Structure of the axonal membrane; Myelination

Polarity of neurons and the neuronal plasma membrane

The axon initial segment and the maintenance of neuronal polarity

Matthew N. Rasband

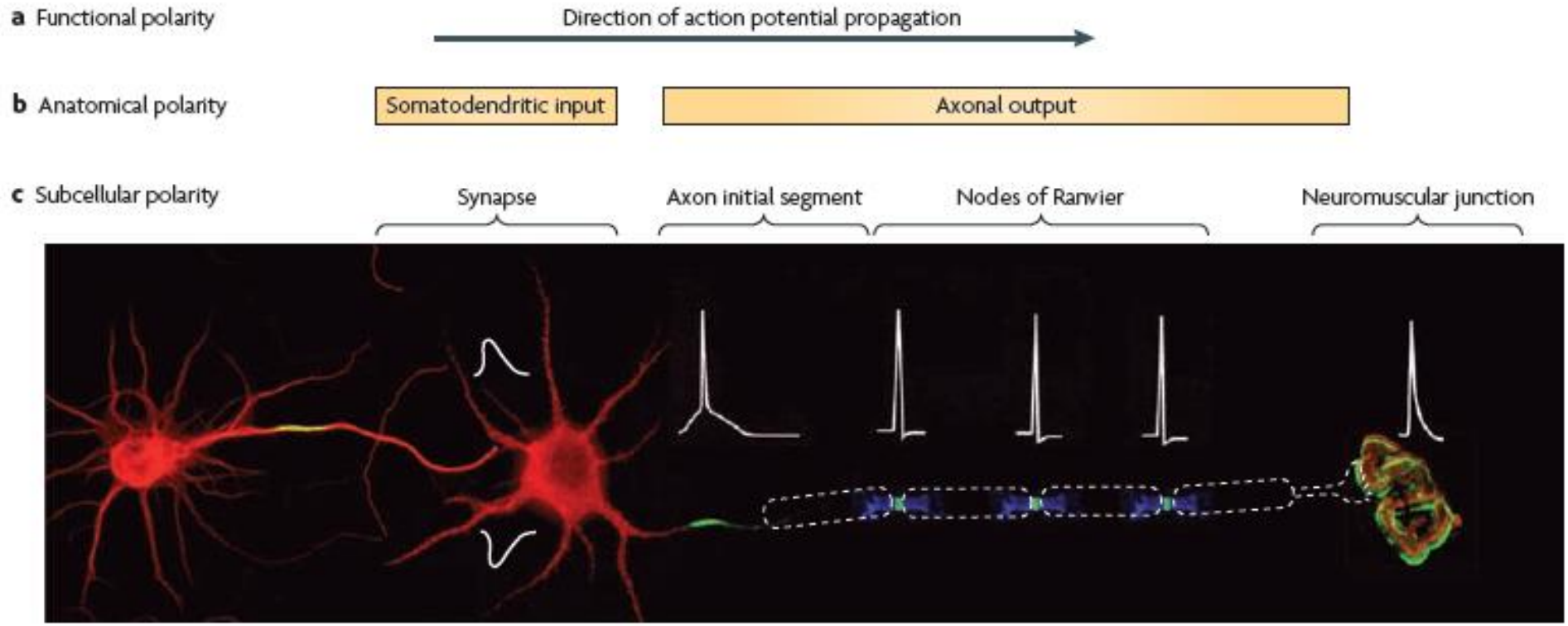
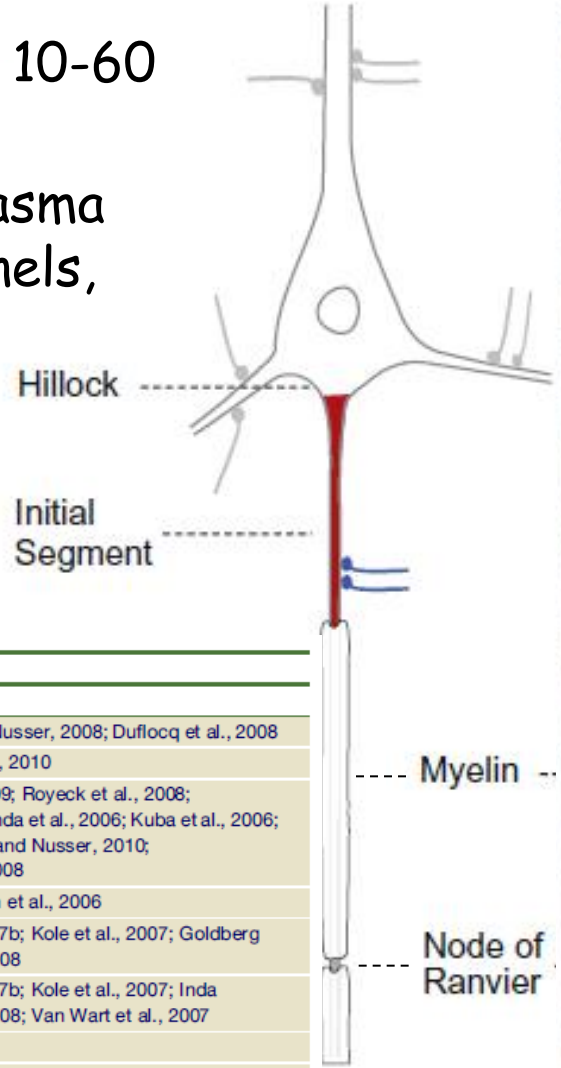
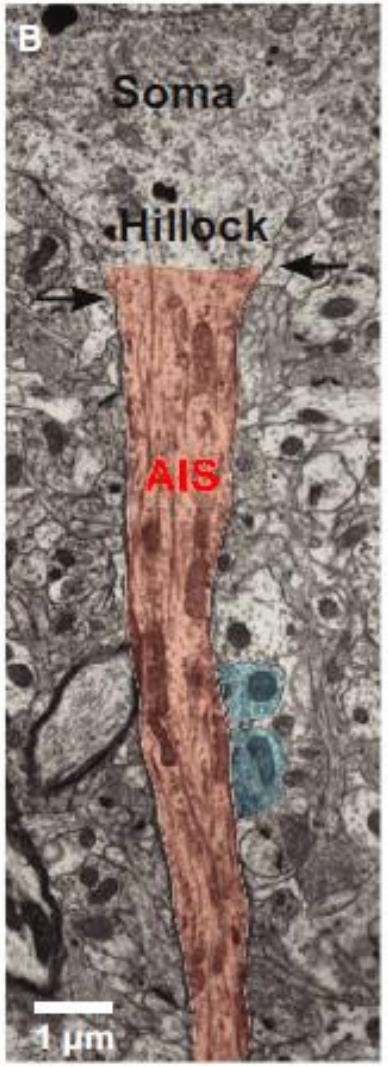


Figure 1 | **Neurons are highly polarized cells. a** | Neurons are functionally polarized because action potentials propagate in a single direction. Excitatory and inhibitory synaptic inputs are integrated at the axon initial segment (AIS). The resulting action potentials then propagate along the axon through the activity of ion channels clustered at nodes. Finally, neurotransmitter is released at the nerve terminal. **b** | Neurons are also anatomically polarized, as they can be subdivided into a somatodendritic input domain and an axonal output domain. The AIS separates these two domains. **c** | Neurons have a high degree of subcellular polarity, and synapses, the AIS, nodes of Ranvier and the neuromuscular junction are the main subcellular domains. Each of these domains is enriched in specific types of ion channels, receptors, adhesion molecules and molecular scaffolds that allow for the unidirectional propagation of action potentials. Each of these subcellular domains can also elicit unique electrophysiological responses (shown in white).

The axonal initial segment (AIS)

- only in vertebrates; non-myelinated, 10-60 μm long axonal segment
- dense granular layer beneath the plasma membrane ~ Ranvier node: ion channels, scaffold proteins
- frequent GABAergic synapses
- ER: Ca^{2+} store (~spine apparatus)





(B) Electron micrograph of the AIS of a cortical pyramidal neuron. The soma, axon hillock, and AIS (red) are indicated. Blue areas indicate presynaptic terminals onto the AIS. Arrows (black) indicate the onset of the dense granular layer beneath the surface membrane indicating the start of the AIS. Adapted from Peters et al. (1968).

Table 1. Ion Channel Expression Patterns in the Axon Initial Segment

Current	Channel	Cell Type	Reference
I_{NaT}	$Na_v1.1$	IN, RGC, MN	Van Wart et al., 2007; Lorincz and Nusser, 2008; Duflocq et al., 2008
	$Na_v1.2$	PC	Hu et al., 2009; Lorincz and Nusser, 2010
	$Na_v1.6$	PC, DG, RGC, PN, IN, MN	Van Wart et al., 2007; Hu et al., 2009; Royeck et al., 2008; Boiko et al., 2003; Catterall, 1981; Inda et al., 2006; Kuba et al., 2006; Lorincz and Nusser, 2008; Lorincz and Nusser, 2010; Kress et al., 2010; Duflocq et al., 2008
I_{NaP}	$Na_v1.?$	PC	Stuart and Sakmann, 1995; Astman et al., 2006
I_D	$K_v1.1$	PC, MNTB, IN	Dodson et al., 2002; Shu et al., 2007b; Kole et al., 2007; Goldberg et al., 2008; Lorincz and Nusser, 2008
	$K_v1.2$	PC, RGC, MNTB, IN	Dodson et al., 2002; Shu et al., 2007b; Kole et al., 2007; Inda et al., 2006; Lorincz and Nusser, 2008; Van Wart et al., 2007
	$K_v2.2$	MNTB	Johnston et al., 2008
I_A	$K_v1.4$	PC	Ogawa et al., 2008
I_M	$K_v7.2$ / $K_v7.3$	PC	Pan et al., 2006; Shah et al., 2008
	$K_v7.2$	MN, DG	Devaux et al., 2004; Klinger et al., 2011
I_{Ca} (T/R-type)	$Ca_v2.3$ / $Ca_v3.2$ / $Ca_v3.1$	CC, PC, PN	Bender and Trussell, 2009
I_{Ca} (P/Q/N-type)	$Ca_v2.1$/$Ca_v2.2$	PC; PN	Callewaert et al., 1996; Yu et al., 2010

IN, interneuron; PC, pyramidal cell; DG, dentate granule cell (hippocampus); PN, Purkinje neuron; RGC, retinal ganglion cell; MNTB, medial nucleus of the trapezoid body; CC, cartwheel cell; MN, spinal cord motoneuron.

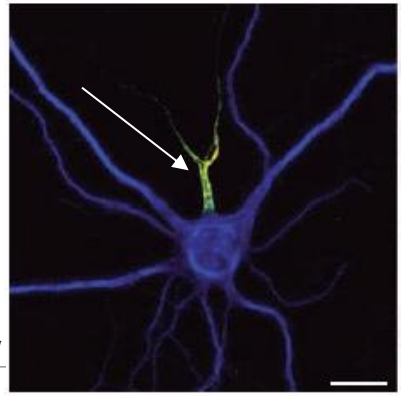
Neuron 73, January 26, 2012

Signal Processing in the Axon Initial Segment

Maarten H.P. Kole[1,2] and Greg J. Stuart[1,*]

The axonal initial segment (AIS)

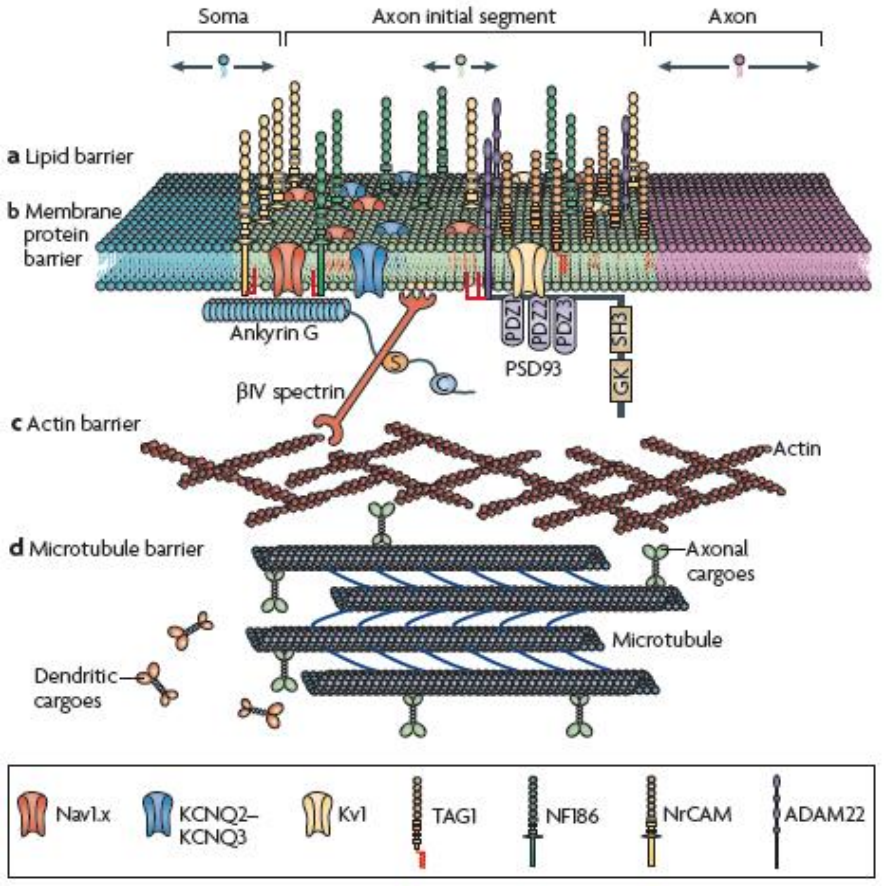
- physical barrier against the lateral diffusion between the axonal / somatodendritic membrane components
  - + cytoplasmic filtering (actin: depending on size? myosin?)
  - + selective passing of vesicles (MT)
- developing in parallel with axonal/dendritic specification
  - before the formation of functional synaptic sites
- voltage-gated Na^+ (Na_V) and K^+ (K_V) channels in high density + small diameter -> action potential
  - 35-45 μm long
  - >50x density (or less?)
- similar structure to the Ranvier-nodes, but AIS formation happens in a glia-independent manner



