A neuronális plaszticitás

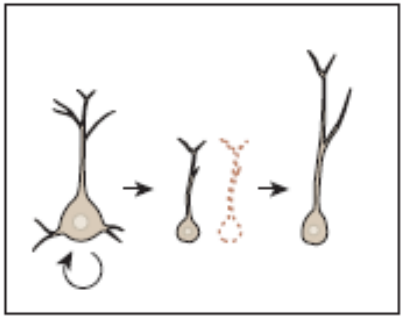
Mi az a neuronális plaszticitás [neuronal plasticity]?

- plaszticitás: a (külső) változásokhoz való adaptív alkalmazkodás
- összemosott fogalmak:
  - külső – belső hatás?
  - milyen szintű változás?
    - komplex élettani, viselkedési változások
    - lokális / távoli hálózatok
    - 2 sejt közötti
    - sejt-autonóm
    - molekuláris
  - milyen típusú változás?
    - struktúrális (morfológiai)
    - funkcionális
    - mennyiségi
  - hogyan és mit mérünk?

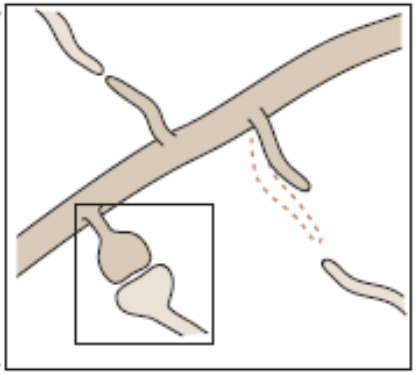
A celluláris plaszticitás

proliferáció / túlélés

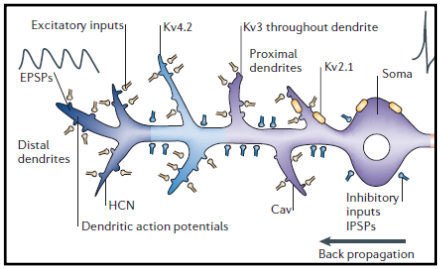
Neurogenesis / apoptosis



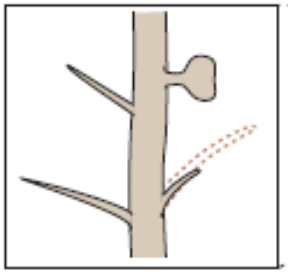
New synapses / pruning



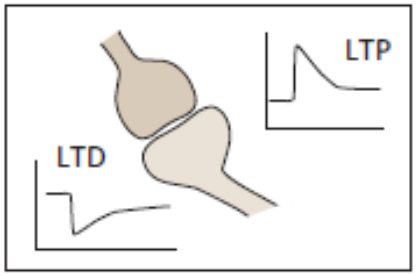
