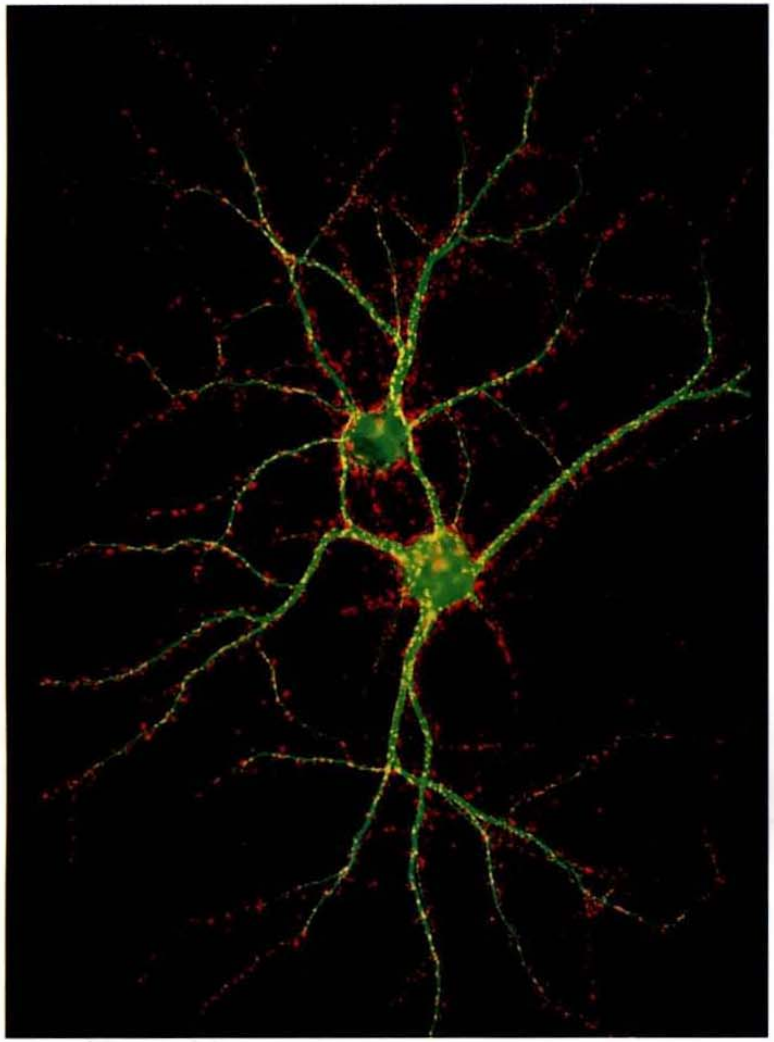
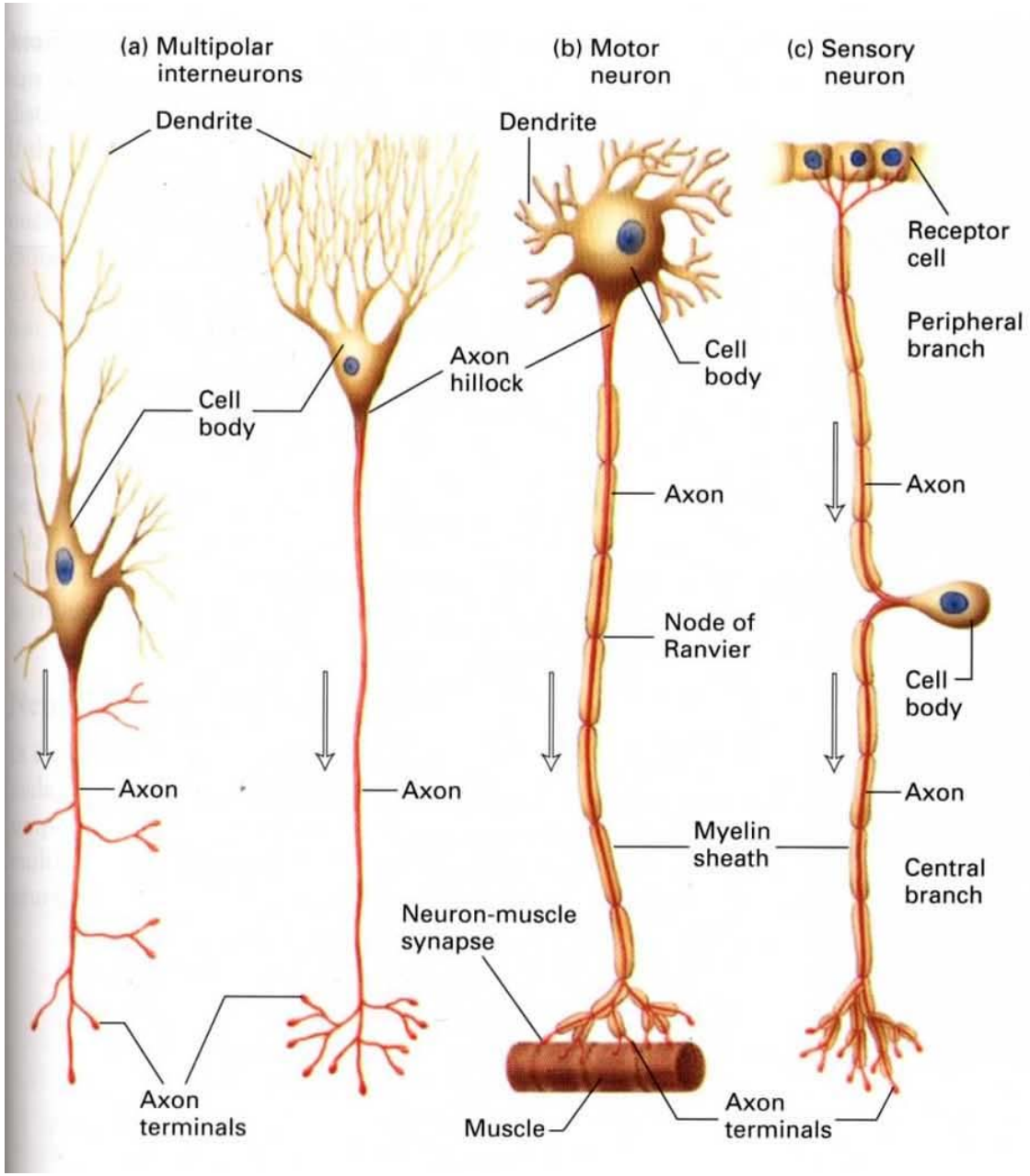
Närvide töö

