Spinal Mechanisms of Pain Processing (Referred Pain)

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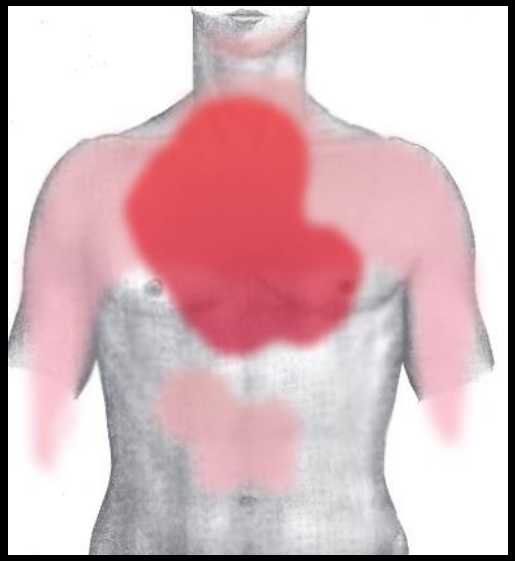
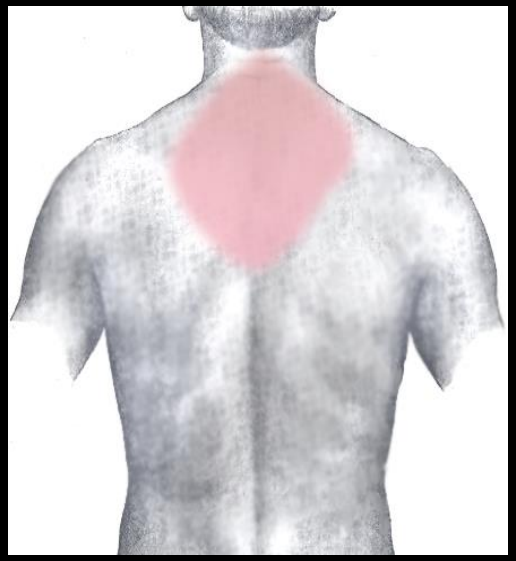
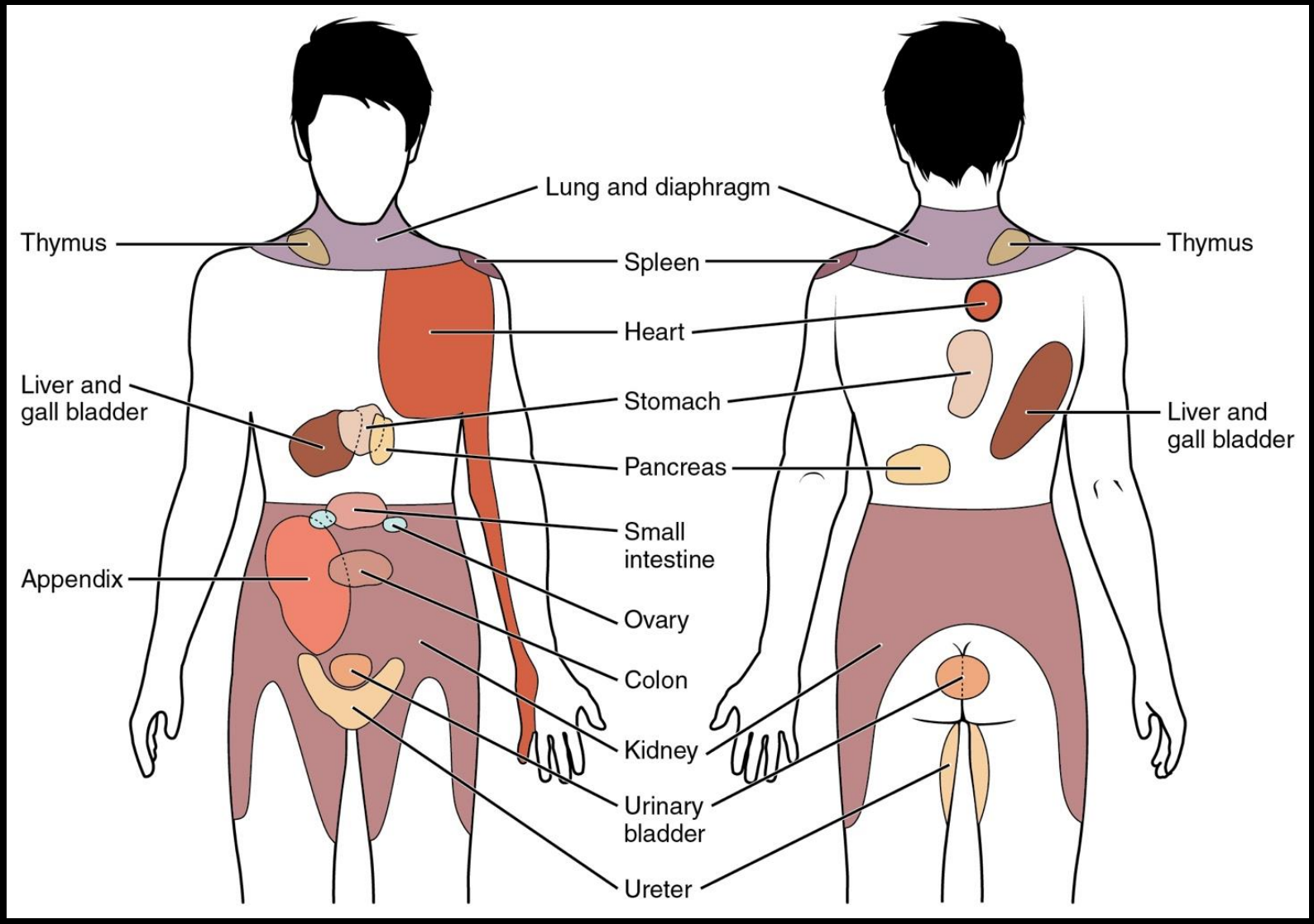
Referred pain is perceived at a location other than the site of the painful stimulus origin.

