1 Ultrastructure of Myelinated and Unmyelinated Axons

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The macroscopic anatomy of peripheral nerves results from the hierarchic arrangement of nerve fibers formed by microscopic groups of motor and sensory neuronal cytoplasmic elongations known as axons [1–8]. The latter enable conduction of electrical impulses along their plasma membranes, as well as chemically mediated signal transduction throughout cytoplasmic organelles. Most peripheral nerves are mixed nerves containing efferent motor fibers, afferent sensory fibers, and sympathetic fibers. The initial segment of an axon (AIS) originates in the soma and is located between the cell body and the beginning of the myelin sheath. This site is a polarized structure containing proteins such as voltage-gated sodium channels (VGCs), which are responsible for producing the inward ionic flow that generates the action potential at the AIS. VCGs at the AIS, together with the linked spectrin–actin membrane cytoskeleton may function as a diffusion barrier preventing axonal proteins from leaking out of the neuron. Nerve fibers have two types of axons, myelinated and unmyelinated. Each myelinated nerve fiber consists of an axon covered by myelin sheaths produced by Schwann cells alternating with areas called nodes of Ranvier [1–4]. The latter are sites of discontinuity between successive myelin sheaths along the axon [5, 6]. Mechanisms regulating the production and distribution of myelin take place in an extremely tight compartment located between the plasma membranes of both neurons and Schwann cells [7]. An inner layer, or basal membrane, and an outer layer, known as the endoneurium, enclose each myelinated nerve fiber. The axon contains an extremely dense cytoplasm, with an estimated viscosity five times greater than that of water. Inside the cytoplasm are microtubules, neurofilaments, mitochondria, vesicles, cisterns of cytoplasmic reticulum, and lysosomes, whereas ribosomes and Golgi apparatus are present uniquely in the AIS [5, 6]. The external diameter of a myelinated axon measures between 2 and 18 μm, whereas its length varies remarkably, ranging from just a few millimeters to as long as 1 m [5, 6].

Schwann cells wrap around axons at regular intervals, leaving uncovered portions known as Ranvier nodes [7]. The internodal distance is the interval between Ranvier nodes, is occupied by alternating Schwann cells, and measures about 0.4–1.2 mm.

Membrane depolarization and repolarization of myelinated axons during the propagation of action potentials occur at the Ranvier nodes; here, the proportion of VGCs is greater than in other unmyelinated areas.

Unmyelinated axons are not enclosed within multilayered myelin sheaths [8]. Instead, a single Schwann cell appears at the center of axonal groups, emitting cytoplasmic prolongations that separate each of the surrounding unmyelinated axons. Here, groups of six to eight axons are held together and partially covered by simple, nonwrapping prolongations originating in a single Schwann cell. In addition, groups of unmyelinated axons contain bundles of collagen fibers that confer mechanical resistance to the axonal group. The diameter of unmyelinated axons measures about 0.1–3 μm (Figs. 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 1.10, 1.11, 1.12, 1.13 and 1.14).

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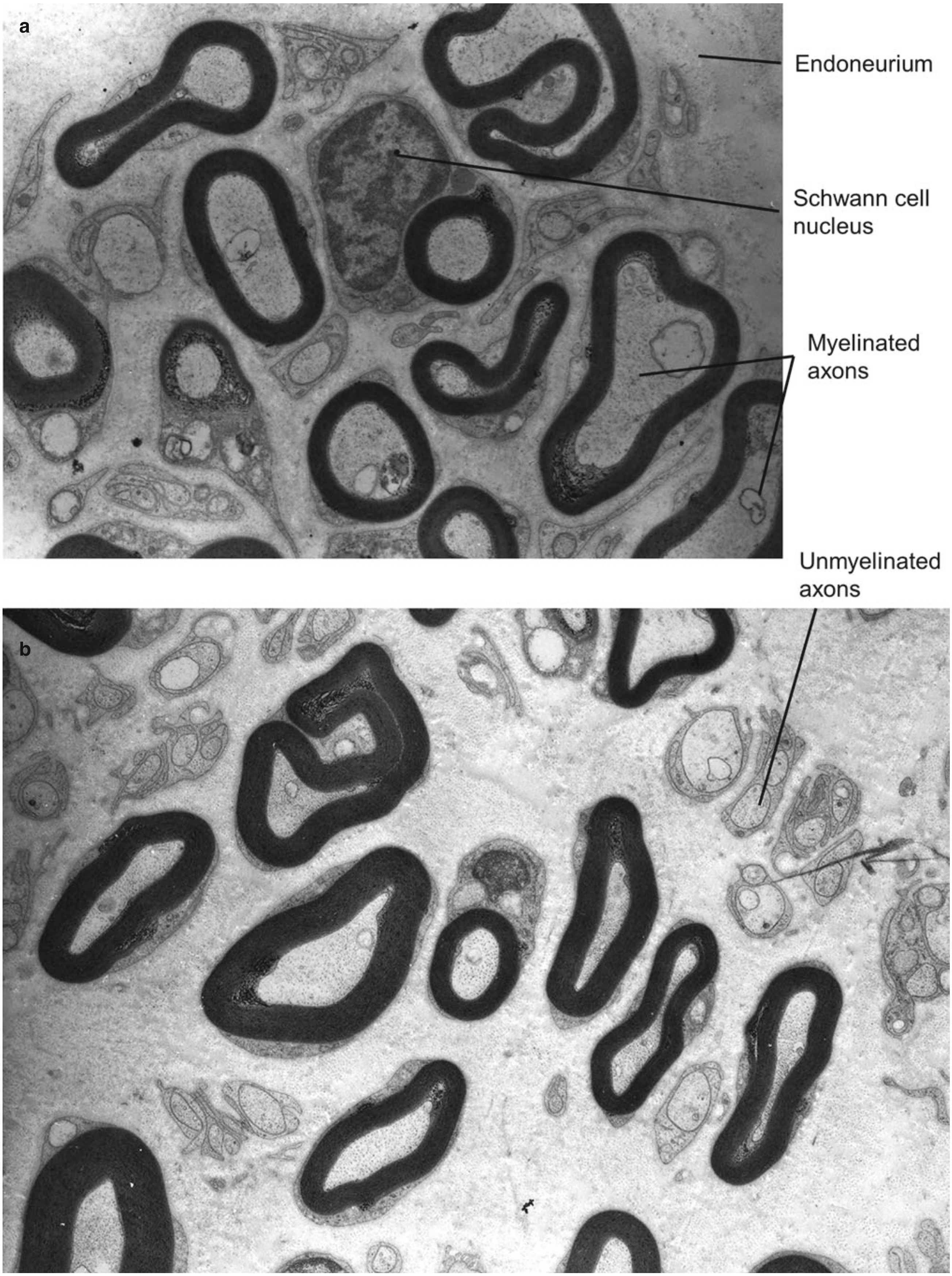

Fig. 1.1 Axons inside fascicles of a sciatic nerve. Transmission electron microscopy, magnification: ×7,000 (**a**); ×3,000 (**b**)

