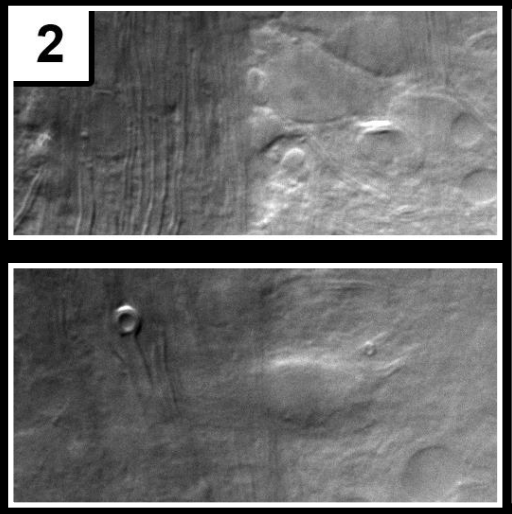


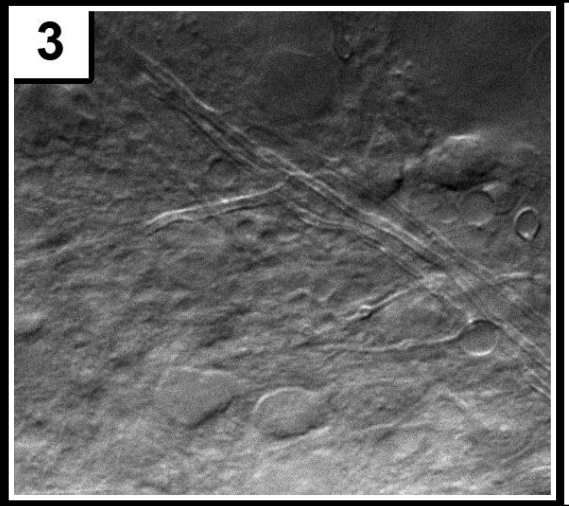


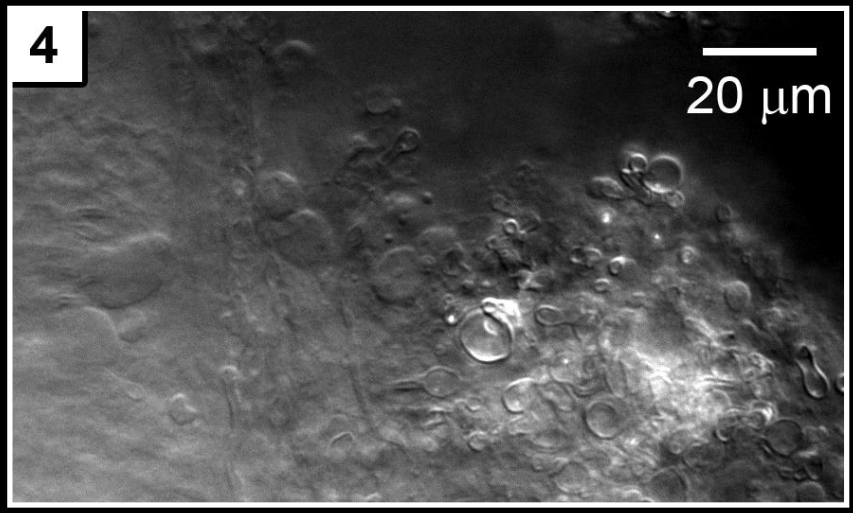
Visualization of lamina I-II neurons



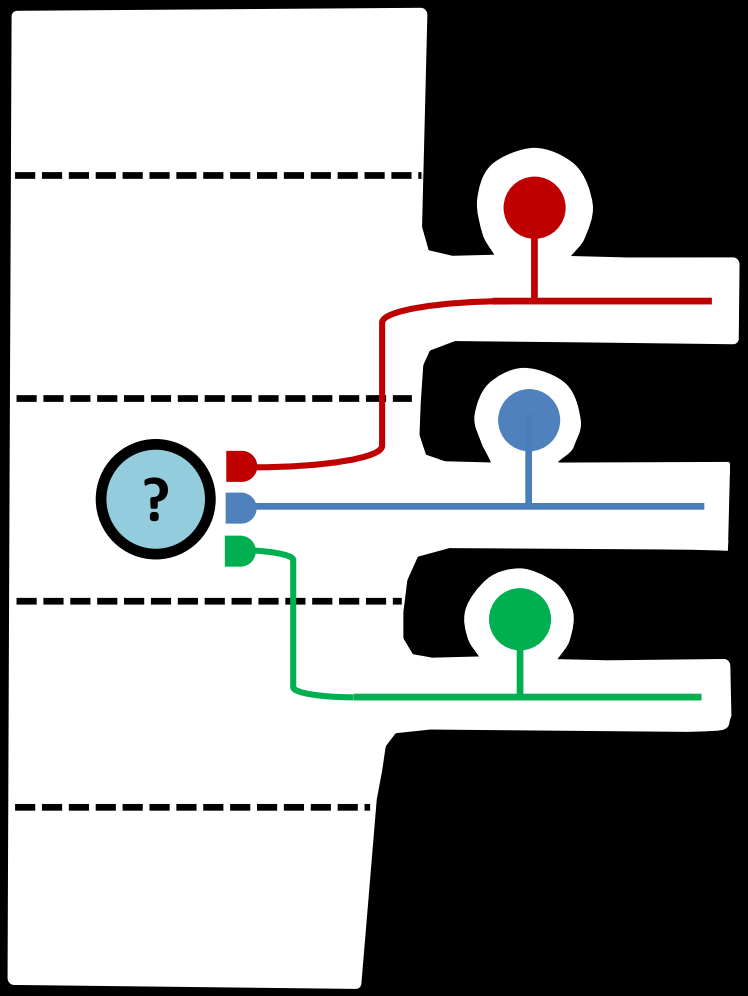






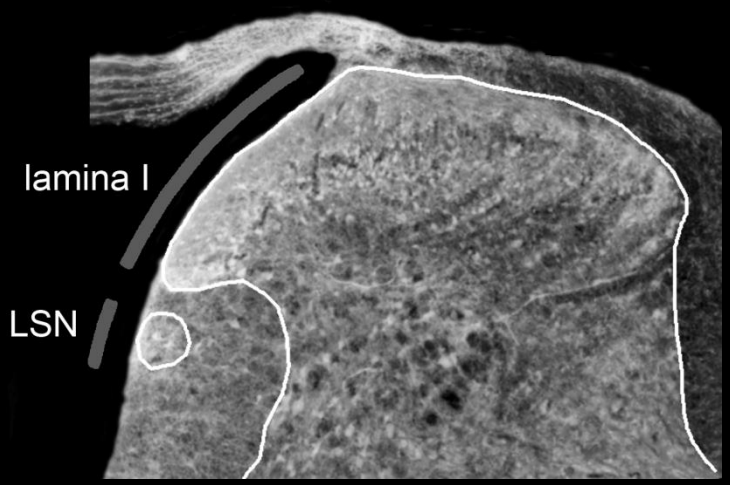


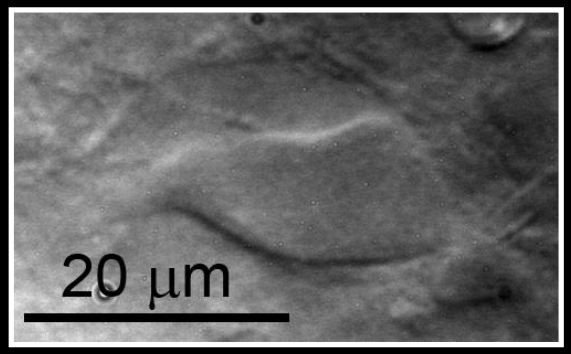
Thin (Aδ and C) afferents from different roots converge at the segment level