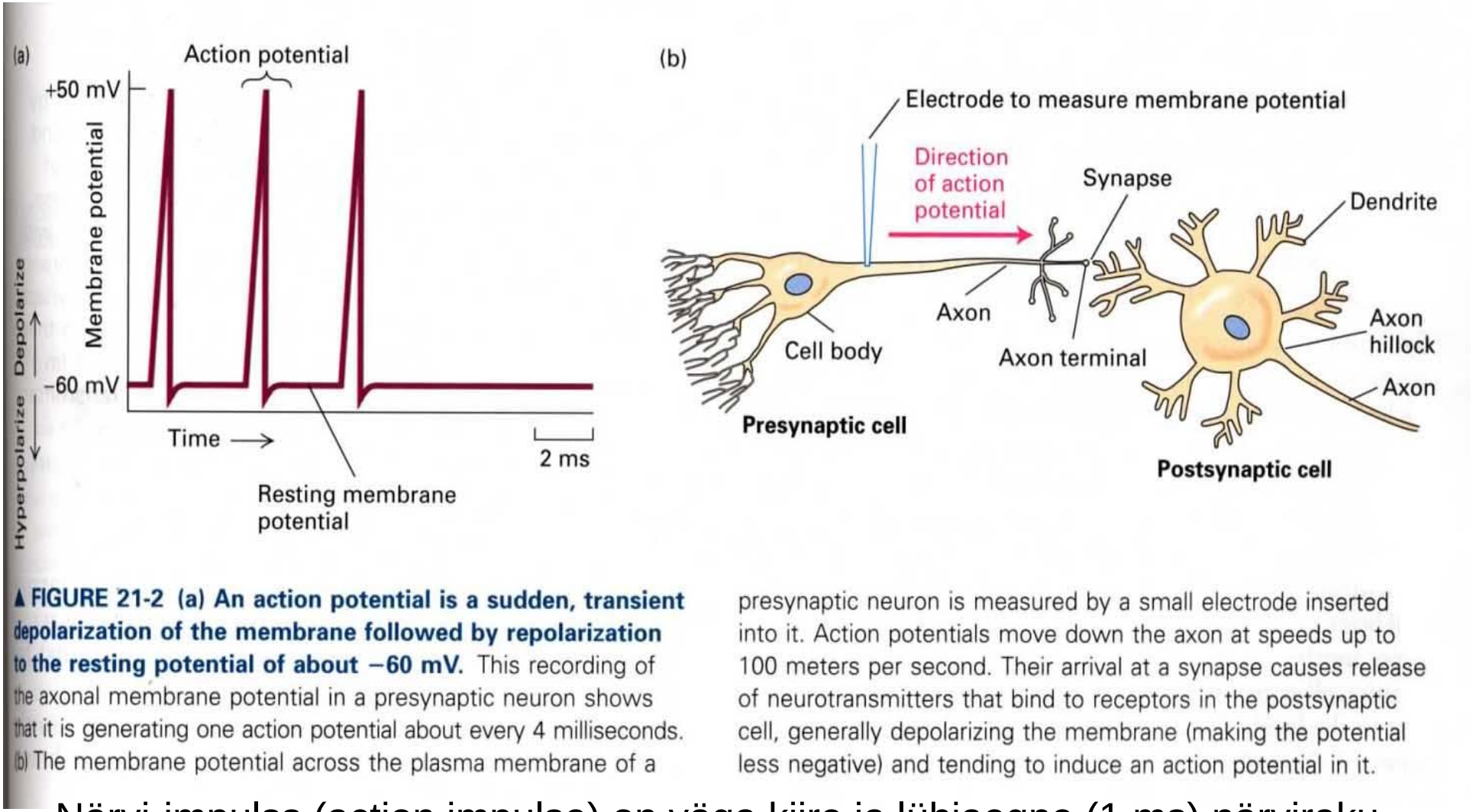


▲ **FIGURE 21-3 Typical interneurons from the hippocampal region of the brain makes about a thousand synapses.** The cells were stained with two fluorescent antibodies: one specific for the microtubule-associated protein MAP2 (green), which is found only in dendrites and cell bodies, and the other specific for synaptotagmin (orange-red) (see Figure 21-31), a protein found in presynaptic axon terminals. Thus the orange-red dots indicate presynaptic axon terminals from neurons that are not visible in this field. [Courtesy of O. Mundigl and P. deCamilli.]