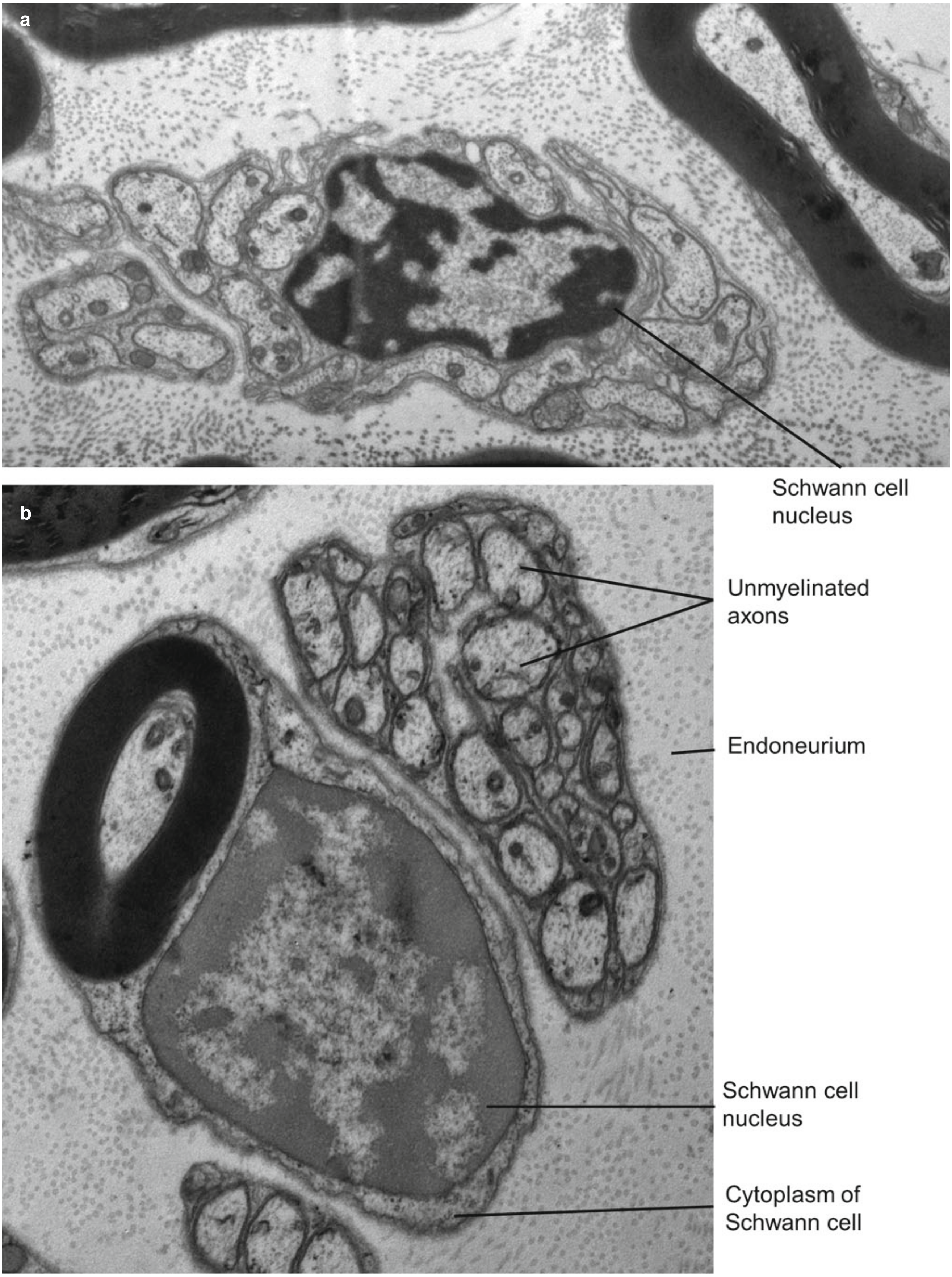

Fig. 1.2 (**a**) Unmyelinated axon of a human nerve rootlet. (**b**) Myelinic axon surrounded by Schwann cells and an unmyelinated axon of a human nerve rootlet. Transmission electron microscopy, magnification: ×15,000 (**a**); ×25,000 (**b**)