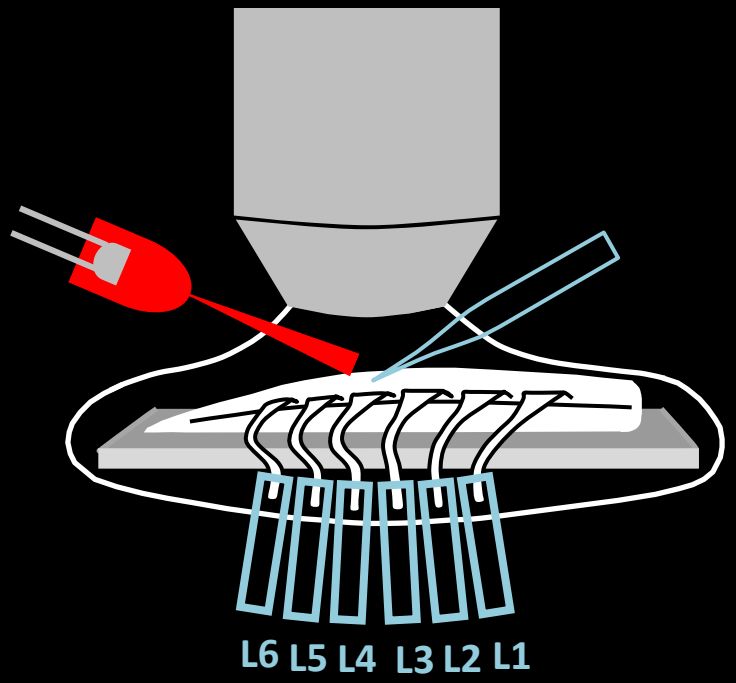


Szentagothai, 1964
Cruz et al., 1987

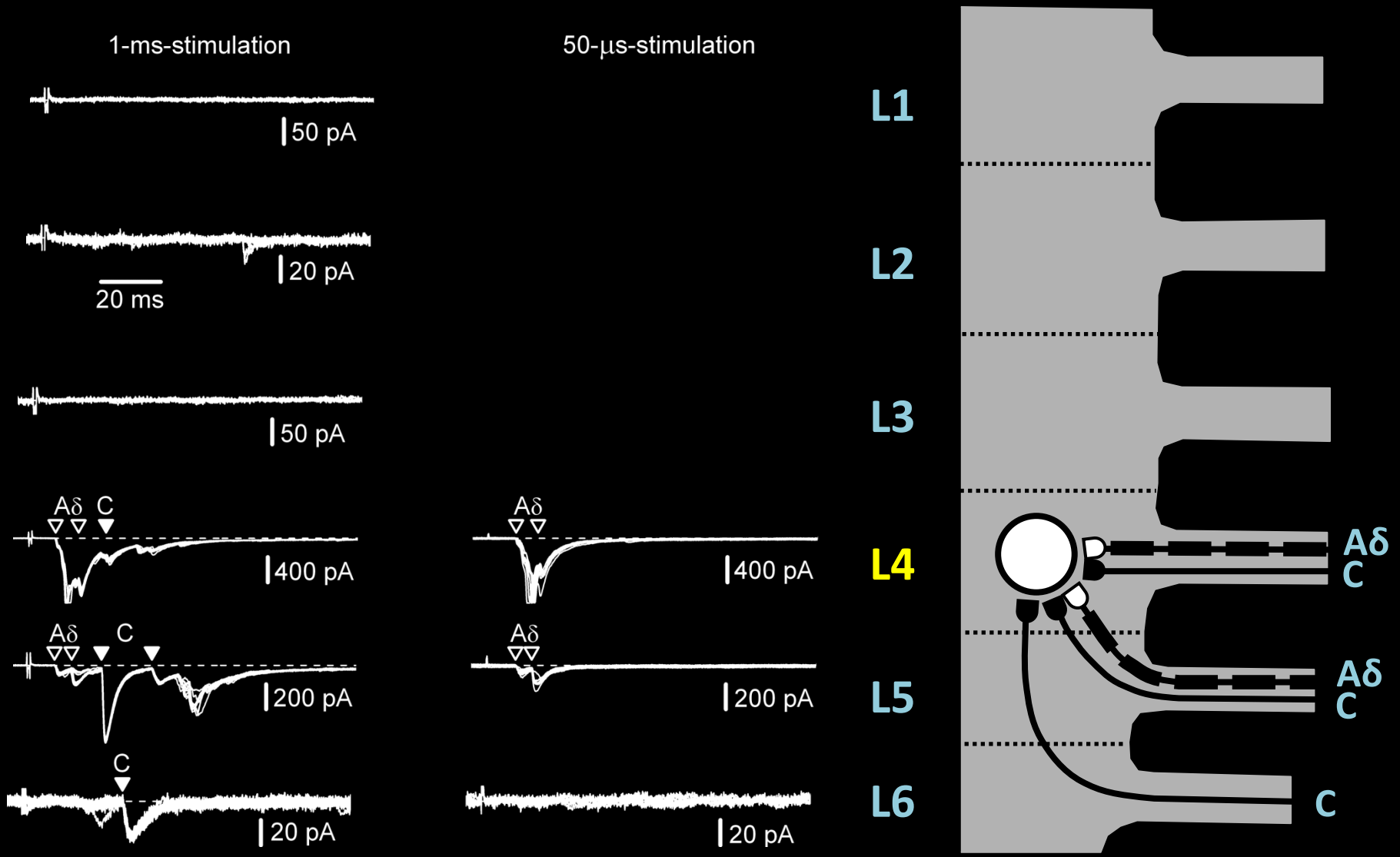
Multi-segmental input to lamina I-II neurons