intrinsic plasticity



Arborization / pruning

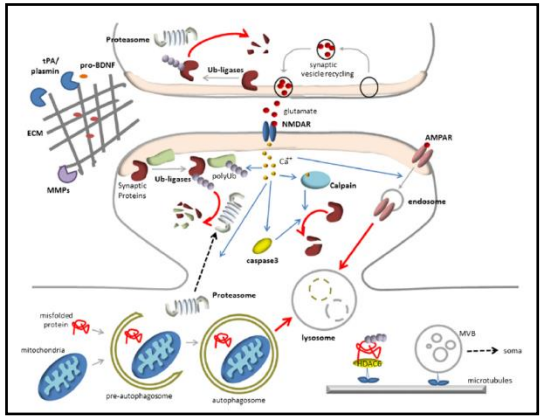


Synaptic strength

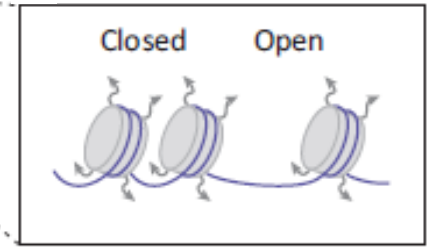


asszociatív (Hebb-féle) szinaptikus plaszticitás

proteome plasticity



Genomic plasticity

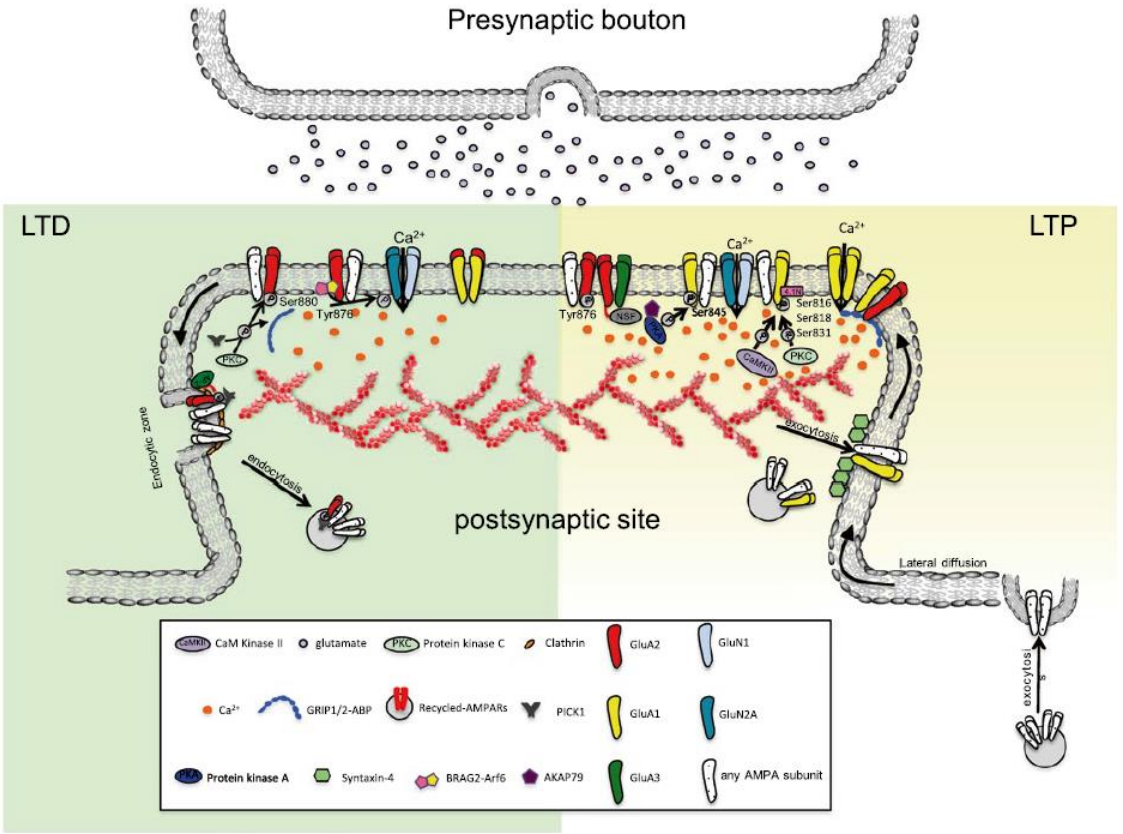


Deconstruction for Reconstruction: The Role of Proteolysis in Neural Plasticity and Disease

Neuronal plasticity and antidepressant actions

A szinaptikus plaszticitás

- szinaptikus plaszticitás: szinaptikus kapcsolat (erősség) kétirányú változása
- asszociatív (Hebb-féle) plaszticitás: a szinaptikus kapcsolat relatív erősségének aktivitás-függő változása; lokális hatás (homo- vagy heteroszinaptikus)
  - rövid távú (facilitáció, depresszió)
  - hosszú távú (LTP, LTD)



