Direct, volitional control of the sensory information that reaches consciousness can be readily demonstrated by suddenly directing your attention to a body part, such as the fingers of your left hand, to which you were initially oblivious as you were attending to this text. Sensations from the fingers flood consciousness until attention is redirected to the text. Neural recordings in somatosensory and visual cortex confirm that neurons change their sensitivity, as reflected in their firing rates, much more so than their selectivity for particular stimuli. At a more abstract level, for example, we can switch our attention from the subject matter of a painting to the artist's technique.

Each primary sensory area of cortex has extensive projections back to its principal afferent relay nucleus in the thalamus. In fact, the number of feedback axons exceeds the number of afferent axons from the thalamus to the cortex. These projections have an important function that is not yet clear. One possibility is that they modulate the activity of certain neurons when attention and vigilance change or during motor tasks.

Centers in the brain are also able to modulate the responsiveness of sensory receptors. For example, neurons in the motor cortex can alter the sensitivity of sensory receptors in skeletal muscle that signal muscle length. Activation of gamma motor neurons by corticospinal pathways enhances the sensory responses of muscle spindle afferents to stretch. Neurons in the brain stem can directly modulate the frequency sensitivity of hair cells in the cochlea. Thus, information about a stimulus sent from peripheral sensory neurons to the brain is conditioned by the entire organism.

Top-Down Learning Mechanisms Influence Sensory Processing

What we perceive is always some combination of the sensory stimulus itself and the memories it both evokes and builds upon. The relationship between perception and memory was originally developed by empiricists, particularly the associationist philosophers James and John Stuart Mill. Their idea was that sensory and perceptual experiences that occur together or in close succession, particularly those that do so repeatedly, become associated so that thereafter the one triggers the other. Association is a powerful mechanism, and much of learning consists of forging associations through repetition.

Contemporary neuroscientists using multineuronal recordings discovered that sensory events evoke sequences of neuronal activation. These patterns of neural activity are believed to trigger memories of previous experiences of such stimulation patterns. For example, as we hear a work of music over and over again, the circuits of our auditory system are modified by the experience, and we learn to anticipate what comes next, completing the phrase before it occurs. Familiarity with the phrasing and harmonies used by a composer allows us to distinguish the operas of Verdi from those of Mozart, and the symphonies of Bruckner from those of Brahms. Likewise, when we drive to an unknown destination, our visual system is initially overwhelmed by new landmarks, as we assess which are important and which are not. With repeated trips, the journey becomes second nature and seems to take less time.

Percepts are uniquely subjective. When we look at a work of art, we superimpose our personal experience on the view; what we see is not just the image projected on the retina, but its contextual meaning to us as individuals. For example, when we view a historic photograph of important events in our lives, or persons we admired or detested, we recall not only the event in the image but also the words spoken and our emotional reactions in the past. The emotional response is muted or absent if we did not experience a direct connection to the event or person illustrated.

How can a network of neurons "recognize" a specific pattern of inputs from a population of presynaptic neurons? One potential mechanism is called *template matching*. Each neuron in the target population has a pattern of excitatory and inhibitory presynaptic connections. If the pattern of arriving action potentials fits the postsynaptic neuron's pattern of synaptic connections even approximately—activating many of its excitatory synapses but mostly avoiding activating its inhibitory synapses—the target neuron fires. The codes may also be combinatorial: the overall activity of a region remains the same with different stimuli, but the specific subset of neurons that are active when a particular input is presented constitute a "tag" specifying that input.

Charles F. Stevens has identified these in very different sensory systems and noted that such *maximum entropy* codes are highly efficient, able to represent many different stimuli for a set number of neurons. Refining our understanding of efficient coding, the Carandini and Harris labs have recently shown that the neural code in mouse visual cortex is indeed efficient and preserves fine detail, but in a manner that retains the ability to generalize by responding similarly to closely related visual stimuli. Such computational or algorithmic views have great promise for our understanding of sensory systems. *Artificial neural networks*, simulated using computers, can be trained on images and taught to "see." Daniel L. Yamins and James J.

DiCarlo have pointed out that as these artificial networks evolve the ability to recognize objects and faces, the properties of neuron-like "units" in particular layers begin to resemble the distribution of activity seen in corresponding cortical areas. Such artificial neural networks are trained by machine learning algorithms that modify the connection strength between units, similar to neuronal learning with repetition and synapse modification.

Precisely how the brain solves the recognition problem is uncertain. There is currently much evidence that the neural representation of a stimulus in the initial pathways of sensory systems is an isomorphic representation of the stimulus. Successive synaptic regions transform these initial representations into abstractions of our environment that we are beginning to decipher. In contrast, we barely understand the top-down mechanisms by which incoming sensory information invokes memories of past occurrences and activates our prejudices and opinions.