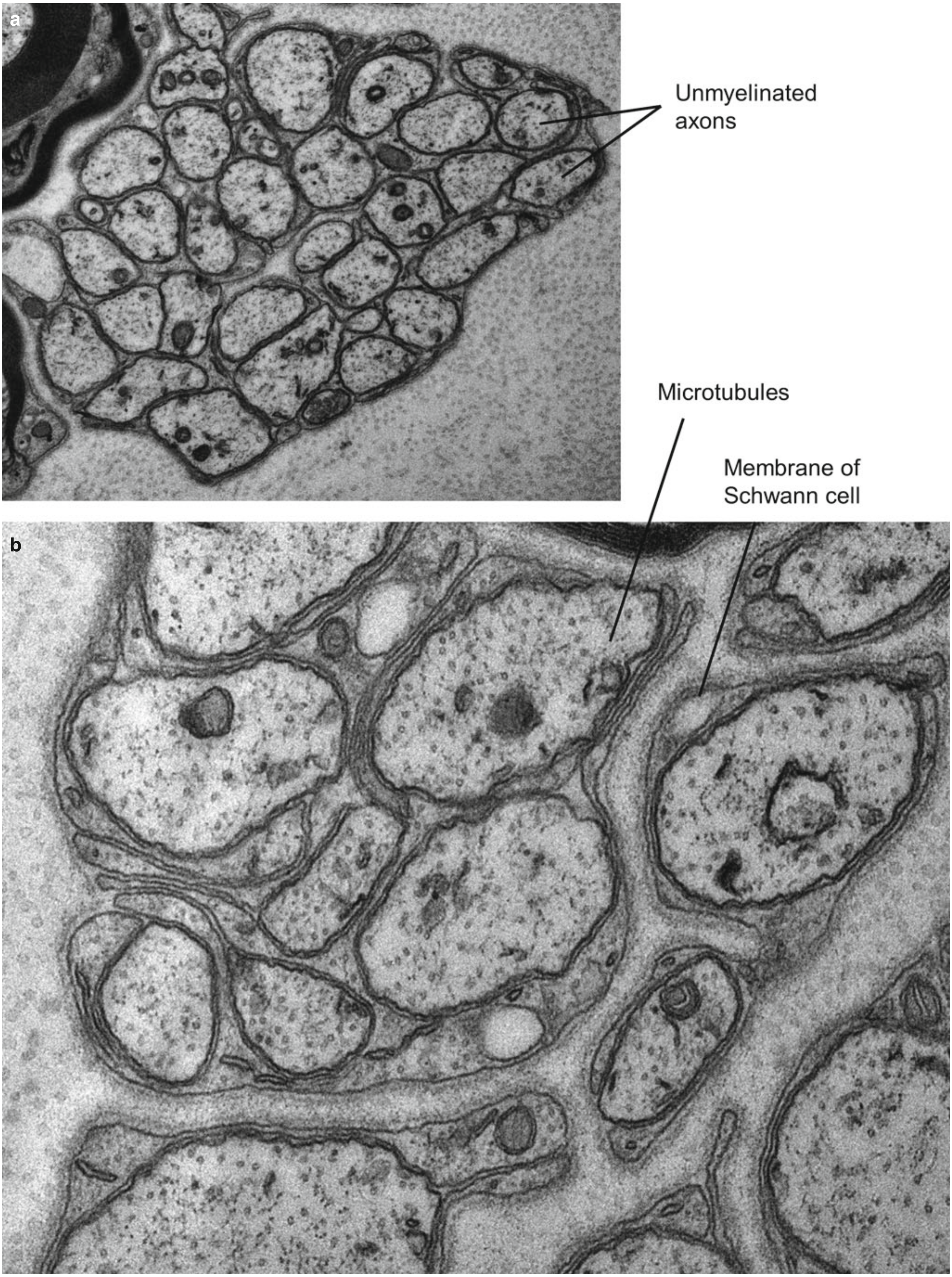

Fig. 1.3 Unmyelinated axon of a human nerve rootlet. Transmission electron microscopy, magnification: ×30,000 (**a**); ×50,000 (**b**)

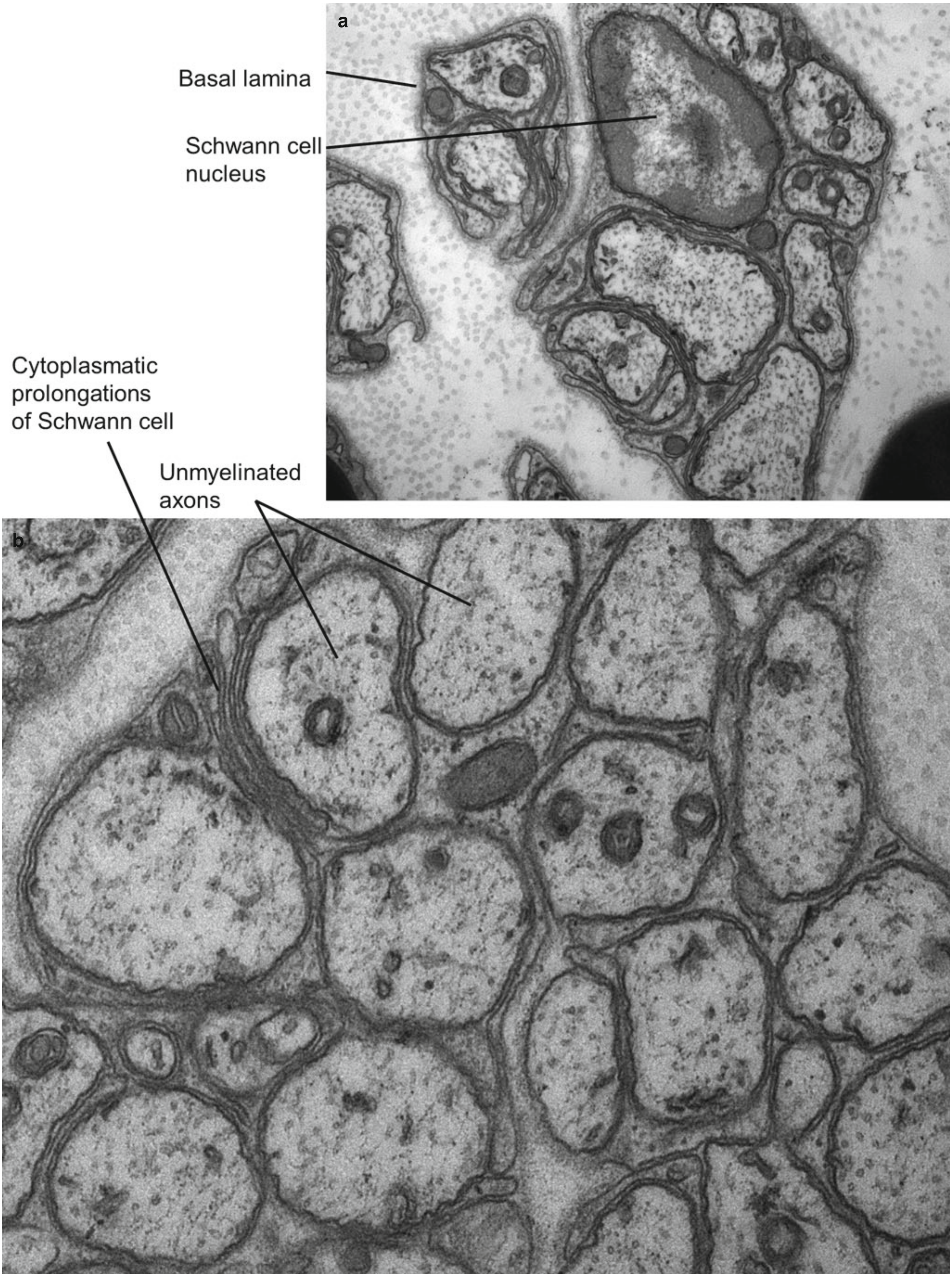

Fig. 1.4 Unmyelinated axon of a human nerve rootlet. Transmission electron microscopy, magnification: ×40,000 (**a**); ×50,000 (**b**)