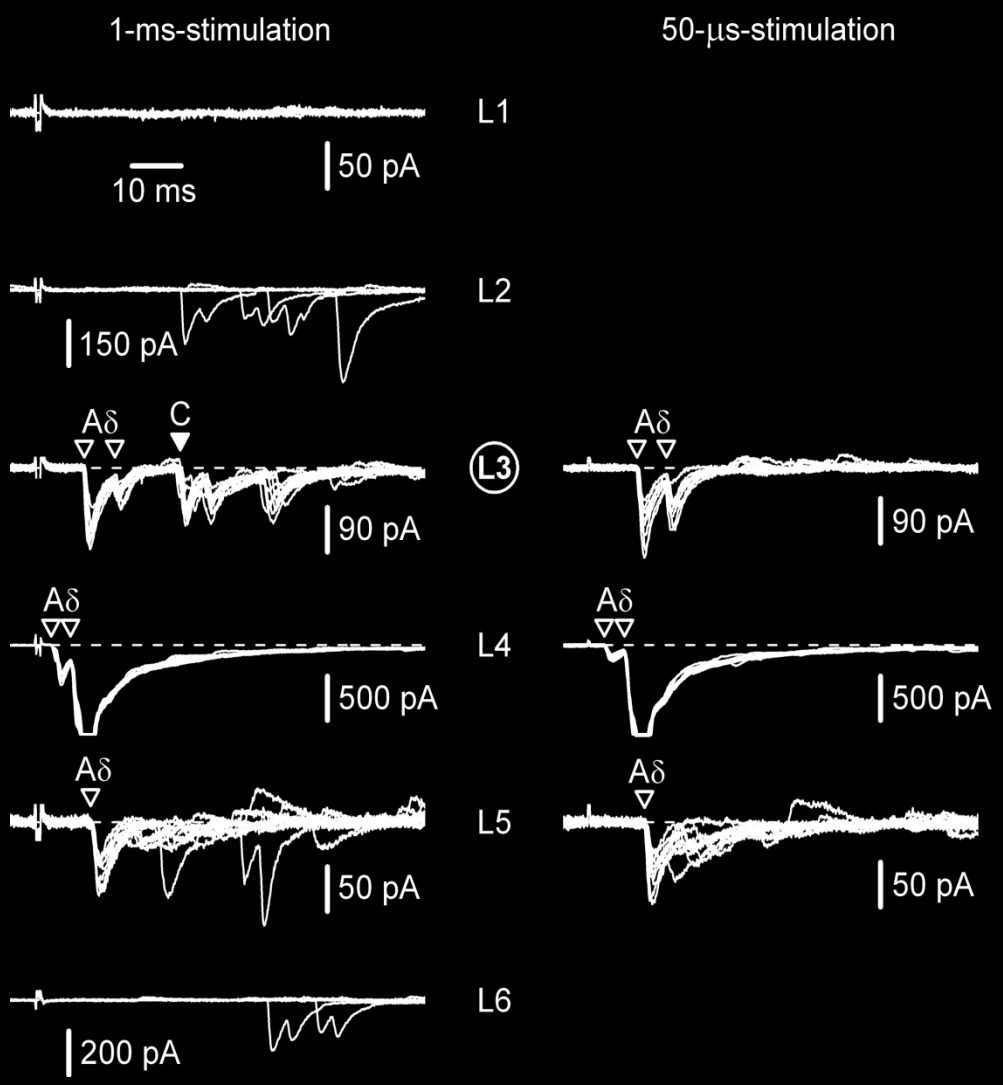


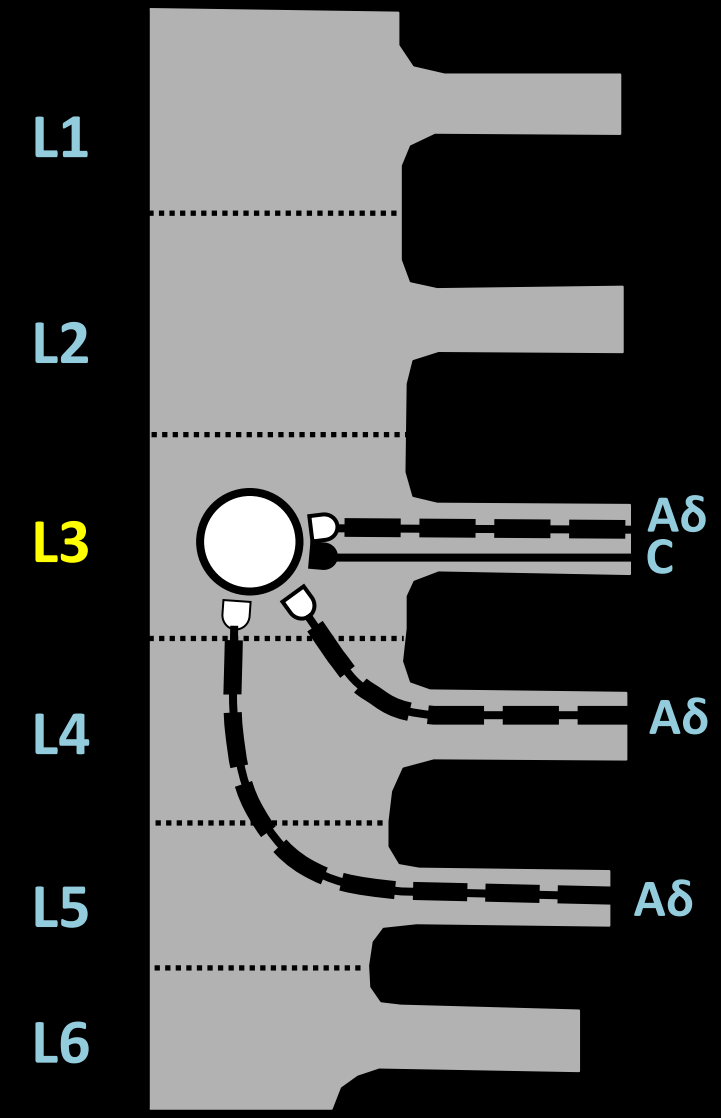


Inputs to a lamina II neuron in L4



Inputs to a lamina II neuron in L3





Interpretation of multi-segmental convergence in lamina II

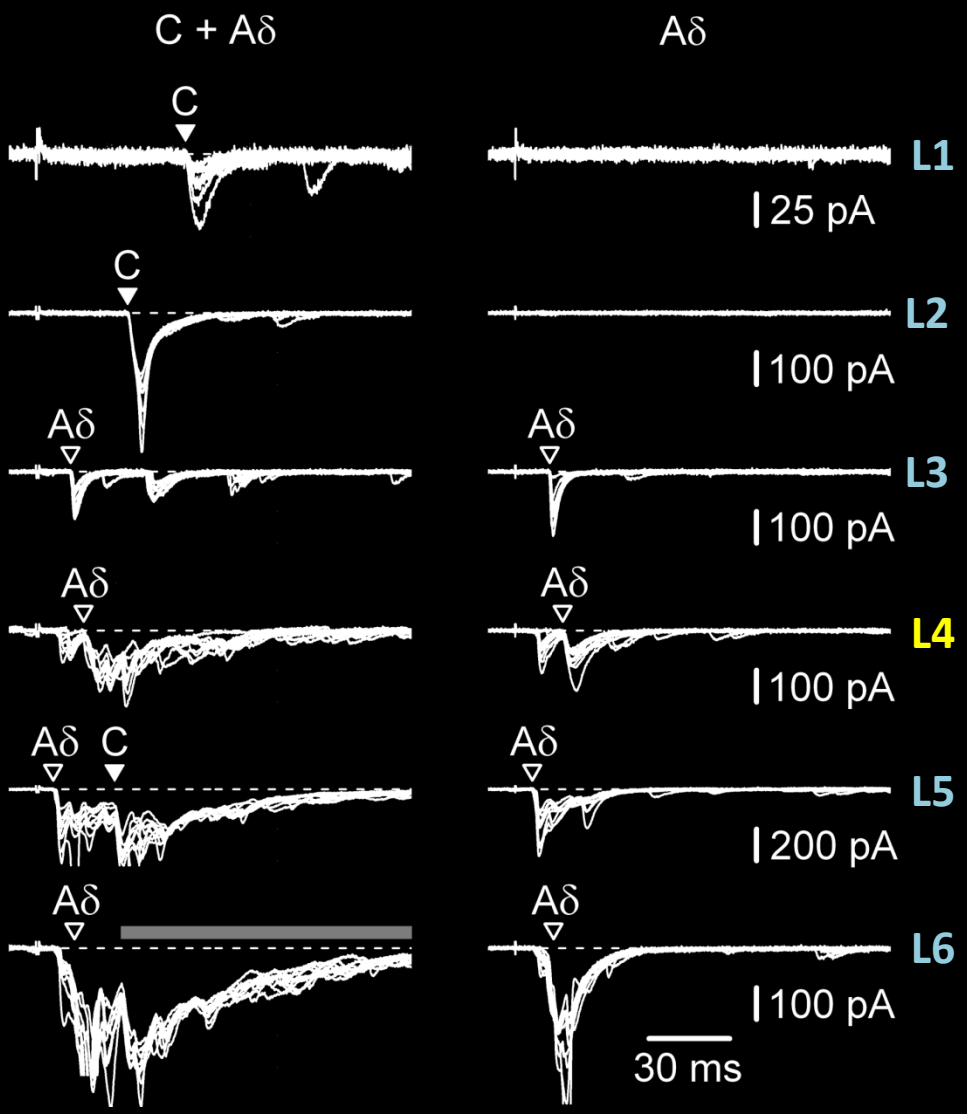
Based on Takahashi et al. (2003) *J. Comp. Neurol.*

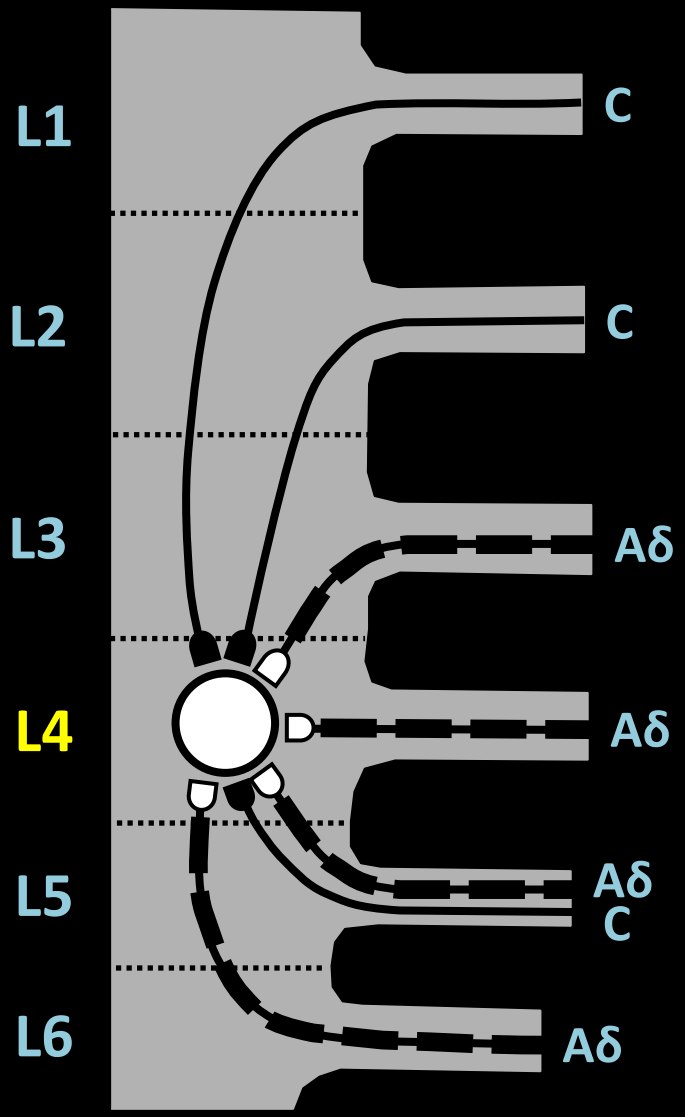
Conclusions (1):

Lamina II: neurons receive monosynaptic inputs from 2-4 segmental roots

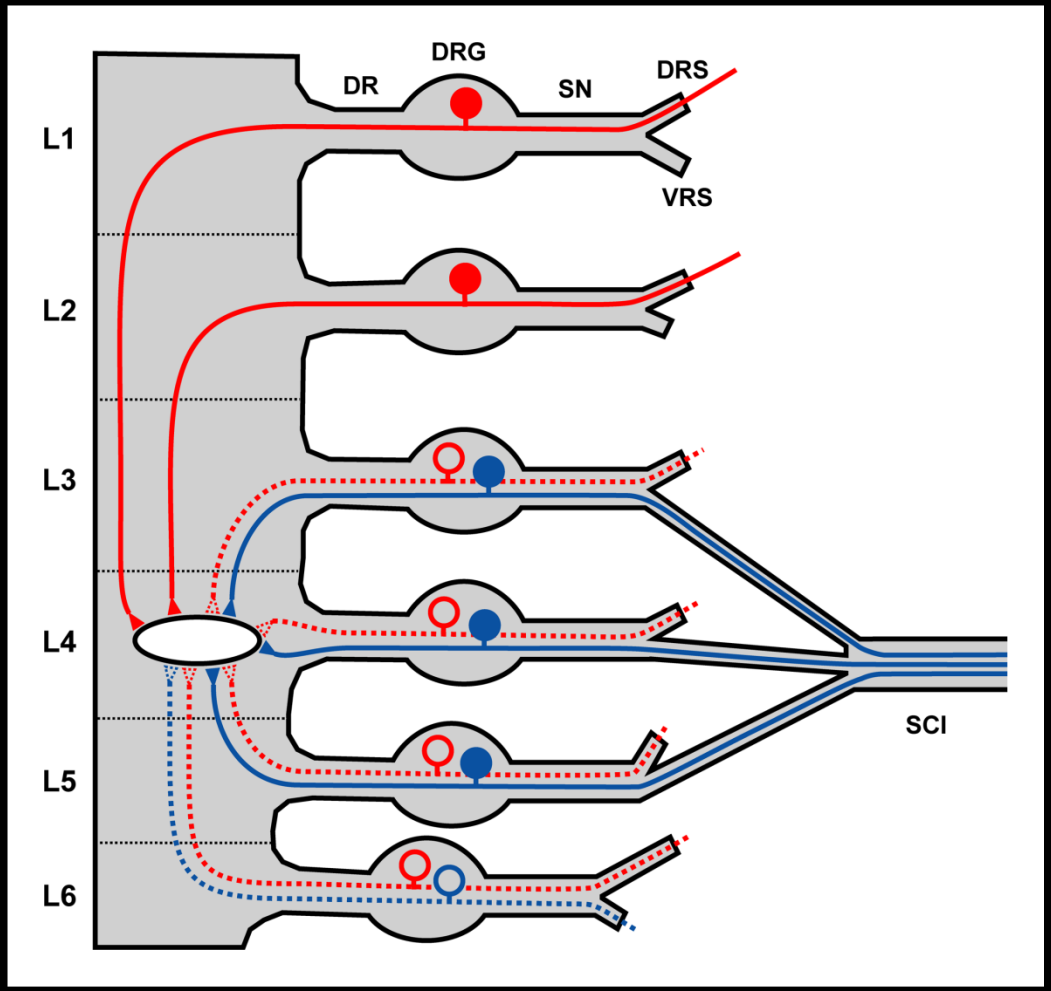
- This organization is important for formation of precise and robust neural maps of the body surface at the spinal cord level

Monosynaptic inputs to a lamina I neuron in L4





Somatovisceral convergence on lamina I neurons ?