AMPAR trafficking in synapse maturation and plasticity

Silvia Bassani · Alessandra Folci · Jonathan Zapata · Maria Passafaro

Cell. Mol. Life Sci. (2013) 70:4411–4430
DOI 10.1007/s00018-013-1309-1

A szinaptikus plaszticitás

Fig. 3 Schematic illustration of known molecular players and mechanisms involved in long-term depression (*left*) and long-term potentiation (*right*). Long-term depression (LTD) is characterized by endocytosis of GluA2-containing AMPARs from synapses and consequent weakening of synaptic strength. LTD is induced by sustained low-level postsynaptic calcium influx as a result of low-frequency glutamate stimulation. The slow rise in intracellular calcium selectively activates phosphatases and kinases of intracellular signaling pathways that effect changes contributing to LTD. Thus, PKC is activated to phosphorylate Ser880 on GluA2, which in turn decreases GluA2 affinity for GRIP-anchoring proteins, and increases GluA2 affinity for PICK1. PICK1-binding enhances AMPAR endocytosis, which occurs in clathrin-positive zones adjacent to the post synaptic density (PSD). By contrast, Tyr876 dephosphorylation allows GluA2 binding to BRAG2 leading to the Arf6 activation crucial for AMPAR internalization. Long-term potentiation is characterized by a marked increase in AMPARs at the synapse with consequent increase in synaptic strength. LTP is induced by high presynaptic glutamate levels which activate postsynaptic NMDARs, leading to a strong calcium influx, followed by further calcium influx though CP-AMPARs. The strong calcium influx activates kinases (PKC, PKA, and CAMKII) involved in GluA1 phosphorylation. GluA1 phosphorylation induces AMPAR exocytosis in extrasynaptic regions. Another consequence of the initiation of LTP is that recycling endosomes deliver AMPARs to the membrane at domains enriched in Stx4, which mediates fusion of endosome with the membrane. Finally, AMPARs diffuse laterally to the synapse and are anchored there by scaffold proteins

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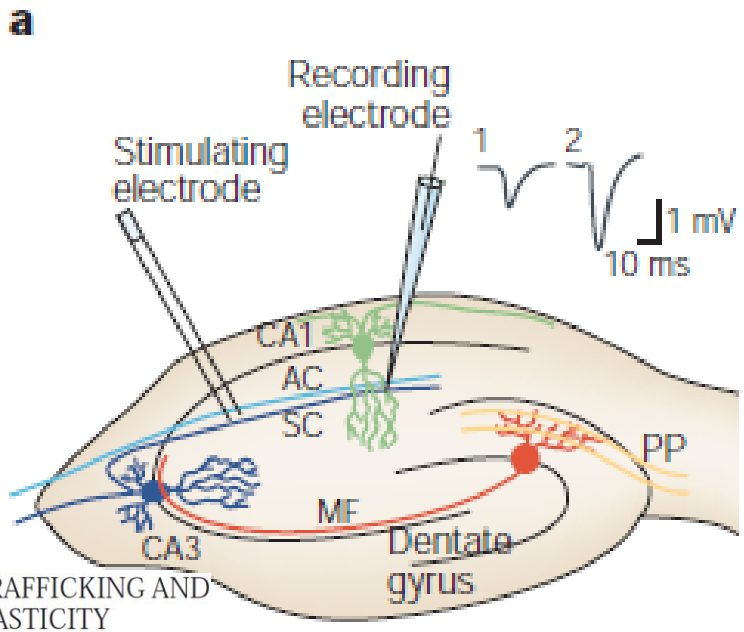
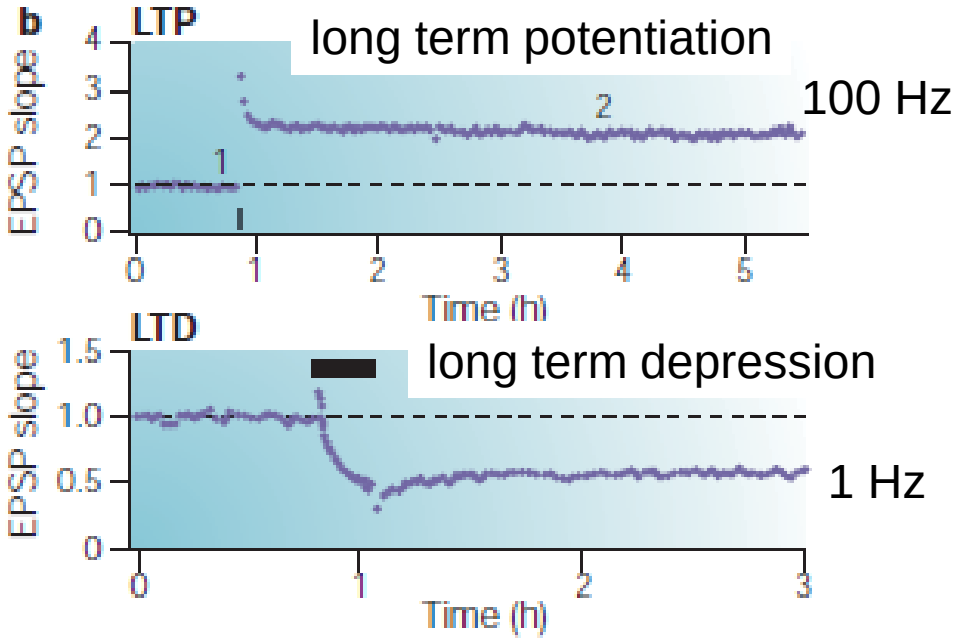
A (hosszú távú) szinaptikus plaszticitás