The axon initial segment and the maintenance of neuronal polarity

Matthew N. Rasband

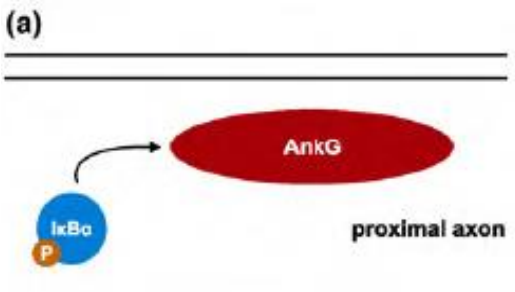
ankyrinG / neurofascin 186

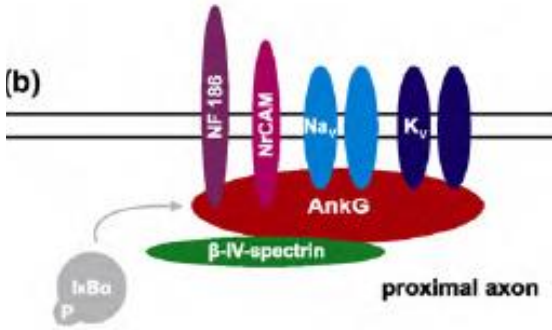


Formation of the AIS

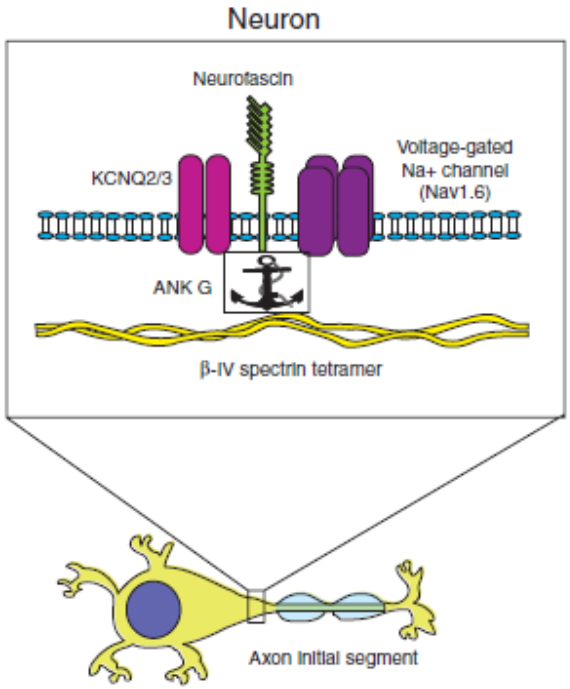
1) deposits of ankyrinG in the proximal axon (promoted by IκBα phosphorylation?)

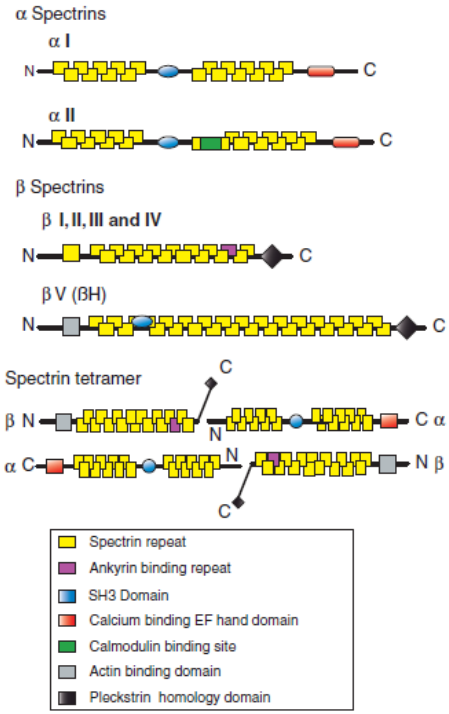
2. ankyrinG: scaffold protein
   - adhesion molecules (NF186 [neurofascin], NrCAM)
   - ankyrinG -> β-IV spectrin -> actin

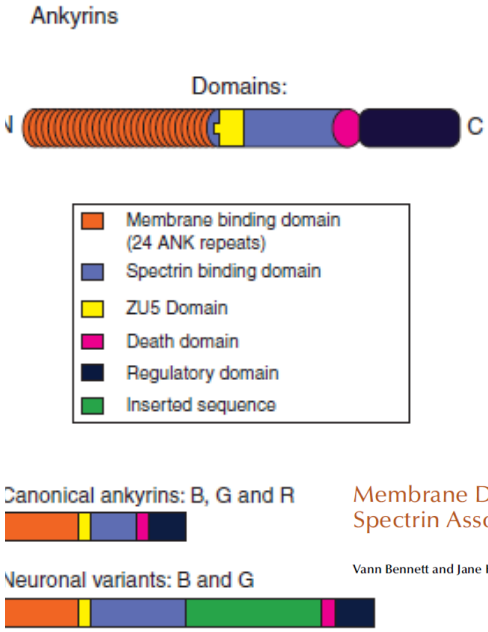




Building and maintaining the axon initial segment
Matthew S Grubb and Juan Burrone







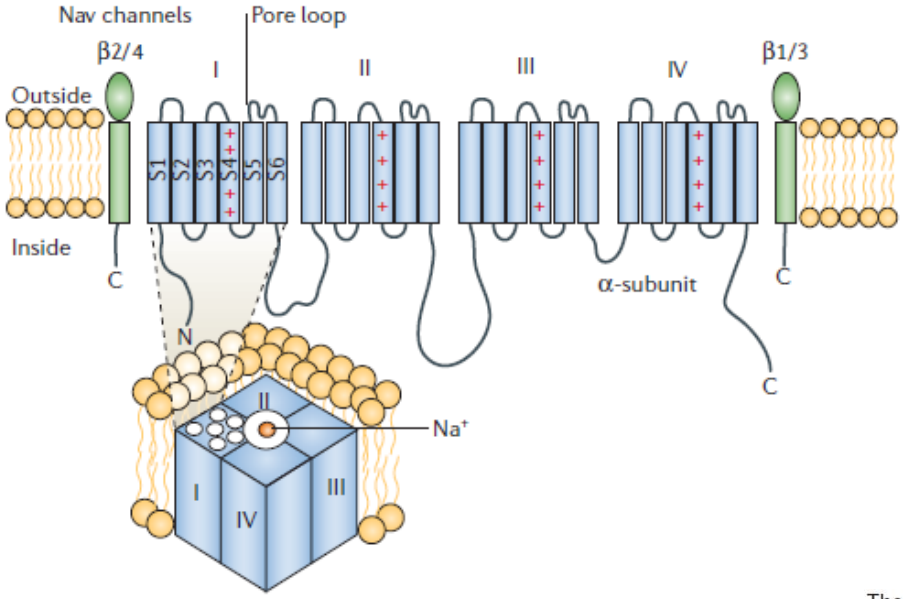
Membrane Domains Based on Ankyrin and Spectrin Associated with Cell–Cell Interactions

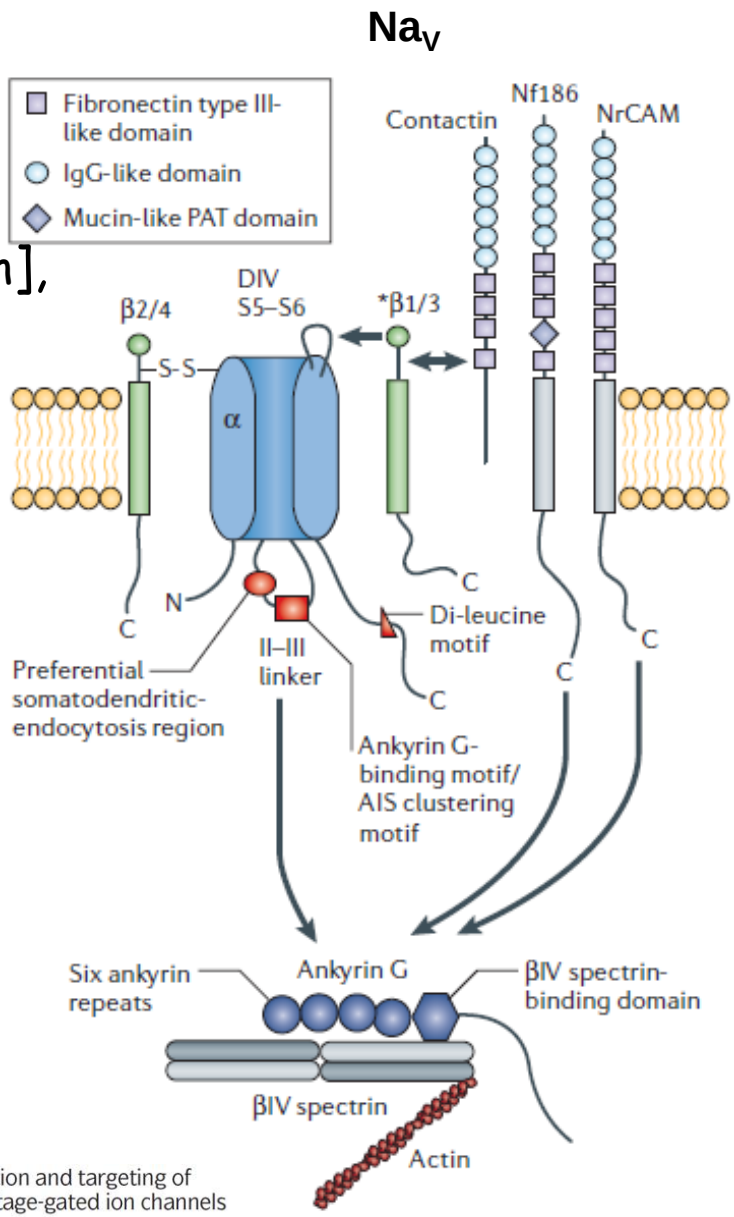
Vann Bennett and Jane Healy

Formation of the AIS

1) deposits of ankyrinG in the proximal axon (promoted by IκBα phosphorylation?)

2. ankyrinG: scaffold protein
   - adhesion molecules (NF186 [neurofascin], NrCAM)
   - ankyrinG -> β-IV spectrin -> actin
   - ion channels





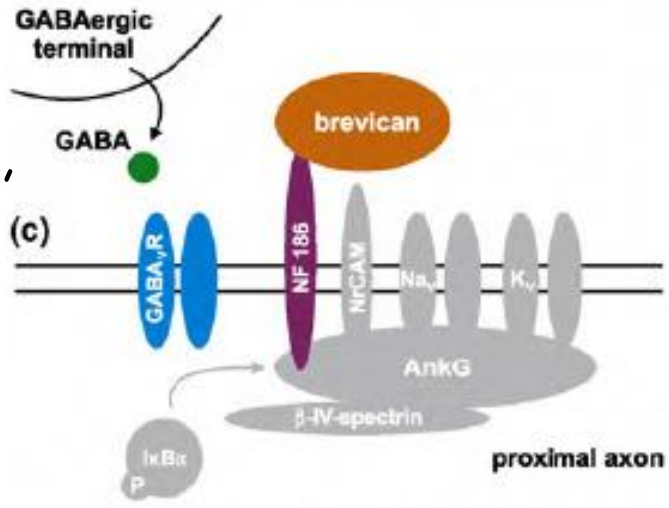
NATURE REVIEWS | NEUROSCIENCE
VOLUME 7 | JULY 2006

The distribution and targeting of neuronal voltage-gated ion channels

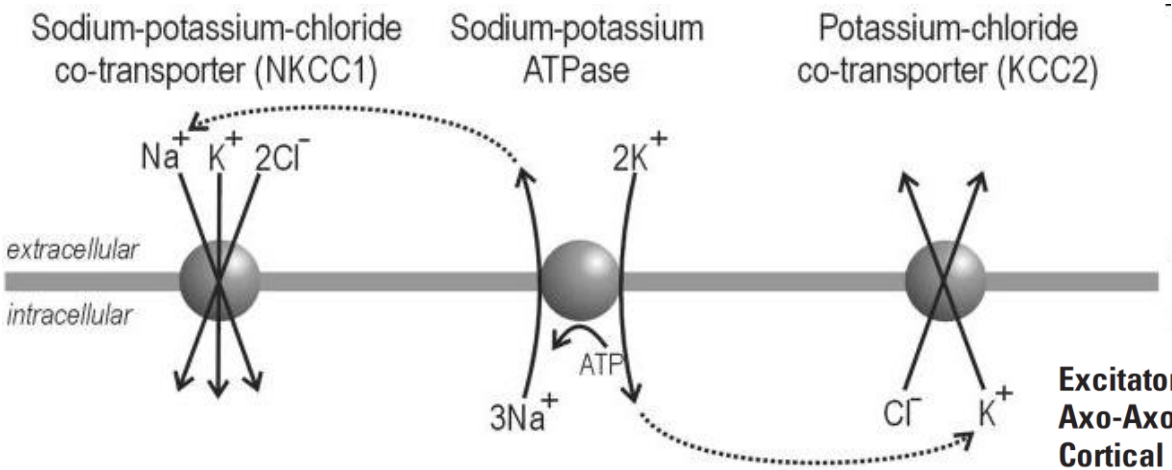
Helen C. Lai* and Lily Y. Jan*

Formation of the AIS

3. neurofascin (NF186):
   - organizing the ECM (brevican, phosphocan, tenascin)
   - GABAerg synaptic inputs -> axo-axonic synapse (chandellier cells)
     - normally very effective inhibition
     - cortical pyramidal cells: excitatory effects!
       - the normally high KCC2 (*K-Cl cotransporter*) density is low within the AIS -> high $[Cl^-]_{IC}$ -> activation of $GABA_AR$ has hypopolarizing (excitatory) effects



Building and maintaining the axon initial segment
Matthew S Grubb and Juan Burrone