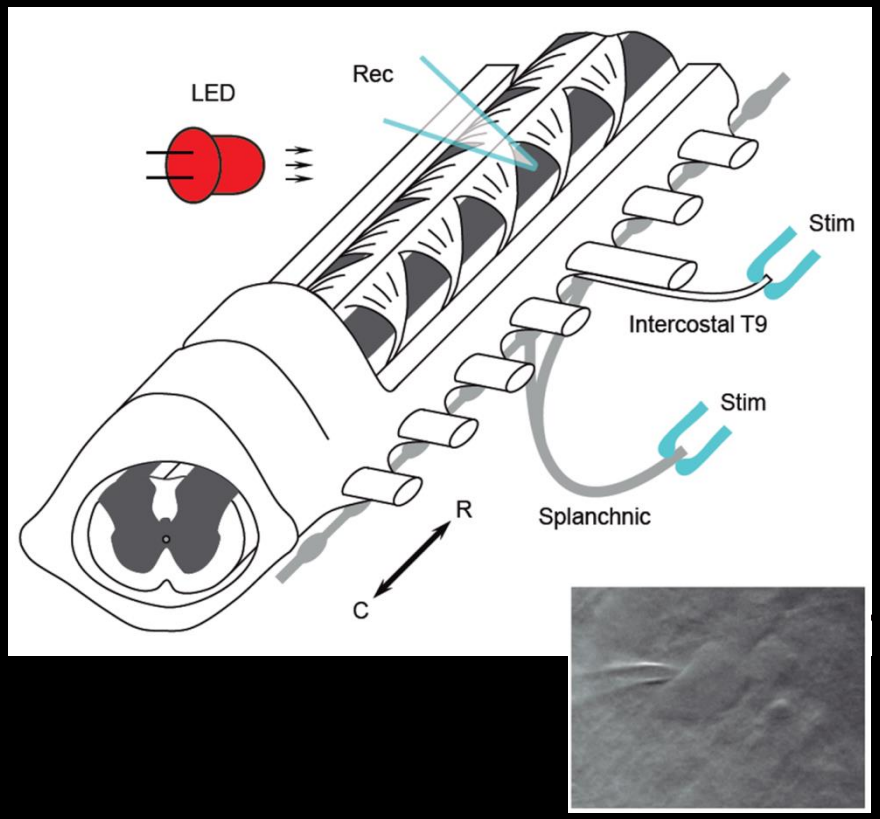


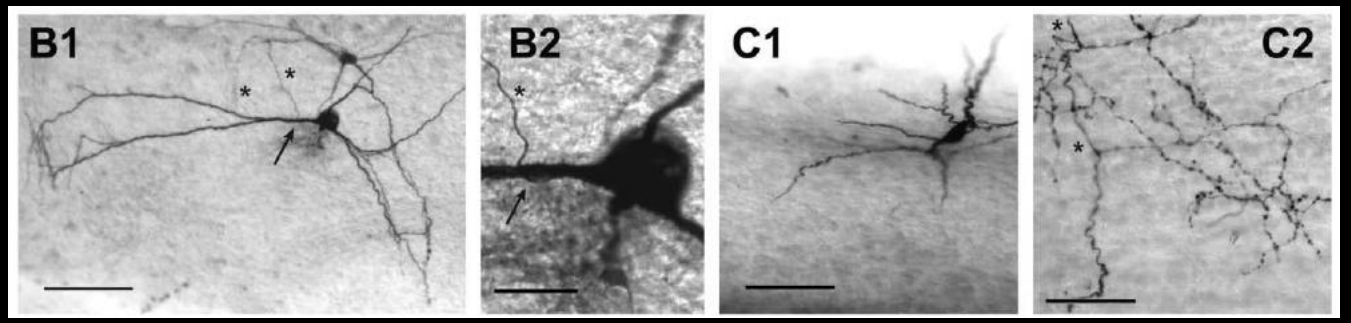
Conclusions (2):

Lamina I: **Aδ- and C-fibers from six roots can directly converge onto one neuron, which functions as an intersegmental integrator of primary afferent inputs**

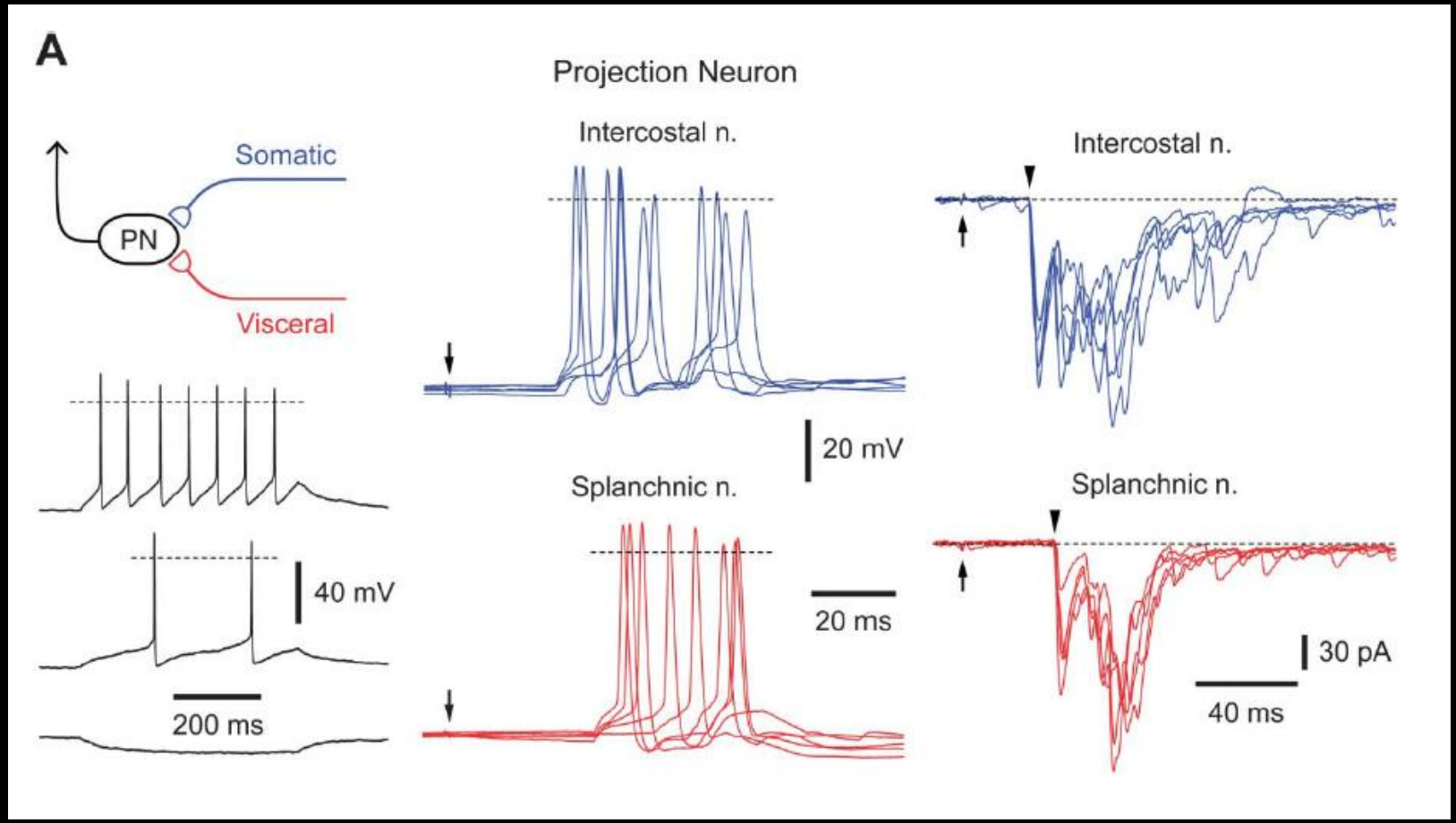
- **Can lamina I neurons integrate somatovisceral inputs and play a role in complex neurological phenomena like referred pain?**