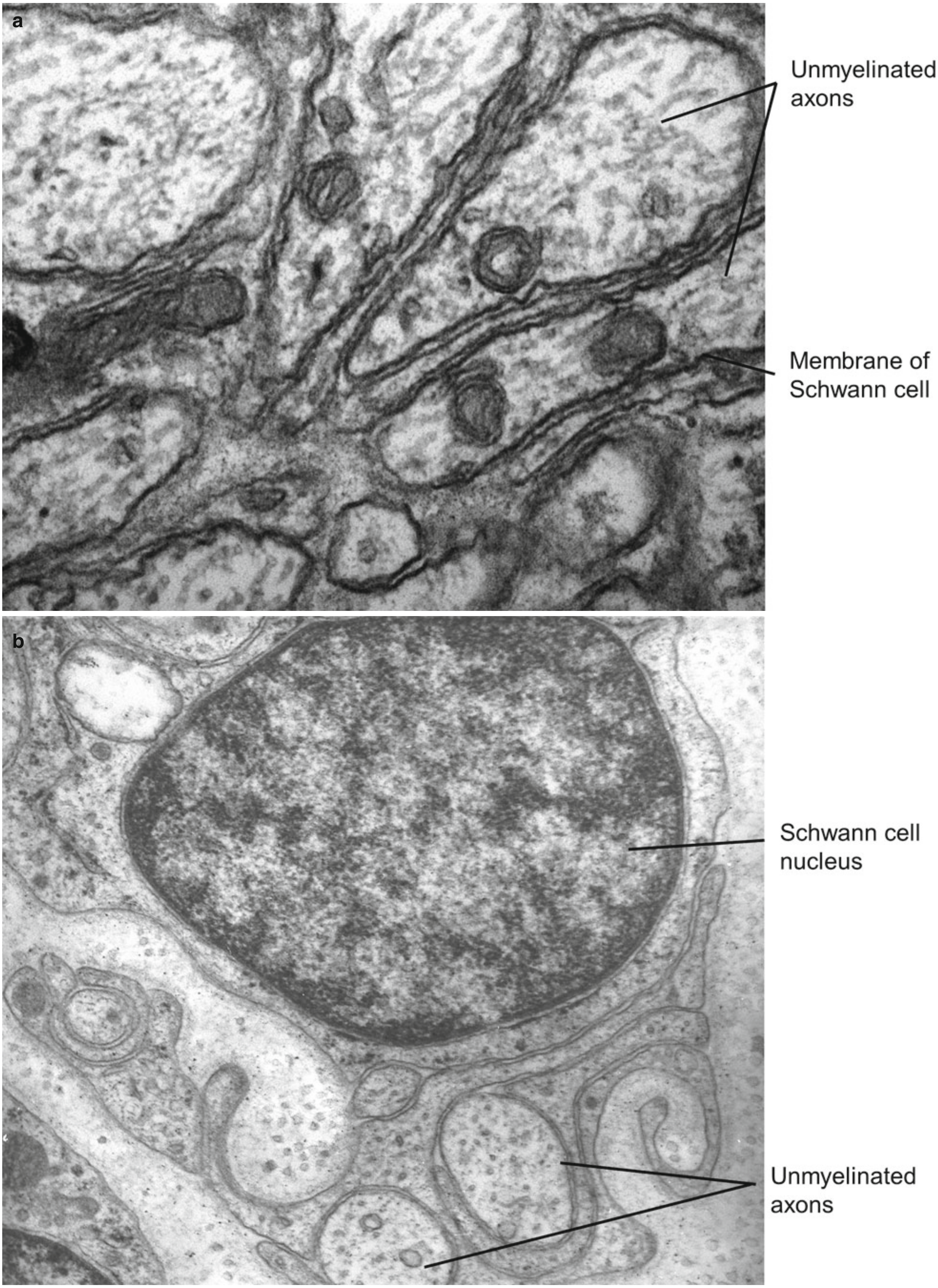

Fig. 1.5 (**a**) Unmyelinated axon of a human nerve rootlet. (**b**) Unmyelinated axon of a sciatic nerve (From De Andrés et al. [4]; with permission) Transmission electron microscopy, magnification: ×100,000 (**a**); ×20,000 (**b**)

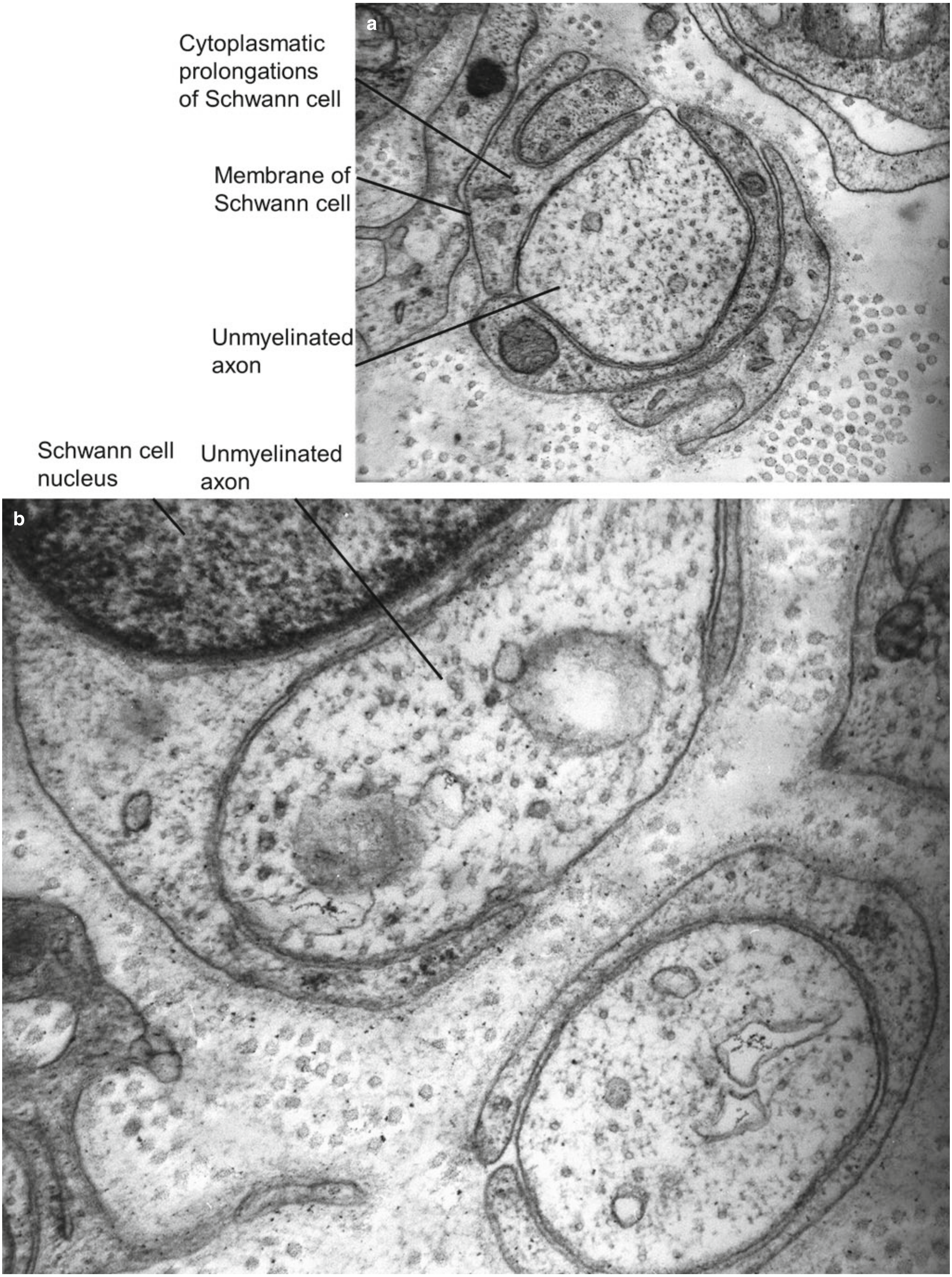

Fig. 1.6 Unmyelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×30,000 (**a**); ×30,000 (**b**)

