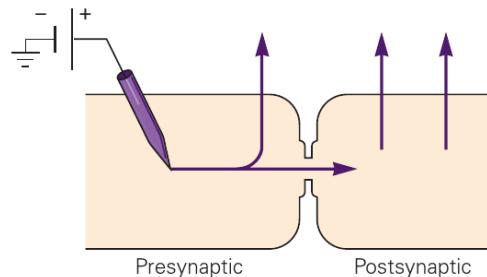


Synaptic transmission

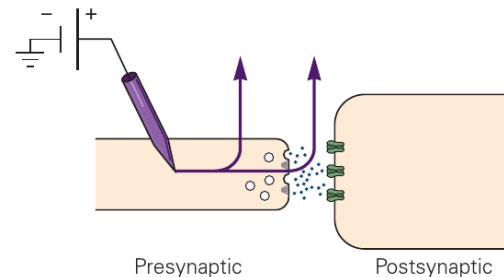
A. Brazhe

Synaptic transmission

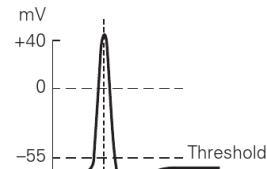
A Current pathways at electrical synapses



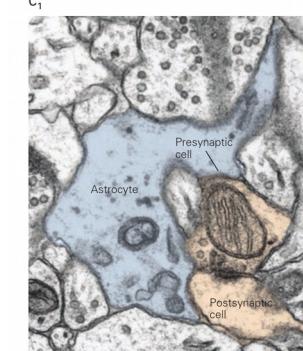
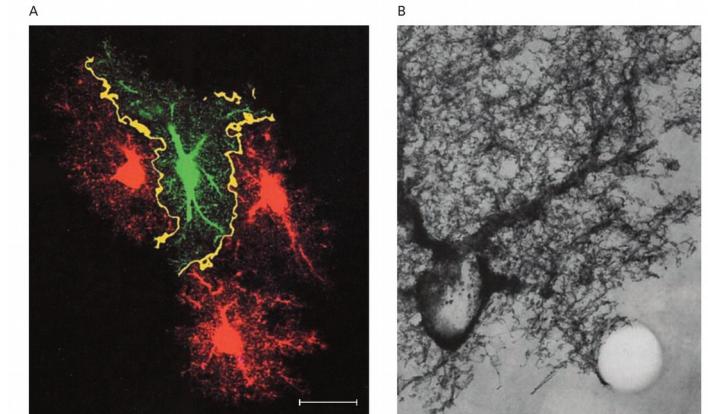
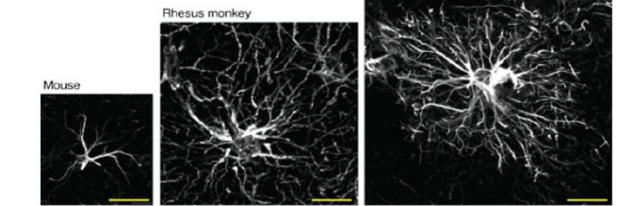
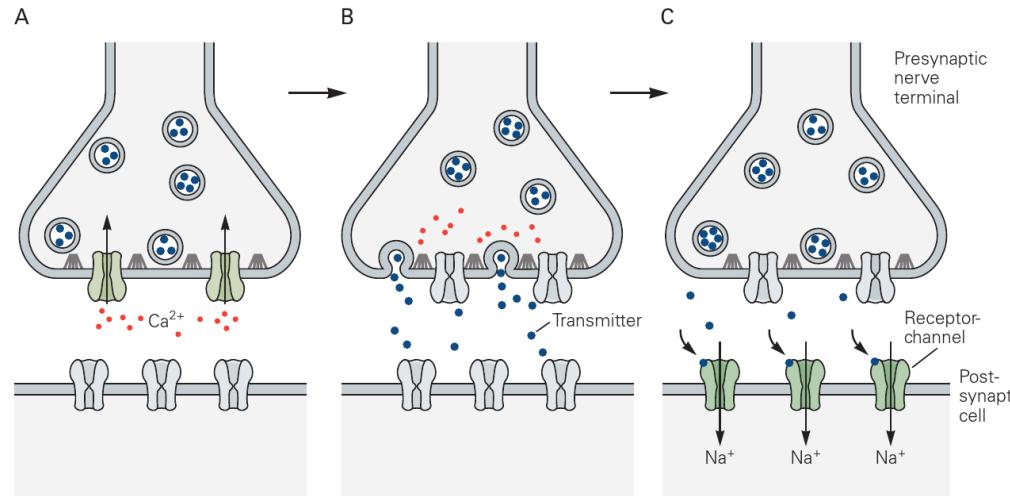
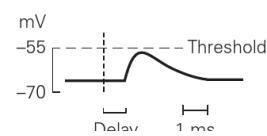
B Current pathways at chemical synapses