Study of somatovisceral convergence

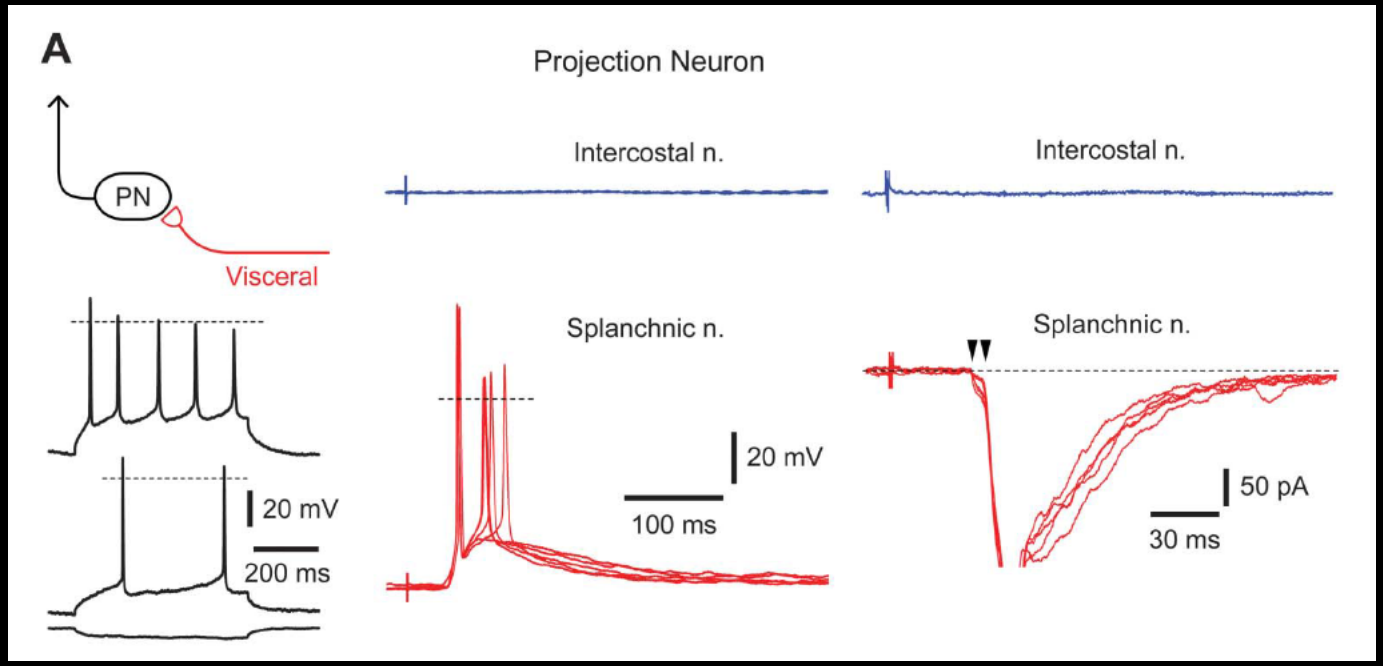




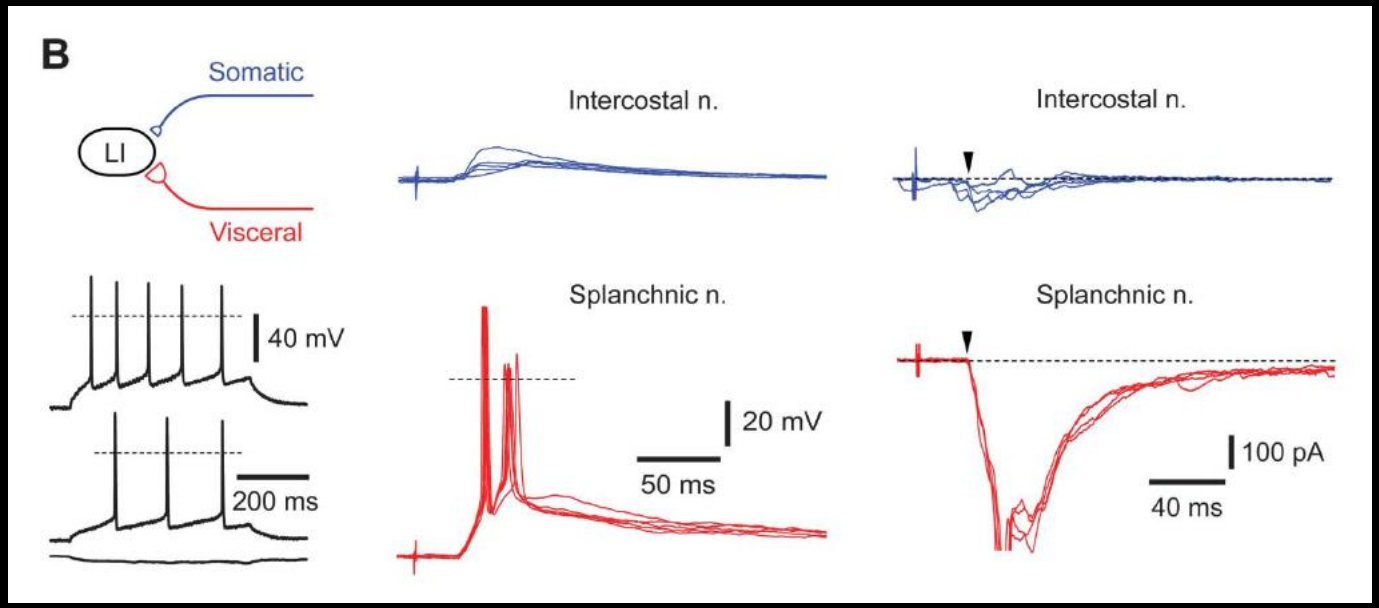
Somatovisceral lamina I neurons



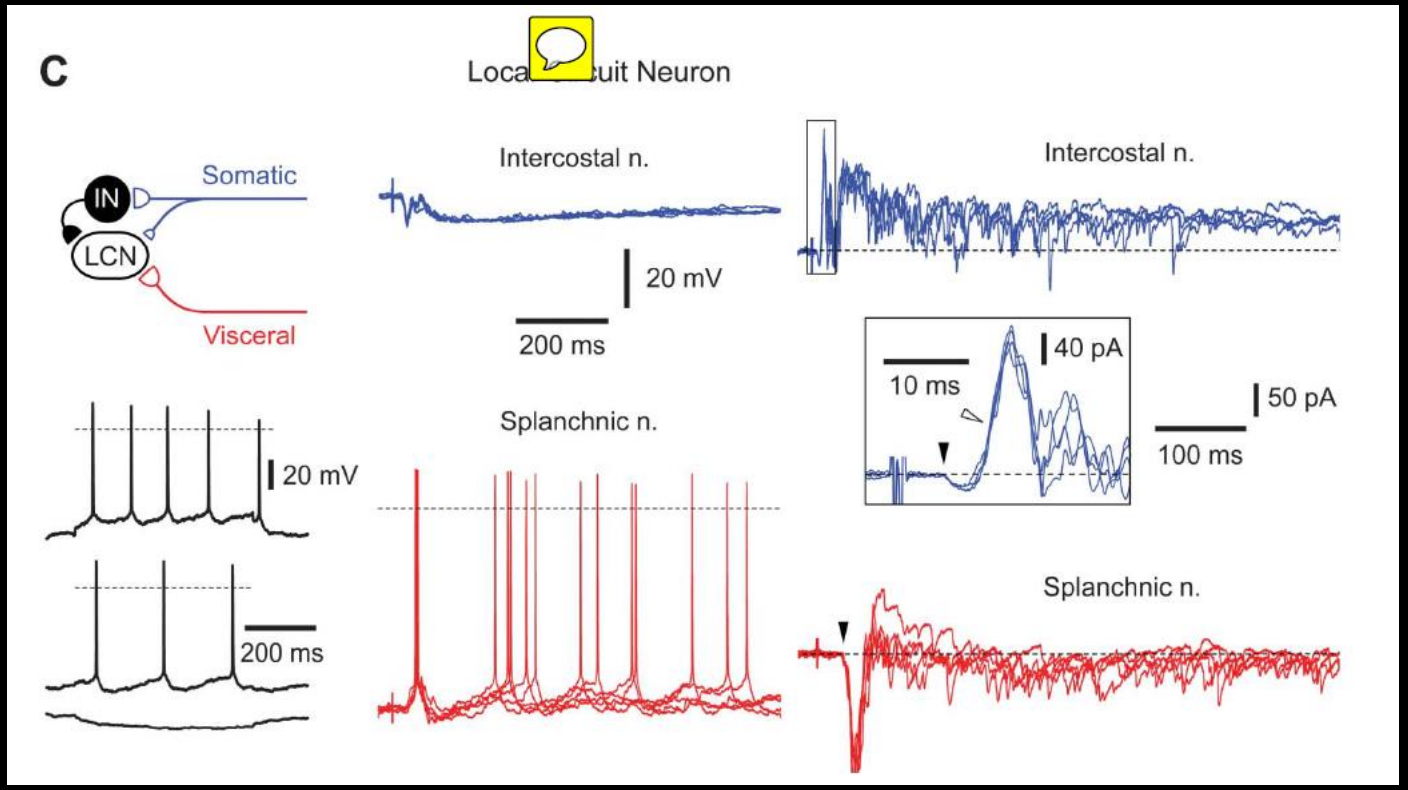
Visceral-specific neuron



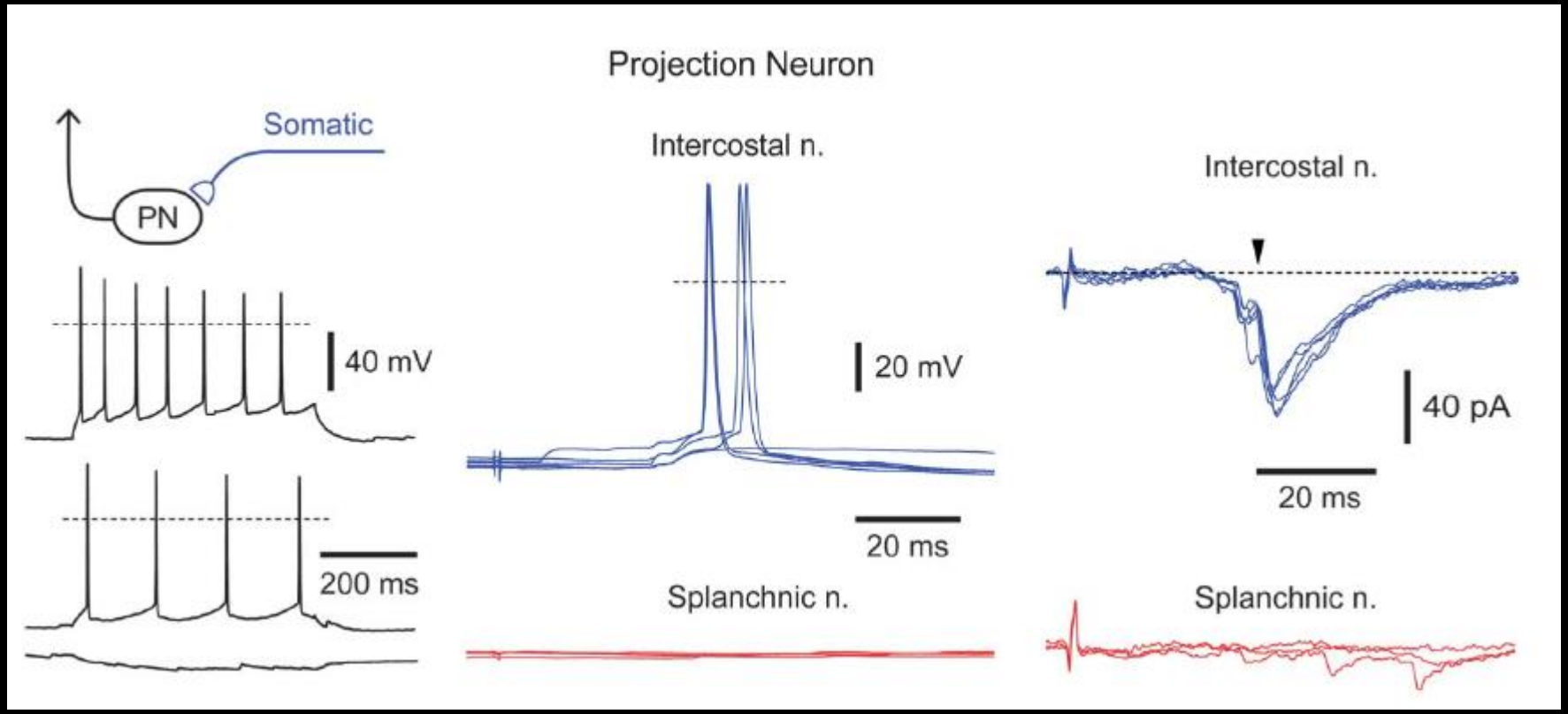
Visceral-specific neuron



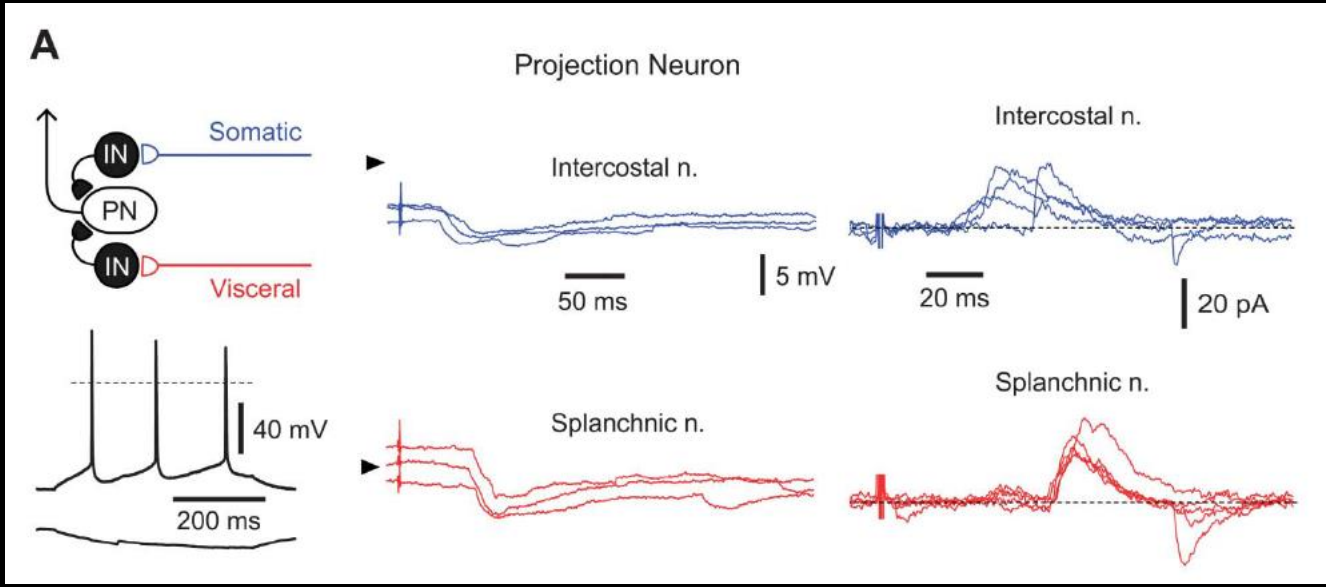
Visceral-specific neuron



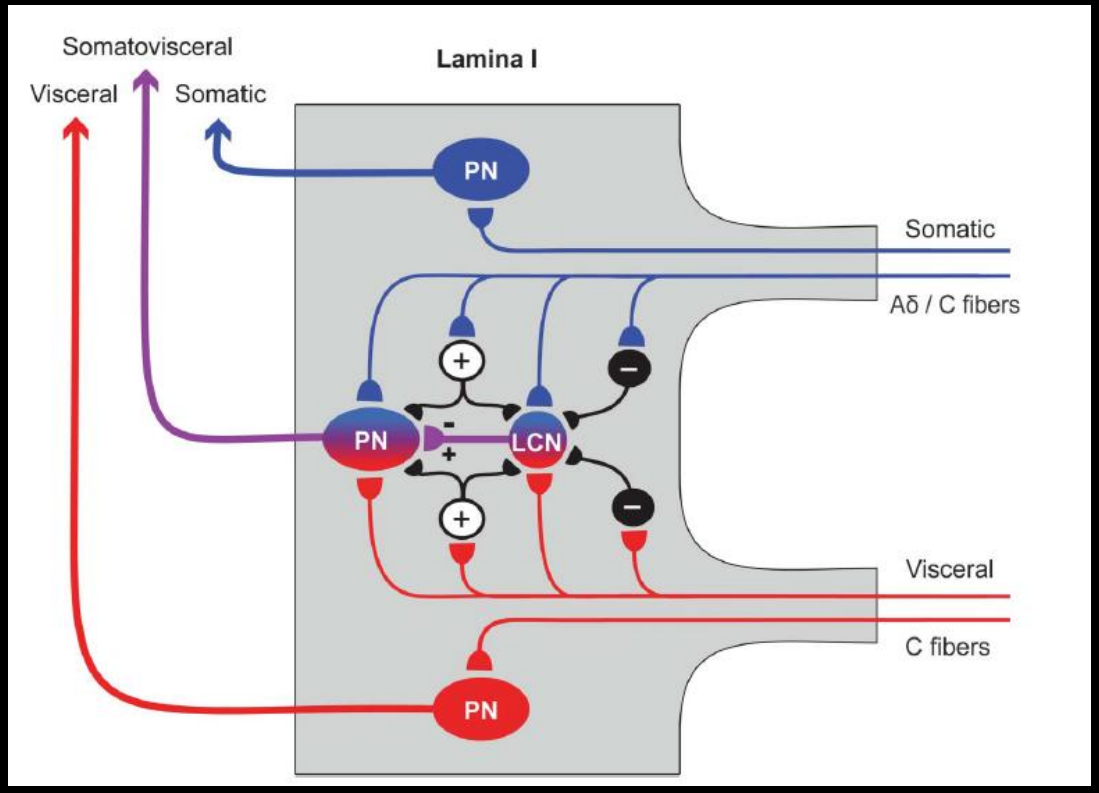
Somatic-specific neuron



‘ Inhibited ’ neuron