Inimajus on umbes 10^{12} närvirakku (neuronit), mis moodustavad ühendusi omavahel ja organitega. Kuna ajust organiteni on pikk tee, peavad need närvirakud olema vastava erilise kujuga, mis ulatuks organismi kaugematessegi osadesse

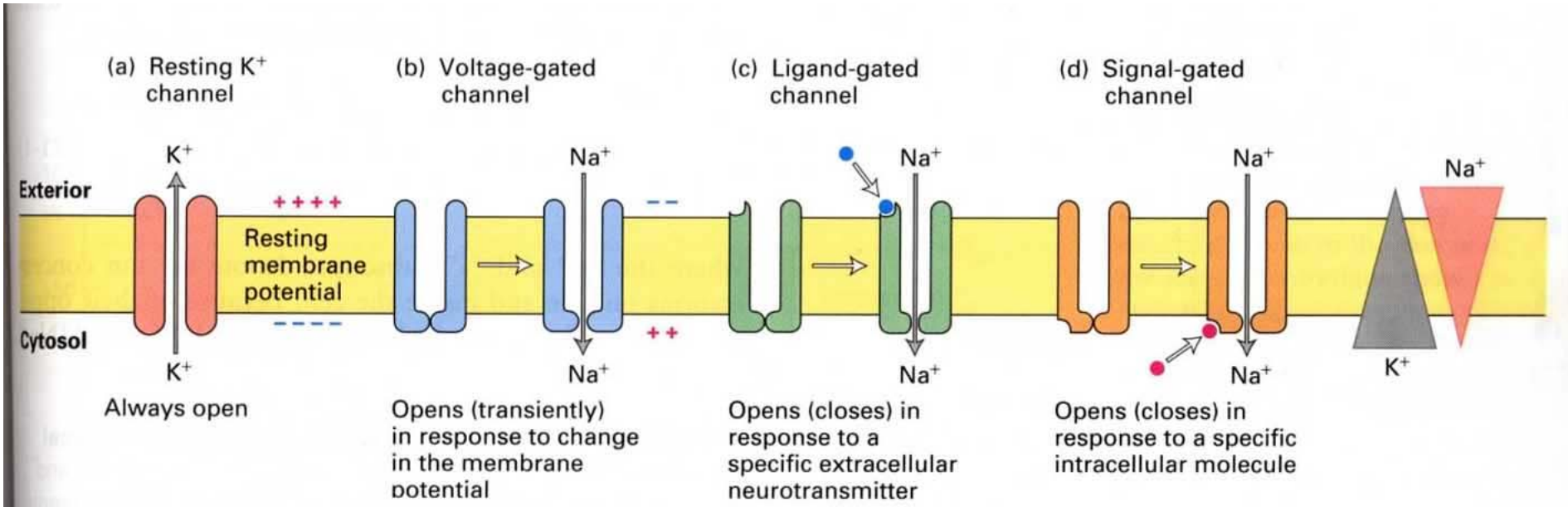


◀ **FIGURE 21-1 Structure of typical mammalian neurons.** Arrows indicate the direction of conduction of action potentials in axons (red). (a) Multipolar interneurons. Each has profusely branched dendrites, which receive signals at synapses with several hundred other neurons, and a single long axon that branches laterally and at its terminus. (b) A motor neuron that innervates a muscle cell. Typically, motor neurons have a single long axon extending from the cell body to the effector cell. In mammalian motor neurons an insulating sheath of myelin usually covers all parts of the axon except at the nodes of Ranvier and the axon terminals. (c) A sensory neuron in which the axon branches just after it leaves the cell body. The peripheral branch carries the nerve impulse from the receptor cell to the cell body, which is located in the dorsal root ganglion near the spinal cord; the central branch carries the impulse from the cell body to the spinal cord or brain. Both branches are structurally and functionally axons, except at their terminal portions, even though the peripheral branch conducts impulses toward, rather than away from, the cell body.