One view of these processes is Bayesian: Our experience and understanding of the world inform a top-down *sensory prior* that describes our likely environment. The primary insight of Bayes's rule is that decisions are made by the likelihood ratio of current evidence from a test stimulus and the subject's previous experience of similar stimuli (priors), all modified by the task contingencies (rewards and hazards). Ongoing sensory information contributes immediate data, and the two combine to form an up-to-the-moment *posterior* estimate of our surroundings and our place in them. When we do understand these neural codes and the algorithms and mechanisms that generate and interpret them, it is likely that we will be on the verge of understanding cognition, the way in which information is coded in our memory and our understanding. That is what makes the study of neural coding so challenging and exciting.

Highlights

1. Our sensory systems provide the means by which we perceive the external world, remain alert, form a body image, and regulate our movements. Sensations arise when external stimuli interact with some of the billion sensory receptors that innervate every organ of the body. The information detected by these receptors is conveyed to the brain as trains of action potentials traveling along individual sensory axons.
2. All sensory systems respond to four elementary features of stimuli—modality, location, intensity, and duration. The diverse sensations we experience—the sensory modalities—reflect different forms of energy that are transformed by receptors into depolarizing or hyperpolarizing electrical signals called receptor potentials. Receptors specialized for particular forms of energy, and sensitive to particular ranges of the energy bandwidth, allow humans to sense many kinds of mechanical, thermal, chemical, and electromagnetic events.
3. The intensity and duration of stimulation are represented by the amplitude and time course of the receptor potential and by the total number of receptors activated. In order to transmit sensory information over long distances, the receptor potential is transformed into a digital pulse code, sequences of action potentials whose frequency of firing is proportional to the strength of the stimulus. The pattern of action potentials in peripheral nerves and in the brain gives rise to sensations whose qualities can be measured directly using a variety of psychophysical paradigms such as magnitude estimation, signal detection methods, and discrimination tasks. The temporal features of a stimulus, such as its duration and changes in magnitude, are signaled by the dynamics of the spike train.
4. The location and spatial dimensions of a stimulus are conveyed through each receptor's receptive field, the precise area in the sensory domain in which stimulation activates the receptor. The identity of the active sensory neurons therefore signals not only the modality of a stimulus but also the place where it occurs.
5. These messages are analyzed centrally by several million sensory neurons performing different, specific functions in parallel. Each sensory neuron extracts highly specific and localized information about the external or internal environment, and in turn has a specific effect on sensation and cognition because it projects to specific places in the brain that have specific sensory, motor, or cognitive functions. To maintain the specificity of each modality within the nervous system, receptor axons are segregated into discrete anatomical pathways that terminate in unimodal nuclei.
6. Sensory information in the central nervous system is processed in stages, in the sequential relay nuclei of the spinal cord, brain stem, thalamus, and cerebral cortex. Each nucleus integrates sensory inputs from adjacent receptors and, using networks of inhibitory neurons, emphasizes the strongest signals. After about a dozen synaptic steps in each sensory system, neural activity

converges on neuronal groups whose function is multisensory and more directly cognitive.

7. Processing of sensory information in the cerebral cortex occurs in multiple cortical areas in parallel and is not strictly hierarchical. Feedback connections from areas of the brain involved in cognition, memory, and motor planning control the incoming stream of sensory information, allowing us to interpret sensory stimulation in the context of past experience and current goals.
8. The richness of sensory experience—the complexity of sounds in a Mahler symphony, the subtle layering of color and texture in views of the Grand Canyon, or the multiple flavors of a salsa—requires the activation of large ensembles of receptors acting in parallel, each one signaling a particular aspect of a stimulus. The neural activity in a set of thousands or millions of neurons should be thought of as coordinated activity that conveys a "neural image" of specific properties of the external world.
9. Our sensory systems are increasingly appreciated as computational and algorithmic encoders, processors, and decoders of information. Insights from machine learning, information theory, artificial neural networks, and Bayesian inference continue to inform our understanding of what we perceive in our bodies and from the world around us.

Esther P. Gardner
Daniel Gardner

Selected Reading

Basbaum AI, Kaneko JH, Shepherd GM, Westheimer G (eds). 2008. *The Senses: A Comprehensive Reference* (6 vols). Oxford: Elsevier.

Dowling JE. 1987. *The Retina: An Approachable Part of the Brain.* Cambridge, MA: Belknap.

Gerstein GL, Perkel DH, Dayhoff JE. 1985. Cooperative firing activity in simultaneously recorded populations of neurons: detection and measurement. J Neurosci 5:881–889.

Green DM, Swets JA. 1966. *Signal Detection Theory and Psychophysics.* New York: Wiley. (Reprinted 1974, Huntington, NY: Robert E. Krieger.)

Kandel ER. 2016. *Reductionism in Art and Brain Science: Bridging the Two Cultures.* New York: Columbia Univ. Press.