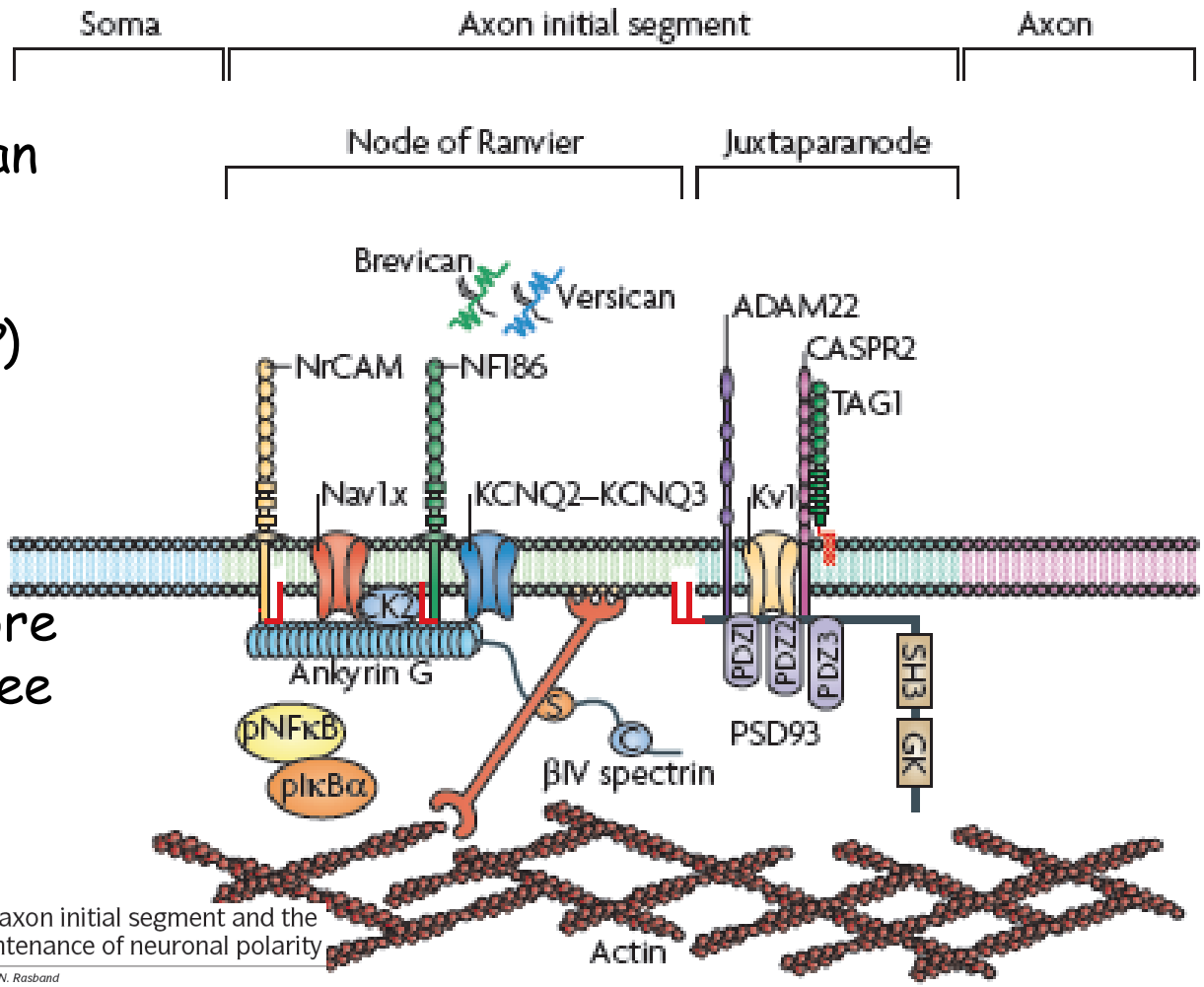


Excitatory Effect of GABAergic Axo-Axonic Cells in Cortical Microcircuits

János Szabadics,[1*] Csaba Varga,[1*] Gábor Molnár,[1*] Szabolcs Oláh,[1] Pál Barzó,[2] Gábor Tamás[1†]

Structure of the AIS and Ranvier-node

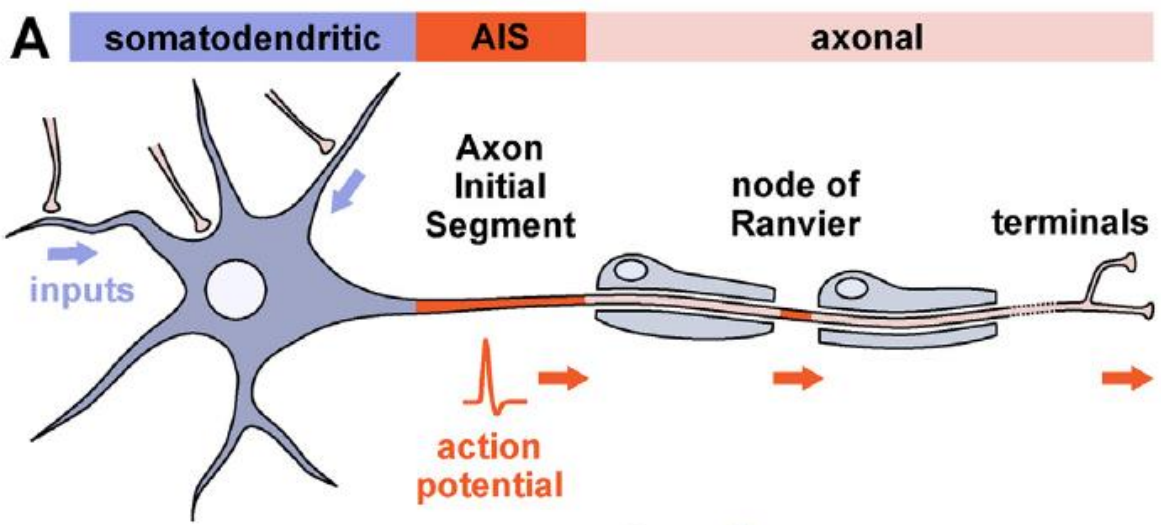
- master scaffold: ankyrinG + βIV spectrin, PSD-93
- voltage-gated Na^+ and K^+ channels [$Na_V1.X$; KCNQ2-KCNQ3, $K_V1.X$]
- adhesion molecules: NrCAM, neurofascin, TAG1
- metalloprotease: ADAM22
- ECM: brevican, versican
- regulatory factors:
  - CK2 (*kasein kinase2*)
  - NFκB / IκBα
- Ranvier-node: even more spatial organization (see later)

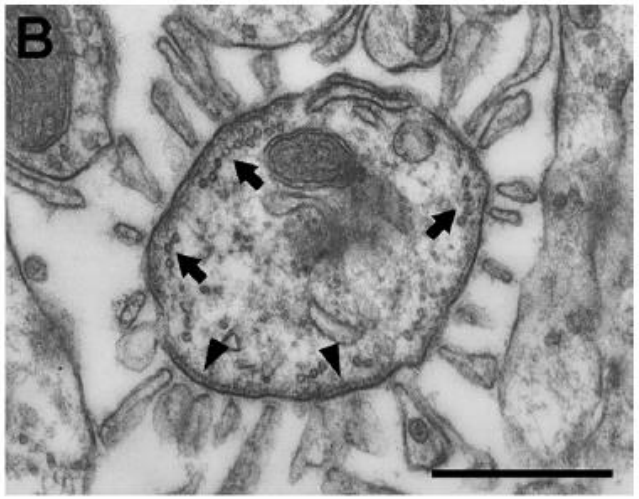


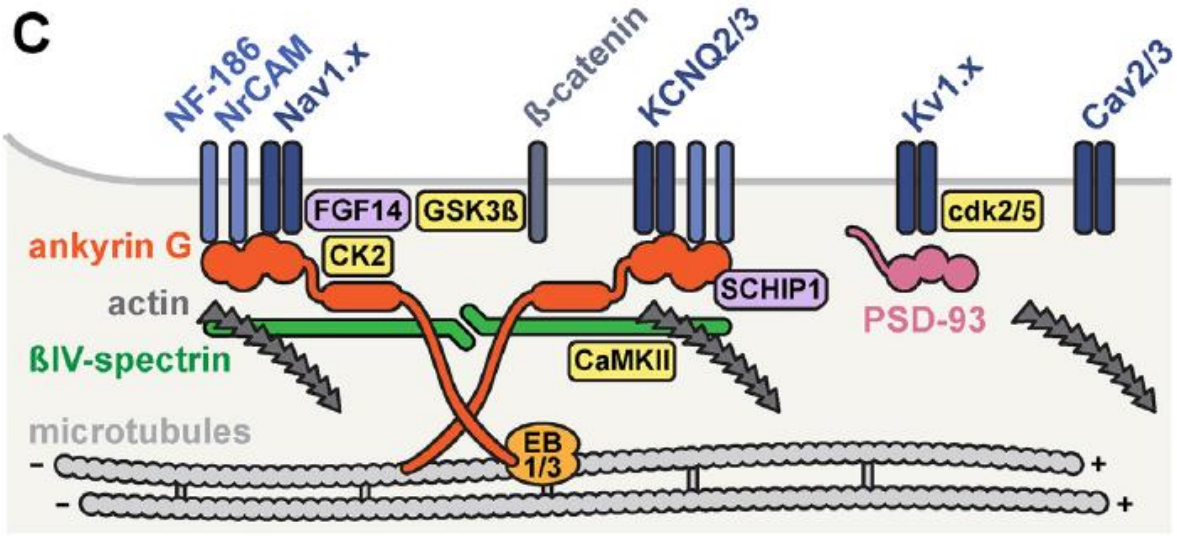
The axon initial segment and the maintenance of neuronal polarity

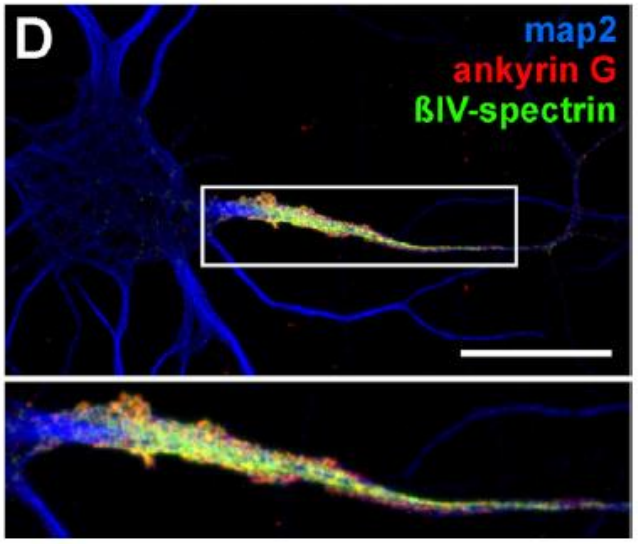
Matthew N. Rasband

Structure of the AIS and Ranvier-node









No Pasaran! Role of the axon initial segment in the regulation of protein transport and the maintenance of axonal identity