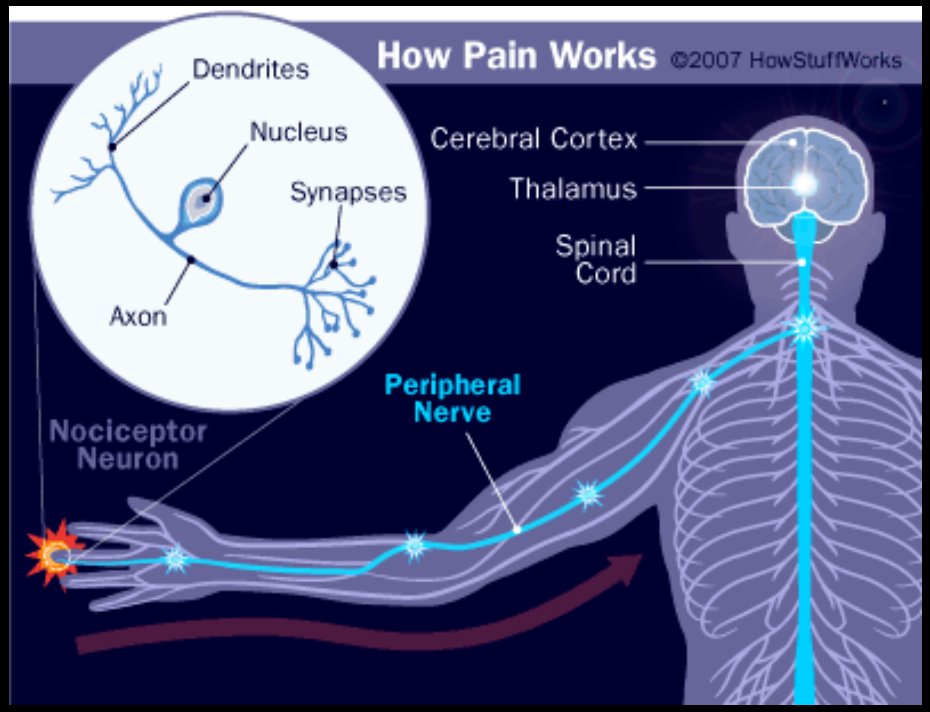




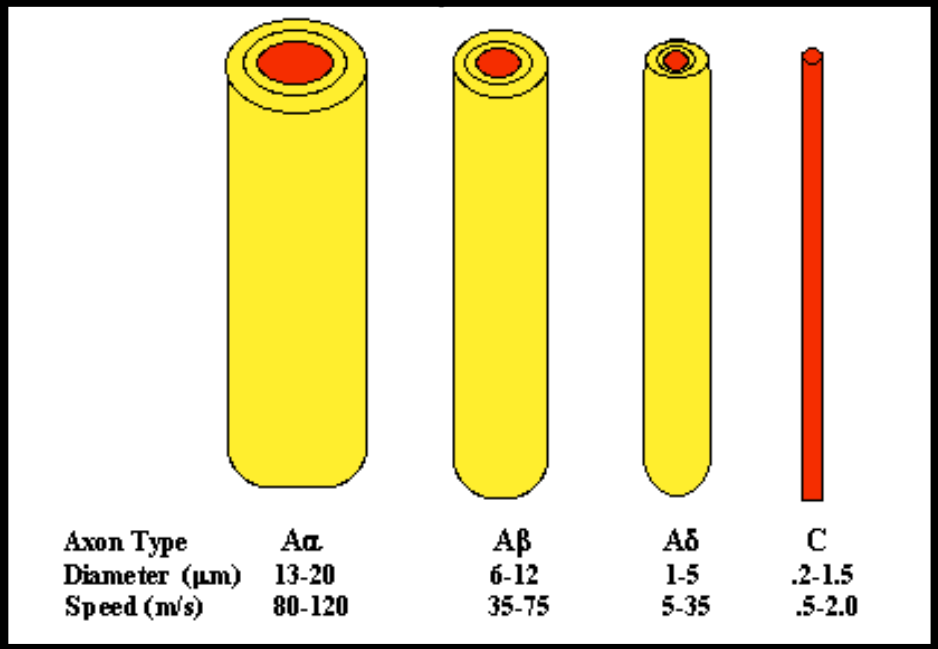
Somatic projections of visceral pain



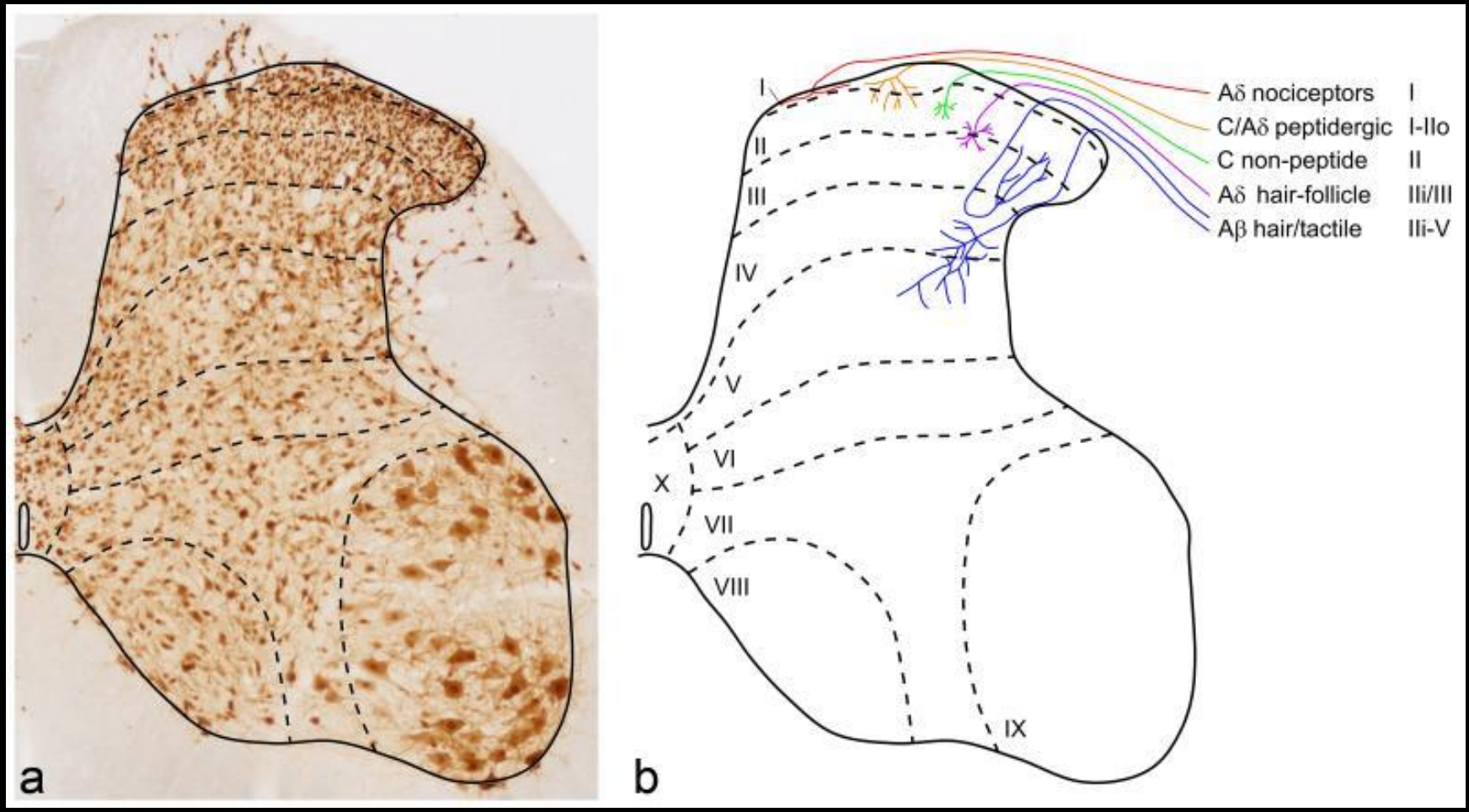
Pain processing pathways



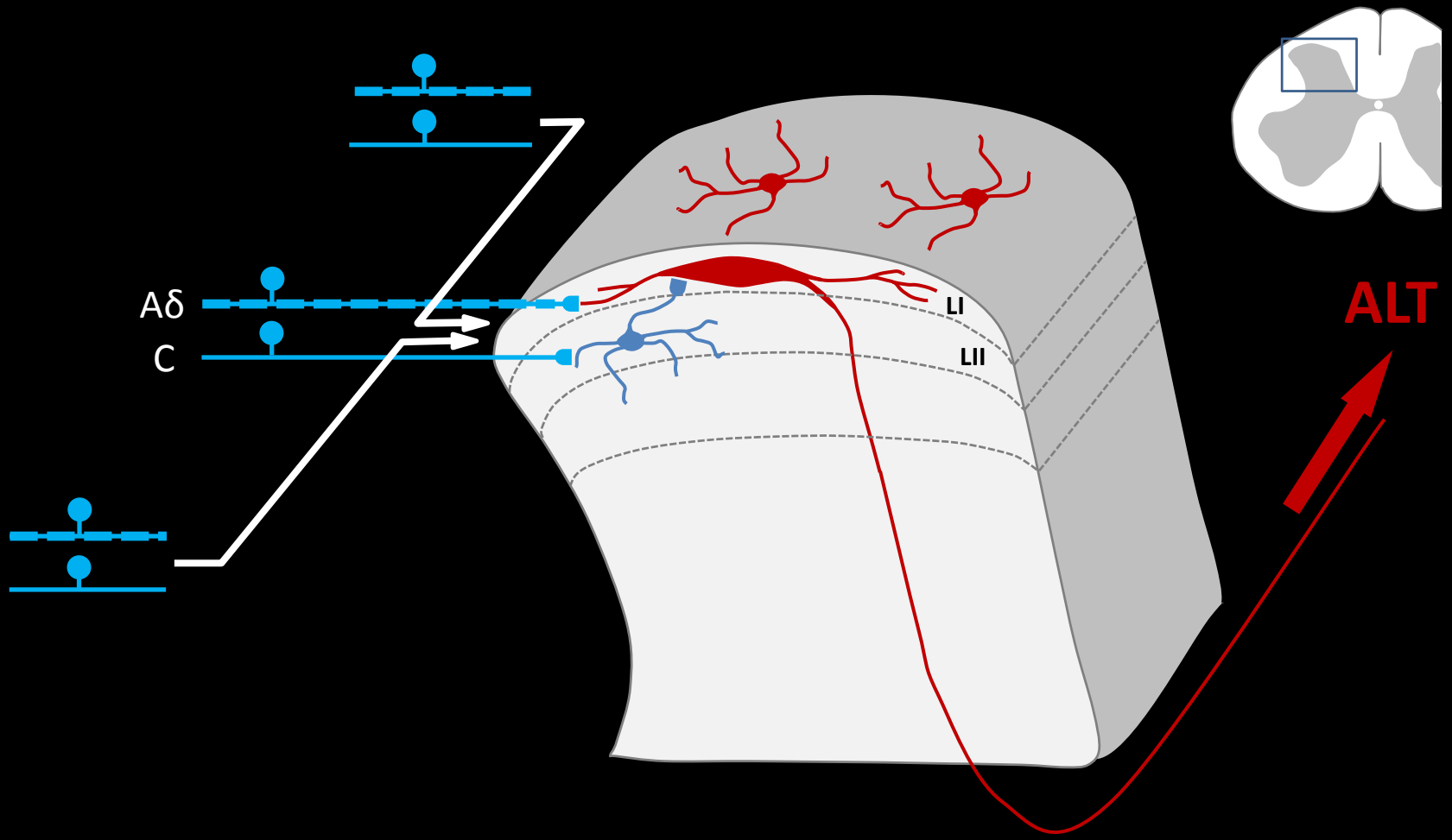
Primary afferent fibers



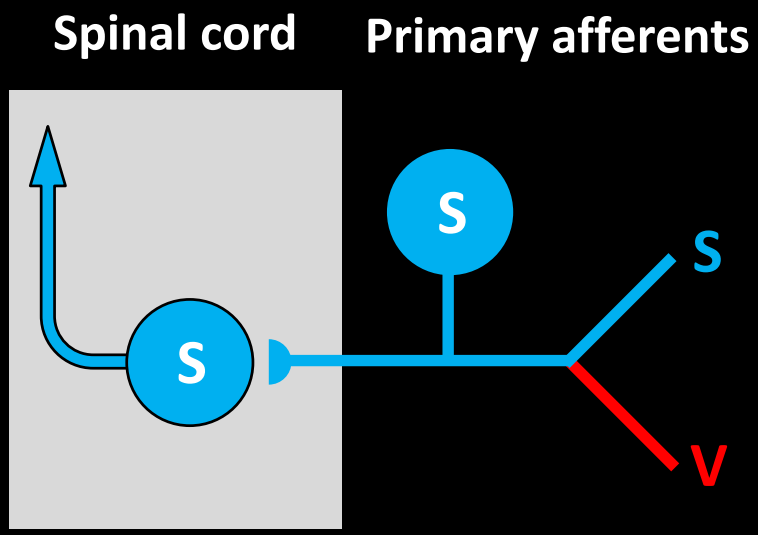
Nociceptors project to laminae I-II



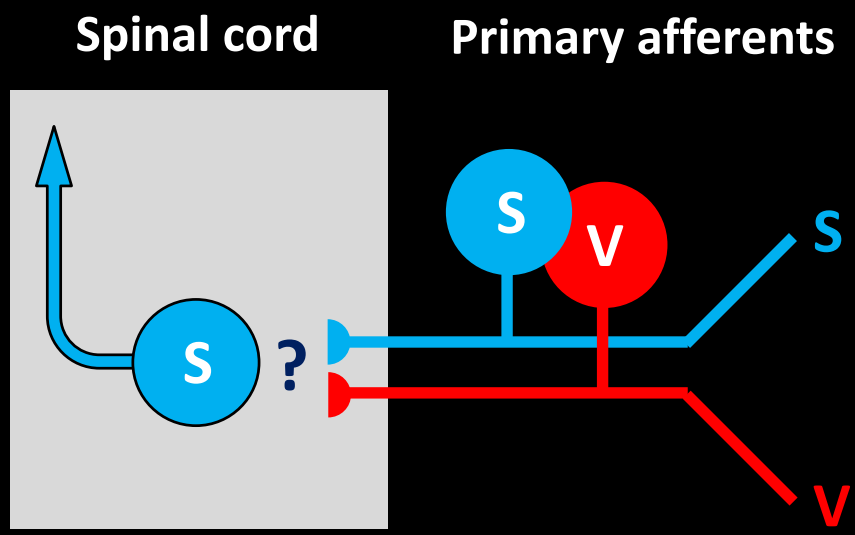
The superficial dorsal horn (laminae I-II)



Theories of referred pain origin

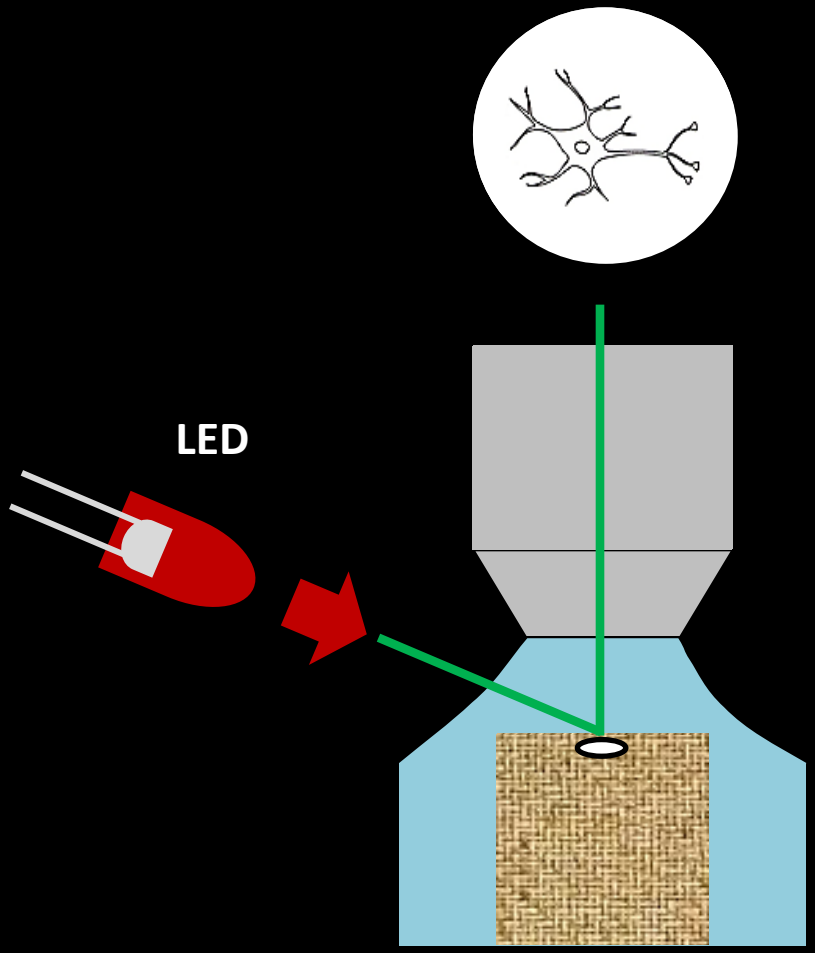


Dichotomizing axons
(are rare)



Spinal cord integration
(how?)