Moore GP, Perkel DH, Segundo JP. 1966. Statistical analysis and functional interpretation of neuronal spike data. Annu Rev Physiol 28:493–522.

Mountcastle VB. 1998. *Perceptual Neuroscience: The Cerebral Cortex*. Cambridge, MA: Harvard Univ. Press.

Singer W. 1999. Neuronal synchrony: a versatile code for the definition of relations? Neuron 24:49–65.

Stevens SS. 1961. The psychophysics of sensory function. In: WA Rosenblith (ed). *Sensory Communication*, pp. 1–33. Cambridge, MA: MIT Press.

Stevens SS. 1975. *Psychophysics: Introduction to Its Perceptual, Neural, and Social Prospects*. New York: Wiley.

References

Adrian ED, Zotterman Y. 1926. The impulses produced by sensory nerve-endings. Part 2. The response of a single end-organ. J Physiol (Lond) 61:151–171.

Albright TD, Stoner GR. 2002. Contextual influences on visual processing. Annu Rev Neurosci 25:339–379.

Andres KH, von Düring M. 1973. Morphology of cutaneous receptors. In: Iggo A (ed). *Handbook of Sensory Physiology*, Vol. 2, *Somatosensory System*, pp. 3–28. Berlin: Springer-Verlag.

Barch DM, Burgess GC, Harms MP, et al. 2013. Function in the human connectome: task-fMRI and individual differences in behavior. Neuroimage 80:169–189.

Berkeley G. [1710] 1957. *A Treatise Concerning the Principles of Human Knowledge*. K Winkler (ed). Indianapolis: Bobbs-Merrill.

Britten KH, Shadlen MN, Newsome WT, Movshon JA. 1992. The analysis of visual motion: a comparison of neuronal and psychophysical performance. J Neurosci 12:4745–4768.

Carandini M, Heeger DJ. 2011. Normalization as a canonical neural computation. Nat Rev Neurosci 13:51–62.

Chang L, Tsao DY. 2017. The code for facial identity in the primate brain. Cell 169:1013–1028.

Colquhoun D. 2014. An investigation of the false discovery rate and the misinterpretation of *p*-values. Royal Soc Open Sci 1:140216.

DiCarlo JJ, Zoccolan D, Rust NC. 2012. How does the brain solve visual object recognition? Neuron 73:415–434.

Dudel J. 1983. General sensory physiology. In: RF Schmitt, G Thews (eds). *Human Physiology*, pp. 177–192. Berlin: Springer-Verlag.

Gandhi SP, Heeger DJ, Boynton GM. 1999. Spatial attention affects brain activity in human primary visual cortex. Proc Natl Acad Sci U S A 96:3314–3319.

Gazzaniga MS (ed). 2009. *The Cognitive Neurosciences*, 4th ed. Cambridge, MA: MIT Press.

Glasser MF, Coalson TS, Robinson EC, et al. 2016. A multimodal parcellation of human cerebral cortex. Nature 536:171–178.

Hubel DH, Wiesel TN. 1968. Receptive fields and functional architecture of monkey striate cortex. J Physiol 195:215–243.

Hume D. [1739] 1984. *A Treatise of Human Nature*. EC Mossner (ed). New York: Penguin.

Johansson RS, Vallbo AB. 1979. Detection of tactile stimuli. thresholds of afferent units related to psychophysical thresholds in the human hand. J Physiol 297:405–422.

Johnson KO, Hsiao SS, Yoshioka T. 2002. Neural coding and the basic law of psychophysics. Neuroscientist 8:111–121.

Kant I. [1781/1787] 1961. *Critique of Pure Reason*. NK Smith (transl.). London: Macmillan.

Kirkland KL, Gerstein GL. 1999. A feedback model of attention and context dependence in visual cortical networks. J Comput Neurosci 7:255–267.

LaMotte RH, Mountcastle VB. 1975. Capacities of humans and monkeys to discriminate between vibratory stimuli of different frequency and amplitude: a correlation between neural events and psychophysical measurements. J Neurophysiol 38:539–559.

Li HH, Rankin J, Rinzel J, Carrasco M, Heeger DJ. 2017. Attention model of binocular rivalry. Proc Natl Acad Sci U S A 114:E6192-E6201.

Livingstone MS, Hubel DH. 1987. Psychophysical evidence for separate channels for the perception of form, color, movement, and depth. J Neurosci 7:3416–3468.

Locke J. 1690. *An Essay Concerning Human Understanding: In Four Books*, Book 2, Chapter 1. London.

Mountcastle VB, Talbot WH, Kornhuber HH. 1966. The neural transformation of mechanical stimuli delivered to the monkey's hand. In: AVS de Reuck, J Knight (eds). *Ciba Foundation Symposium: Touch, Heat and Pain*, pp. 325–351. London: Churchill.