Christophe Leterrier*, Bénédicte Dargent

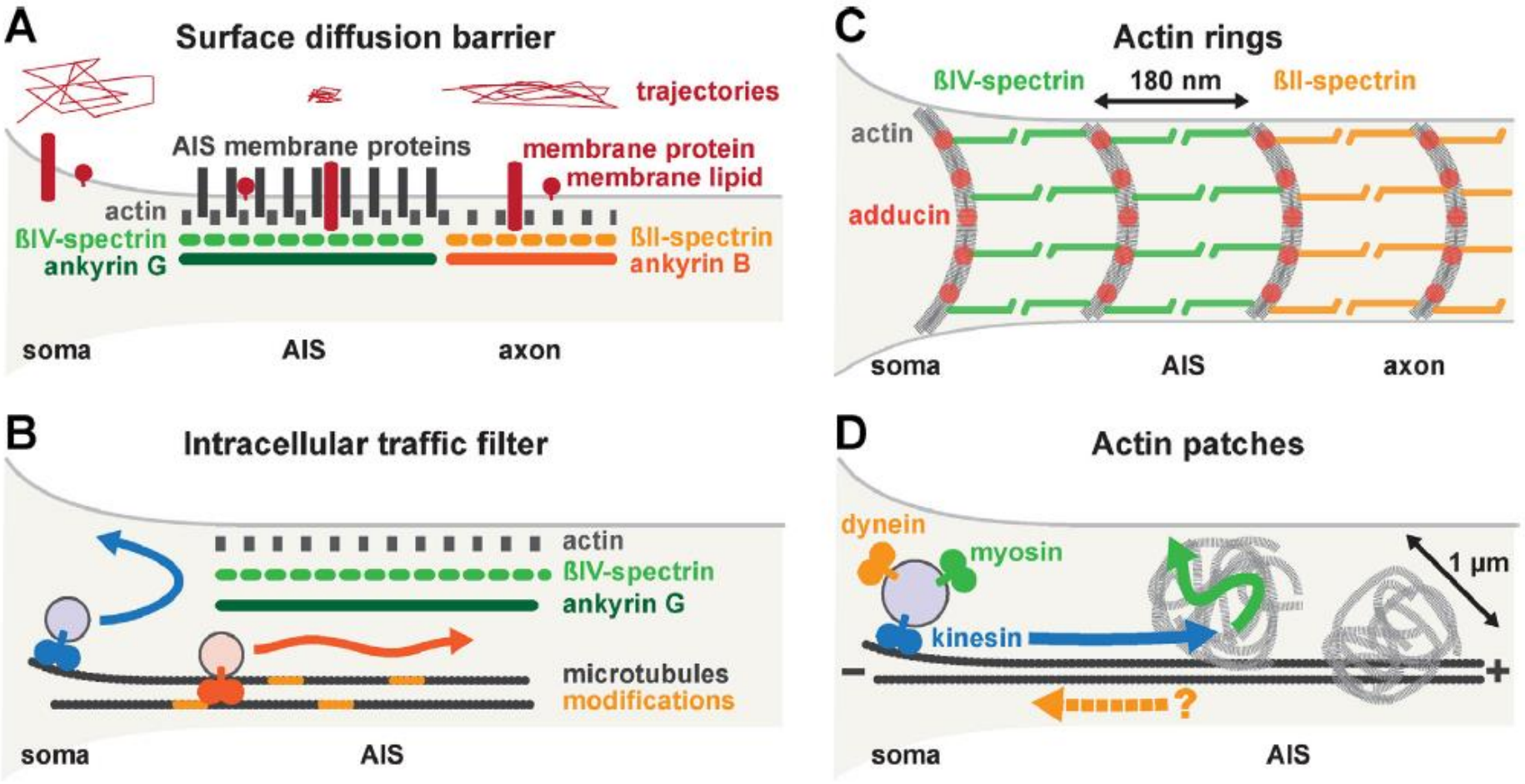
Structure of the AIS and Ranvier-node

Fig. 1. The axon initial segment (AIS). (A) The neuron integrates inputs received in the somatodendritic compartment (blue). The AIS (red), located at the beginning of the axon, generates the action potential that propagates up to the terminals (light red), and is regenerated at nodes of Ranvier (red) across internodes. (B) The AIS of a Purkinje cell (transverse section, right). This electron microscopy image demonstrates two morphological features of the AIS: microtubule fascicles (arrows) and the membrane undercoat (arrowheads). Adapted with permission from Synapse Web (J. Spacek and K. Harris, PI, http://synapses.clm.utexas.edu). Scale bar, 0.5 μm. (C) The AIS of a cultured rat hippocampal neuron labeled for ankG (red) and βIV-spectrin (green). Map2 (blue) is excluded from the axon and delineates the somatodendritic compartment. Scale bar, 20 μm. (D) The AIS components. The main AIS scaffold is ankG (orange), linked to βIV-spectrin (green) that in turn binds to actin filaments (dark gray). AnkG binds to Nav1.x channels and Kv7.2/7.3 channels (dark blue), as well as adhesion proteins NF-186 and NrCAM (blue). EB1/3 proteins (light orange) link ankG to microtubules (light gray). AnkG also binds to SCHIP1 (purple). Other channels present at the AIS are Kv1.x channels linked to PSD-93 (pink), and Cav2/3 channels. Kinases are shown in yellow (see details in main text).

No Pasaran! Role of the axon initial segment in the regulation of protein transport and the maintenance of axonal identity

Christophe Leterrier*, Bénédicte Dargent

Role and importance of the AIS



No Pasaran! Role of the axon initial segment in the regulation of protein transport and the maintenance of axonal identity

Seminars in Cell & Developmental Biology 27 (2014) 44–51

Role and importance of the AIS

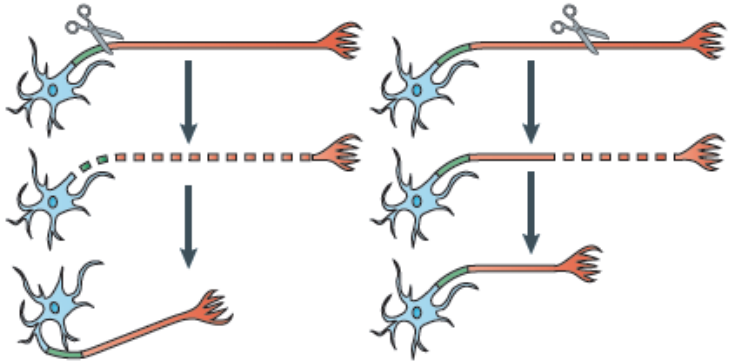
Fig. 2. Regulation of protein mobility and actin structures in the AIS. (A) The AIS diffusion barrier. Lipids and membrane proteins (red) diffusion is impeded in the AIS, due to corralling from the submembrane scaffold (green) and the concentration of AIS membrane proteins (gray). Diffusion along distal axon and soma is less restricted, as measured from trajectories of individual molecules (above, red), despite the presence of the distal axon ankB/βII-spectrin scaffold (orange). (B) The AIS traffic filter. Vesicles containing somatodendritic proteins (blue) are excluded from entering the axon (blue arrow), whereas vesicles transporting axonal proteins (orange) can proceed through the AIS (orange arrow). Specific recruitment of axonal kinesins is helped by cues on microtubule such as post-translational modifications (light orange). (C) Actin rings along the axon [15]. Rings of actin filaments (gray) capped by adducing (red) are spaced regularly every ~180 nm along the axon. Longitudinal β-spectrin dimers (βIV-spectrin in the AIS, green, and βII-spectrin in the distal axon, orange) join two adjacent rings. (D) Actin patches size (~1 μm in size) inside the AIS [16]. Somatodendritic vesicles transported along microtubules (blue arrow) by kinesins (blue) also bear myosins (green), causing them to stop at these actin patches and keeping them from entering the axon (green arrow). Also depicted is the hypothetical role of dynein in transporting non-axonal cargoes back to the soma (orange).

No Pasaran! Role of the axon initial segment in the regulation of protein transport and the maintenance of axonal identity

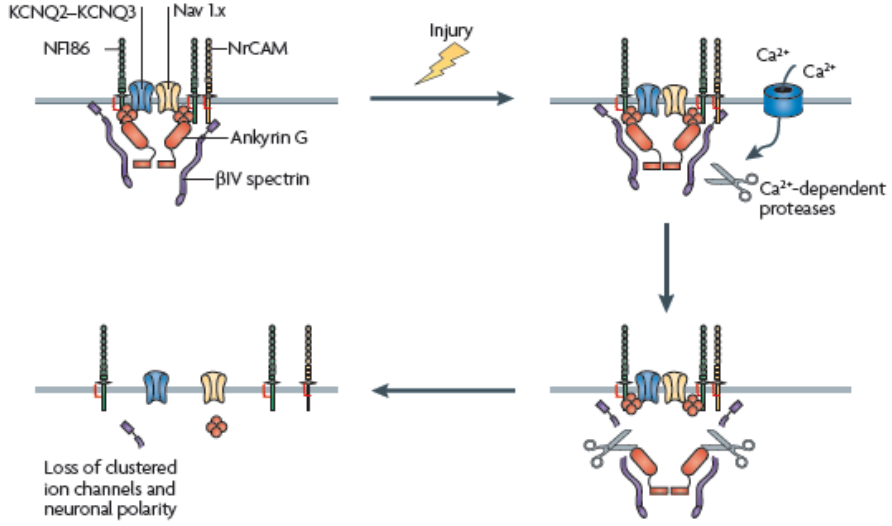
Seminars in Cell & Developmental Biology 27 (2014) 44–51

Role and importance of the AIS

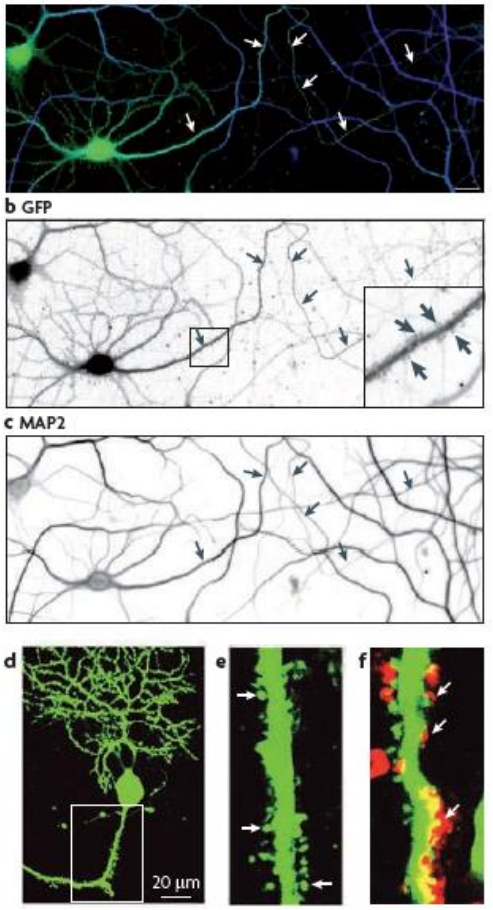
- plasticity: AIS spatial position influences excitability (the further the AIS -> the higher the AP firing threshold is)
- ankyrinG silencing -> „dendritisation"
- axonal injury: neurite regeneration depends on the integrity of the AIS (or from MT stability)

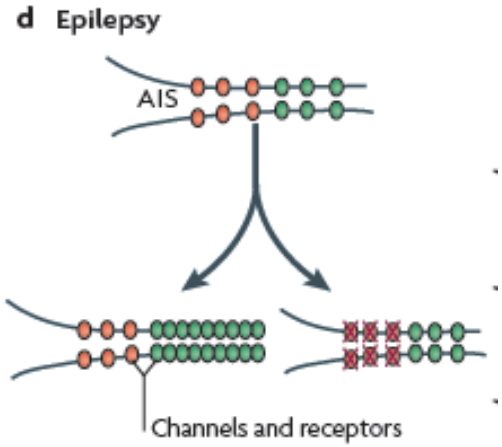


- schizophrenia, epilepsy, MS: aberrant AIS and/or ion channel distribution
- ischemia: Ca^{2+}-dependent proteolysis -> AIS disintegration, more distal localisation



ankyrinG siRNA





The axon initial segment and the maintenance of neuronal polarity

Matthew N. Rasband

Role and importance of the AIS

Figure 5 | **Nervous system injury and disease alters neuronal polarity. a** | Ischaemic injury (that is, stroke) disrupts the axon initial segment (AIS) cytoskeleton. The micrograph shows AIS stained for the cytoskeletal protein βIV spectrin (green), neurons labelled with NeuroTrace (red) and nuclei labelled with Hoechst stain (blue). The dashed line indicates the transition from the injured brain, in which the AISs are missing, to the area not exposed to ischaemia, where the AISs remain intact. The scale bars represent 50 μm. **b** | The cascade of events leading to loss of neuronal polarity after injury. Injury increases cytoplasmic Ca^{2+}, which activates the Ca^{2+}-dependent cysteine-protease calpain. Calpain (indicated by the scissors) cleaves ankyrin G (AnkG, also known as ANK3) and βIV spectrin, leading to the declustering of ion channels and loss of polarity. **c** | The type and location of axonal injury determines the consequence for neuronal polarity. Axonal transection near the cell body causes a dendrite-to-axon identity switch (left panel), whereas transection far from the cell body does not (right panel). **d** | Disruption of channel and receptor density, function or location can cause or result from altered nervous system function. For example, epilepsy can increase channel densities (left) or result from altered AIS channel function (right). Demyelination leads to altered subcellular polarity of axons. Parts **a** and **b** are modified, with permission, from REF. 64 © (2009) The Society for Neuroscience.