RECEPTOR TRAFFICKING AND SYNAPTIC PLASTICITY

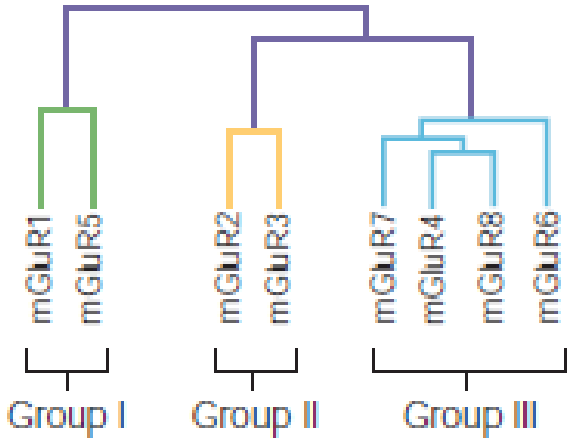
Graham L. Collingridge*†, John T. R. Isaac*§ and Yu Tian Wang‡



Ionotropic glutamate receptors (iGluRs)			
AMPARs	KainateRs	NMDARs	DeltaRs
GluA1	GluK1 GluK4	GluN1* GluN2A GluN3A*	GluD1
GluA2	GluK2 GluK5	GluN2B GluN3B*	GluD2*
GluA3	GluK3	GluN2C	
GluA4		GluN2D	

* These subunits bind glycine or D-serine.