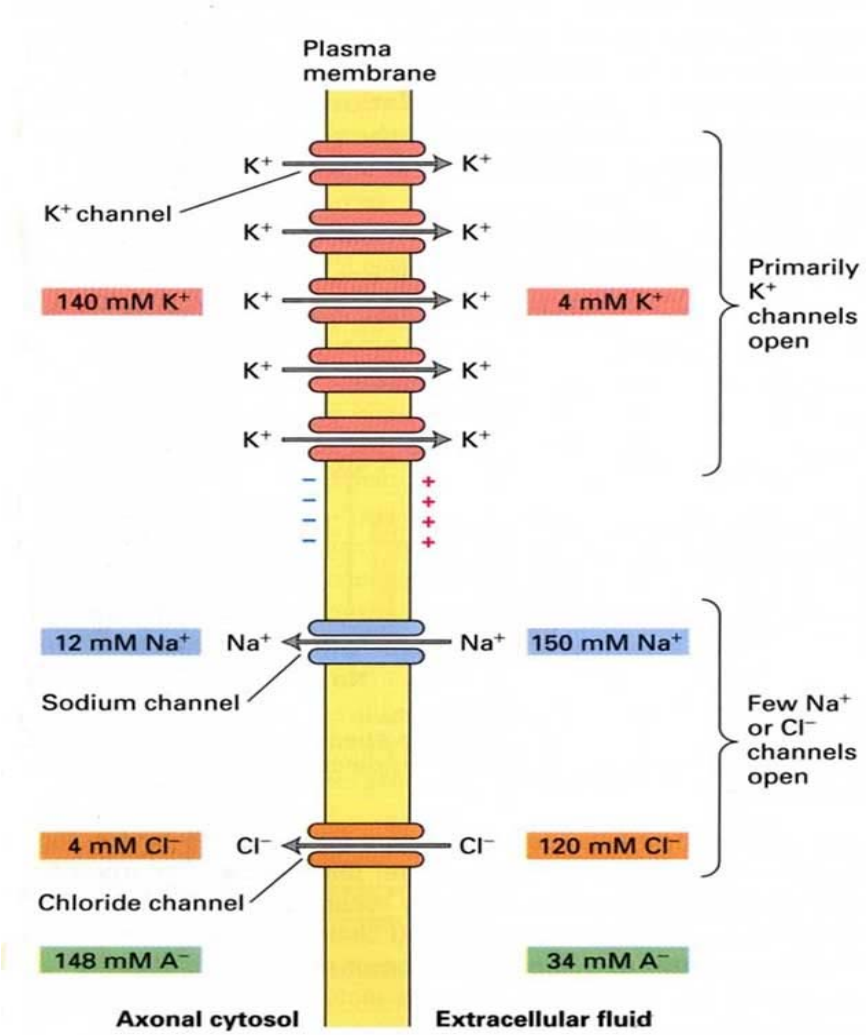
▲ **FIGURE 21-2 (a) An action potential is a sudden, transient depolarization of the membrane followed by repolarization to the resting potential of about −60 mV.** This recording of the axonal membrane potential in a presynaptic neuron shows that it is generating one action potential about every 4 milliseconds. (b) The membrane potential across the plasma membrane of a presynaptic neuron is measured by a small electrode inserted into it. Action potentials move down the axon at speeds up to 100 meters per second. Their arrival at a synapse causes release of neurotransmitters that bind to receptors in the postsynaptic cell, generally depolarizing the membrane (making the potential less negative) and tending to induce an action potential in it.

Närvi-impulss (action impulse) on väga kiire ja lühiaegne (1 ms) närviraku membraanipotenstiaali suuna vahetus, puhkeseisundis -60 mV (raku sisemus negatiivne) väärtuselt umbes +50 mV –ni impulsis ja jälle tagasi.Niisuguseid impulsse genereeritakse korduvalt, iga 4 ms järel. Närvi-impulsid liiguvad aksonites kiirusega 100 m/s