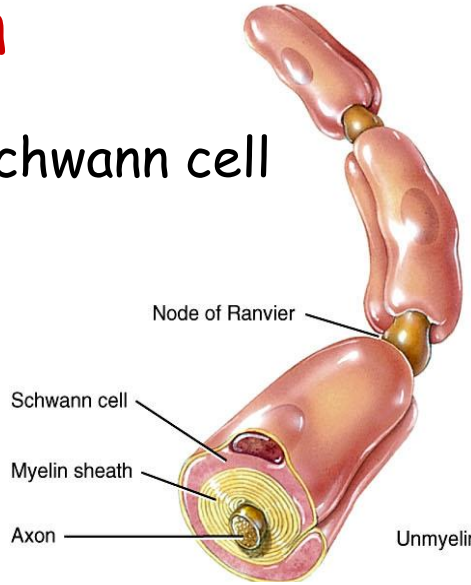
Myelination

peripheral nervous system

CNS

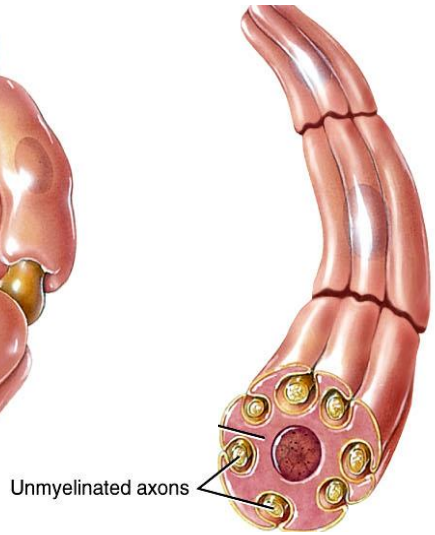
oligodendroglia

Schwann cell

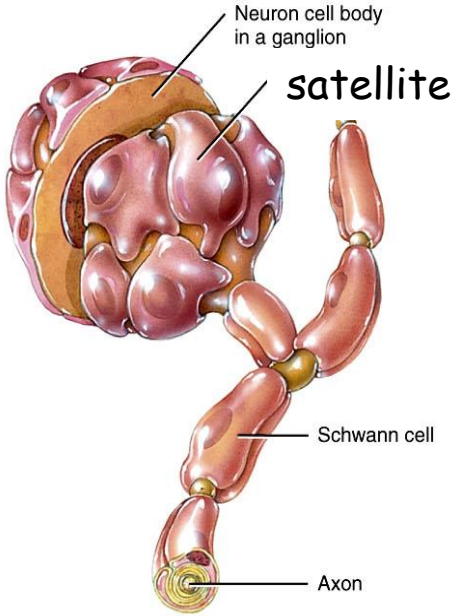


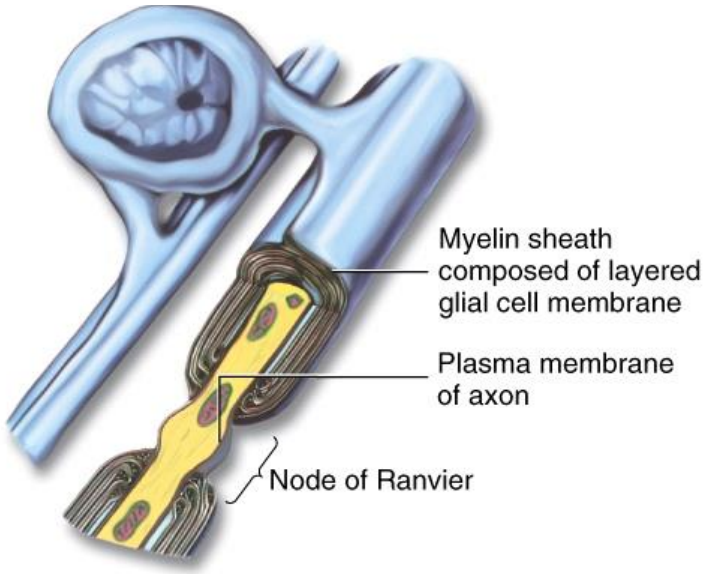
myelinated axon

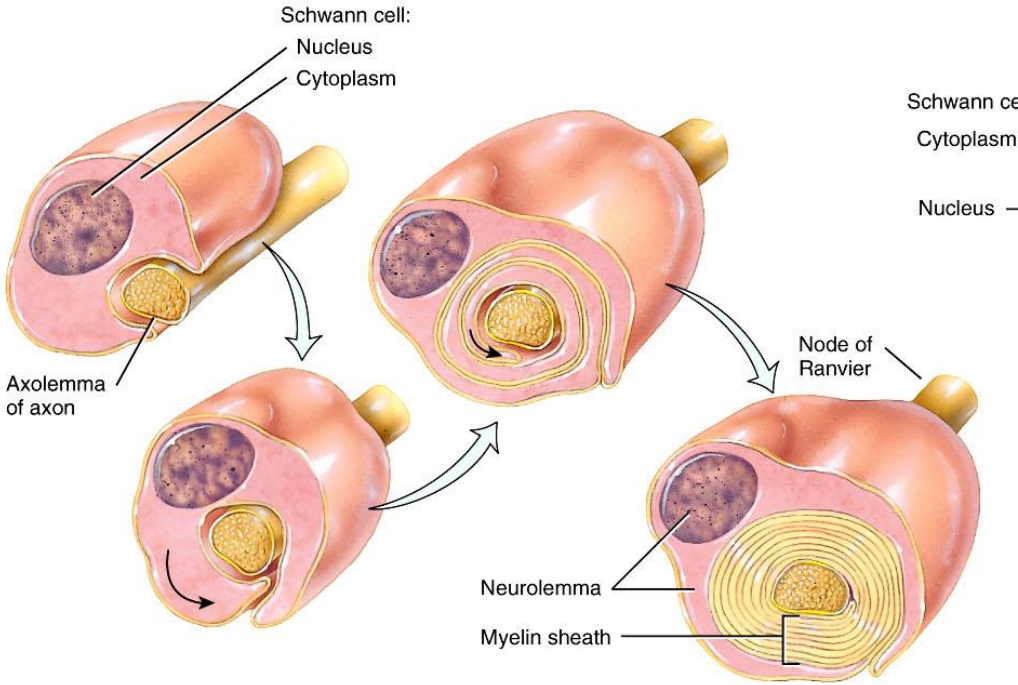
Remak cell



more, non-myelinated axons



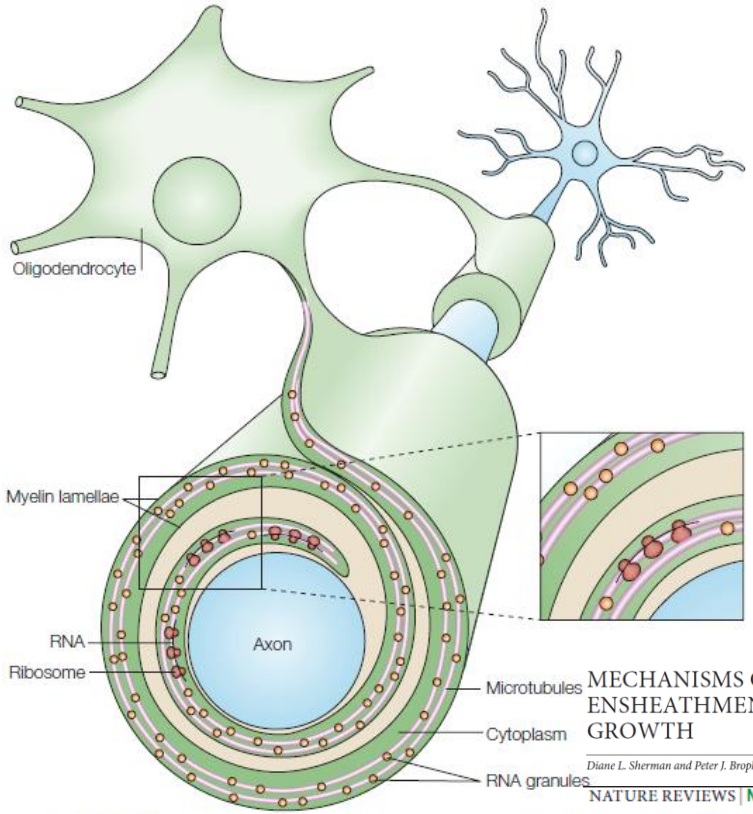




Formation of the myelin sheath

- synthesis of myelin basic protein (MBP) at the periphery -> localized RNA granules
  - bound and transported along the MTs
  - oligodendroglia: „reeled-up" MT, gap junctions
  - Schwann cell: microvilli, Cajal-bands (dystrophin-periaxin complex)

CNS

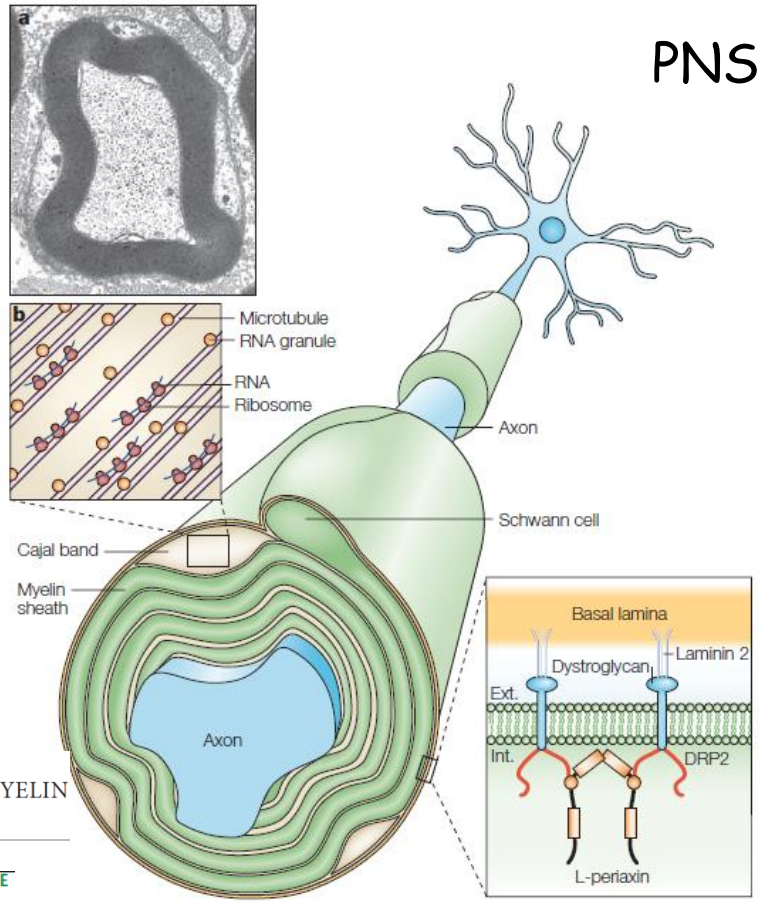


MECHANISMS OF AXON ENSHEATHMENT AND MYELIN GROWTH

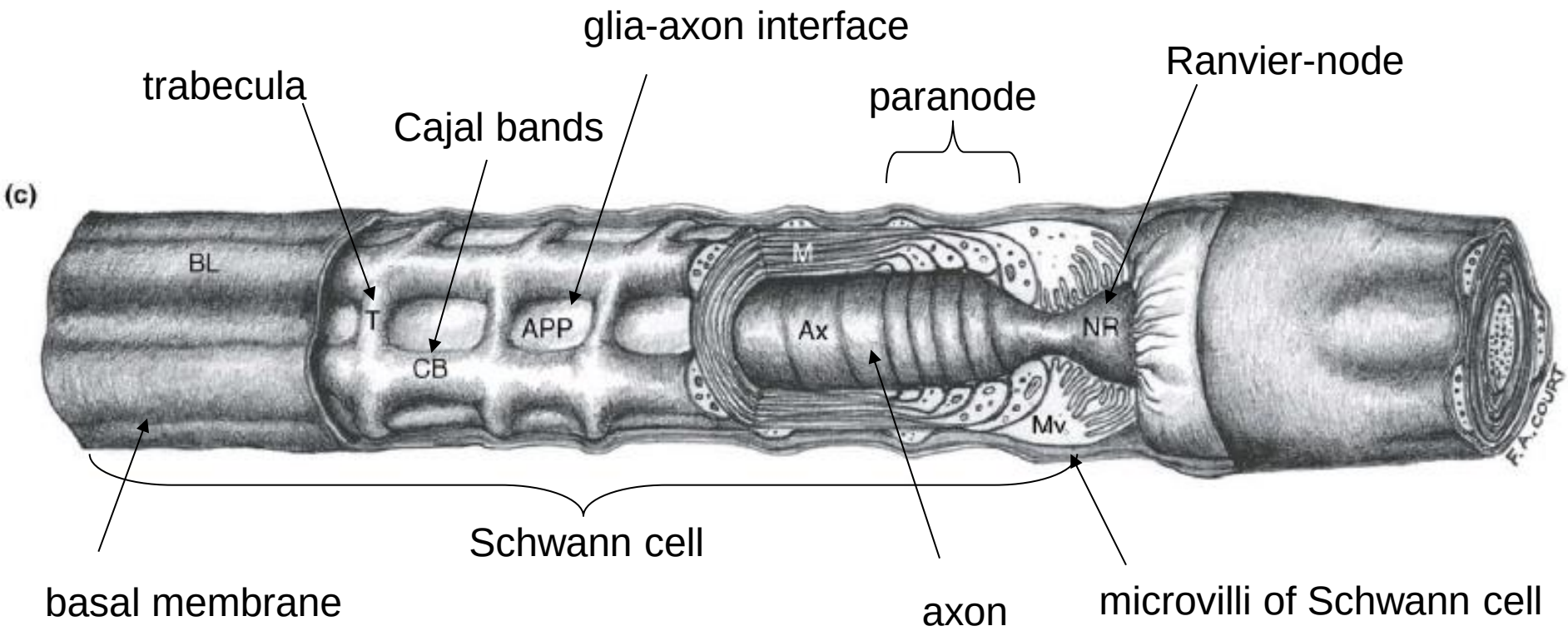
Diane L. Sherman and Peter J. Brophy

NATURE REVIEWS | NEUROSCIENCE

PNS



Myelin sheath within the PNS



Schematic drawing with cut away sections displays the architecture of the myelinated fiber. Abbreviations: App: apposition; Ax: axon; BL: basal lamina; CB: Cajal Band; M: myelin; Mv: microvilli; NR: node of Ranvier; T: trabecula.

Basal lamina: Schwann cells wrap to the rhythm of space-time
Felipe A Court, Lawrence Wrabetz and M Laura Feltri
Current Opinion in Neurobiology 2006, 16:501–507