Metabotropic glutamate receptors

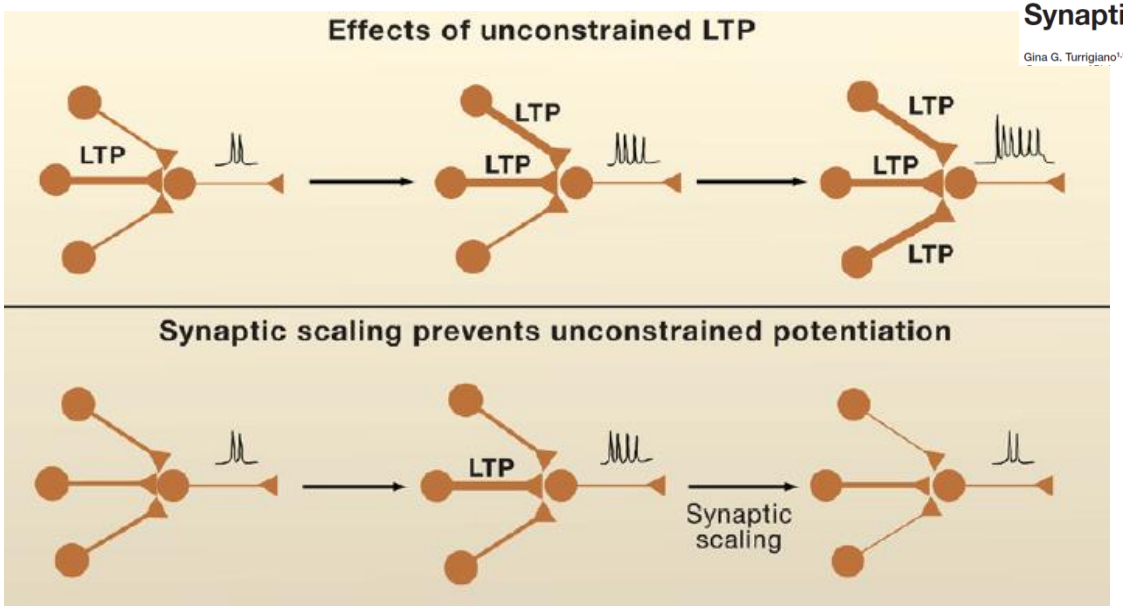


A szinaptikus plaszticitás

- hosszú távú hatásokat le is kell állítani! különben öngerjesztés indul be

The Self-Tuning Neuron:
Synaptic Scaling of Excitatory Synapses

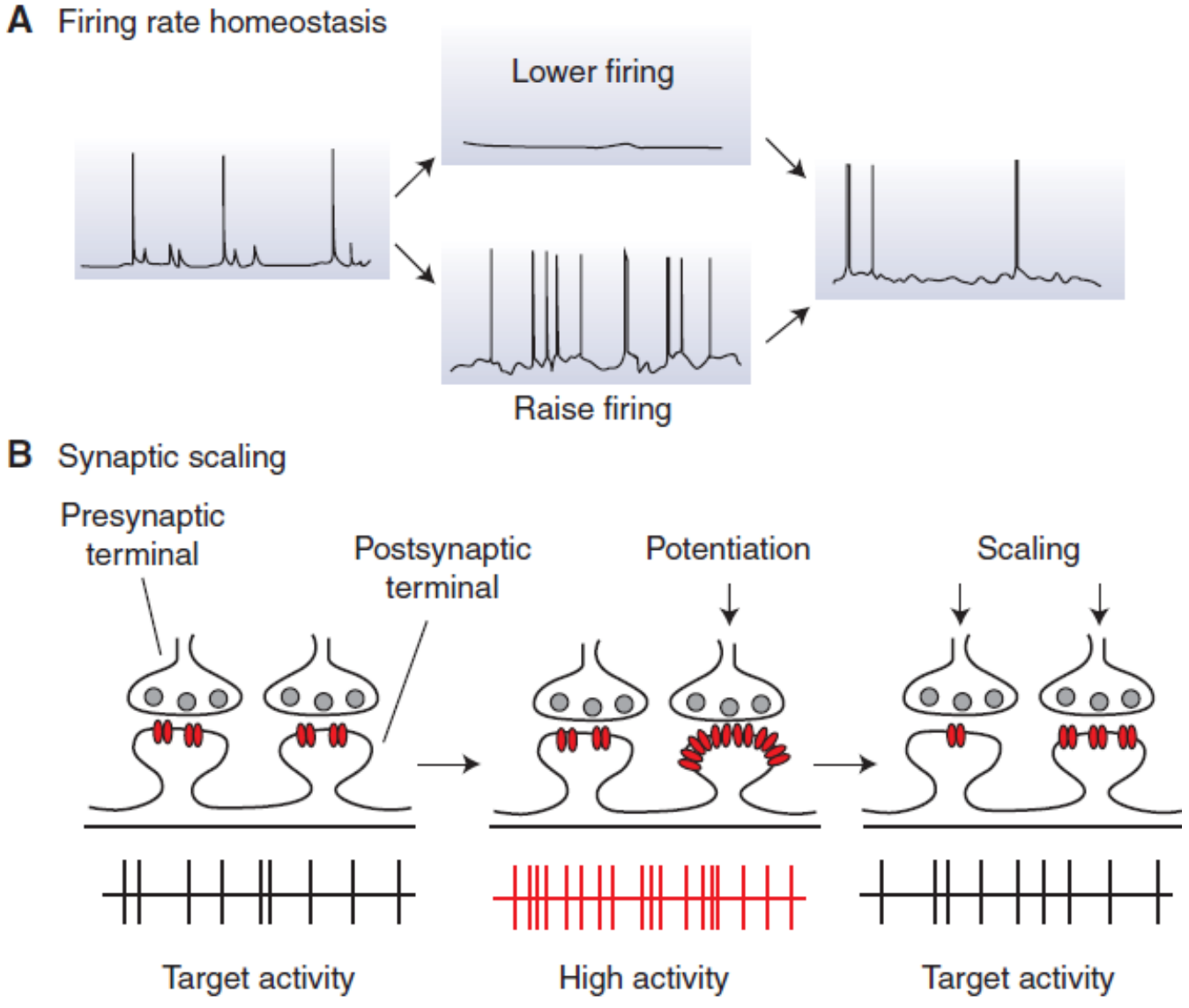
Gina G. Turrigiano[1,*]



- homeosztatikus plaszticitás: aktivitás-függő negatív feedback a hálózati aktivitás stabilizálására

  - globális (teljes sejtre kiterjedő) hatás
  - szinaptikus „scaling"

A homeosztatikus szinaptikus plaszticitás (HSP)



Homeostatic Synaptic Plasticity: Local and Global Mechanisms for Stabilizing Neuronal Function