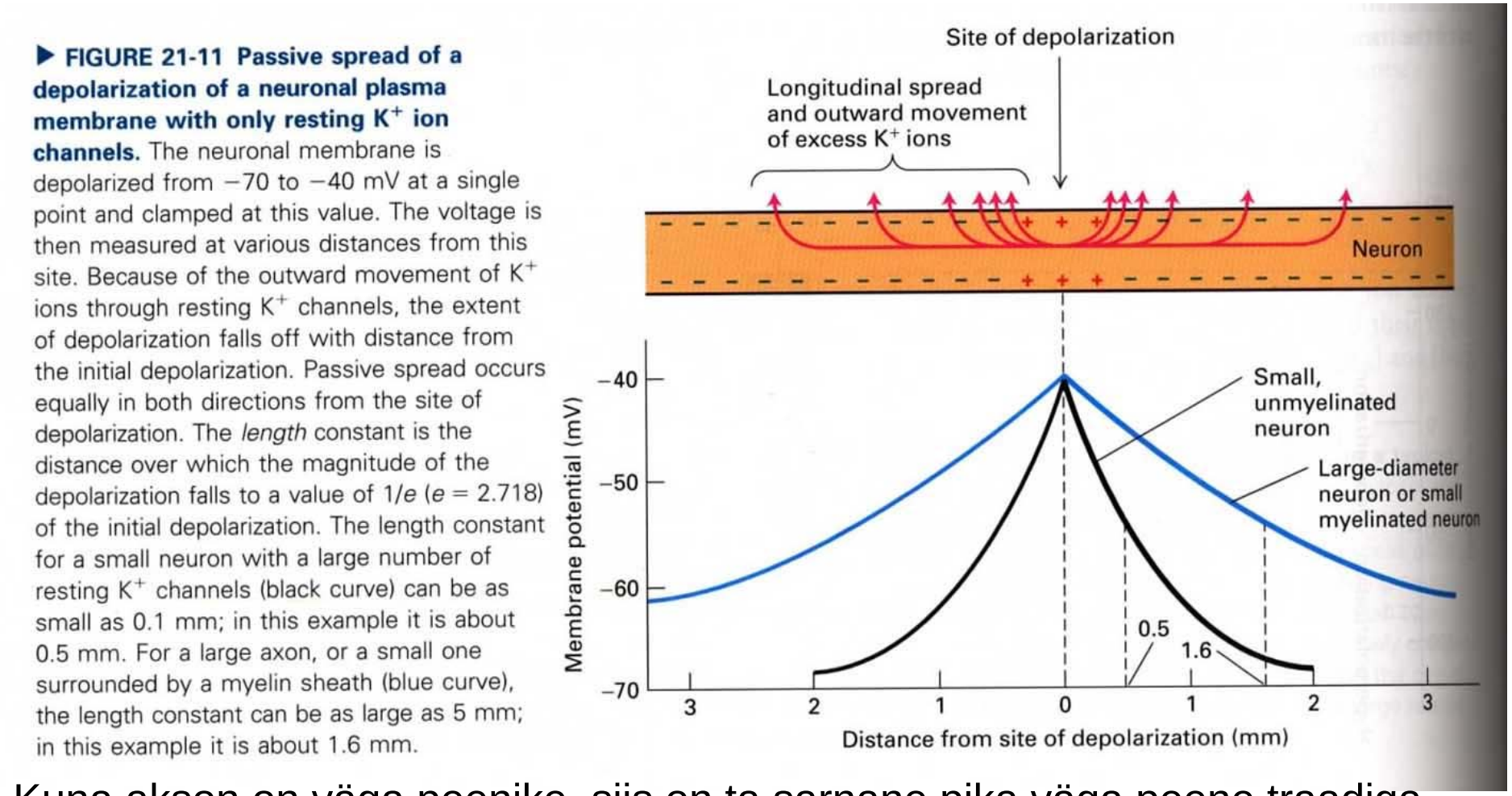
▲ FIGURE 21-8 Ion channels in neuronal plasma membranes. Each type of channel protein has a specific function in the electrical activity of neurons. (a) Resting K^+ channels are responsible for generating the resting potential across the membrane. (b) Voltage-gated channels are responsible for propagating action potentials along the axonal membrane. (c, d) Two types of ion channels in dendrites and cell bodies are responsible for generating electric signals in postsynaptic cells. One type (c) has a site for binding a specific extracellular neurotransmitter (blue circle). The other type (d) is coupled to a neurotransmitter receptor via a G protein; it responds to intracellular signals (red circle) induced by binding of neurotransmitter to a separate receptor protein (not shown). Signals activating different channels include Ca^{2+}, cyclic GMP, and the $G_{\beta\gamma}$ subunits of trimeric G proteins (Chapter 20).

Puhkepotentsiaal on tingitud K-kanalite avatud olekust, aga neid kanaleid on suhteliselt vähe. Närvi-impulss algab liganditundliku Na kanali (c, d) signaal-indutseeritud avanemisega. Tekkiv kohalik suhteliselt nõrk depolarisatsioon annab alguse pingetundlike Na kanalite (b) laviinikujulisele avanemisele. Need kanalid aga on isesulguvad (vt järgm. Joonis), nii et depolarisatsioon jääb lühikeseks. Siiski, seesama depolarisatsioon indutseerib suure arvu K kanalite avanemise, mis kiiresti repolariseerib membraani puhkepotentsiaalile tagasi.