Ochoa J, Torebjörk E. 1983. Sensations evoked by intraneural microstimulation of single mechanoreceptor units innervating the human hand. J Physiol 342:633–654.

Raichle ME. 2011. The restless brain. Brain Connect 1:3–12.

Roy A, Steinmetz PN, Hsiao SS, Johnson KO, Niebur E. 2007. Synchrony: a neural correlate of somatosensory attention. J Neurophysiol 98:1645–1661.

Shepherd GM. 1994. *Neurobiology*, 3rd ed. New York: Oxford Univ. Press.

Smith SM, Beckmann CF, Andersson J, et al. 2013. Resting-state fMRI in the Human Connectome Project. Neuroimage 80:144–168.

Stevens CF. 2015. What the fly's nose tells the fly's brain. Proc Natl Acad Sci U S A 112:9460–9465.

Stevens CF. 2018. Conserved features of the primate face code. Proc Natl Acad Sci U S A 115:584–588.

Stringer C, Pachitariu M, Steinmetz N, Carandini M, Harris KD. 2019. High-dimensional geometry of population responses in visual cortex. Nature 571:361–365.

Swets JA. 1973. The relative operating characteristic in psychology: a technique for isolating effects of response bias finds wide use in the study of perception and cognition. Science 182:990–1000.

Swets JA. 1986. Indices of discrimination or diagnostic accuracy: their ROCs and implied models. Psychol Bull 99:100–117.

Talbot WH, Darian-Smith I, Kornhuber HH, Mountcastle VB. 1968. The sense of flutter-vibration: comparison of the human capacity with response patterns of mechanoreceptive afferents from the monkey hand. J Neurophysiol 31:301–334.

Tanner WP, Swets JA. 1954. A decision-making theory of visual detection. Psychol Rev 61:401–409.

Thurstone LL. 1927. A law of comparative judgment. Psychol Rev 34:273–286.

Ungerleider LG, Mishkin M. 1982. Two cortical visual systems. In: DG Ingle, MA Goodale, RJW Mansfield (eds). *Analysis of Visual Behavior*, pp. 549–586. Cambridge, MA: MIT Press.

Yamins DLK, DiCarlo JJ. 2016. Using goal-driven deep learning models to understand sensory cortex. Nat Neurosci 19:356–365.

18

Receptors of the Somatosensory System

Neurophysiological studies of the individual sensory modalities were first conducted in the somatosensory system (Greek *soma*, the body), the system that transmits information coded by receptors distributed throughout the body. Charles Sherrington, one of the earliest investigators of these bodily senses, noted that the somatosensory system serves three major functions: proprioception, exteroception, and interoception.

Proprioception is the sense of oneself (Latin *proprius*, one's own). Receptors in skeletal muscle, joint capsules, and the skin enable us to have conscious awareness of the posture and movements of our own body, particularly the four limbs and the head. Although one can move parts of the body without sensory feedback from proprioceptors, the movements are often clumsy, poorly coordinated, and inadequately adapted to complex tasks, particularly if visual guidance is absent.

Exteroception is the sense of direct interaction with the external world as it impacts the body. The principal mode of exteroception is the sense of *touch*, which includes sensations of contact, pressure, stroking, motion, and vibration, and is used to identify objects. Some touch involves an active motor component—stroking, tapping, grasping, or pressing—whereby a part of the body is moved against another surface or organism. The sensory and motor components of touch are intimately connected anatomically in the brain and are important in guiding behavior.

Exteroception also includes the *thermal senses* of heat and cold. Thermal sensations are important controllers of behavior and homeostatic mechanisms needed to maintain the body temperature near 37°C (98.6°F). Finally, exteroception includes the sense of *pain*, or nociception, a response to external events that damage or harm the body. Nociception is a prime motivator of actions necessary for survival, such as fight or flight.

The third component of somatic sensation, *interoception*, is the sense of the function of the major organ systems of the body and its internal state.

The information conveyed by receptors in the viscera is crucial for regulating autonomic functions, particularly in the cardiovascular, respiratory, digestive, and renal systems, although most of the stimuli registered by these receptors do not lead to conscious sensations. Interoceptors are primarily chemoreceptors that monitor organ function through such indicators as blood gases and pH, and mechanoreceptors that sense tissue distention, which may be perceived as painful.

This diverse group of sensory functions may seem an unlikely combination to form a sensory system. We treat all of the somatic senses in one introductory chapter because they are mediated by one class of sensory neurons, the dorsal root ganglion (DRG) neurons. Somatosensory information from the skin, muscles, joint capsules, and viscera is conveyed by DRG neurons innervating the limbs and trunk or by trigeminal sensory neurons that innervate cranial structures (the face, lips, oral cavity, conjunctiva, and dura mater). These sensory neurons perform two major functions: the transduction and encoding of stimuli into electrical signals and the transmission of those signals to the central nervous system.