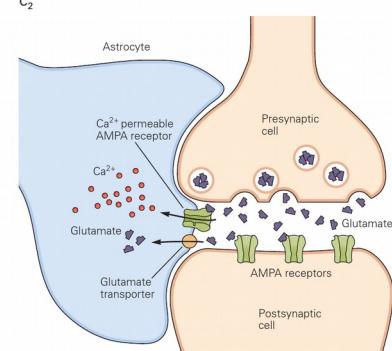
Presynaptic action potential



Excitatory postsynaptic potential



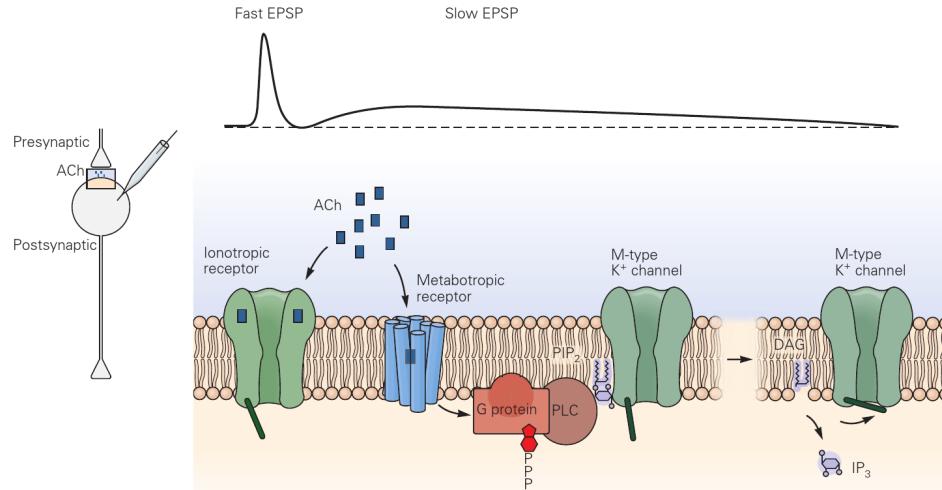
C₁



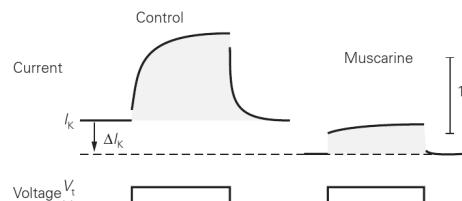
Astrocytes and the synapse³

Slow modulation of synaptic transmission (plasticity)

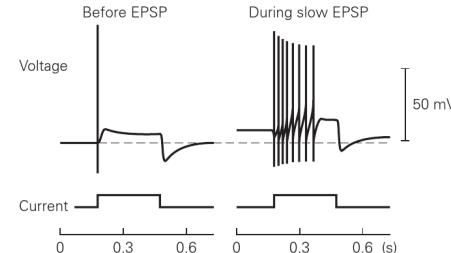
A Fast and slow synaptic transmission



B The effect of muscarine on the M-type K⁺ current



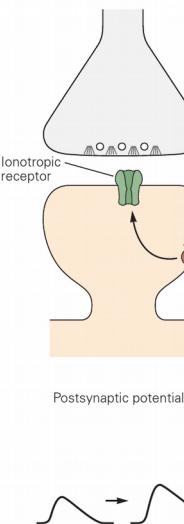
C The anti-accommodation effect of M-type K⁺ current inhibition