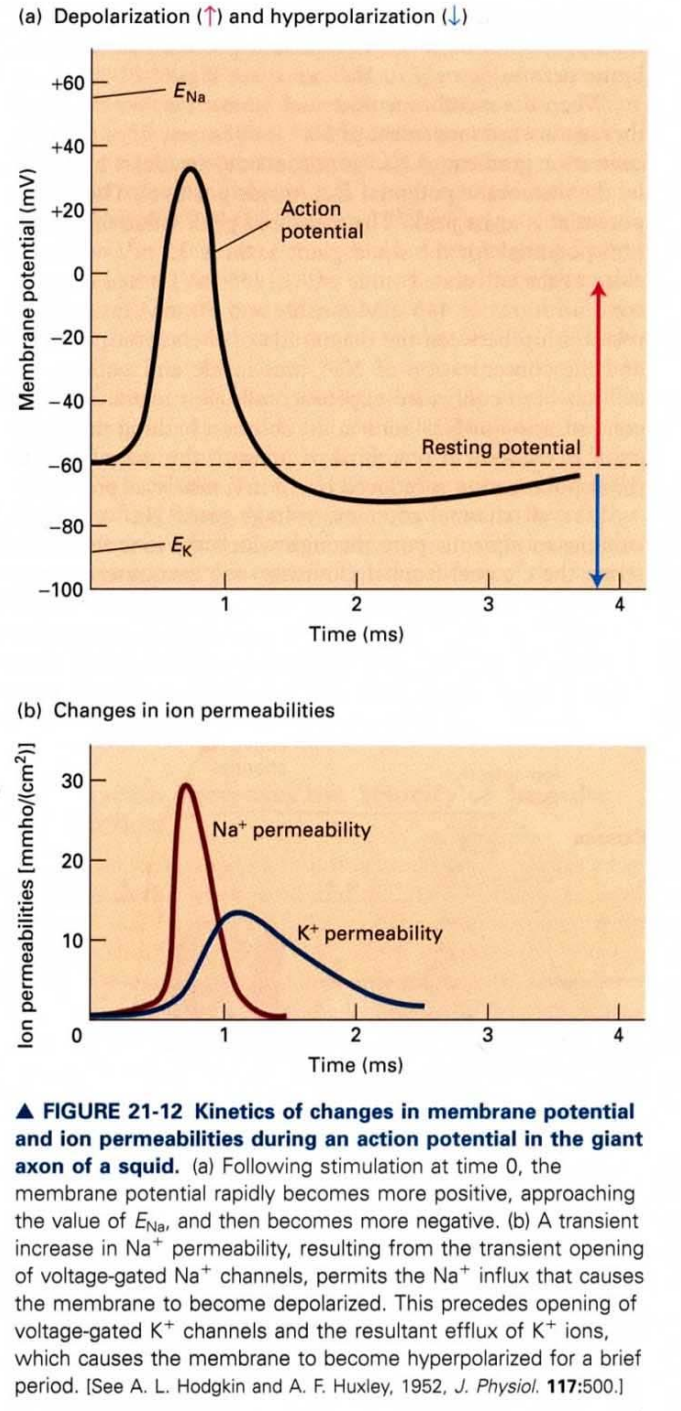
◀ **FIGURE 21-9 Origin of the resting potential in a typical vertebrate neuron.** The ionic compositions of the cytosol and of the surrounding extracellular fluid are different. A^- represents negatively charged proteins, which neutralize the excess positive charges contributed by Na^+ and K^+ ions. In the resting neuron there are about ten times more open K^+ channels than open Na^+ or Cl^- channels; as a consequence more positively charged K^+ ions exit the cell than Na^+ or Cl^- ions enter, and the outside of the plasma membrane acquires a net positive charge relative to the inside.

See pilt ilustreerib puhkepotentsiaali olukorda. Pange tähele kõrget K kontsentratsiooni rakus ja madalat väljaspool, Na suhtes aga vastupidi. K kanlite kogujuhtivus ei ole suur, kuid siiski palju suurem kui suletud Na kanalite juhtivus, nii et membraanipotenstsiaal on lähedane K-ga määratud nernsti potentsiaalile. Na-kanalite avanemisega algab närvi-impulss. Ka Cl kanalid osalevad membraani depolarisatsioonis.



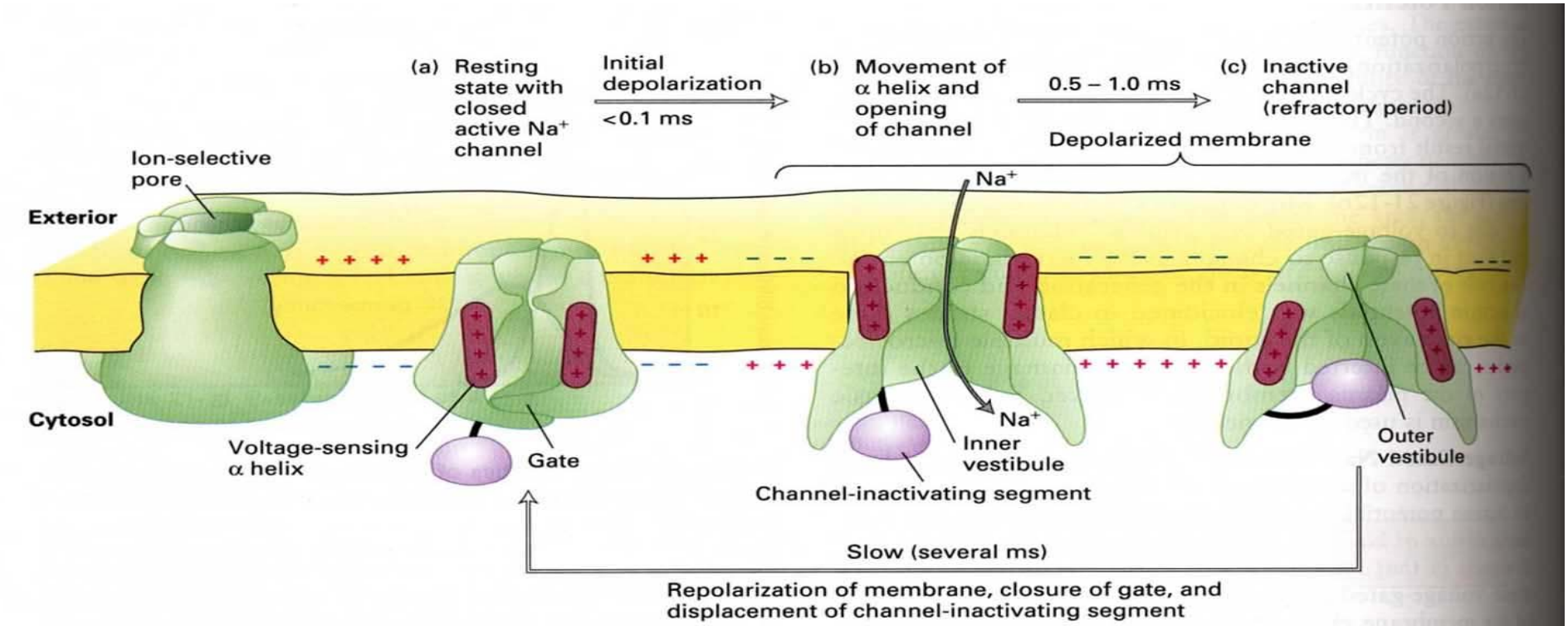
▶ **FIGURE 21-11 Passive spread of a depolarization of a neuronal plasma membrane with only resting K^+ ion channels.** The neuronal membrane is depolarized from −70 to −40 mV at a single point and clamped at this value. The voltage is then measured at various distances from this site. Because of the outward movement of K^+ ions through resting K^+ channels, the extent of depolarization falls off with distance from the initial depolarization. Passive spread occurs equally in both directions from the site of depolarization. The *length* constant is the distance over which the magnitude of the depolarization falls to a value of $1/e$ ($e = 2.718$) of the initial depolarization. The length constant for a small neuron with a large number of resting K^+ channels (black curve) can be as small as 0.1 mm; in this example it is about 0.5 mm. For a large axon, or a small one surrounded by a myelin sheath (blue curve), the length constant can be as large as 5 mm; in this example it is about 1.6 mm.