The study of somatic sensation has been revolutionized in the past 10 years by three important advances. First, the development of transgenic mice with fluorescent reporters of gene expression in DRG neurons has allowed neuroscientists to assess the physiological responses of specific receptor classes and their anatomical projections to sensory receptors in the body and in the central nervous system. Functional imaging of individual DRG neurons expressing genetically encoded calcium sensors such as GCaMP6 enables simultaneous optical recordings of activity from populations of receptor neurons innervating a specific region of the body, thereby providing a useful tool for analyzing ensemble responses to somatosensory stimuli. Second, studies of isolated DRG neurons in vitro, or in reduced skin-nerve preparations, enable biophysical assessment of receptor responses and characterization of ion channels expressed in individual somatosensory neurons. Third, the identification of Piezo protein ion channels as the molecular transducers of touch and proprioception in mammalian mechanoreceptors has provided a novel system for assessing the role of these channels in the senses of touch, proprioception, and visceral function.

In this chapter, we consider the principles common to all DRG neurons and those that distinguish their individual sensory function. We begin with a description of the peripheral nerves and their organization, followed by a survey of the receptor classes responsible for each of the major bodily senses. We also examine the sensory transduction mechanisms that convert various stimulus energies into electrical signals. We then describe the integration of information by the parent axon from multiple receptors in its receptive field and conclude with a discussion of the central processing centers for each submodality in the spinal cord and brain stem. Higher-order processing of touch, pain, proprioception, and autonomic regulation of viscera is described in later chapters.

Dorsal Root Ganglion Neurons Are the Primary Sensory Receptor Cells of the Somatosensory System

The cell body of a DRG neuron lies in a ganglion on the dorsal root of a spinal or cranial nerve. Dorsal root ganglion neurons originate from the neural crest and are intimately associated with the nearby segment of the spinal cord. Individual neurons in a DRG respond selectively to specific types of stimuli because of morphological and molecular specializations of their peripheral terminals.

Dorsal root ganglion neurons are a type of bipolar cell, called pseudo-unipolar cells. The axon of a DRG neuron has two branches, one projecting to the periphery and one projecting to the central nervous system (Figure 18–1). The peripheral terminals of individual DRG neurons innervate the skin, muscle, joint capsules, or viscera and contain receptors specialized for particular kinds of stimuli. The region of the body innervated by these sensory endings is called a *dermatome* (see Figure 18-13). Sensory peripheral nerve endings differ in receptor morphology and stimulus selectivity, allowing them to detect mechanical, thermal, or chemical events. The central branches terminate in the spinal cord or brain stem, forming the first synapses in somatosensory pathways. Thus, the axon of each DRG cell serves as a single transmission line with one polarity between the receptor terminal and the central nervous system. This axon is called the *primary afferent fiber*.

Individual primary afferent fibers innervating a particular region of the body, such as the thumb or fingers, are grouped together into bundles or fascicles of axons forming the *peripheral nerves*. They are guided during development to a specific location in the body by various trophic factors such as brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT3), neurotrophin-4 (NT4), or nerve growth factor (NGF). The peripheral nerves also include motor axons innervating nearby muscles, blood vessels, glands, or viscera.

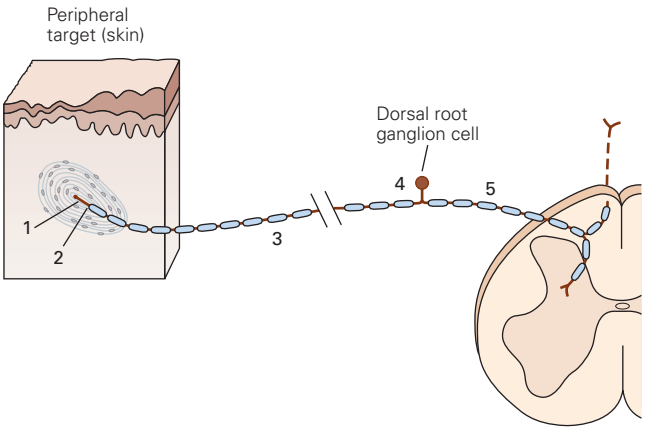

Figure 18–1 The dorsal root ganglion neuron is the primary sensory cell of the somatosensory system. The cell body is located in a dorsal root ganglion (**DRG**) adjacent to the spinal cord. The axon has two branches, one projecting to the body, where its specialized terminal contains receptors for a particular form of stimulus energy, and one projecting to the spinal cord or brain stem, where the afferent signals are processed. All DRG neurons contain five functional zones: **1.** The *distal terminals* in skin, muscle, or viscera contain specialized receptor-channels that convert specific types of stimulus energy (mechanical, thermal, or chemical) into a depolarizing receptor potential. DRG neurons typically have multiple sensory endings. **2.** The *spike generation site* contains voltage-gated Na^+ and K^+ channels (Na_V and K_V) that are located near the initial segment of the axon within the receptor capsule; they convert the receptor potential into a stream of action potentials. **3.** The *peripheral nerve fiber* transmits action potentials from the spike initiation site to the DRG cell body. **4.** The *cell body* of the DRG neuron is contained within a ganglion adjacent to the spinal cord or brain stem. **5.** A *spinal or cranial nerve* connects the DRG or trigeminal neuron to the ipsilateral spinal cord or brain stem.