Somatovisceral integration in Lamina I



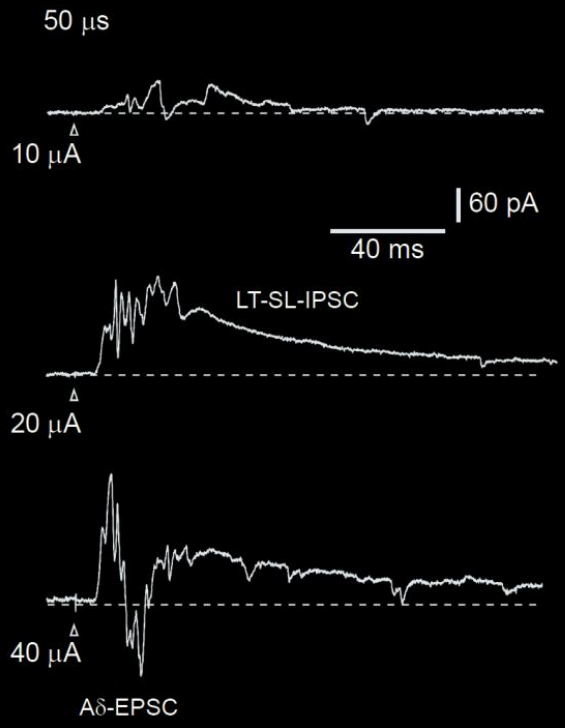
Conclusions (3):

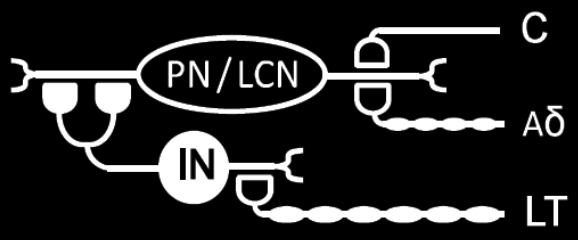
Lamina I:

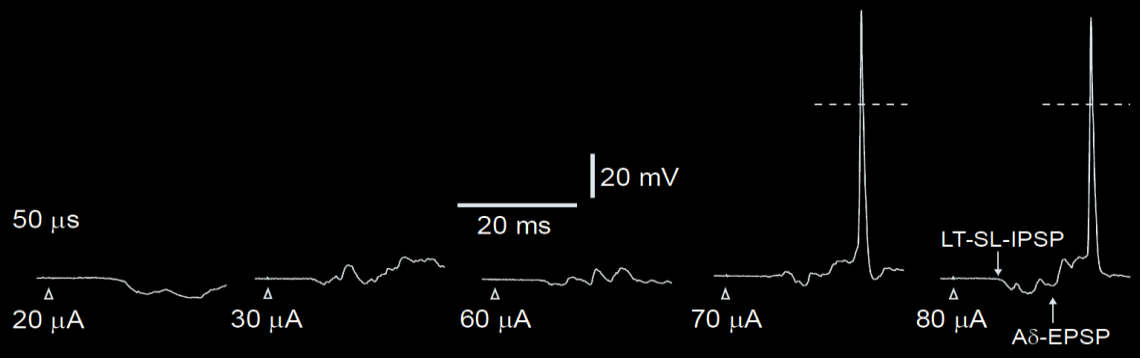
- **There is a monosynaptic somatovisceral convergence on lamina I neurons, which**

- **Can underlie complex neurological phenomena like referred pain**

Low-threshold afferent-driven inhibition of lamina I neurons: a ‘postsynaptic gate’