Kuna akson on väga peenike, siis on ta sarnane pika väga peene traadiga. Kui ühes punktis tekitada potentsiaali muutus, siis see sumbub kiiresti traadi takistuse tõttu, levides ehk ainult mõne mm kaugusele. Telefoni kaugekõnede hea kuuldavuse tagamiseks on traatides aeg-ajalt võimendusjaamad, mis annavad lisa sumbuvale potentsiaalile. Närvirakkudes on selleks pingetundlikud Na kanalid, mis samuti võimendavad sumbuvat depolarisatsiooni-lainet.



▲ FIGURE 21-12 Kinetics of changes in membrane potential and ion permeabilities during an action potential in the giant axon of a squid. (a) Following stimulation at time 0, the membrane potential rapidly becomes more positive, approaching the value of E_{Na}, and then becomes more negative. (b) A transient increase in Na^+ permeability, resulting from the transient opening of voltage-gated Na^+ channels, permits the Na^+ influx that causes the membrane to become depolarized. This precedes opening of voltage-gated K^+ channels and the resultant efflux of K^+ ions, which causes the membrane to become hyperpolarized for a brief period. [See A. L. Hodgkin and A. F. Huxley, 1952, *J. Physiol.* **117**:500.]

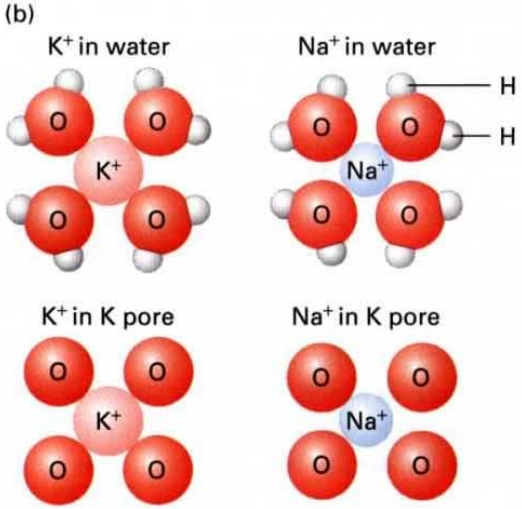
Mõõtmised näitavad, et Na kanalite avanemisega põhjustatud depolarisatsioon lõpeb väga kiiresti, asendudes isegi väikese hüperpolarisatsiooniga, mis laheneb puhkepotentsiaalile (a). Viimane näitab, et repolarisatsioonil osalevad K kanalid, mis avanevad depolarisatsiooni ajal pingetundlikult, püüdes depolarisatsiooni kaotada (b).Niisugune Na-Ka kanalite omavaheline “võitlus” peab aga olem hästi koordineeritud, et mõlemad ei oleks korraga laialt avatud ja ei “lühistaks” Ka-Na konsentratsioonide erinevusi. Seda koordinatsiooni kindlustab Na kanalite eriline ehitus, mis avab kanalid pingetundlikult, suleb aga lihtsalt kindla aja pärast, mitte mingiule signaalile reageerides