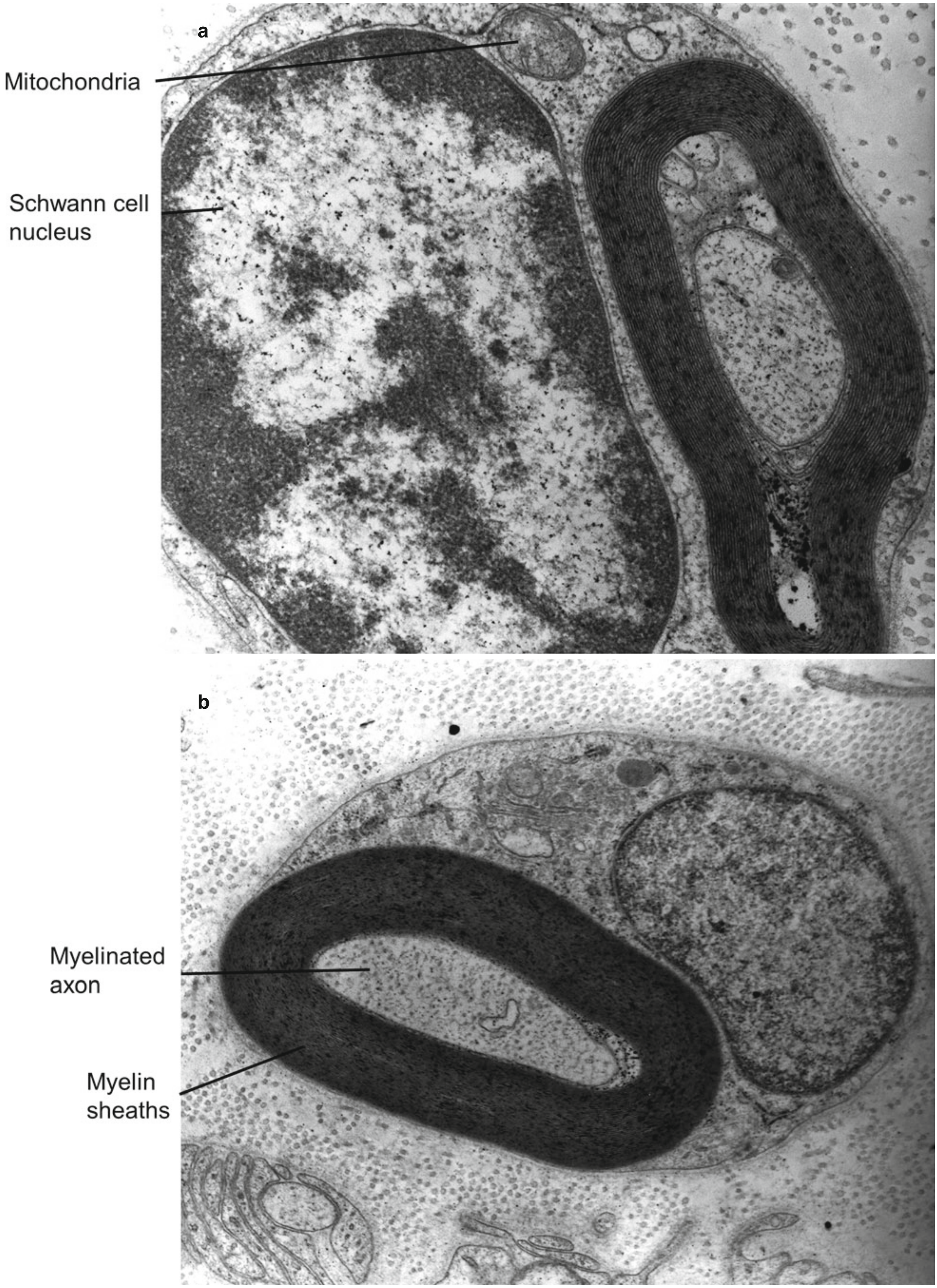

Fig. 1.7 Myelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×20,000 (**a**); ×12,000 (**b**) (Panel **b** from Reina et al. [1]; with permission)

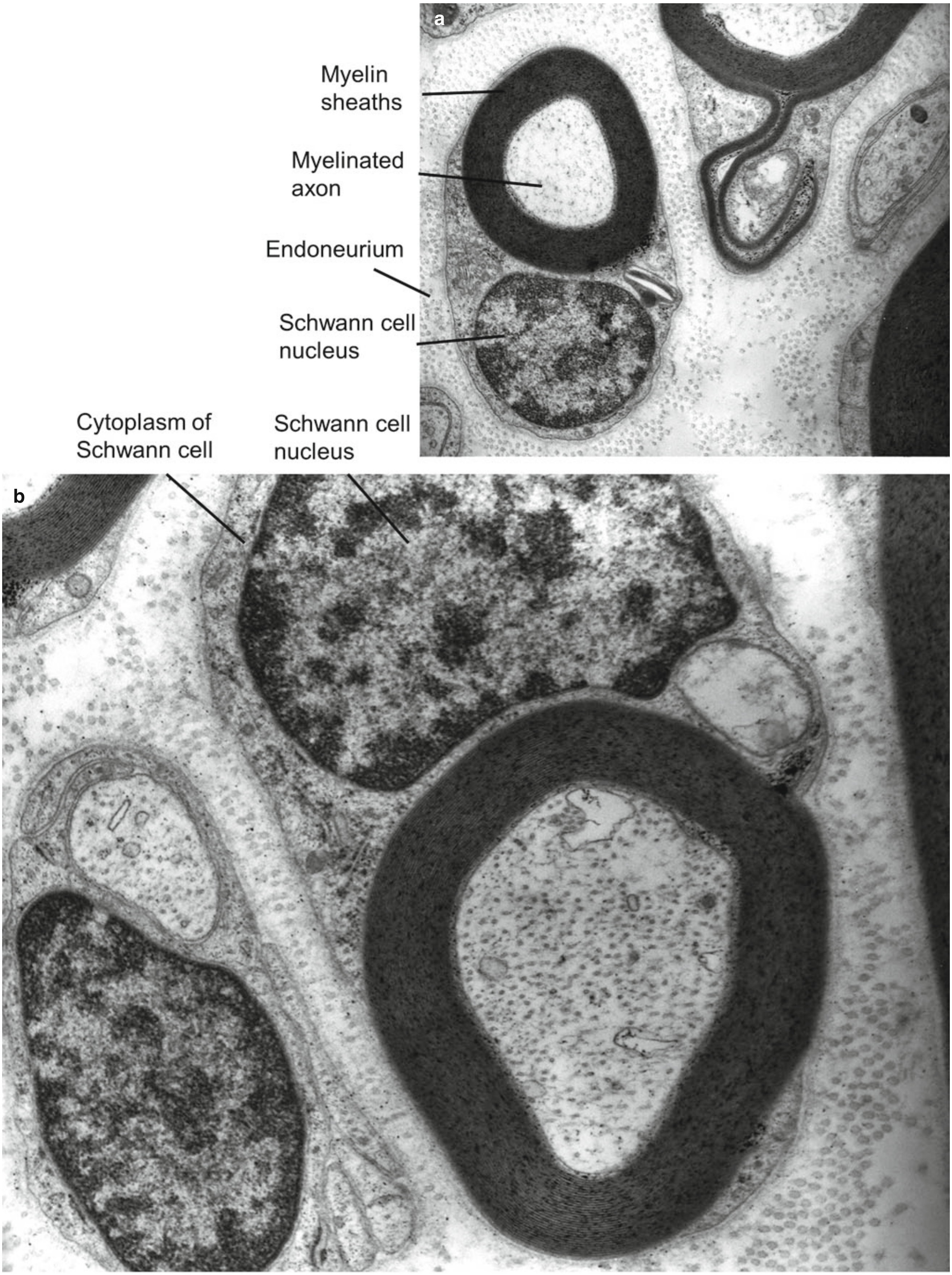

Fig. 1.8 Myelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×12,000 (**a**); ×12,000 (**b**)