Cell imaging in thick tissues: The basic idea

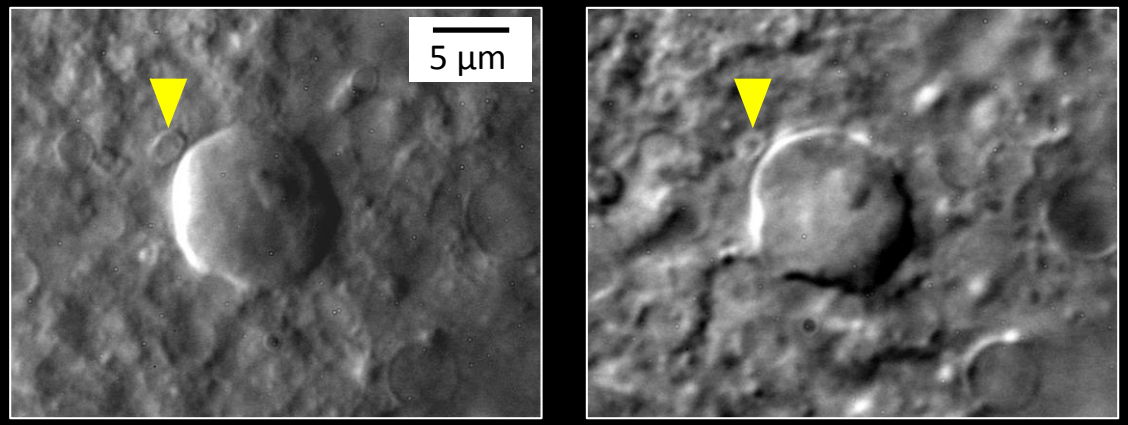


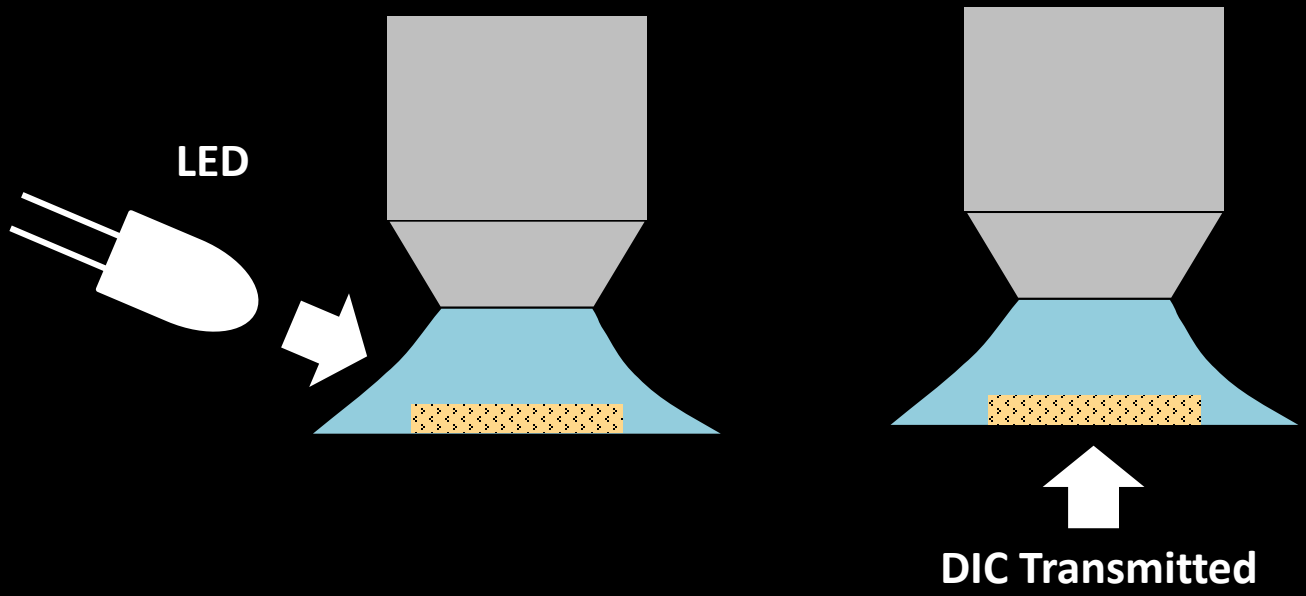
The Fresnel equation

Refractive indices n_1=1.33 n_2=1.35

Angle

LED *versus* DIC in a 200-µm slice



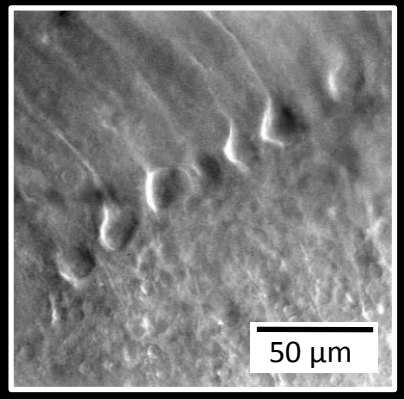


Oblique LED illumination

Whole brain

metal plate

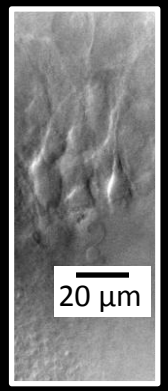
cerebellar cortex



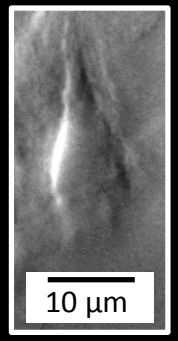
Purkinje cell layer

soma

cerebral cortex

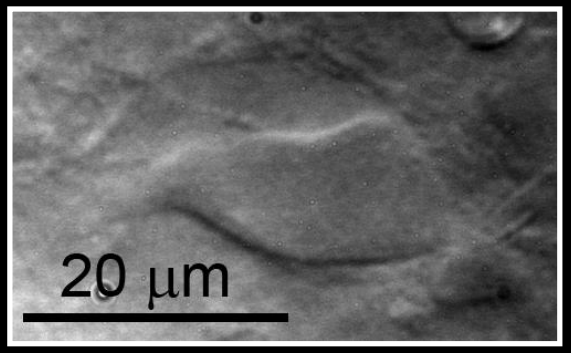


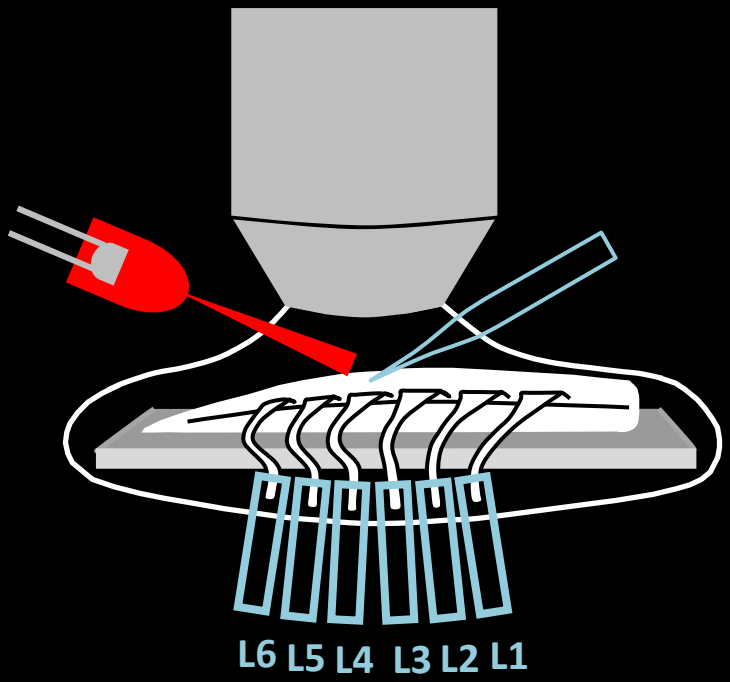
cell layer



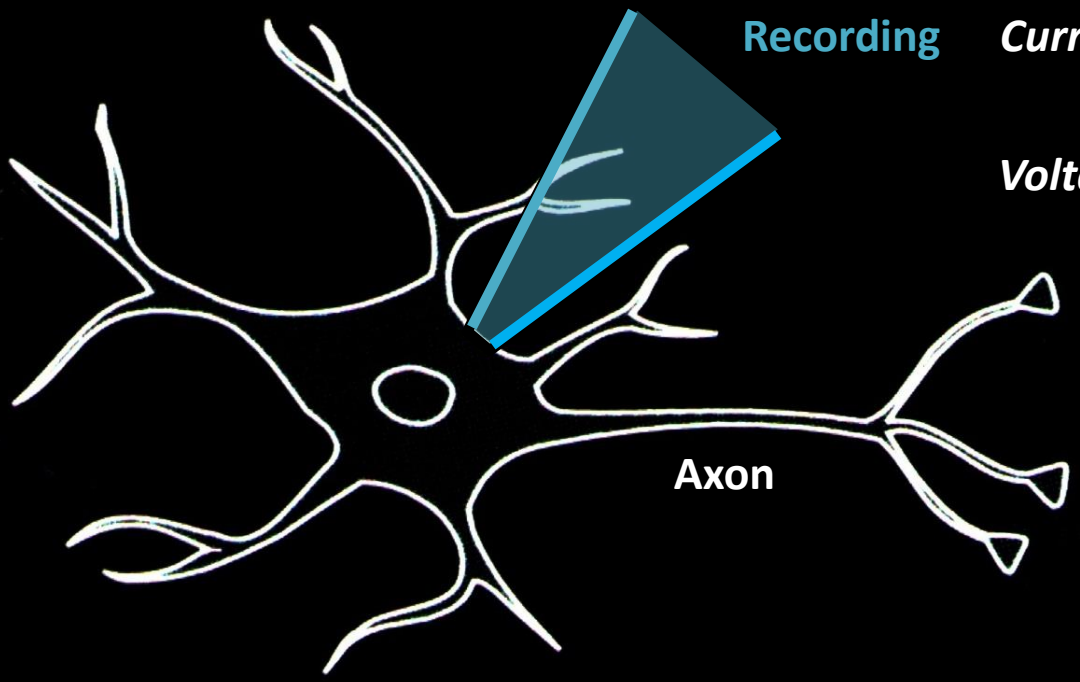
soma

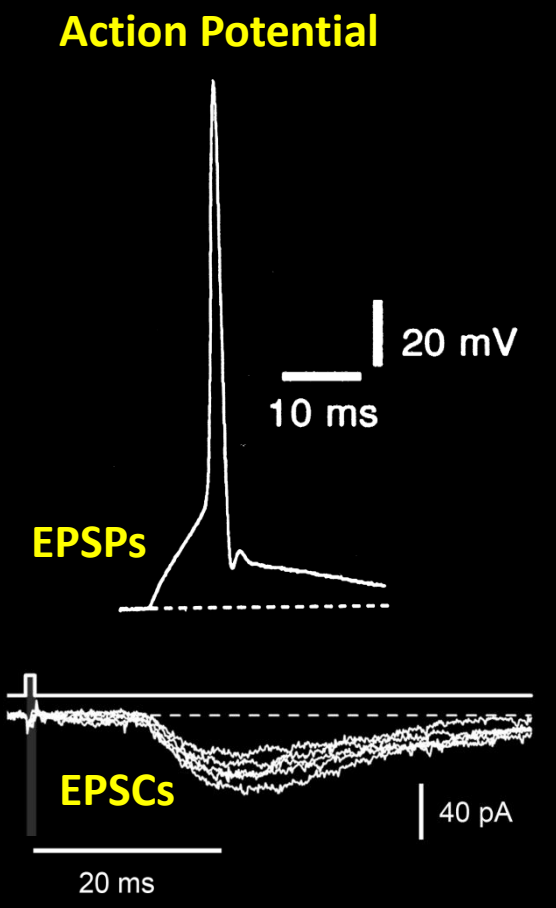
Multi-segmental input to lamina I neurons