Gina Turrigiano *Cold Spring Harb Perspect Biol* 2012;4:a005736

A homeosztatikus szinaptikus plaszticitás (HSP)

Figure 1. Homeostasis of neuronal firing through homeostatic synaptic plasticity. (*A*) Cartoon illustration of the phenomenon of firing rate homeostasis in dissociated neocortical networks; perturbing firing in either direction results in the homeostatic regulation of synaptic and intrinsic properties so that baseline firing rates are restored. (*B*) One mechanism contributing to the firing rate homeostasis illustrated in A is synaptic scaling. When activity is perturbed (illustrated here as the potentiation of some inputs through Hebbian mechanisms) this triggers synaptic scaling, which produces a proportional reduction in strength at all synapses of the right magnitude to return firing to baseline levels. Note that, because this mechanism scales synaptic strength up or down proportionally, the relative difference in synaptic strengths induced by Hebbian mechanisms is preserved.

Homeostatic Synaptic Plasticity: Local and Global Mechanisms for Stabilizing Neuronal Function

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A homeosztatikus szinaptikus plaszticitás (HSP)

- szinaptikus „scaling" : hálózati aktivitás tartós gátlása (48h TTX) vagy túlserkentése (48h bicuculline) kompenzációként felszíni AMPAR gyarapodást (scaling up), illetve csökkenést (scaling down) vált ki

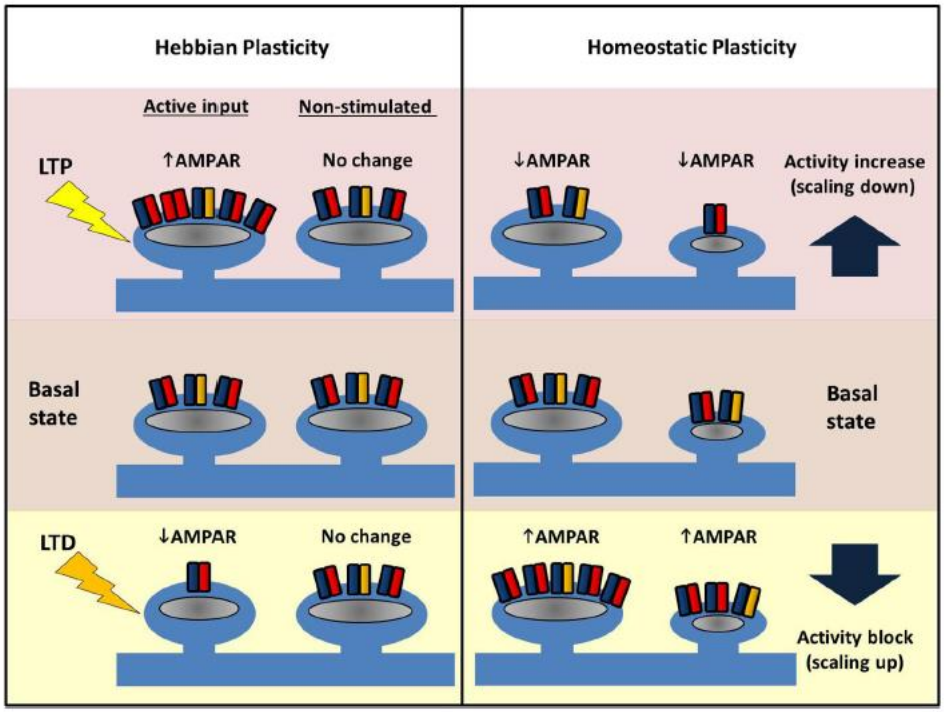

FIGURE 4 | Comparing Hebbian and homeostatic plasticity. During Hebbian forms of plasticity synapses change their number of AMPARs in an input-specific fashion. Different patterns of activity can either cause strengthening (LTP, top left) or weakening of synapses (LTD, bottom left) via AMPAR trafficking. Potentiation or depression is limited to stimulated synapses, and neighbors are unaffected. In contrast, during homeostatic plasticity altered levels of neuronal activity drives changes in synaptic AMPAR number across the entire dendritic arbor. Blocking pre- and postsynaptic spiking with TTX causes AMPARs to accumulate at excitatory synapses (bottom right). Conversely increasing network activity (for example with a $GABA_AR$ antagonist) causes a reduction in synaptic AMPAR (top right). Crucially this form of plasticity conserves the relative strength difference between synapses.