Fig. 1.9 Myelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×7,000 (**a**); ×25,000 (**b**)

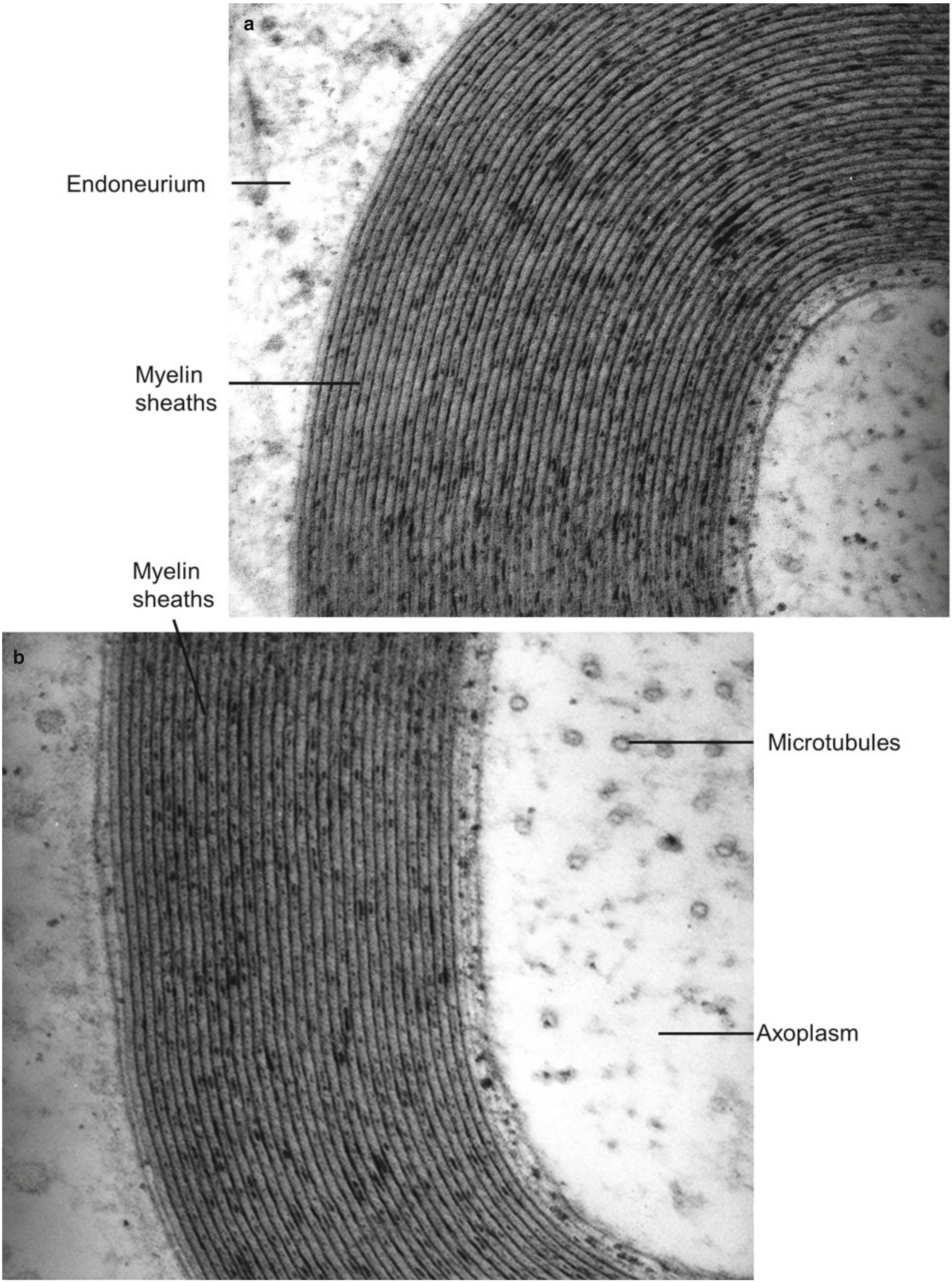

Fig. 1.10 Myelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×85,000 (**a**); ×85,000 (**b**) (Panel **a** from De Andrés et al. [4]; with permission)