Patch-clamp recording from spinal neurons

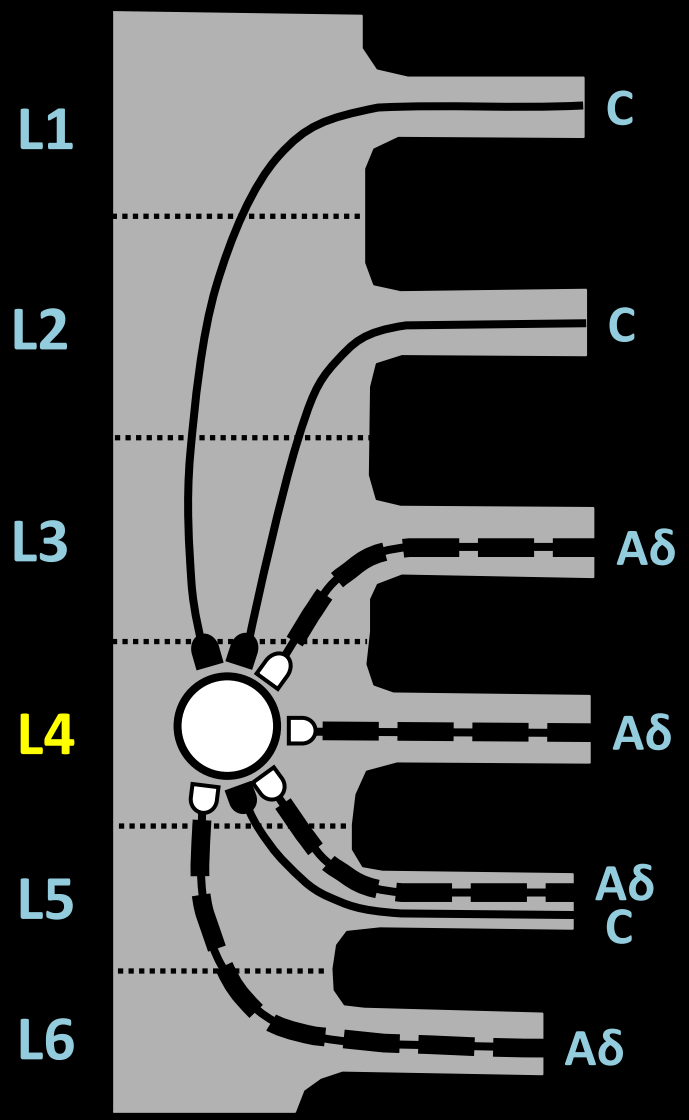




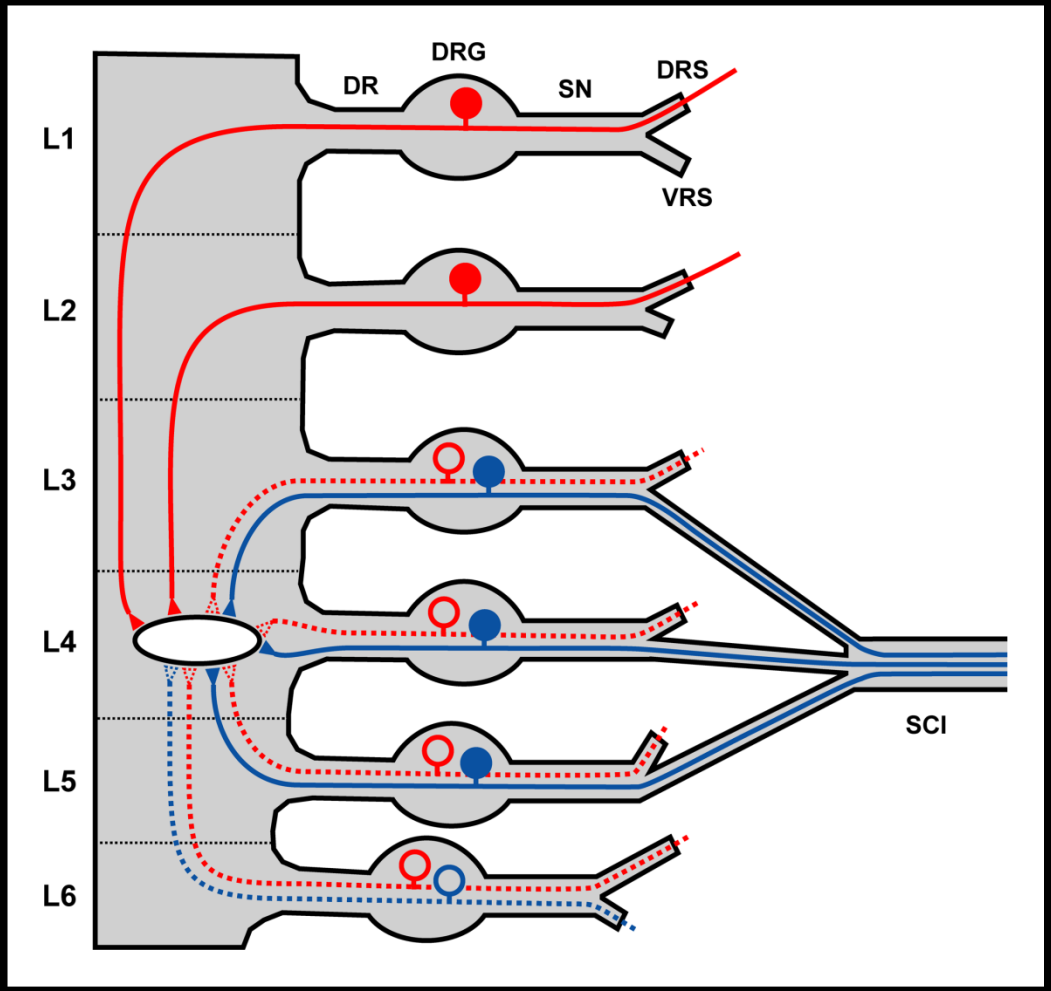
Broad monosynaptic inputs to lamina I neurons

Aδ + C

Aδ



Somatovisceral convergence on lamina I neurons?

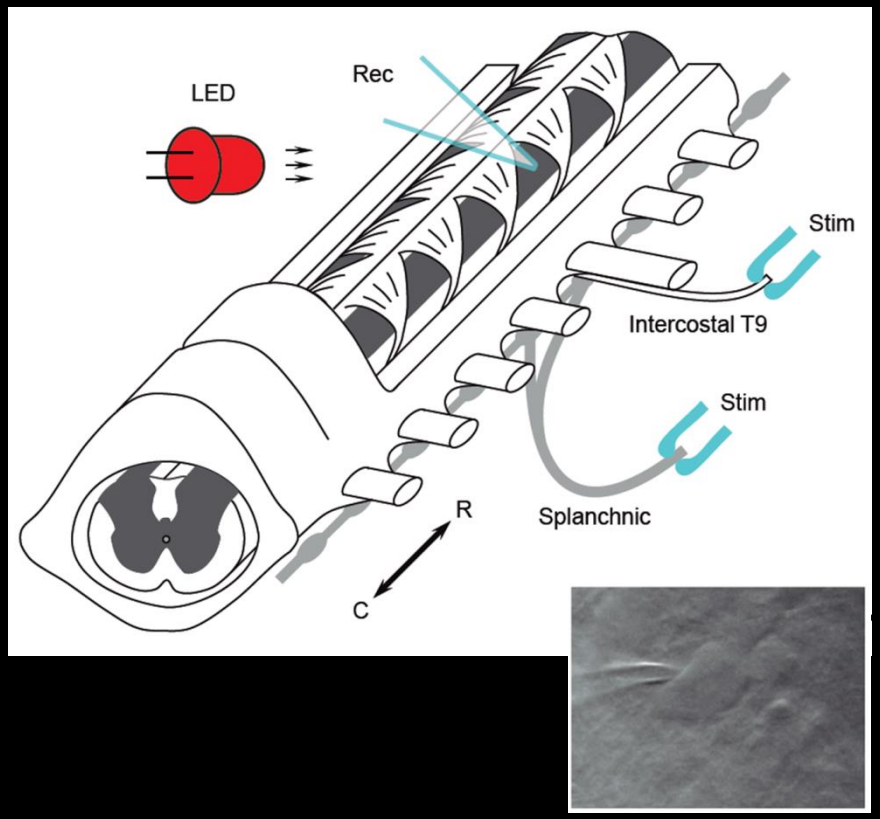


Preliminary conclusions:

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

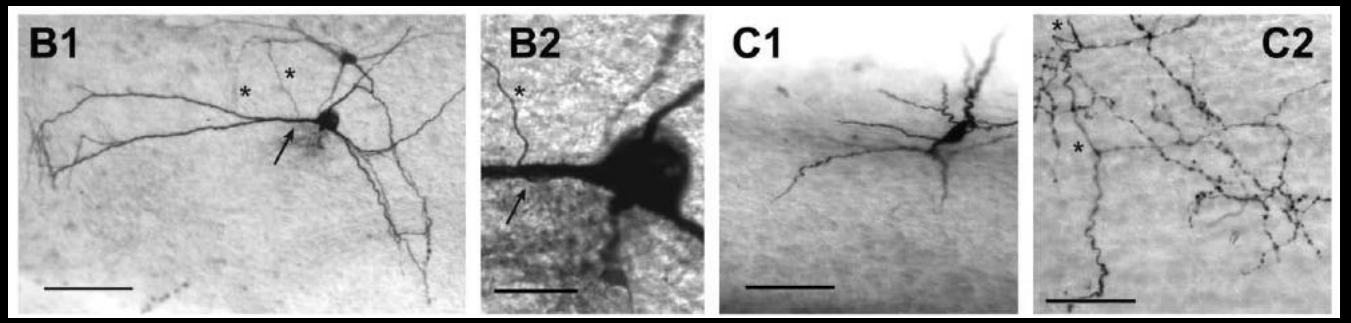
- Can lamina I neurons integrate somatovisceral inputs and serve as neuronal substrates of referred pain?