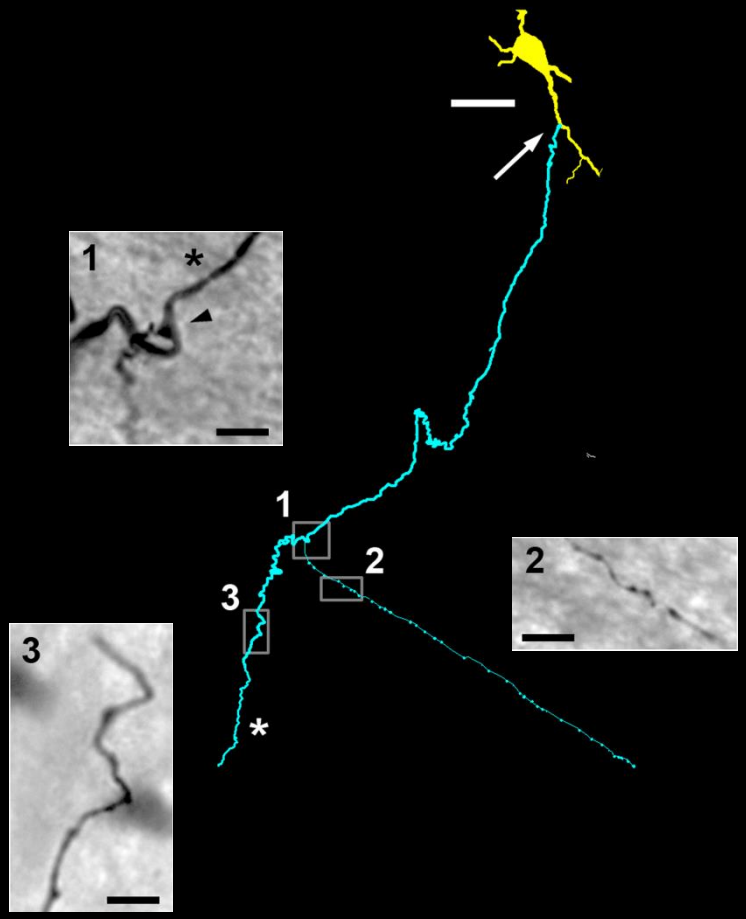


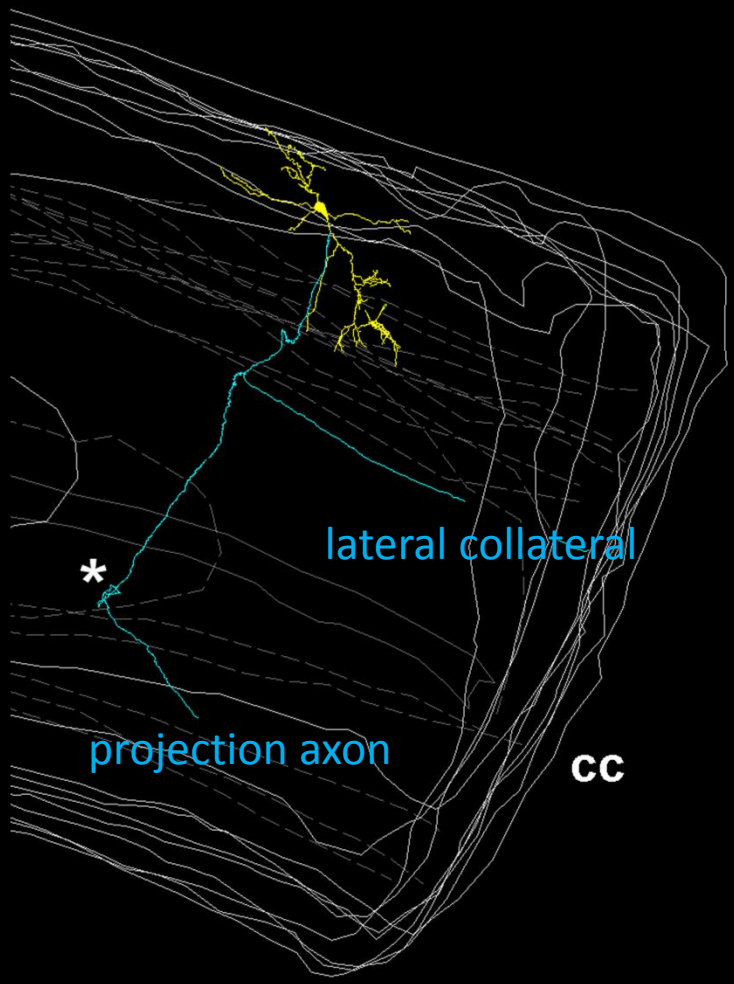
Conclusions (4):

Lamina I **local-circuit** and **projection neurons** receive low-threshold afferent-driven inhibition, which, in many cases, is disynaptic and temporally precedes classical high-threshold excitatory inputs

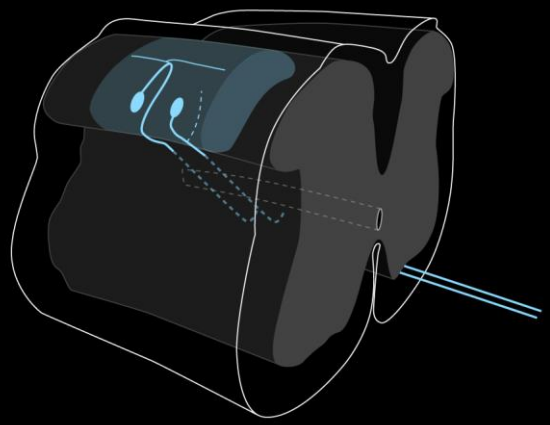
This direct inhibitory link between low-threshold afferents and **projection neurons** can function as **a postsynaptic gate** controlling the nociceptive information flow in the spinal cord

Local axon collaterals of ALT-projection neurons





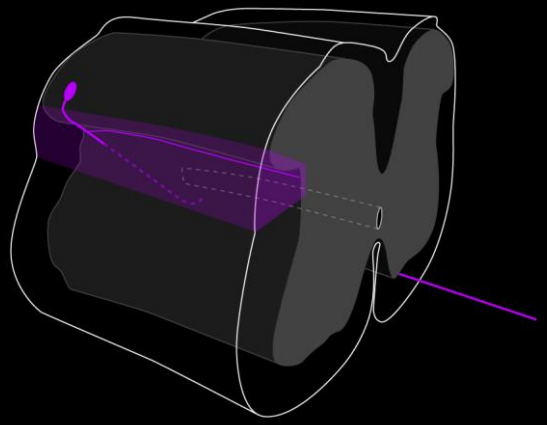
Axon collaterals of ALT-projection neurons