Myelin sheath within the PNS

Molecular mechanisms regulating myelination in the peripheral nervous system

Jorge A. Pereira, Frédéric Lebrun-Julien and Ueli Suter

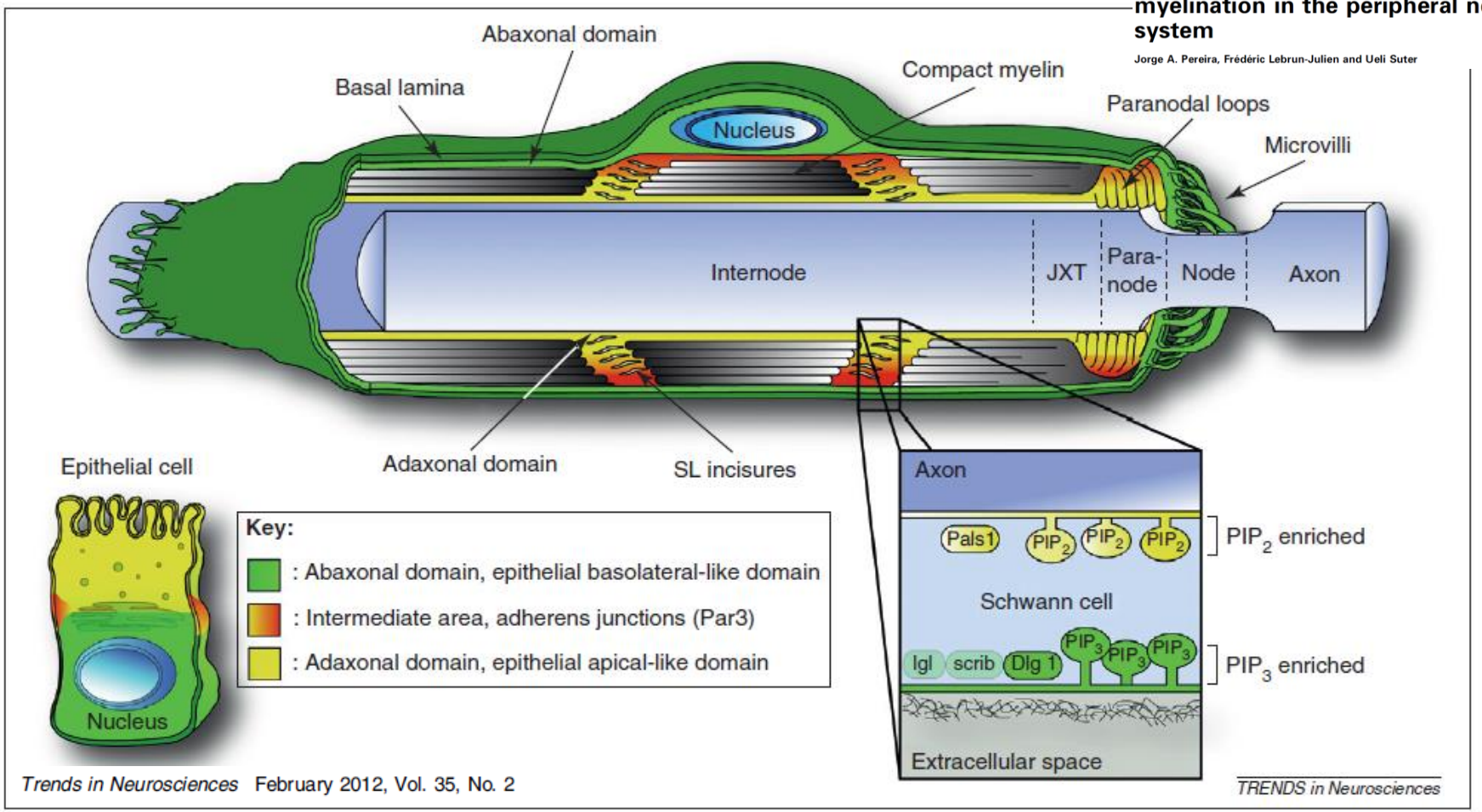
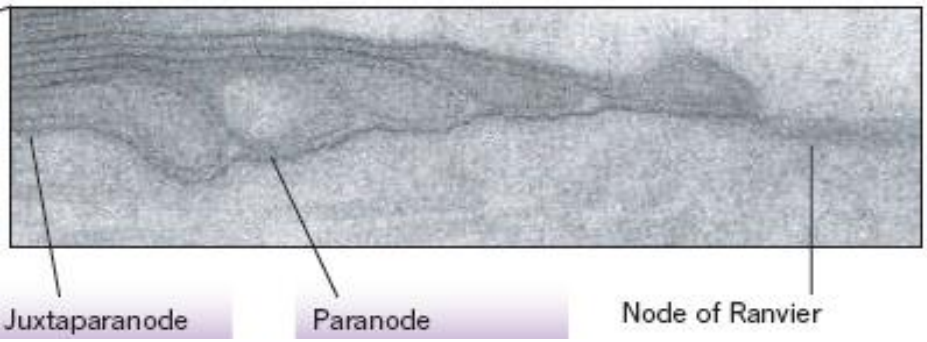


Figure 2. Polarized structure of the adult myelinating SC. Myelinating SCs cover a segment of the axon, designated the internode, and organize their subcellular domains in a polarized fashion, both in the longitudinal and radial axes. Longitudinally, SCs display the nucleus at the center. At the edge of the internode, cytoplasm-filled SC paranodal loops tether the internode to the axon and define the juxtaparanodal region (JXT). SC microvilli project into the nodal area. Radial polarity of SCs is also striking, with the nucleus being localized in the outermost wrap of the myelin sheath (abaxonal domain), followed by compact myelin and the innermost wrap facing the axon (adaxonal domain). Cytoplasm-filled spiral-shaped channels, Schmidt–Lantermann (SL) incisures, connect the adaxonal and abaxonal cytoplasm. The abaxonal domain is in tight contact with the basal lamina, a thin layer of highly organized ECM components synthesized by SCs, whereas the adaxonal domain is in close contact with the axolemma. This radial polarity organization shows similarities to epithelial cell polarization with an apical and a basolateral domain. Adult myelinating SCs show distributions of intrinsic polarity-regulatory proteins similar to those of epithelial cells, with Dlg1 being enriched in the abaxonal domain (basolateral-like), Pals1 concentrated in the adaxonal domain, SL incisures and paranodal loops (apical-like), and Par3 being localized to adherens junctions in outer regions of paranodal loops and SL incisures (between both domains). The asymmetric distribution of polarity proteins is coupled to a polar distribution of phosphoinositides. In mature myelinating SCs, PIP2 is enriched in the adaxonal domain and PIP3 is concentrated at the abaxonal domain. These enriched distributions of polarity proteins and PIPs relate to adult myelinating SCs. Note that when SC polarity is established and further enhanced during the myelination process, localization of these proteins and lipids is dynamic with different effects on signaling, as exemplified by Par3 recruitment to the SC–axon interphase at myelination initiation (Figure 3).

Myelin sheath at the Ranvier node

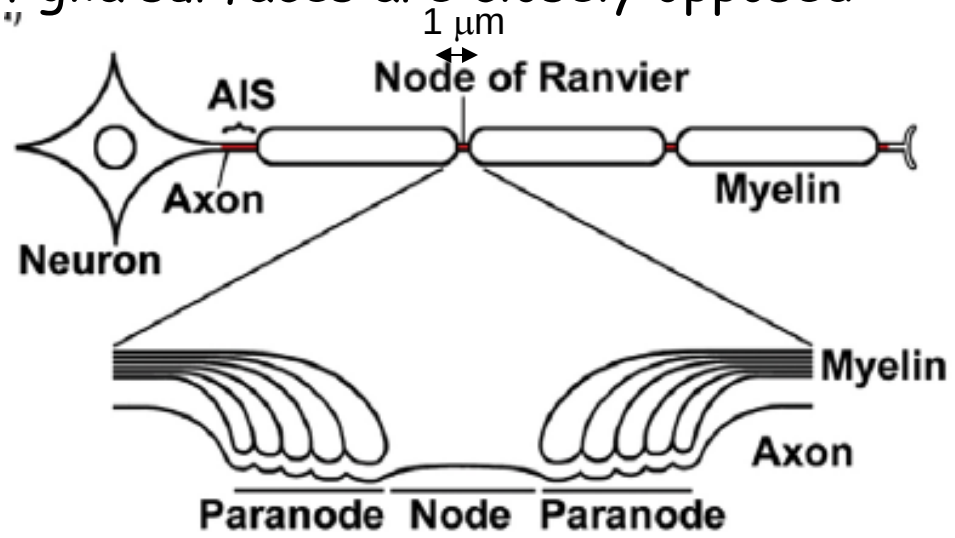
- electric „insulation": membrane resistance ⇧, capacitance ⇩ -> faster conductance (> 100x)
- energy need ⇩ -> less than 0.1% of the plasma membrane contains Na/K ATPases
- regions:
  - node ~ AIS
  - paranode: edge of the myelin sheath; largest adhesive complex
  - juxtaparanode: specific barrier (5-15 μm; K_V + Caspr2, TAG-1)
  - internode: myelin sheath, axon-glia surfaces are closely opposed



Myelination and support of axonal integrity by glia

Klaus-Armin Nave[1]

244 | NATURE | VOL 468 | 11 NOVEMBER 2010



Molecular mechanisms of node of Ranvier formation

Keiichiro Susuki and Matthew N Rasband

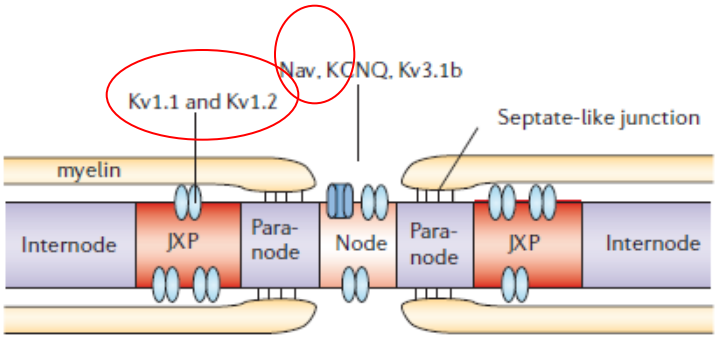
Current Opinion in Cell Biology 2008, 20:616–623

Myelin sheath at the Ranvier node

- regulated spatial distribution of axonal voltage-gated ion channels
  - Na_V: depolarisation - conducting AP within the node
  - K_V1: hyperpolarisation -> inhibiting the spread of AP over the juxtaparanode

The distribution and targeting of neuronal voltage-gated ion channels

Helen C. Lai* and Lily Y. Jan†



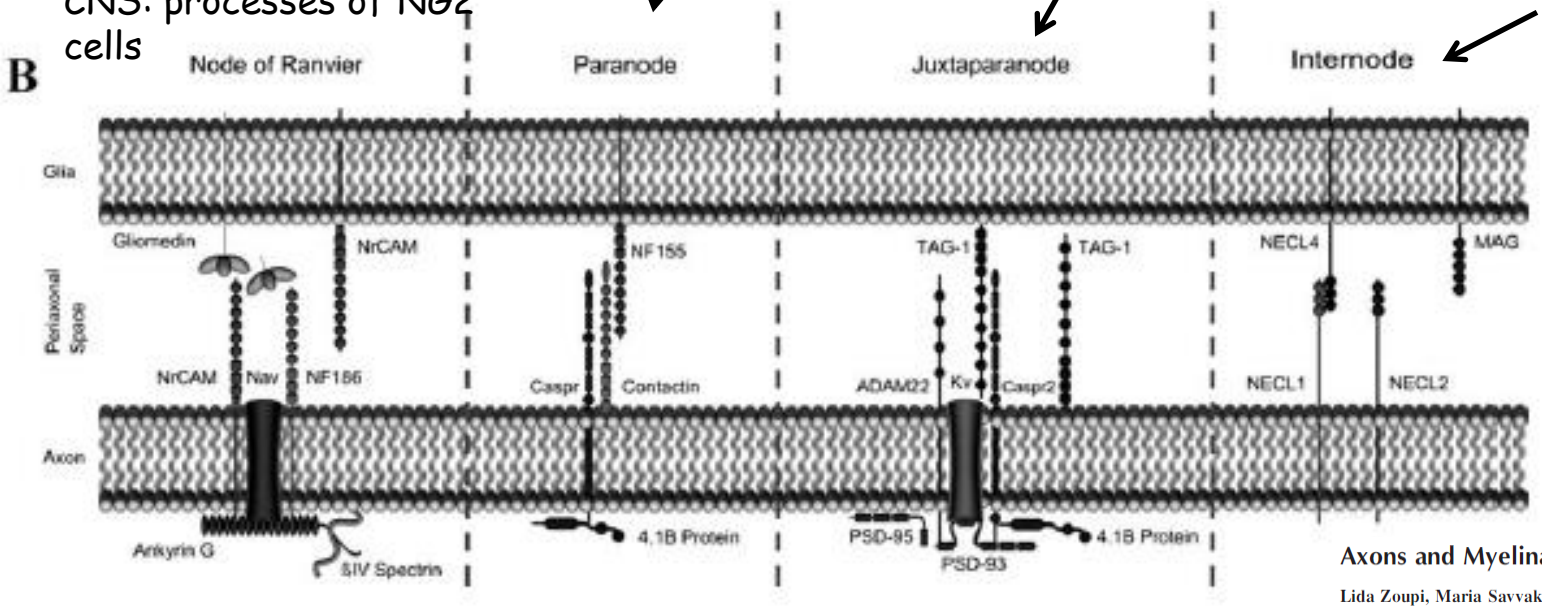
- adhesion complexes

separation of K_V and Na_V channels

position of K_V channels

adherence of the myelin sheath, myelin growth

PNS: microvilli
CNS: processes of NG2 cells

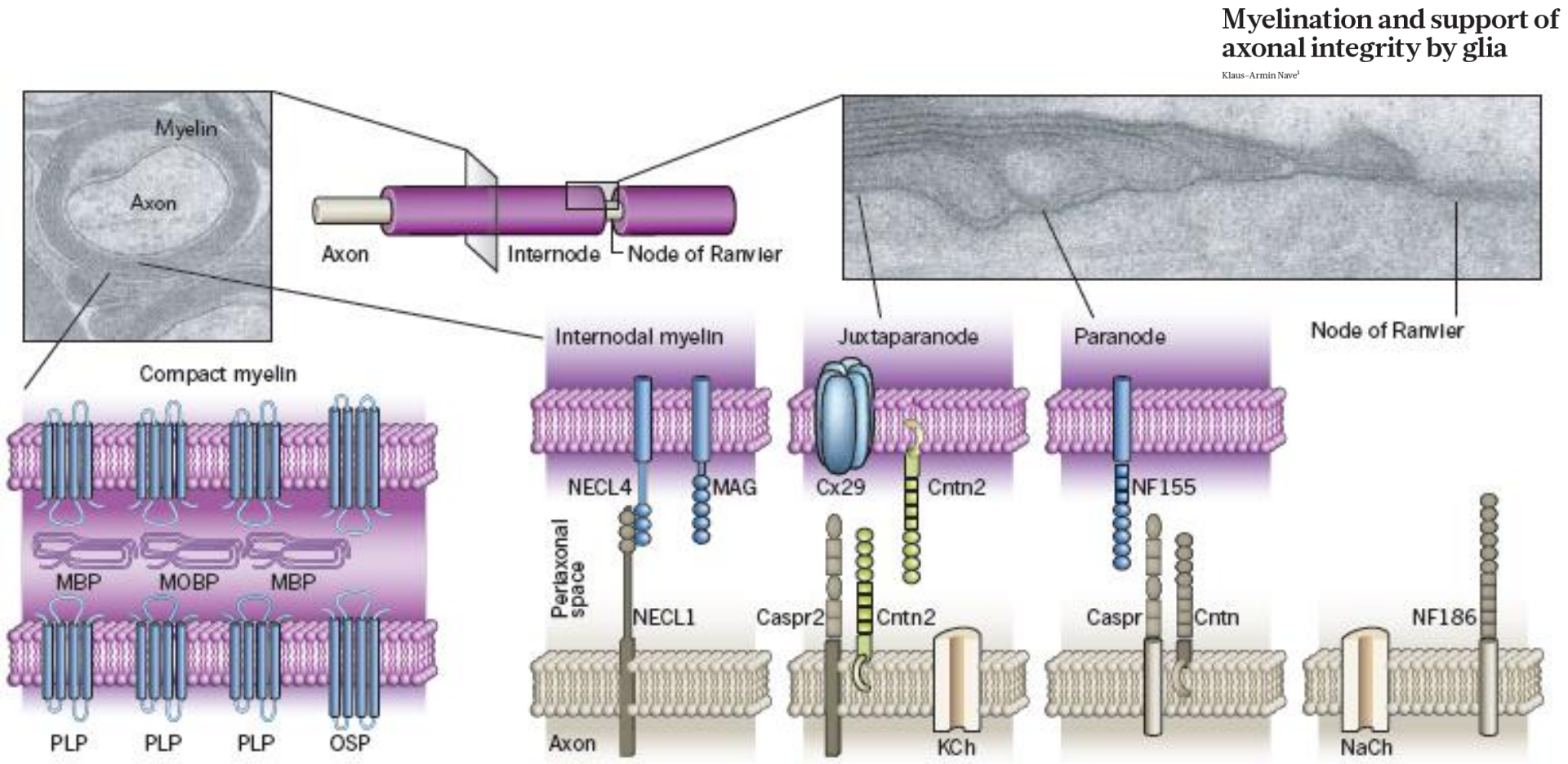


Axons and Myelinating Glia: An Intimate Contact

Lida Zoupi, Maria Savvaki and Domna Karagogeos

Structure of the myelin sheath

- lipid rafts: high cholesterol and galactolipid content



Caspr: contactin-associated protein; **Cntn**: contactin (Cntn2 is also known as Tag1); **Cx29**: connexin 29 kDa; **KCh**: fast potassium channels; **MAG**: myelin-associated glycoprotein; **MBP**: myelin basic protein; **MOBP**: myelin oligodendrocyte basic protein; **NaCh**: voltage-gated sodium channels; **NECL**: nectin-like protein/synCAM; **NF155/186**: neurofascin 155 kDa/186 kDa; **OSP**: oligodendrocytespecific protein; **PLP**: proteolipid protein