Study of somatovisceral convergence

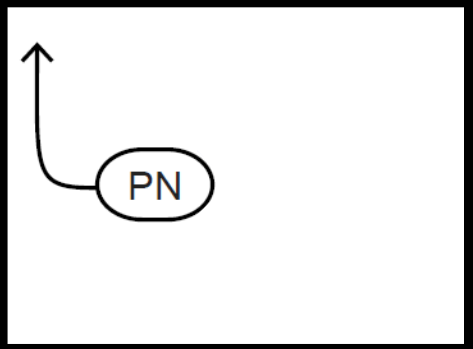


Somatic: Intercostal nerve

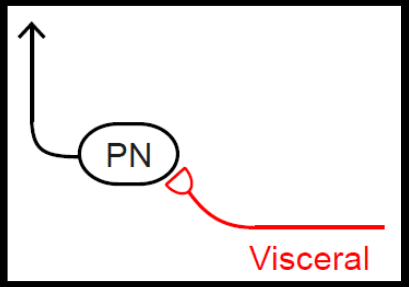
Visceral: Splanchnic nerve

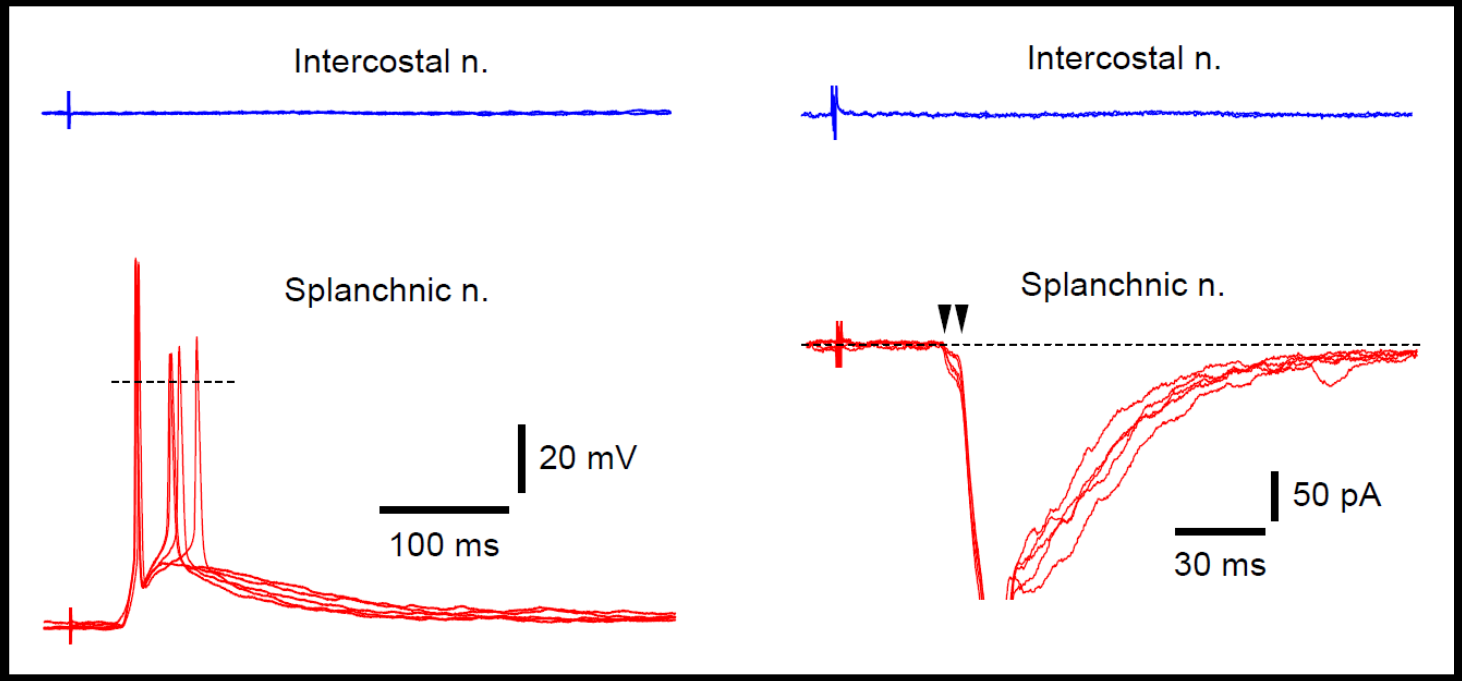


Somatovisceral lamina I neuron

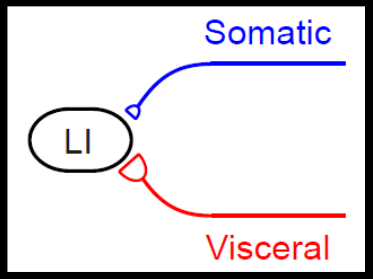


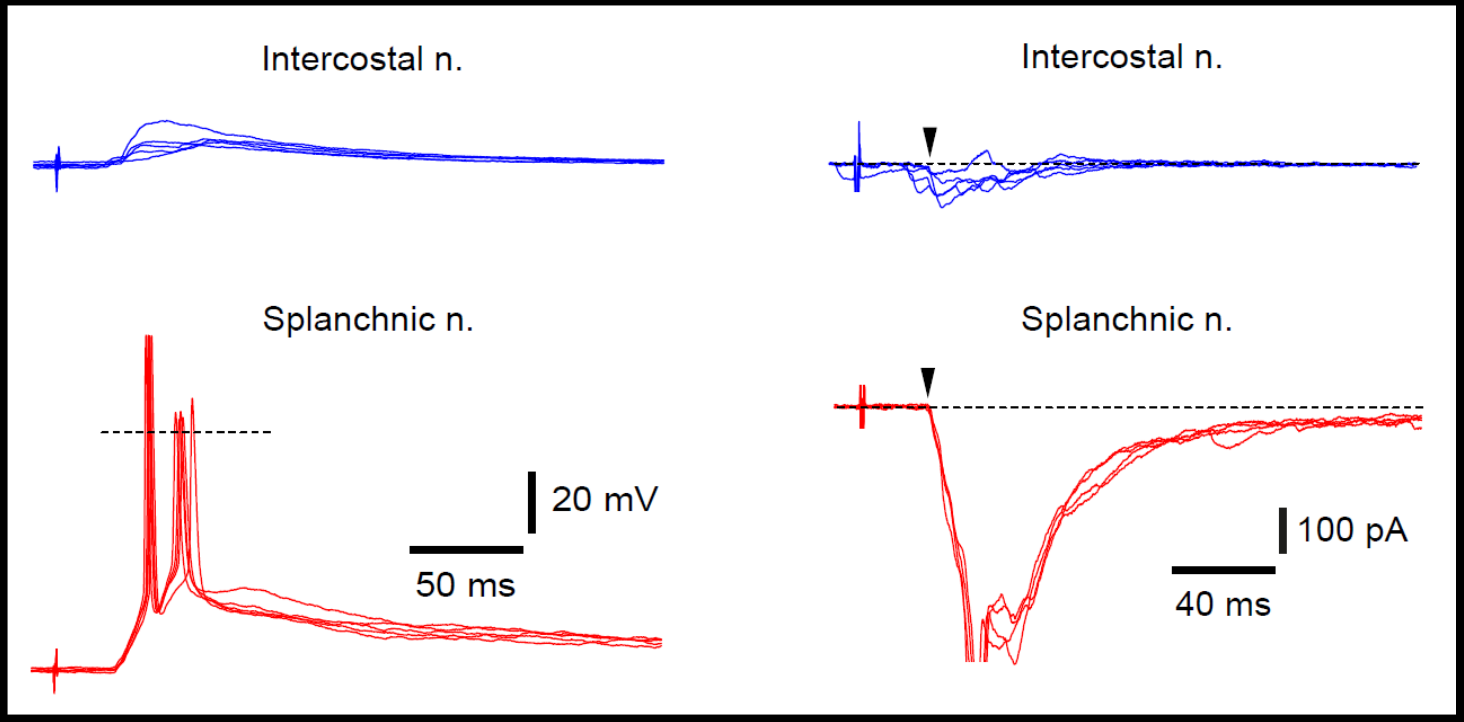
Visceral-specific neuron: Type 1



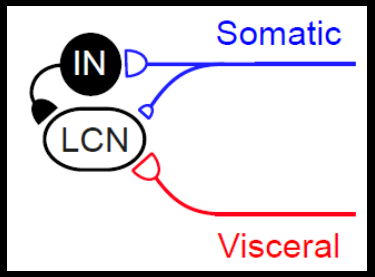


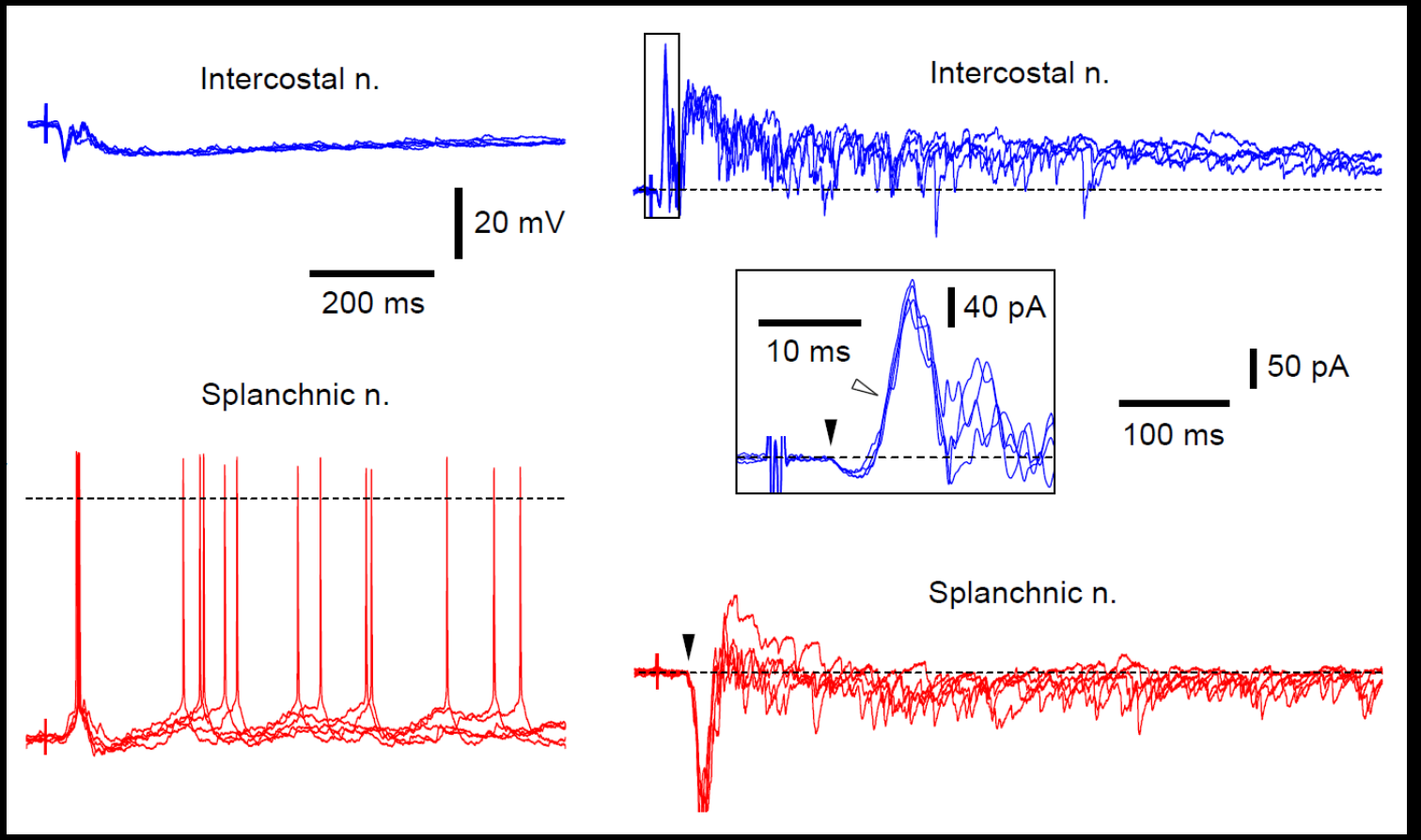
Visceral-specific neuron: Type 2