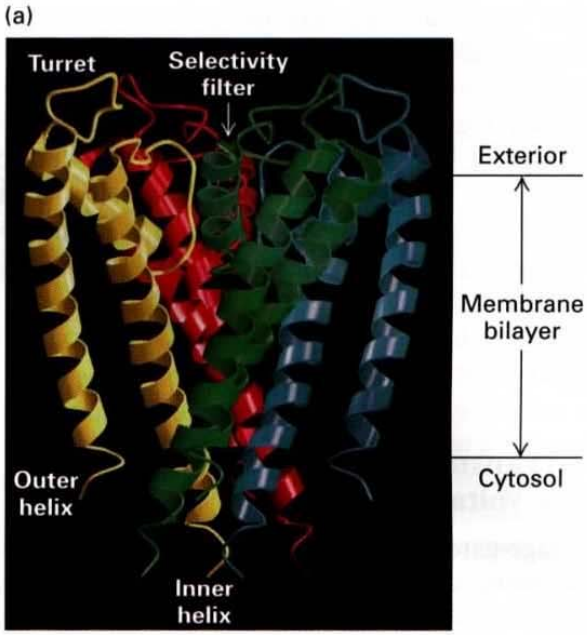


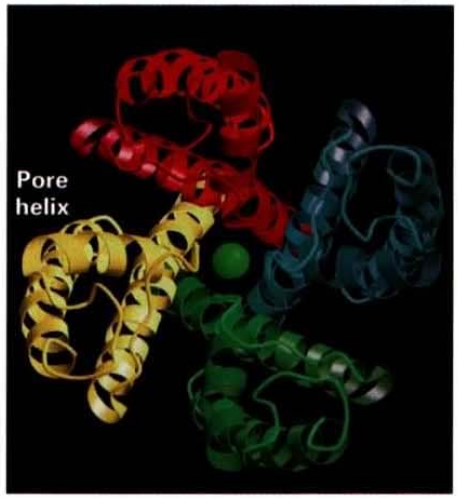
▲ **FIGURE 21-13 Structure and function of the voltage-gated Na^+ channel.** *(Left)* Like all voltage-gated channels, it contains four transmembrane domains, each of which contributes to the central pore through which ions move. The critical components that control movement of Na^+ ions are shown in the cutaway views. (a) In the closed, resting state, the gate obstructs the channel, inhibiting Na^+ movement, and the channel-inactivating segment is free in the cytosol. The channel protein contains four voltage-sensing α helices (maroon), which have positively charged side chains every third residue. The attraction of these charges for the negative interior of resting cells helps keep the channel closed. (b) When the membrane becomes depolarized (outside negative), the voltage-sensing helices move toward the outer plasma membrane surface, causing an immediate conformational change in the gate segment that opens the channel for influx of Na^+ ions. (c) Within a millisecond after opening, the voltage-sensing helices return to the resting position and the channel-inactivating segment (purple) moves into the open channel, preventing further ion movements. When the membrane potential is reversed so that the inside is again negative, the gate moves back into the blocking position (not shown). After 1–2 ms the channel-inactivating segment is displaced from the channel opening and the protein reverts to the closed, resting state (a) where it can be opened again by depolarization. [Adapted from C. Miller, 1991, *Science* **252:**1092, and C. Armstrong and B. Hille, 1998, *Neuron* **20:**371.]

Pingetundliku kanali avavad laengutega heeliksid, suleb aga stopper-segment, mis pöördub avatud kanali ette umbes millisekundiga. Alles selle järel kanal ise pöördub algasendisse, laengud endistele kohtadele ja stopper-segment ooteseisundisse. Stopper-segmendi vajadus on ilmne, sest kord avatud pingetundlik kanal enam ei sulgukski

FIGURE 21-25 Mechanism of ion selectivity in a resting K^+ channel from the bacterium *Streptomyces lividans*. (a) The three-dimensional structure of the pore in this channel, viewed from the side *(upper)* and from the top, or extracellular, side *(lower)*, reveals that the two membrane-spanning α helices in each of the four subunits are tilted relative to the vertical, forming an "inverted teepee." These helices, analogous to S5 and S6 in the Shaker channel, are connected by a P segment comprising a nonhelical "turret," which lines the outer part of the pore; a short α helix; and an extended loop, which forms the ion-selectivity filter. Selectivity of K^+ over Na^+ is due mainly to the carboxyl groups on two highly conserved glycine residues and one tyrosine on each of these loops, which protrude into the narrowest part of the channel. (b) Potassium ions, hydrated in solution, lose their bound water molecules as they pass through the selectivity filter and become coordinated instead to four backbone carbonyl oxygens, one from a glycine in the channel-lining loop of each P segment. Na^+ ions, being smaller, cannot perfectly coordinate with these oxygens and therefore pass through the channel only rarely. [Part (a) from D. A. Doyle et al., 1998, Science **280**:69, courtesy of R. MacKinnon. Part (b) adapted from C. Armstrong, 1998, Science **280**:56.]







Ka ja Na kanali tähtsaim omadus on nede vahel vahet teha. Ioonide mõõdud on väga sarnased ja kui tegu oleks lihtsalt auguga, siis väiksem ioon läbiks suuremale mõeldud kanalit. Kuna nii ei ole, siis tegelikult moodustuvad koordinatsioonisid emed metalli ja poori seinte aatomite vahel. Nende sidemete täpne pikkus kindlustab selektiivsuse.