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The role of AMPA receptors in postsynaptic mechanisms of synaptic plasticity

*Thomas E. Chater * and Yukiko Goda*

A homeosztatikus szinaptikus plaszticitás (HSP)

- AP küszöb beállítás: AIS plaszticitás
  - AIS diszlokáció:túlzott serkentés hatására az AIS reverzibilisen disztálisan eltolódik, alacsony aktivitásnál pedig proximálisan helyezkedik el – lassú változás
  - AIS gyors változása: sejtfelszíni ioncsatorna-készlet / foszforilációs állapot megváltozása

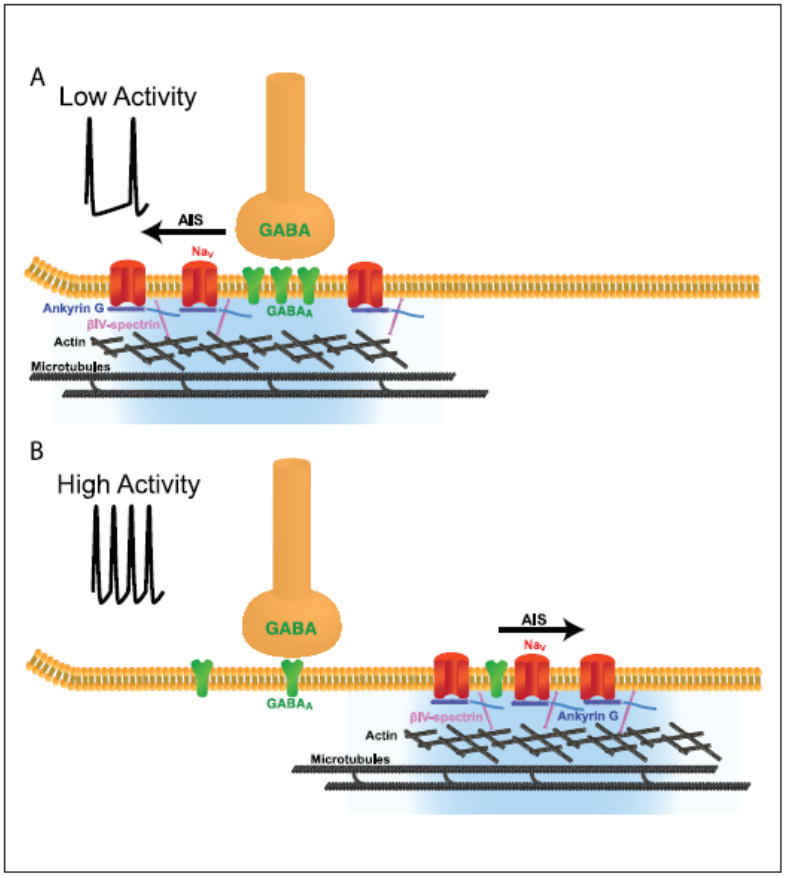
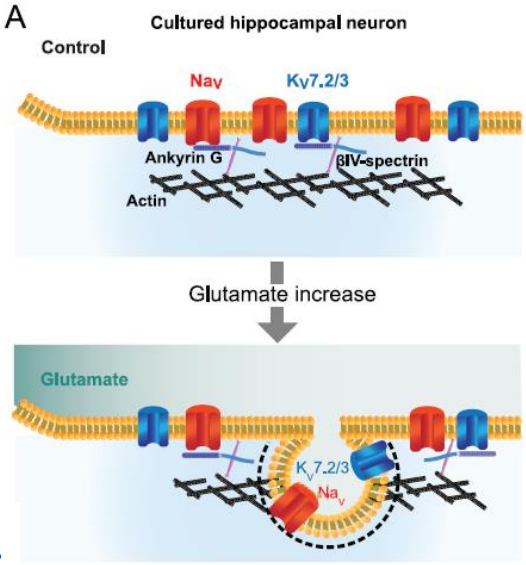


Figure 2. Structural plasticity of the axon initial segment (AIS) of excitatory neurons. (A) Low neuronal activity induces the shifting of the AIS toward the soma. (B) High activity triggers the shifting of the AIS toward the periphery. The position of GABAergic synapses is not altered. However, the time spent by $GABA_A$ receptors inside synapses is decreased.



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

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

The Neuroscientist
1–10
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