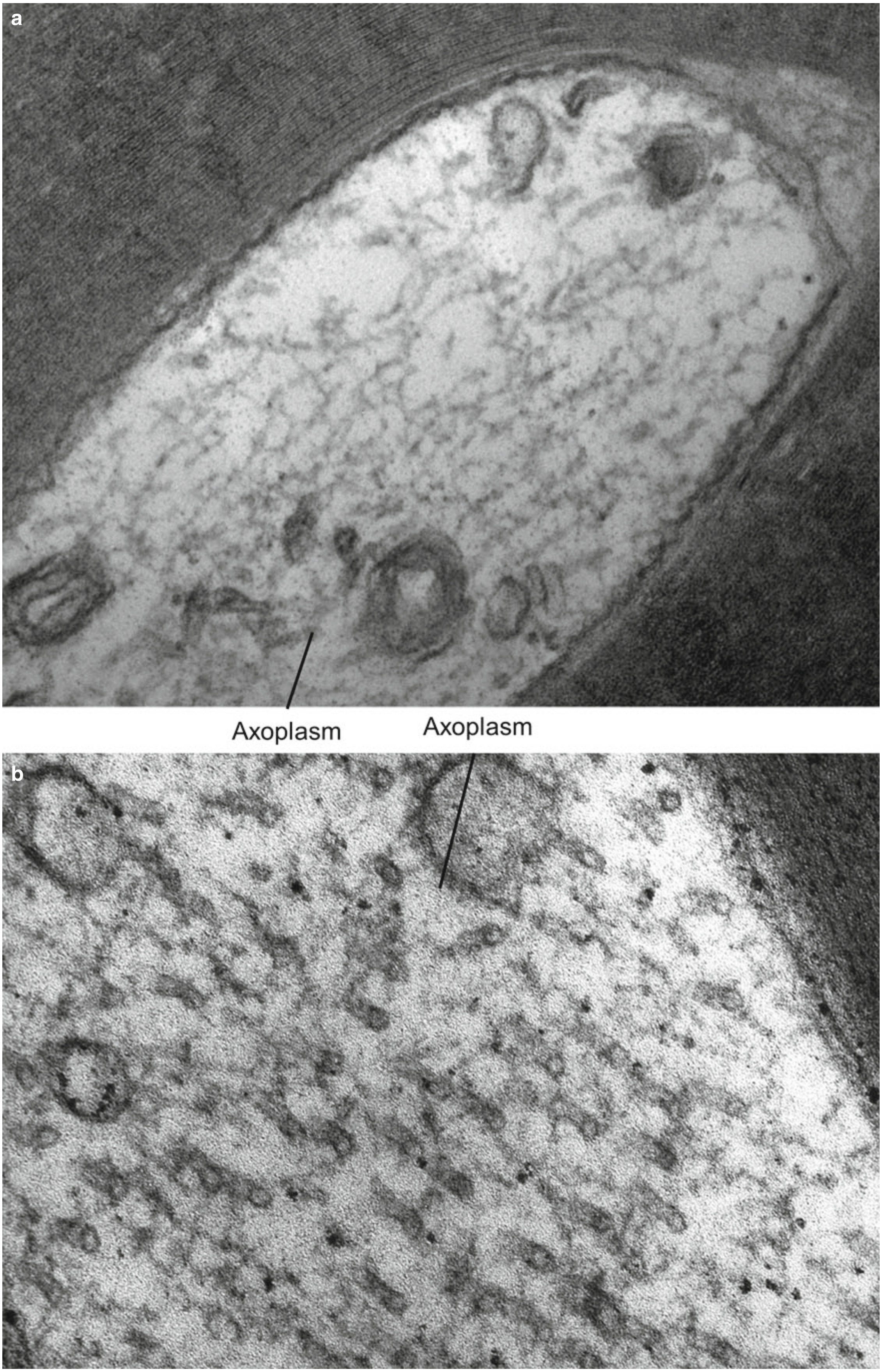

Fig. 1.11 Myelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×120,000 (**a**); ×140,000 (**b**)

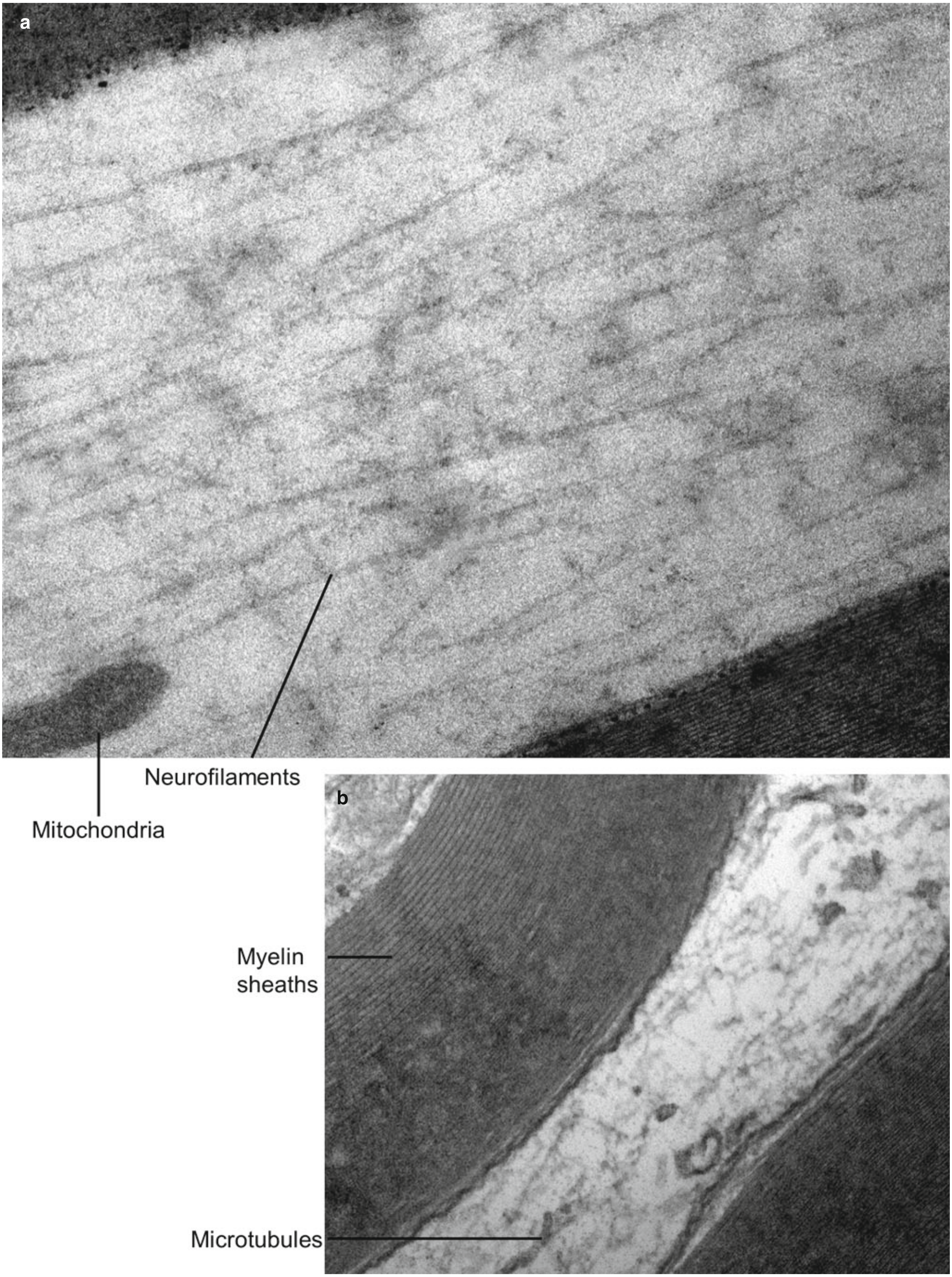

Fig. 1.12 Myelinated axon of a sciatic nerve. Transmission electron microscopy, magnification: ×60,000 (**a**); ×120,000 (**b**)