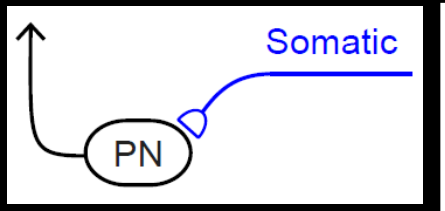


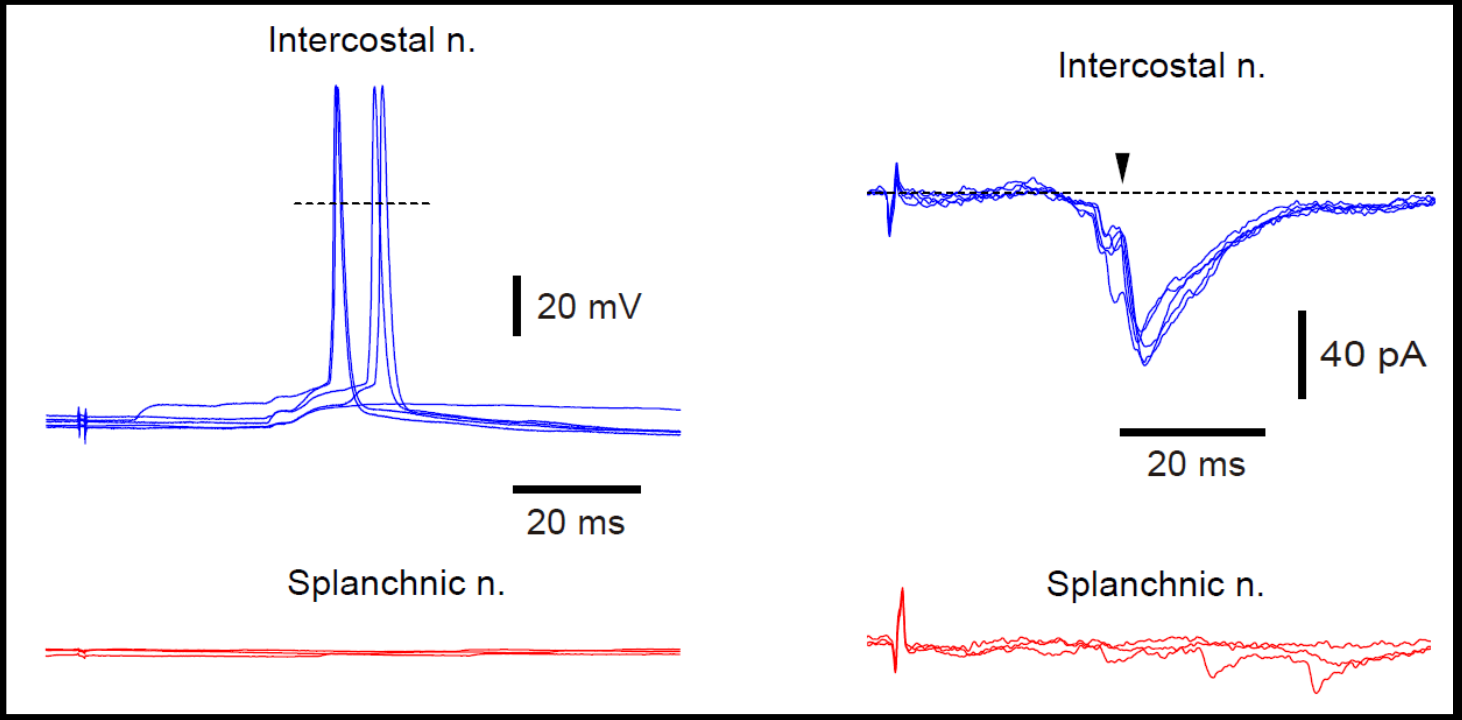
Visceral-specific neuron: Type 3



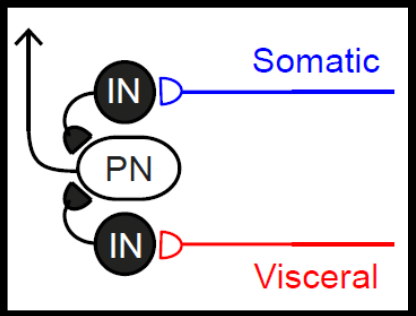


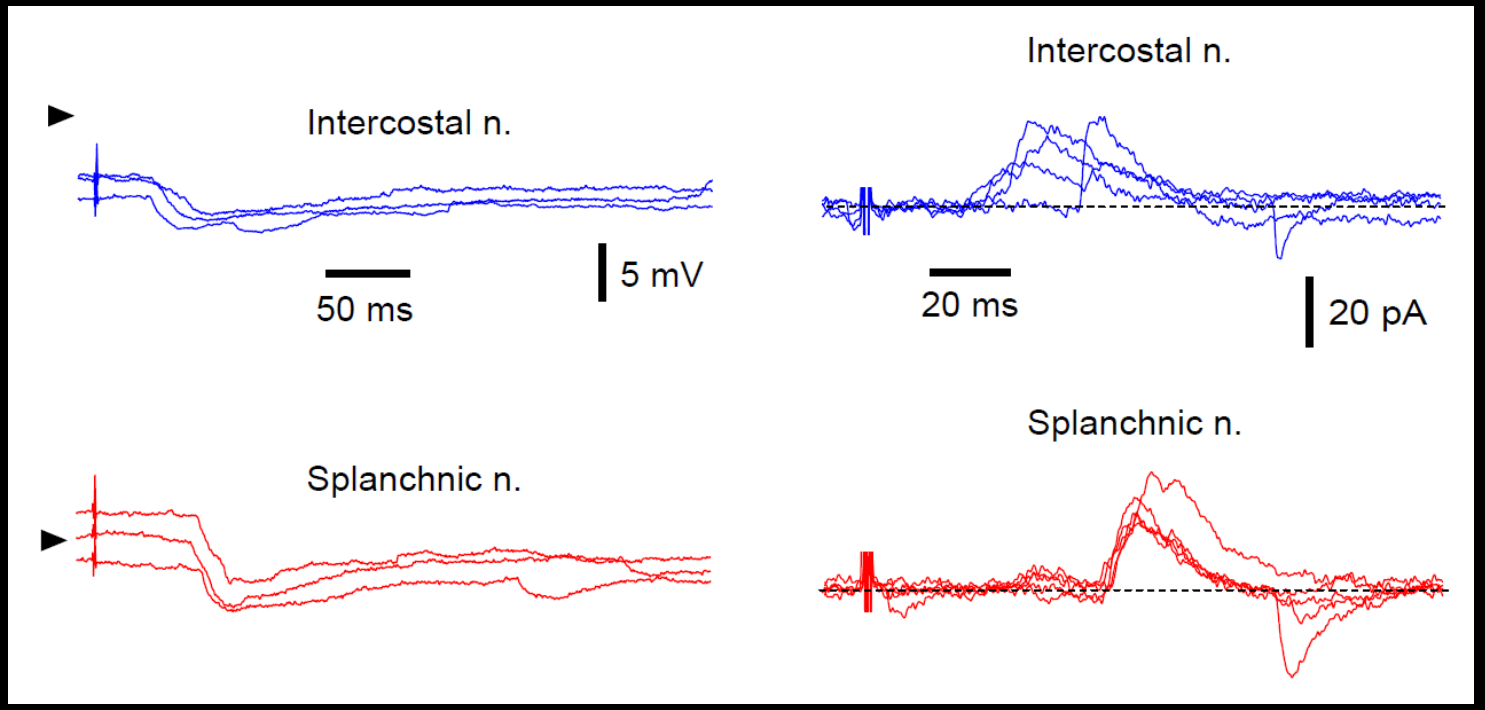
Somatic-specific neuron



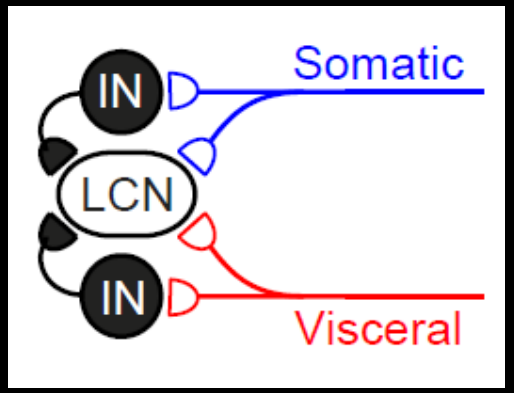


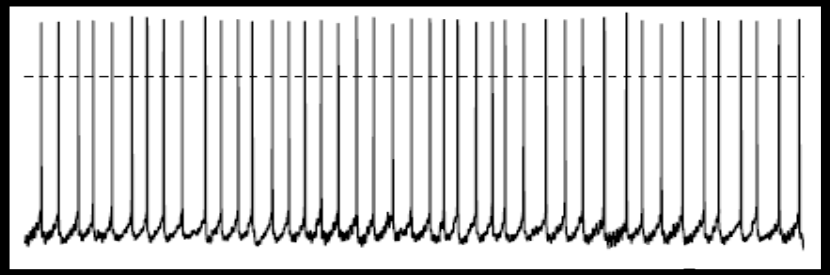
‘Inhibited’ neuron: Type 1

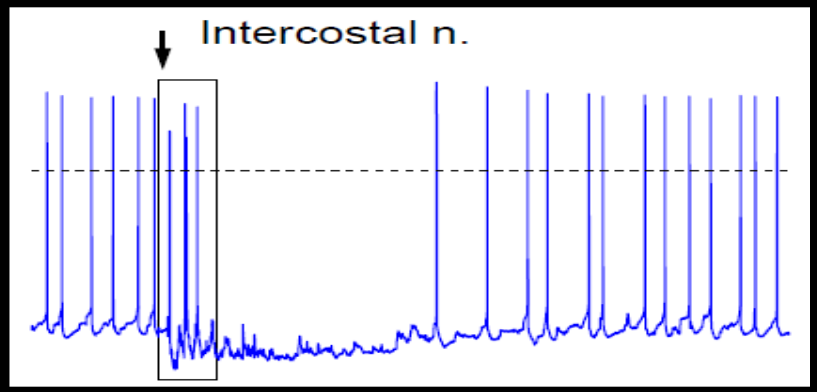


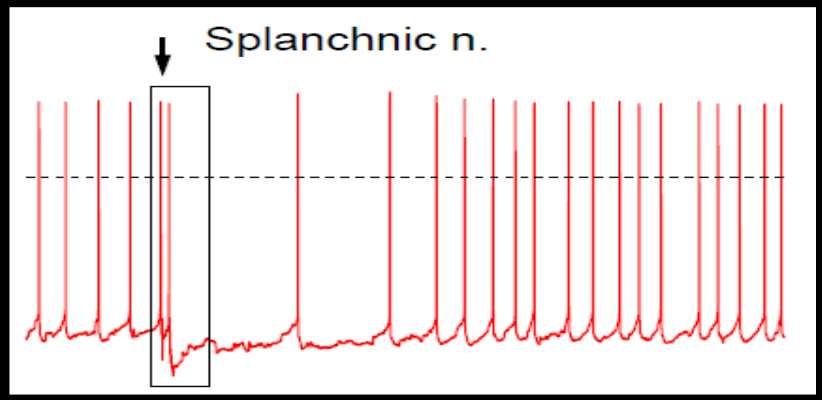


‘Inhibited’ neuron: Type 2

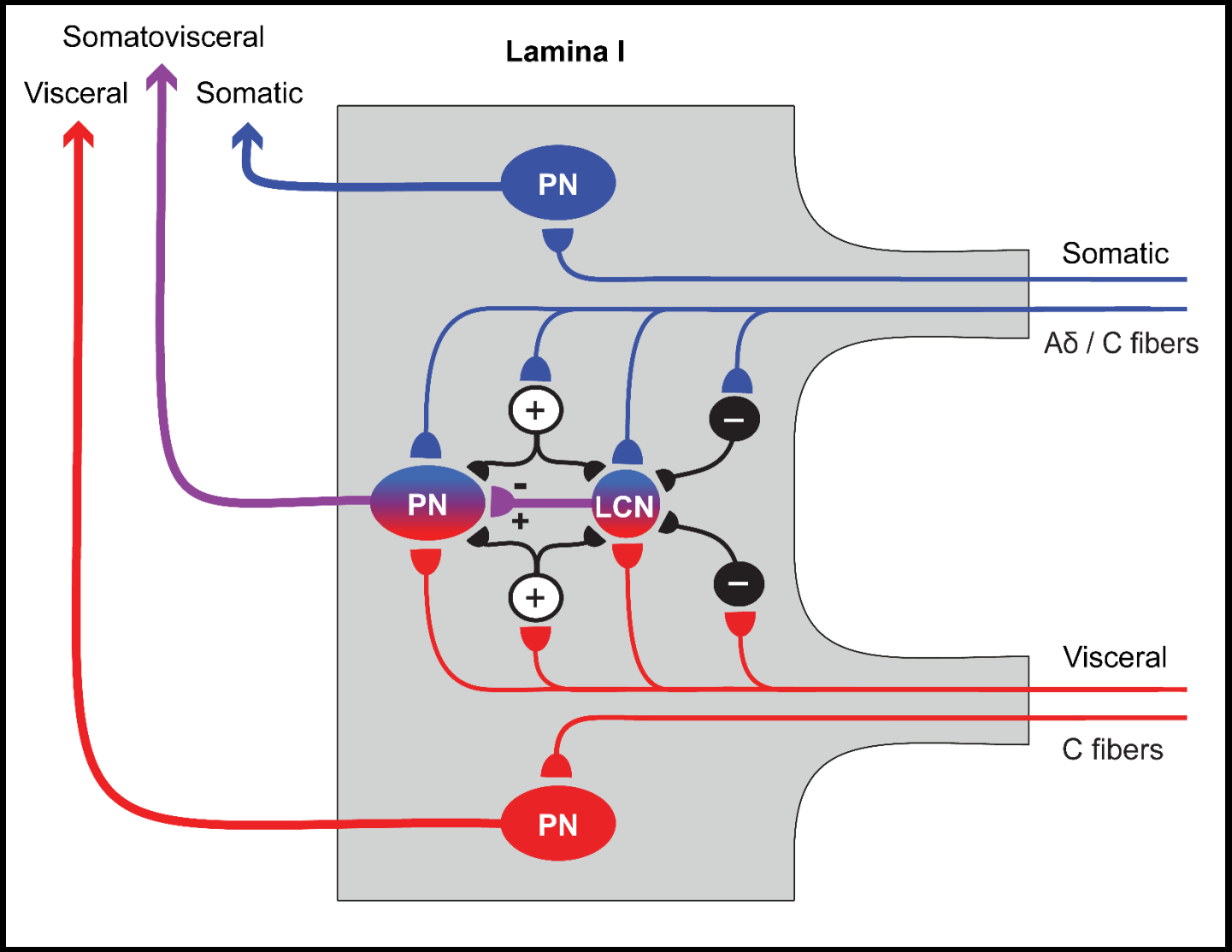