Formation of the myelin sheath

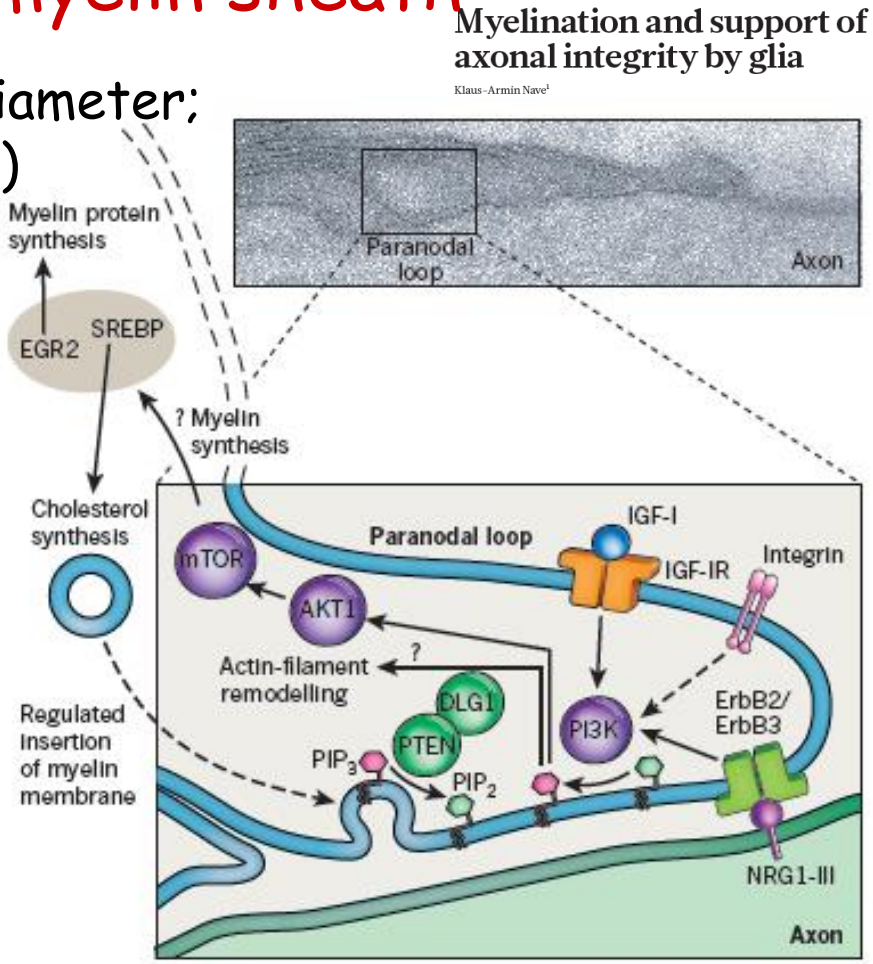
- g ratio: axon diameter/ (axon+myelin) diameter; ~0,6 – 0,7 (smaller after re-myelination)

➢ PNS – upon axonal activity:

- neuregulin-1 / ErbB -> myelin synthesis ⇧, actin polymerisation, transformation within the Schwann cells
- no myelination without axonal signals: inductive effects

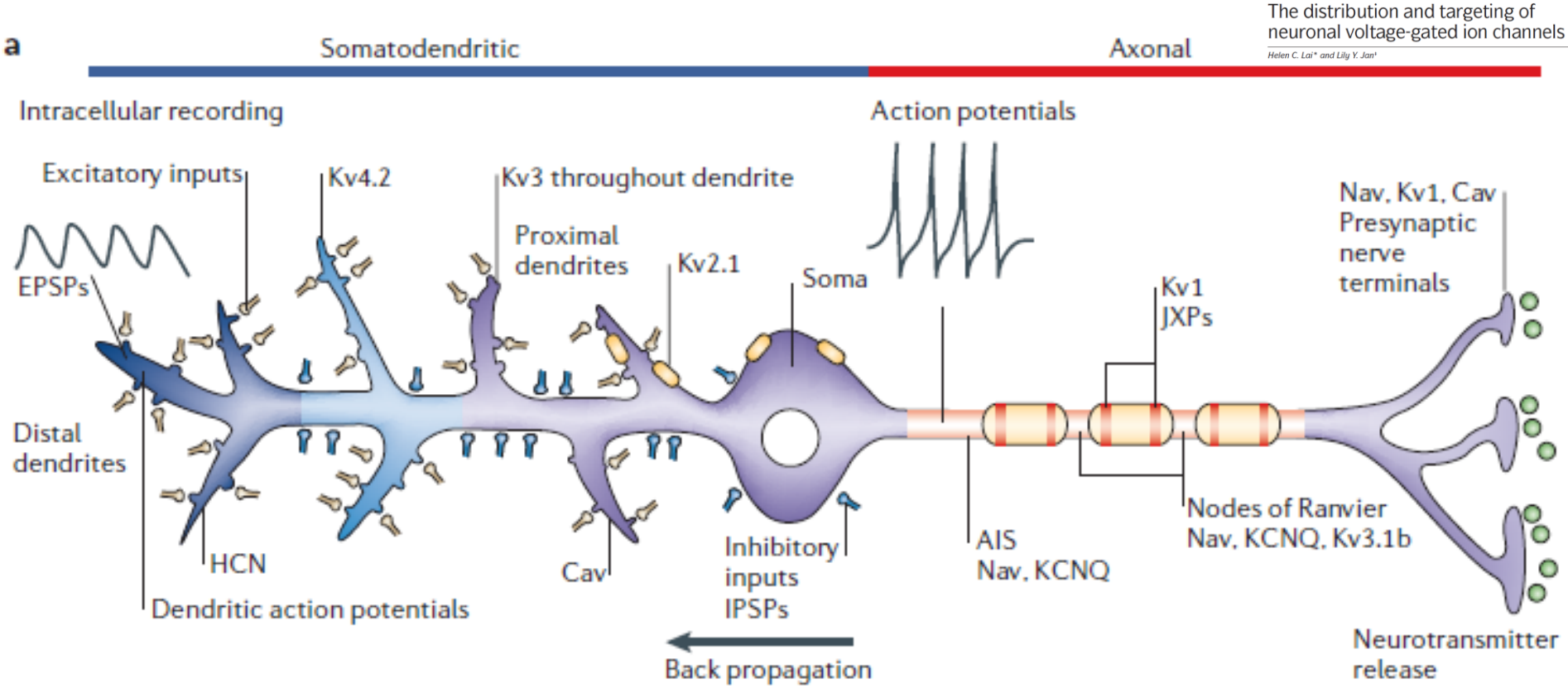
➢ CNS:

- takes place without NRG/ErB or electrical activity, also around fixated axons -> axonal signals are not inductive
- axonal membrane: permissive effects
- many signals: BDNF, CNTF, PDGF, LIF…



NRG1-III: neuregulin-1 type III; **ErbB**: epidermal growth factor receptor; **PI3K**: phosphatidylinositol-3-kinase; **DLG1**: mammalian discs large homolog 1; **PTEN**: phosphatase and tensin homologue; **BACE**: β-site amyloid precursor protein-cleaving enzyme 1; **EGR2**: early growth response protein 2 (also known as Krox20); **ErbB2/ ErbB3**: heterodimeric NRG1 receptor tyrosine kinases; **IGF-1R**: IGF-1 receptor; PIP2: phosphatidylinositol-4,5-bisphosphate; **SREBP**: sterol regulatory element binding protein.

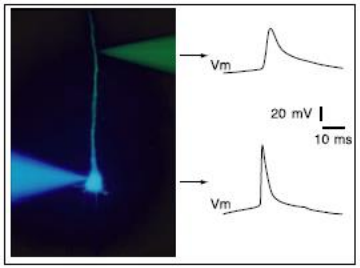
Mosaic diversity of the neuronal membrane surface



General localization of voltage-gated ion channels in a model neuron. In general, **Nav channels** are found in the axon initial segment (AIS), nodes of Ranvier and presynaptic terminals. Voltage-gated potassium **Kv1 channels** are found at the juxtaparanodes (JXPs) in adult myelinated axons and presynaptic terminals. The Kv channel **KCNQ** is found at the AIS and nodes of Ranvier, and **Kv3.1b channels** are also found at the nodes of Ranvier. Canonically, excitatory and inhibitory inputs (EPSPs and IPSPs — excitatory and inhibitory postsynaptic potentials; yellow and blue presynaptic nerve terminals, respectively) from the somatodendritic region spread passively to the AIS where action potentials are generated by depolarization, and travel by saltatory conduction to the presynaptic nerve terminals to activate voltage-gated calcium (**Cav**) **channels** that increase intracellular calcium levels, thereby triggering neurotransmitter release. Hyperpolarization-activated cyclic-nucleotide-gated (**HCN**) **channels** have a gradient distribution that increases in density from the soma to the distal dendrites (dark blue shading). **Kv2.1 channels** are found in clusters on the soma and proximal dendrites (light yellow ovals). **Kv3 channels** are found throughout the dendrite. **Kv4.2 channels** are located more prominently on distal dendrites (light blue shading). Kv channels in the dendrites contribute to controlling back propagation. Strong enough inputs in the dendritic region can generate dendritic action potentials. **Dendritic Cav channels** increase in density toward the proximal dendrites and the soma.

Backpropagating action potential (BAC)

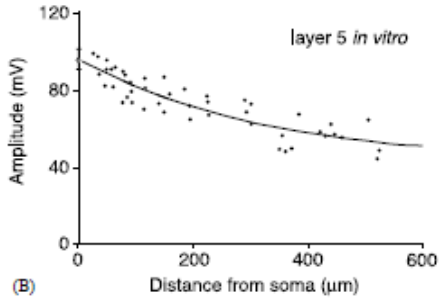
- AP formed within the AIS can backpropagate into the dendrites, depending on
  - the distance from the soma
  - cell type
  - morphology of the dendritic tree
  - type and distribution of ion channels
    - HCN [hyperpolarisation activated cation channels]: increased density towards the distal dendrites
    - voltage gated Na^+, Ca^{2+} and K^+ channels

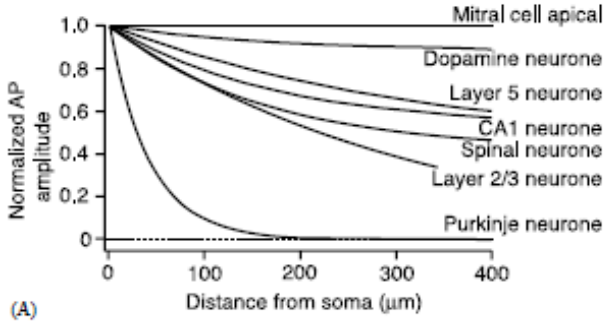


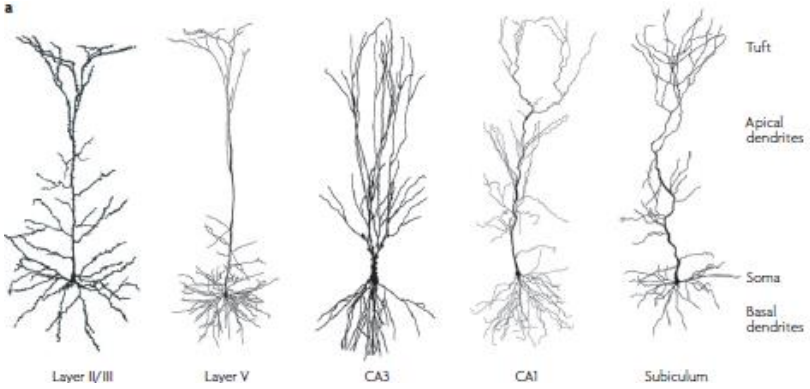
Backpropagating action potentials in neurones: measurement, mechanisms and potential functions