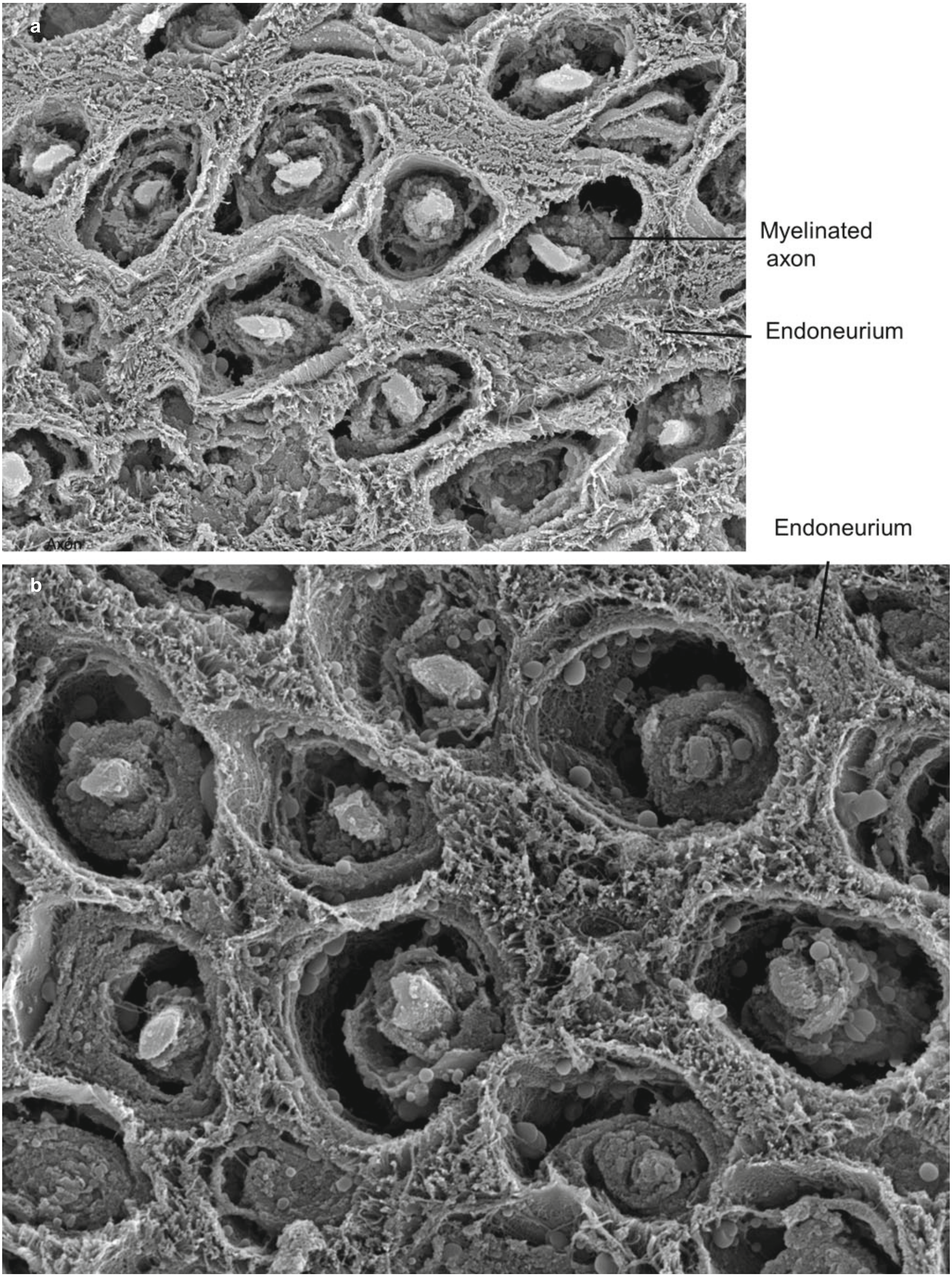

Fig. 1.13 Myelinated axon of a sciatic nerve. Scanning electron microscopy, magnification: ×1,900 (**a**); ×2,000 (**b**)

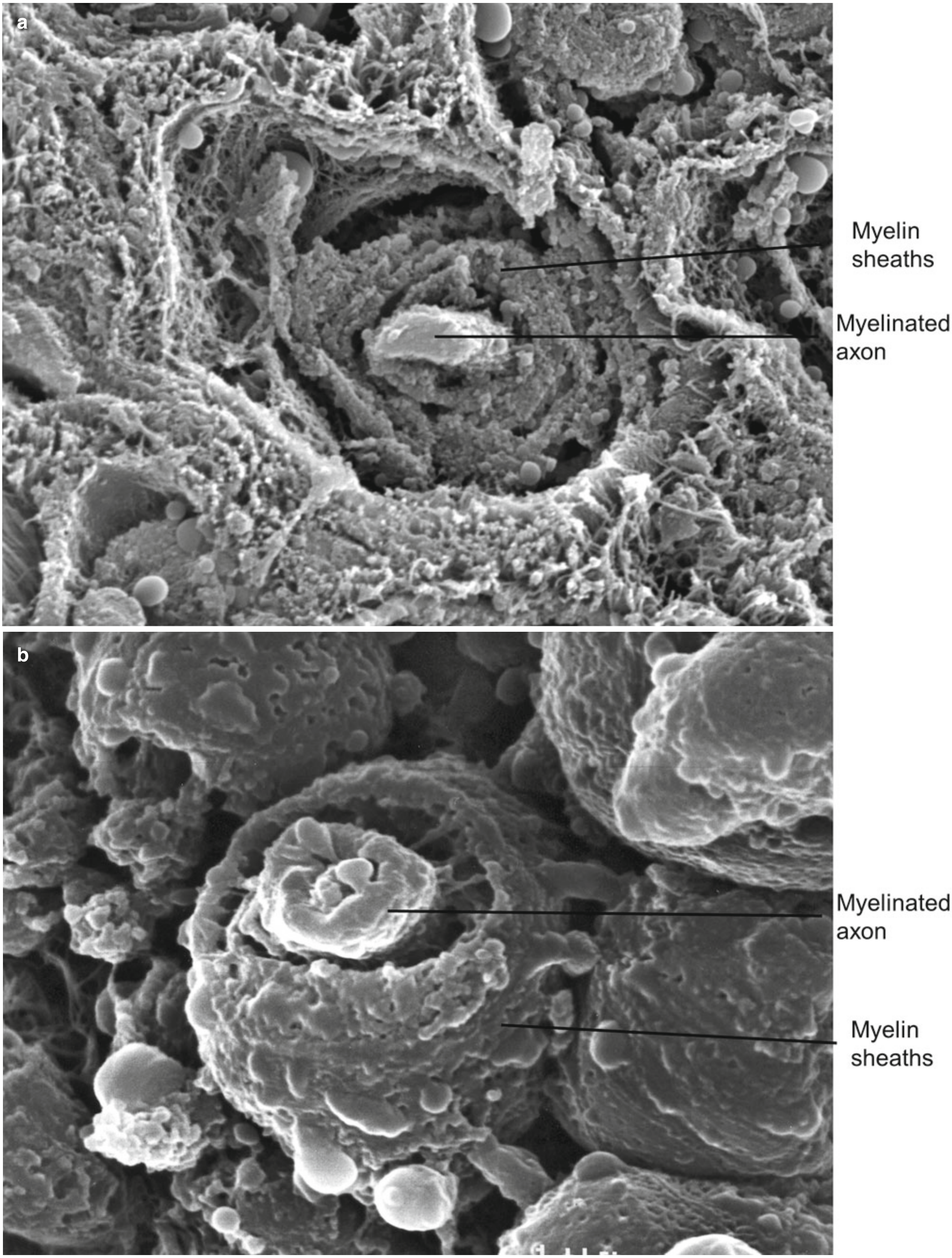

Fig. 1.14 Myelinated axon of a sciatic nerve. Scanning electron microscopy, magnification: ×4,000 (**a**); ×5,000 (**b**)

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