Somatovisceral integration in lamina I

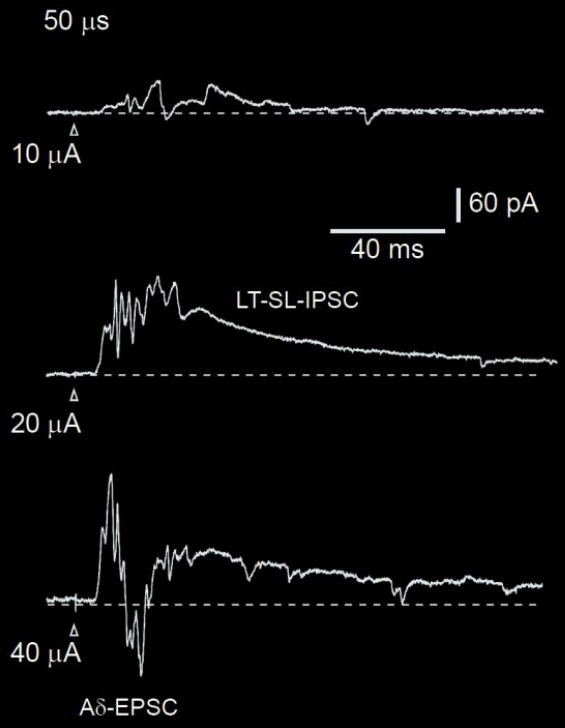


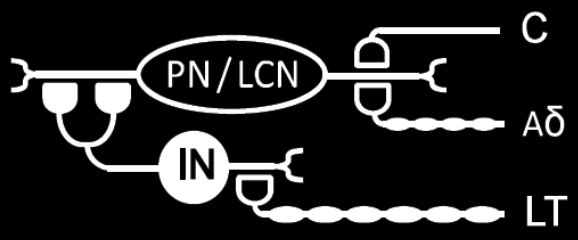
Conclusions:

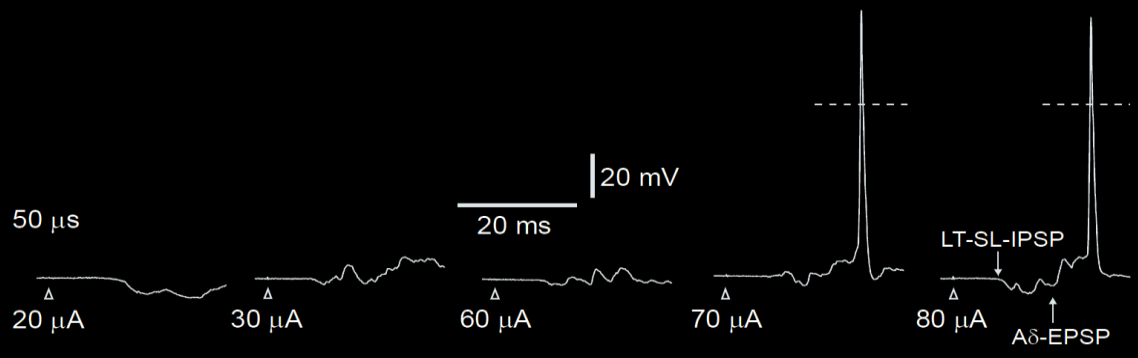
There is a monosynaptic somatovisceral afferent convergence on lamina I neurons, which

Can underlie complex neurological phenomenon of Referred Pain

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





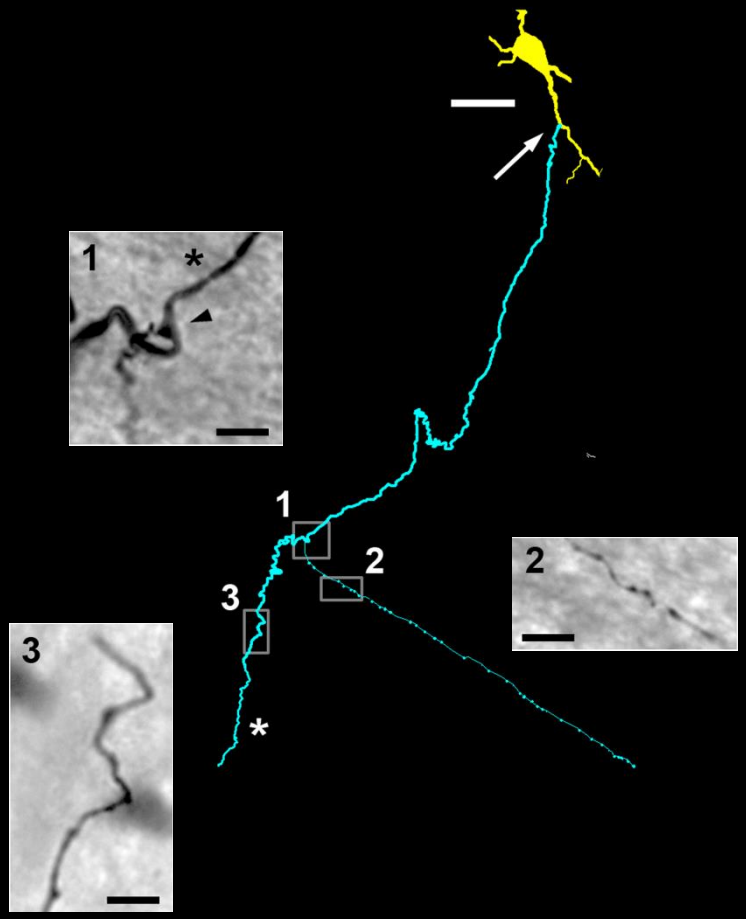


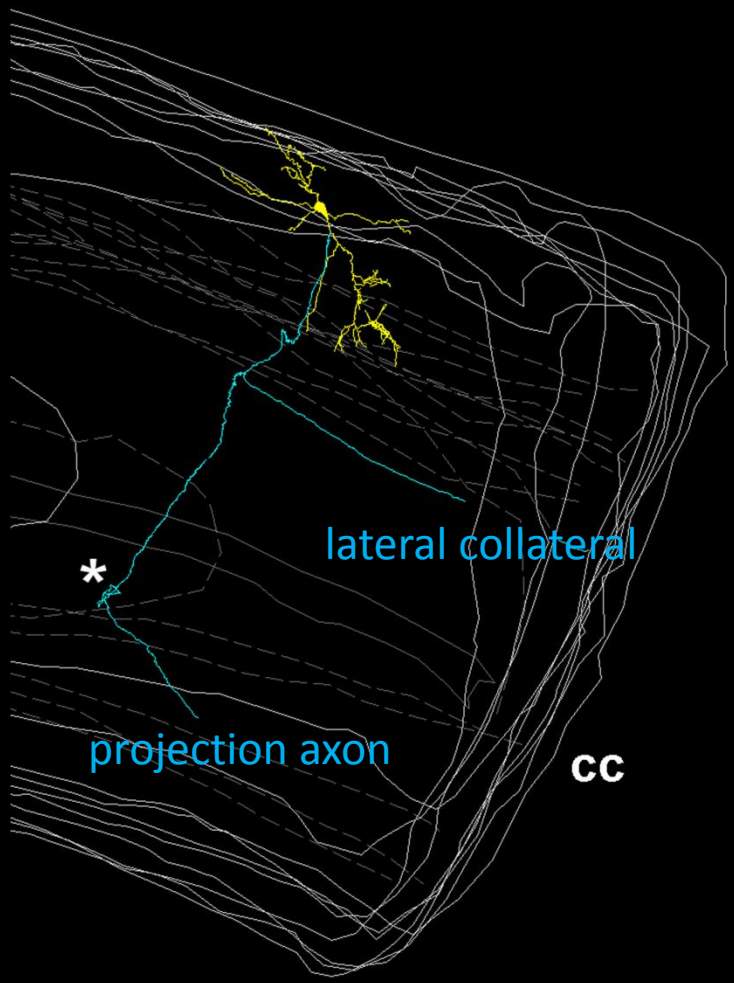
Conclusions:

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

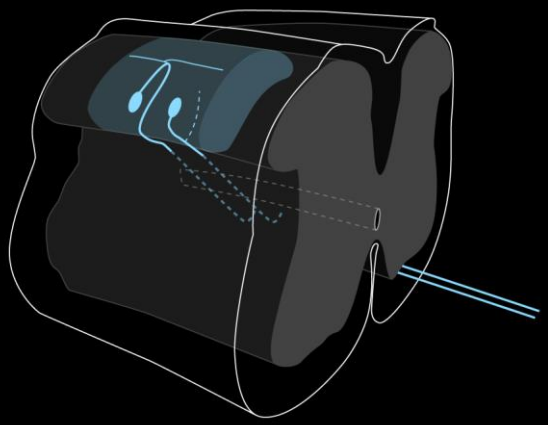
This direct inhibitory link between low-threshold afferents and **projection neurons** can function as **a postsynaptic gate** controlling the nociceptive information flow in the spinal cord

Local axon collaterals of ALT-projection neurons





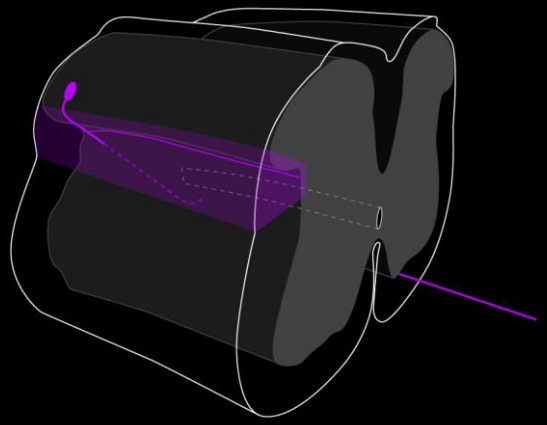
Axon collaterals of ALT-projection neurons



Dorsal Collateral Type I & II

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

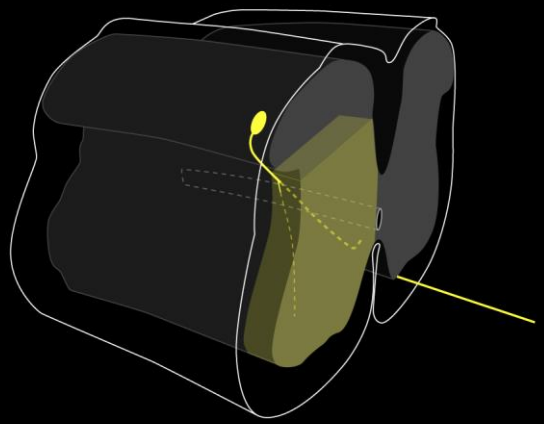
- Local segmental circuits



Lateral Collateral Type

Project to rostral and caudal segments

- Intersegmental connections
- Propriospinal projections

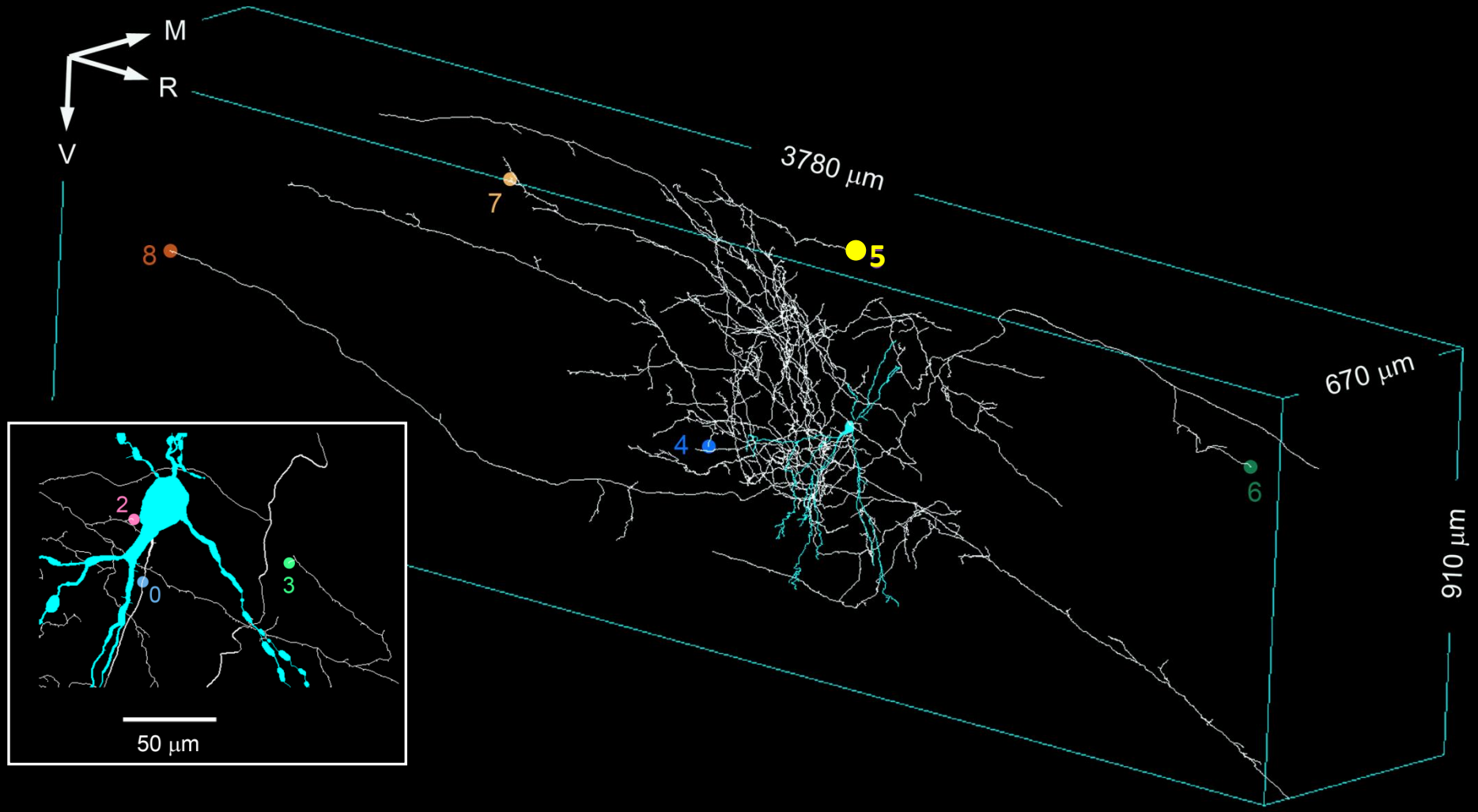


Ventral Collateral Type

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

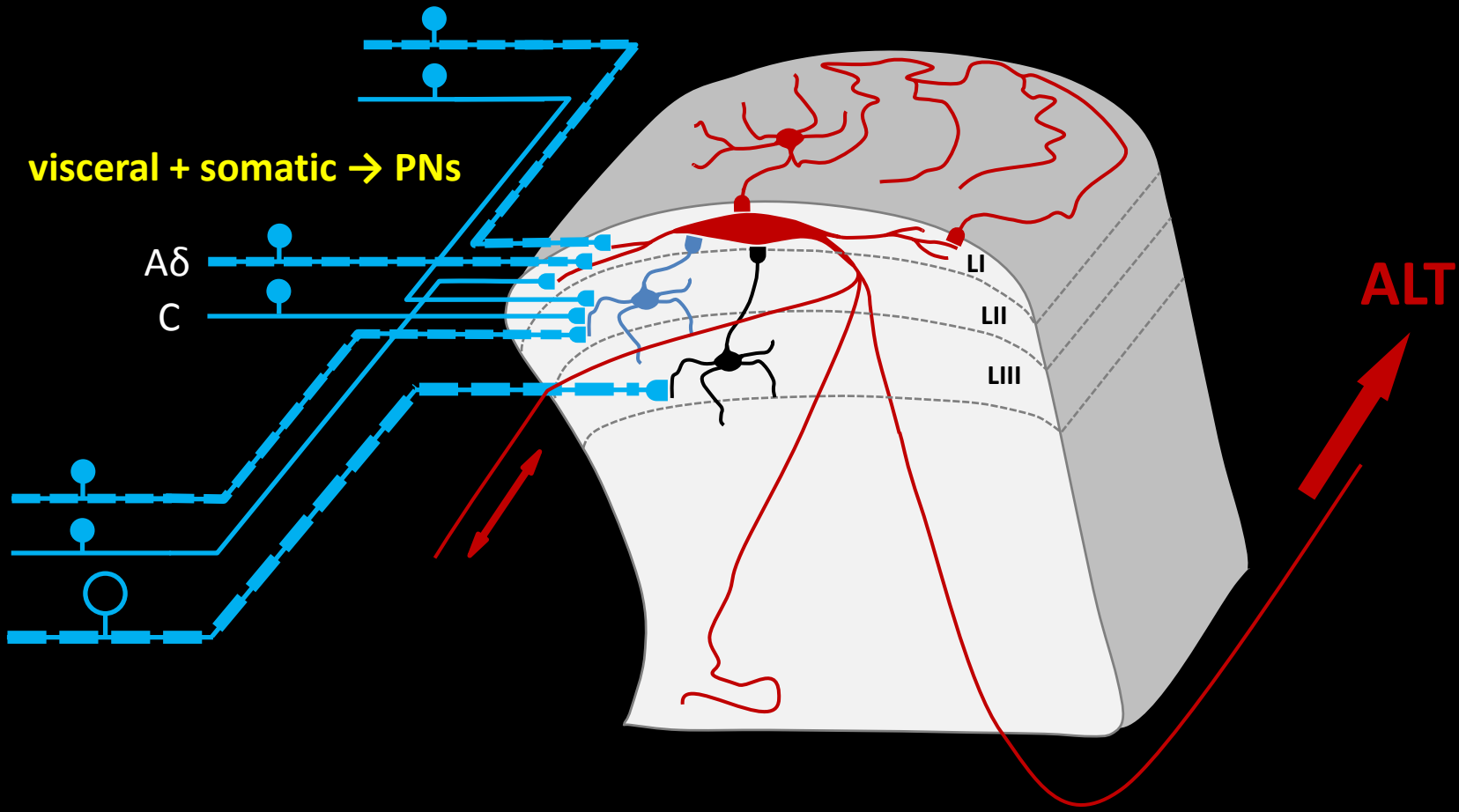


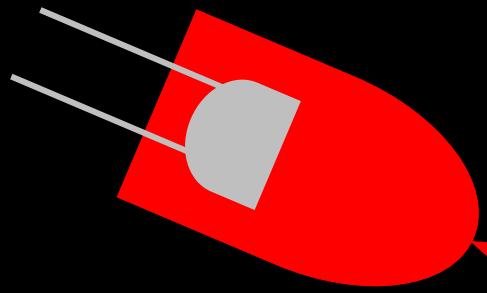
Conclusions:

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:





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