Jack Waters*,1, Andreas Schaefer1, Bert Sakmann

Progress in Biophysics and Molecular Biology 87 (2005) 145–170

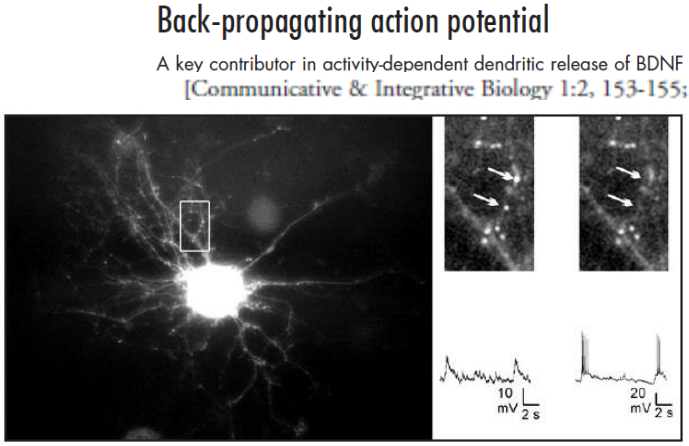


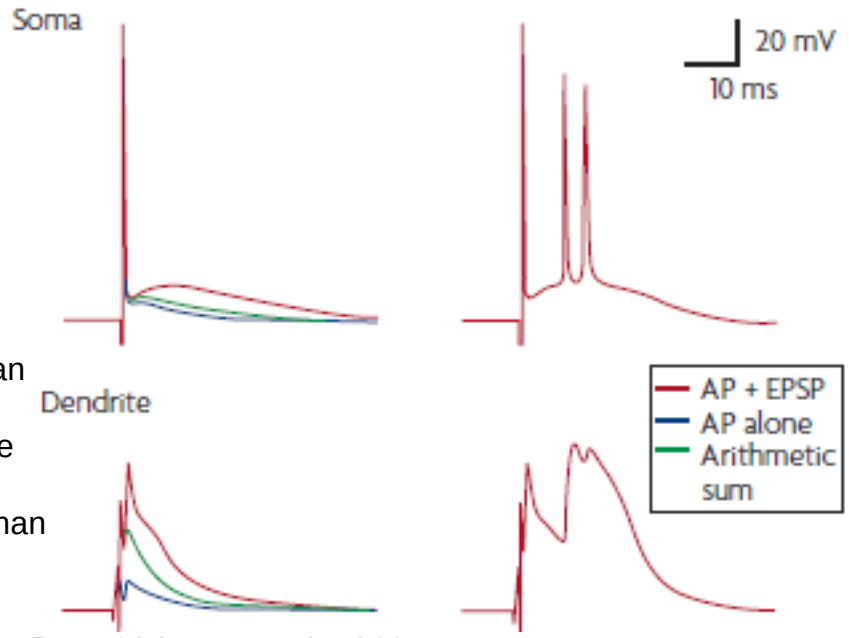




Backpropagating action potential (BAC)

- important role in:
  - retrograde information about neuronal output (eg, firing) – detection of coincidence, LTP formation, etc
  - increasing dendritic $[Ca^{2+}]_{IC}$: eg., regulating BDNF release
  - influencing synaptic integration





Amplification of backpropagating action potentials by dendritic EPSPs can lead to bursting. The two lefthand plots show somatic (top) and dendritic (bottom) responses to an antidromic action potential (AP) activated alone (blue trace) or in combination with a dendritic EPSP-like response to dendritic current injection. The combined response (red trace) is larger than the linear sum of the action potential and the EPSP separately (green trace). The two right-hand plots are from another trial in which the EPSP triggered a second action potential that backpropagated even more effectively, leading to a large dendritic spike that triggered another action potential and hence a burst.

Pyramidal neurons: dendritic structure and synaptic integration

Nelson Spruston

VOLUME 9 | MARCH 2008 |
NATURE REVIEWS | NEUROSCIENCE

Essay questions (choose one)

Describe the role and physiological functions of the axonal initial segment (AIS)! List its main molecular components and explain their importance! / Milyen sejtélettani szerep jellemző az axon iniciális szegmentumára (AIS)? Ismertesse azokat a komponenseket, amelyek részt vesznek a kialakításában és röviden jellemezze ezek szerepét/funkcióját is!

Describe the formation of the axonal initial segment (AIS)! Explain the similarities and also, the differences between the AIS and the Ranvier node! / Hogyan alakul ki az axon iniciális szegmentuma (AIS)? Mennyire és miben hasonló ez a struktúra a Ranvier-féle befűződésekhez?

What kind of cells are responsible for myelin formation within the central and the peripheral nervous system? Explain the main differences and similarities between myelination within the CNS or PNS! / Milyen sejt(ek) és hogyan végzi(k) el a mielinizációt a központi és a perifériás idegrendszerben? Miben hasonló és miben különbözik a mielin hüvely kialakulása a periférián és a központi idegrendszerben?

Describe the organization of the myelin sheath and the Ranvier node! / Hogyan épül fel a mielinhüvely és a Ranvier-féle befűződés?

Neuronal plasma membrane is a mosaic surface. List evidences for this statement, describing different membrane compartments. / Az idegsejtek membránja mozaikos felépítésű. Milyen példákkal tudja ezt az állítást alátámasztani? Milyen főbb területeket tudna elkülöníteni?

Recommended literature

No Pasaran! Role of the axon initial segment in the regulation of protein transport and the maintenance of axonal identity

Christophe Leterrier*, Bénédicte Dargent

Seminars in Cell & Developmental Biology 27 (2014) 44–51

Molecular mechanisms regulating myelination in the peripheral nervous system

Jorge A. Pereira, Frédéric Lebrun-Julien and Ueli Suter

Trends in Neurosciences, February 2012, Vol. 35, No. 2

Plasticity of the Axon Initial Segment: Fast and Slow Processes with Multiple Functional Roles

The Neuroscientist
1–10
© The Author(s) 2016

Anders Victor Petersen[1], Florence Cotel[2], and Jean-François Perrier[1]

Molecular mechanisms of node of Ranvier formation

Keiichiro Susuki and Matthew N Rasband

Current Opinion in Cell Biology 2008, 20:616–623

Excitatory Effect of GABAergic Axo-Axonic Cells in Cortical Microcircuits

János Szabadics,[1*] Csaba Varga,[1*] Gábor Molnár,[1*] Szabolcs Oláh,[1] Pál Barzó,[2] Gábor Tamás[1†]

SCIENCE VOL 311 13 JANUARY 2006

The distribution and targeting of neuronal voltage-gated ion channels

Helen C. Lai and Lily Y. Jan‡*

NATURE REVIEWS | NEUROSCIENCE

548 | JULY 2006 | VOLUME 7

The axon initial segment and the maintenance of neuronal polarity

Matthew N. Rasband

NATURE REVIEWS | NEUROSCIENCE

552 | AUGUST 2010 | VOLUME 11

Backpropagating action potentials in neurones: measurement, mechanisms and potential functions

Jack Waters*[,1], Andreas Schaefer[1], Bert Sakmann

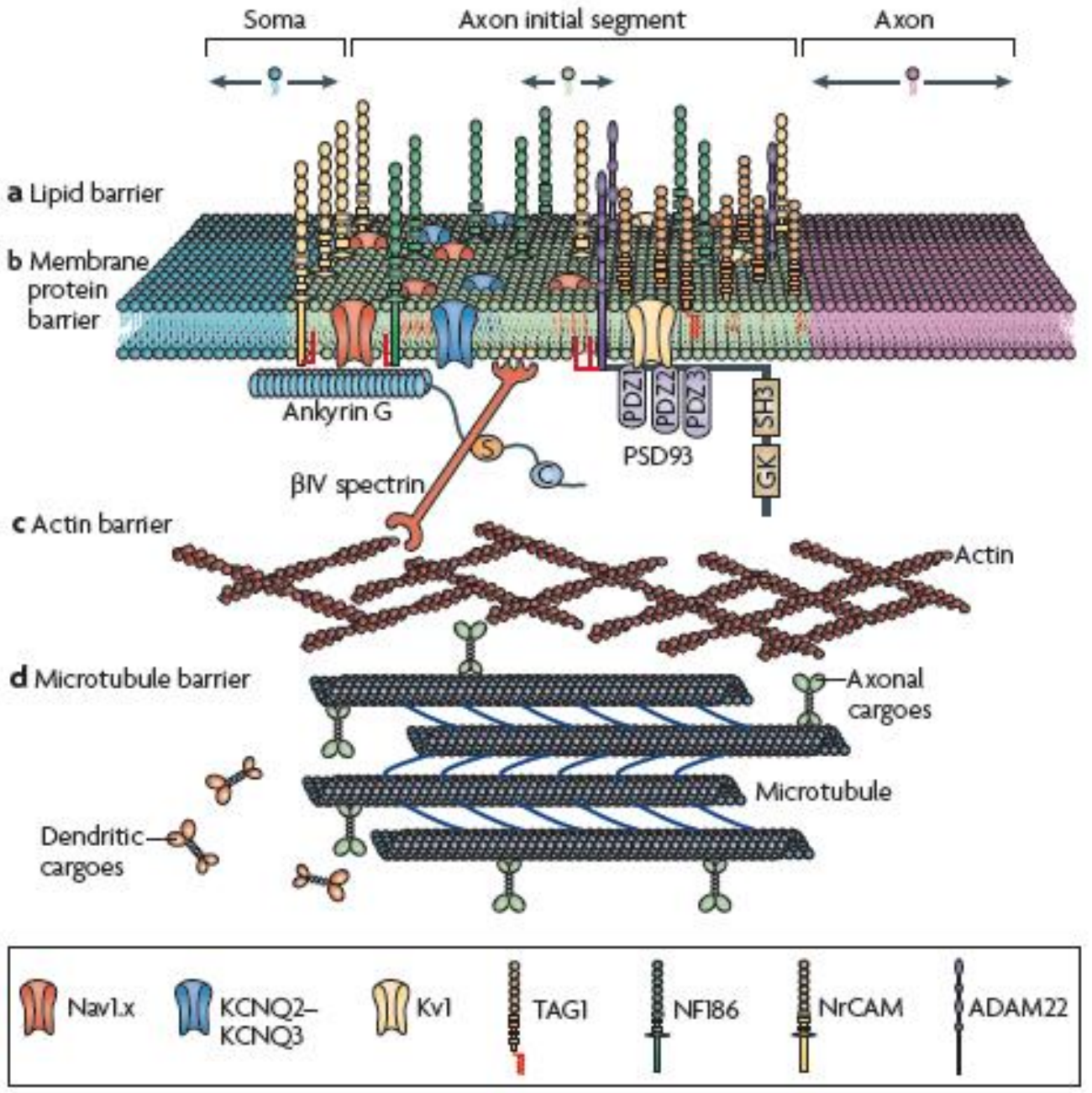
Progress in Biophysics and Molecular Biology 87 (2005) 145–170

Enlarged figures

The AIS

The axon initial segment and the maintenance of neuronal polarity

Matthew N. Rasband



Molecular substrates of the axon initial segment barrier. Four potential mechanisms have been proposed to contribute to the axon initial segment (AIS) barrier. **a** | The lipid composition of the AIS plasma membrane may directly influence mobility and diffusion rates in the AIS. The lipid composition can be directly regulated by post-translational modifications of membrane and cytoplasmic proteins or by phospholipid–cytoskeleton interactions. **b** | The high density of membrane proteins creates a membrane diffusion barrier that limits the lateral mobility of other transmembrane proteins and lipids at the AIS. The high density of these proteins is established through binding to ankyrin G. **c** | Actin filaments can contribute to the maintenance of neuronal polarity and the AIS barrier by limiting the entry of cytoplasmic proteins into the axon and by contributing to the maintenance of protein density at the AIS membrane through interactions with βIV spectrin. **d** | Microtubule fascicles with unique cross-bridges at the AIS allow axonal cargoes but not dendritic cargoes to enter the axon, thus contributing to the maintenance of neuronal polarity. ADAM22, a disintegrin and metalloproteinase domain-containing protein 22; GK, guanylate kinase; NF186, neurofascin 186; NrCAM, neuronal cell adhesion molecule; PDZ, PSD95/discs large/zonula occludens; PSD93, postsynaptic density protein 93; SH3, SRC homology 3; TAG1, transient axonal glycoprotein 1 (also known as contactin 2).

Structure of the AIS and Ranvier-node

The axon initial segment and the maintenance of neuronal polarity

Matthew N. Rasband

The axon initial segment and nodes of ranvier are prototypical examples of subcellular polarity. a | A cultured hippocampal neuron with high densities of ankyrin G (AnkG, also known as ANK3) (green) and neurofascin 186 (NF186) (the overlap between AnkG and NF186 is shown in yellow) at the axon initial segment (AIS). Microtubule-associated protein 2 (MAP2) (blue) is confined to the somatodendritic domain. The scale bar represents 20 μm. b | Nodes of Ranvier show a highly polarized organization that includes nodal Na+ channels (green), paranodal contactin-associated protein (Caspr) (red) and juxtaparanodal K+ channels (blue). The scale bar represents 5 μm. c | The molecular organization of the AIS, which has many features in common with nodes of Ranvier and juxtaparanodes. These domains are comprised of ion channels (Nav1.x, KCNQ2–KCNQ3 and Kv1.x), cell adhesion molecules (neuronal cell adhesion molecule (NrCAM), neurofascin 186 (NF186), a disintegrin and metalloproteinase domain-containing protein 22 (ADAM22), transient axonal glycoprotein 1 (TAG1, also known as contactin 2) and CASPR2), extracellular matrix molecules (brevican and versican), cytoskeletal scaffolds (AnkG, βIV spectrin and postsynaptic density protein 93 (PSD93)) and other signalling proteins, some with unknown roles (casein kinase II (CK2), phosphorylated nuclear factor-κB (pNFκB) and phosphorylated inhibitor of κBα (pIκBα)). Intriguingly, both nodal and juxtaparanodal proteins are located at the AIS, but they occupy mutually exclusive domains in myelinated axons. GK, guanylate kinase; PDZ, PSD95/discs large/zonula occludens; SH3, SRC homology 3.