Damage to peripheral nerves or their targets in the brain may produce sensory deficits in more than one somatosensory submodality or motor deficits in specific muscle groups. Knowledge of where somatosensory modalities overlap morphologically, and where they diverge, facilitates diagnosis of neurological disorders and malfunction.

Each DRG neuron can be subdivided into five functional zones: the receptive zone, the spike generation site, the peripheral nerve fiber, the DRG cell body, and the spinal or cranial nerve (Figure 18–1). The receptive zone, at the distal end of the DRG axon, contains specialized receptor proteins that sense mechanical force, thermal events, or chemicals in the local environment and translate these signals into a local depolarization of the axonal terminals, called the *receptor potential* (see Figure 3–9A). This local depolarization spreads passively toward the central axon where action potentials are generated, usually at the initial segment (distal to the first node of Ranvier in myelinated fibers) (see Figure 3–10A). Stimuli of sufficient strength produce action potentials that are transmitted along the peripheral nerve fiber, through the cell soma, and into the central branch that terminates in the spinal cord or brain stem.

The soma of a DRG neuron contains the cell nucleus. Sensory receptor proteins are expressed in the soma, providing a convenient expression system for characterizing their conductance properties in vitro. Isolated DRG neurons have been widely used in patch-clamp studies of sensory receptor currents and voltage-gated action potential channels.

DRG neurons differ in the size of their cell soma, gene expression profile, conduction velocity of their axons, sensory transduction molecule(s), innervation pattern in the body, and physiological function. For example, DRGs that innervate mechanoreceptors that sense touch and proprioception have the largest cell bodies and large myelinated axons; they express proteins such as Npy2r or parvalbumin (PV) (Figure 18–2). In contrast, DRG neurons that sense temperature or irritant chemicals have small cell bodies and unmyelinated axons; they express calcitonin gene-related peptide (CGRP) or the lectin IB4 (Figure 18–2C,D). As these fluorescent molecular labels extend through the axons to their peripheral endings in the body and in the central nervous system, David Ginty and colleagues were able to characterize the pattern of somatosensory nerve endings in the body (Figure 18–2H) and trace their central projections to the spinal cord (Figure 18–2G) and brain stem.

Peripheral Somatosensory Nerve Fibers Conduct Action Potentials at Different Rates

The peripheral nerves that transmit spike trains from the site of spike generation to the central nervous system have classically served as the primary recording sites for neurophysiological studies of somatosensory receptor mechanisms. Individual peripheral nerve fibers in animals are typically dissected from the main axon bundle and placed on fine wires that serve as recording electrodes. Microelectrodes—manufactured from sharpened tungsten or platinum wires—have also been inserted through the skin into the peripheral nerves of humans (a technique known as *microneurography*) to measure sensory responses to various somatic stimuli (Chapter 19).

Peripheral nerve fibers are classified into functional groups based on properties related to axon diameter