Dorsal Collateral Type I & II

Project to laminae I or II–IV of the same segment

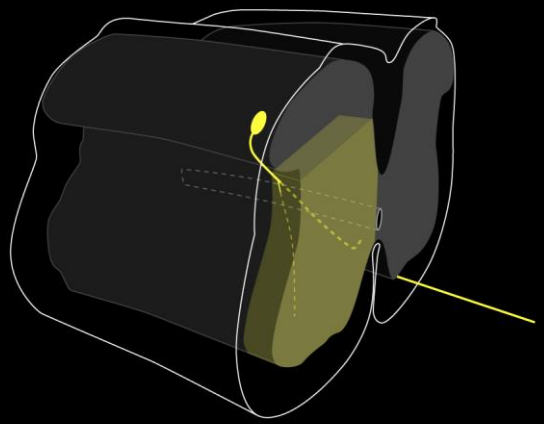
- Local segmental circuits



Lateral Collateral Type

Project to rostral and caudal segments

- Intersegmental connections
- Propriospinal projections

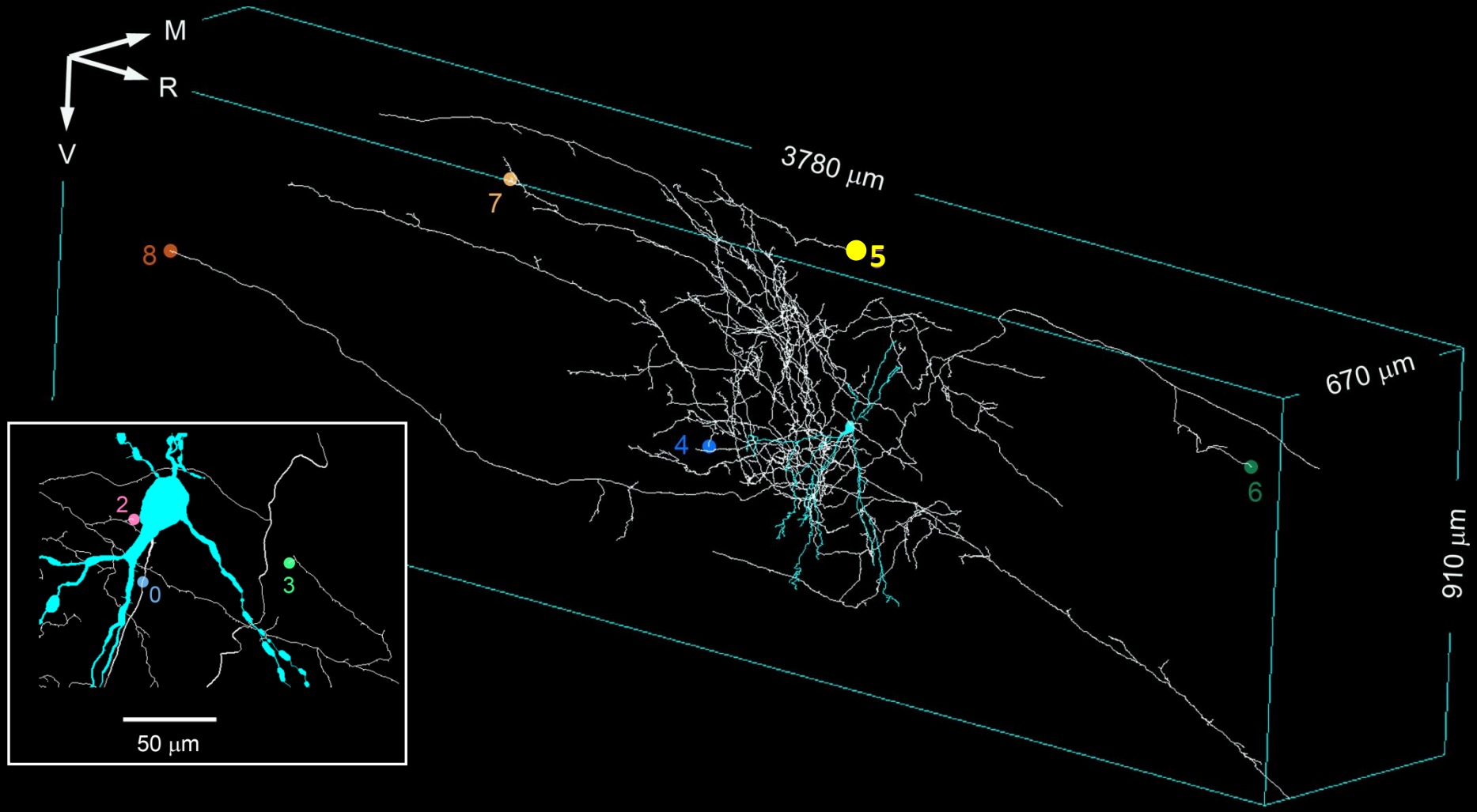


Ventral Collateral Type

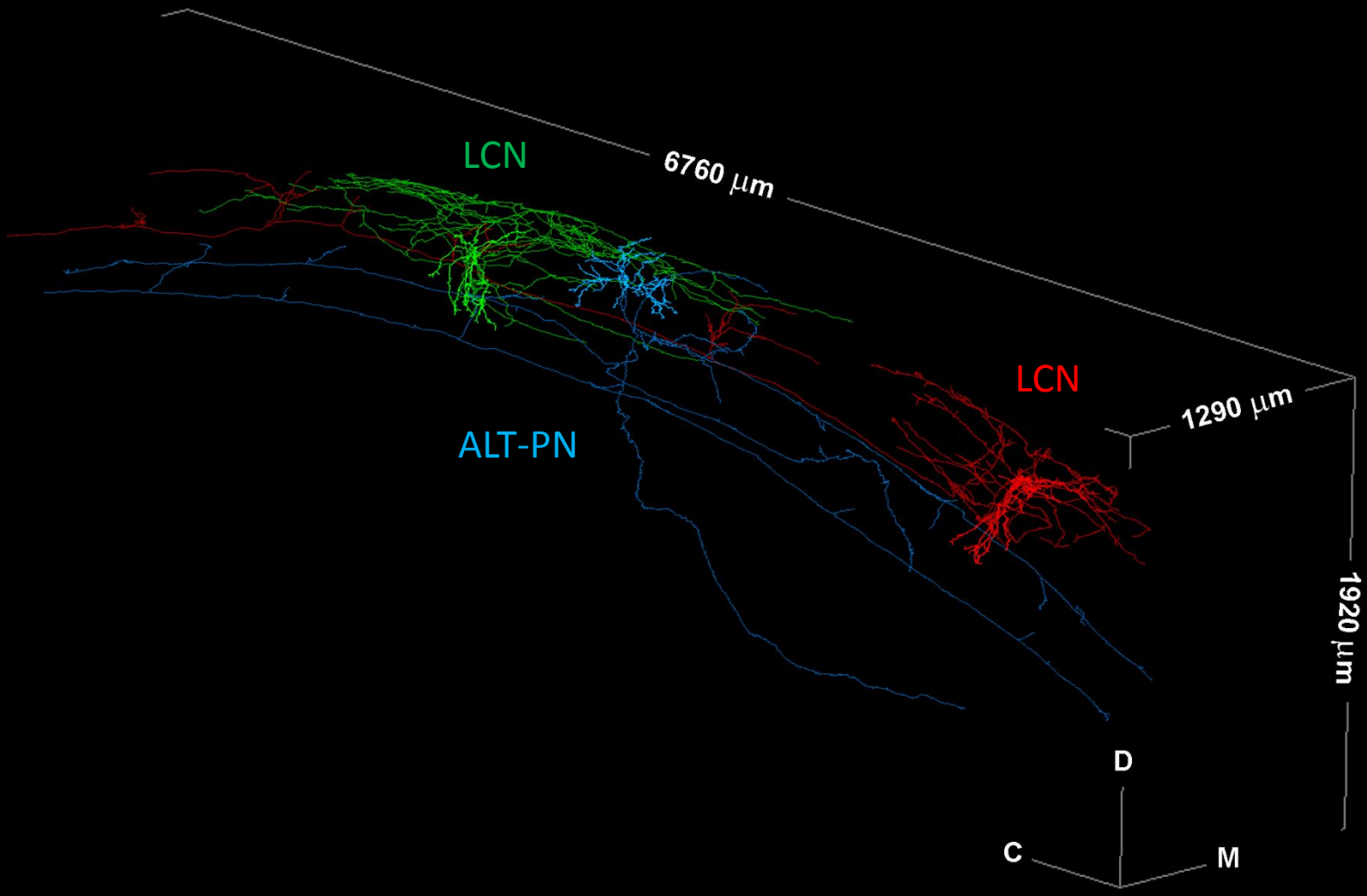
Project to laminae V-VII

- Intrasegmental connections with deep laminae
- Can link parallel pain pathways originating from lamina I and lamina V

Axon of a local-circuit neuron in 3D



Axons of lamina I local-circuit neurons (LCNs)

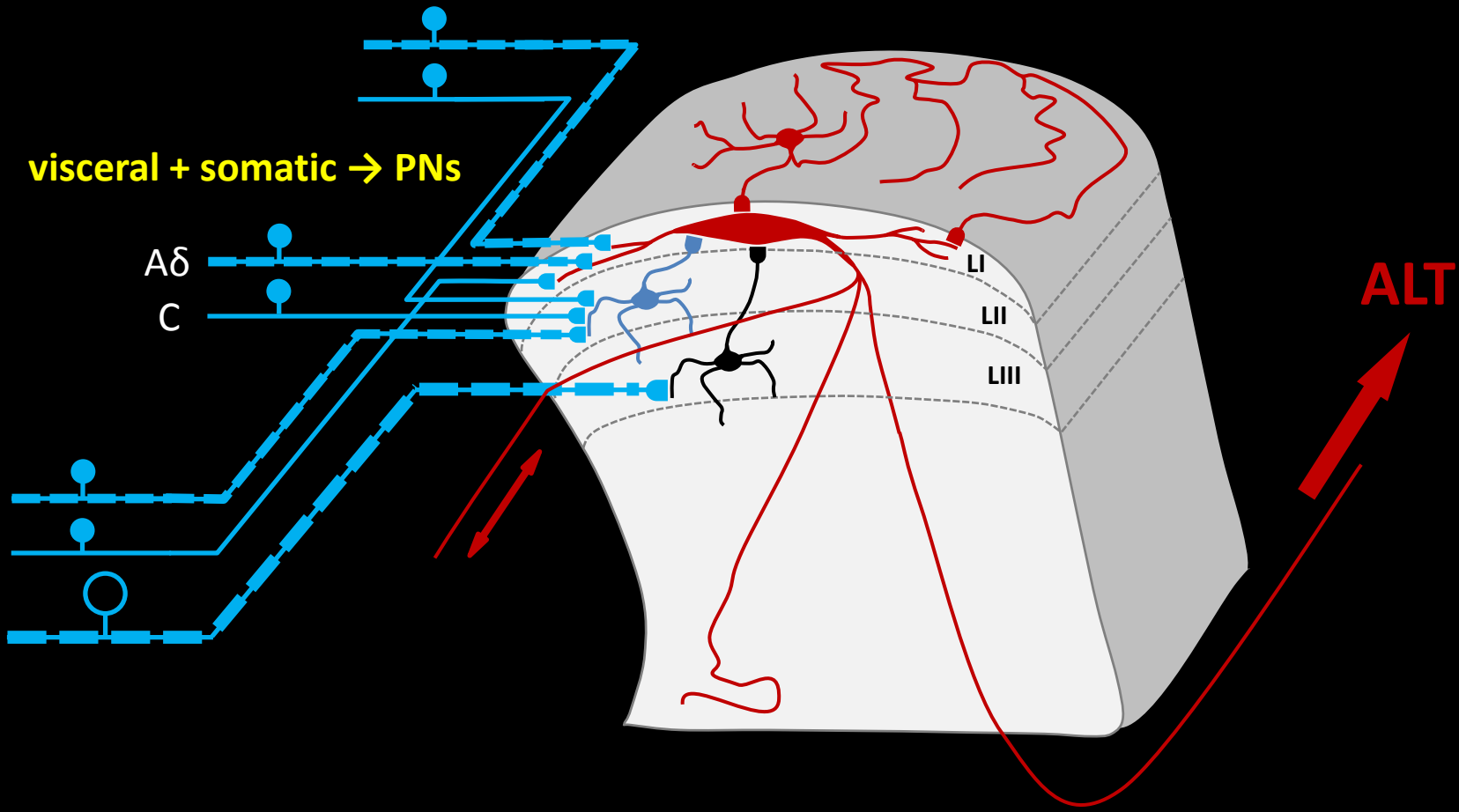


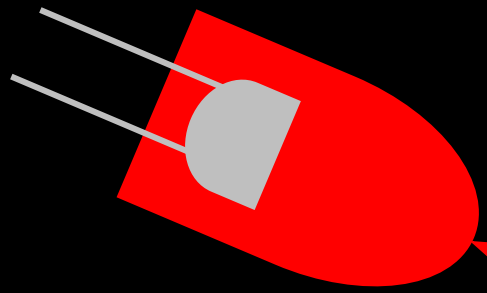
Conclusions (5):

Lamina I ALT-projection neurons, besides their principal role, can also function as local-circuit and propriospinal neurons participating in intra- and intersegmental processing

Lamina I local-circuit neurons form intersegmental as well as interlaminar connections and may control large numbers of neurons, providing anatomical substrate for rostrocaudal ‘‘processing units’’ in the dorsal horn

Final Conclusions:





Peter Szucs
Vitor Pinto
Liliana Luz
Elisabete Fernandes
Victor Derkach