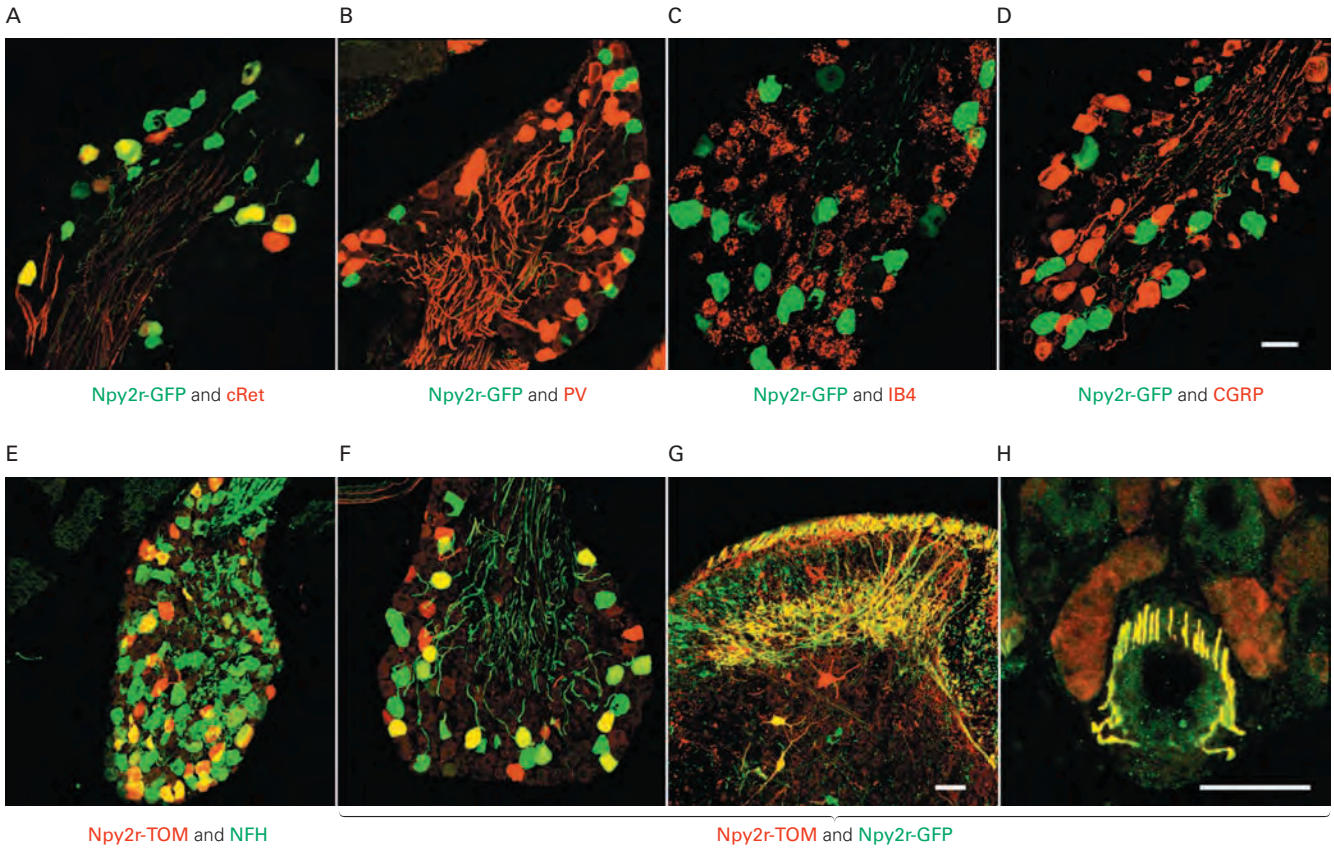

Figure 18–2 **Dorsal root ganglion neurons differ in size, gene expression, and skin innervation patterns.** (Reproduced, with permission, from Li et al. 2011. Copyright © 2011 Elsevier Inc.)

Panels **A–F** show double immunostaining of histological sections through a thoracic dorsal root ganglion. Individual dorsal root ganglion (DRG) neurons in these sections express genetic markers for specific classes of somatosensory nerve fibers. The G protein–coupled receptor Npy2r-GFP (**green**) or Npy2r-TOM (**red**) labels physiologically identified Aβ rapidly adapting low-threshold mechanoreceptors (Aβ RA-LTMRs). These fibers also express neurofilament heavy polypeptide (**NFH**), a marker of heavily myelinated axons (**E**), form longitudinal lanceolate (comb-like) endings surrounding individual guard hairs or awl/auchene hairs in hairy skin (**H**), and terminate in laminae III to V of the dorsal horn (**G**). Double-labeled neurons or fibers are stained **yellow.**

A. Aβ RA-LTMRs express the receptor tyrosine kinase *Ret* early in development (named early *Ret* and stained **red**). A majority of these neurons also express Npy2r-GFP (**green**); neurons that express both markers are stained **yellow**. Aβ RA-LTMRs have medium-sized cell bodies.

B. Aβ RA-LTMRs (**green**) have smaller cell bodies than proprioceptors such as muscle spindle afferents and Golgi tendon organs that express parvalbumin (**PV**, **red**).

C, D. Aβ RA-LTMRs (Npy2r-GFP, **green**) have larger cell bodies than unmyelinated purinergic C fibers that release ATP as cotransmitters (**IB4, red**) and peptidergic Aδ LTMRs that express calcitonin gene-related peptide (**CGRP, red**).

E. Heavily myelinated peripheral nerve fibers with large cell bodies express neurofilament heavy polypeptide (**NFH**, **green**). These include group Ia and Ib muscle afferents, Aβ SA-LTMRs, and Aβ RA-LTMRs (also labeled with Npy2r-tdTom [**red**]). Only Aβ RA-LTMRs express both markers and are stained **yellow**.

F–H. Double immunostaining with Npy2r-GFP (**green**) and Npy2r-tdTomato (**red**) of thoracic DRG neurons (**F**), their central processes in lamina III through V in the spinal cord dorsal horn (**G**), and their peripheral lanceolate endings at hair follicles in hairy skin sections (**H**) shows that the labeled peripheral and central Aβ RA-LTMR neurons largely overlap with each other (**yellow**) and that such genetic markers are useful for tracing sensory nerve endings.

and myelination, conduction velocity, and whether they are sensory or motor. The first nerve classification scheme was devised in 1894 by Charles Sherrington, who measured the diameter of myelin-stained axons in sensory nerves, and subsequently codified by David Lloyd (Table 18–1). They found two or three overlapping groups of axonal diameters (Figure 18–3). It was later discovered that these anatomical groupings are functionally important. Group I axons in *muscle* nerves innervate muscle spindle receptors and Golgi tendon

Table 18–1 Classification of Sensory Fibers in Peripheral Nerves[1]

	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 18–2.

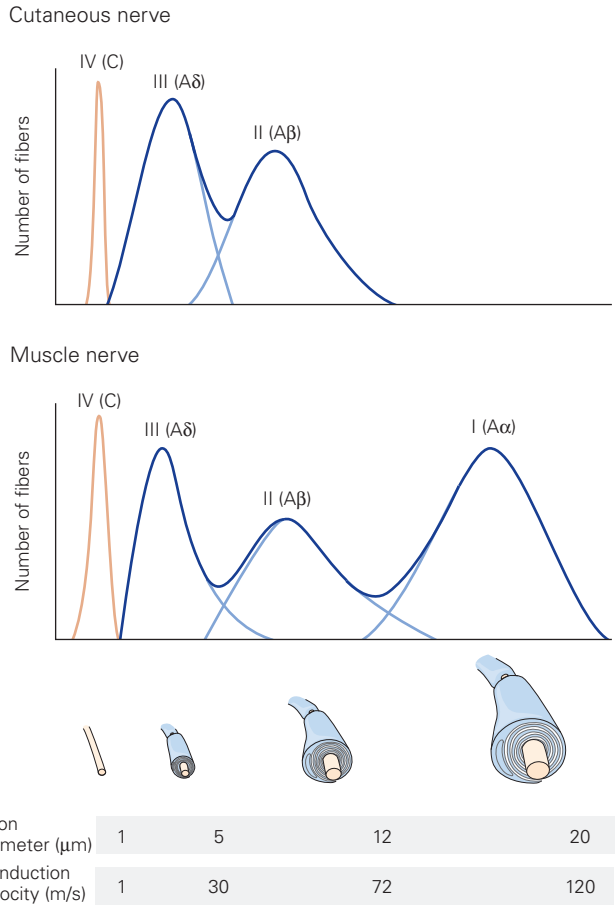

Figure 18–3 Classification of mammalian peripheral nerve fibers. The histograms illustrate the distribution of axon diameter for four groups of sensory nerve fibers innervating skeletal muscle and the skin. Each group has a characteristic axon diameter and conduction velocity (see Table 18–1). **Light blue lines** mark the boundaries of fiber profiles in each group in the zones of overlap. The conduction velocity (m/s) of myelinated peripheral nerve fibers is approximately six times the fiber diameter (μm). (Adapted, with permission, from Boyd and Davey 1968.)

organs, which signal muscle length and contractile force. Group II fibers innervate secondary spindle endings and receptors in joint capsules; these receptors also mediate proprioception. Group III fibers, the smallest myelinated muscle afferents, and the unmyelinated group IV afferents signal trauma or injuries in muscles and joints that are sensed as painful.

Nerves that innervate the skin contain two sets of myelinated fibers: Group II fibers innervate cutaneous mechanoreceptors that respond to touch, and group III fibers mediate thermal and noxious stimuli, as well as light touch in hairy skin. Unmyelinated group IV cutaneous afferents, like those in muscle, also mediate thermal and noxious stimuli.

Another method for classifying peripheral nerve fibers is based on electrical stimulation of whole nerves. In this widely used diagnostic technique, nerve conduction velocities are measured between pairs of stimulating and recording electrodes placed on the skin above a peripheral nerve. When studying conduction in the median or ulnar nerve, for example, the stimulation electrode might be placed at the wrist and the recording electrode on the upper arm. Brief electrical pulses applied through the stimulating electrode evoke action potentials in the nerve. The neural signal recorded a short time later in the arm represents the summed action potentials of all of the nerve fibers excited by the stimulus pulse and is called the *compound action potential* (Chapter 9). It increases in amplitude as more nerve fibers are stimulated; the summed activity is roughly proportional to the total number of active nerve fibers.

Electrical stimuli of increasing strength evoke action potentials first in the largest axons, because they have the lowest electrical resistance, and then progressively in smaller axons (Figure 18–4). Large-diameter fibers conduct action potentials more rapidly because