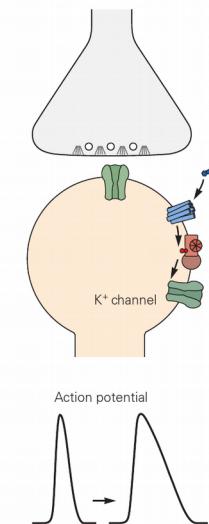
A Presynaptic modulation



B Postsynaptic modulation

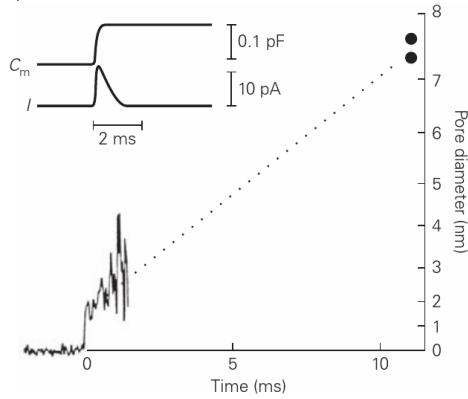
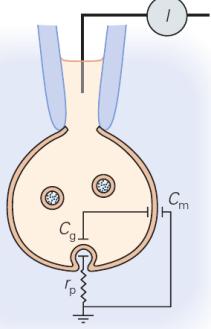


C Modulation in cell body

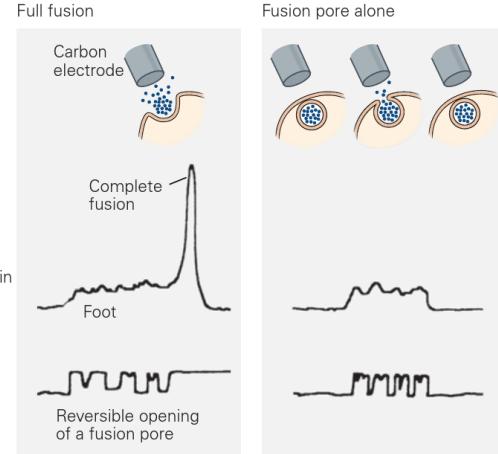
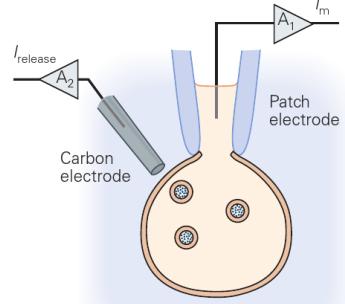


Mechanism of transmitter release

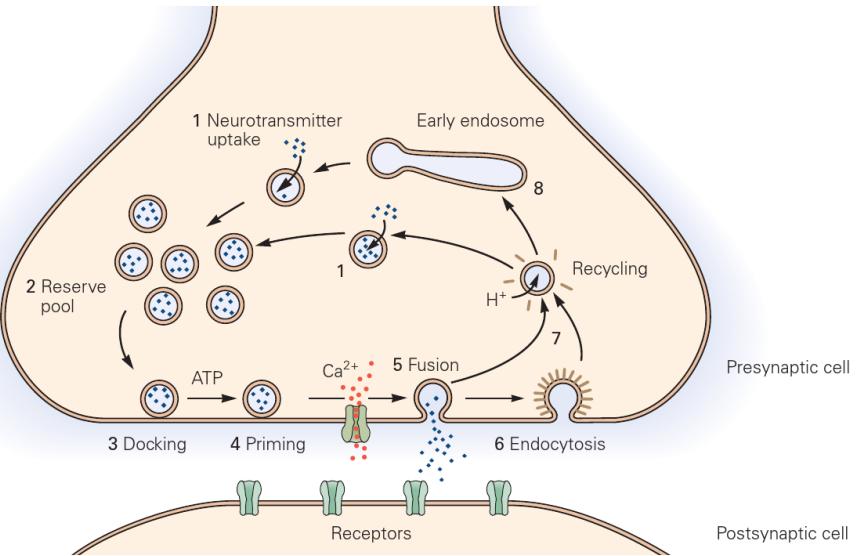
A Electrical events associated with opening of fusion pore



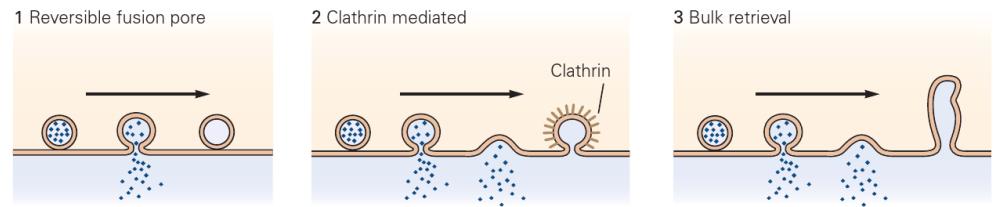
B Transmitter release through fusion pore



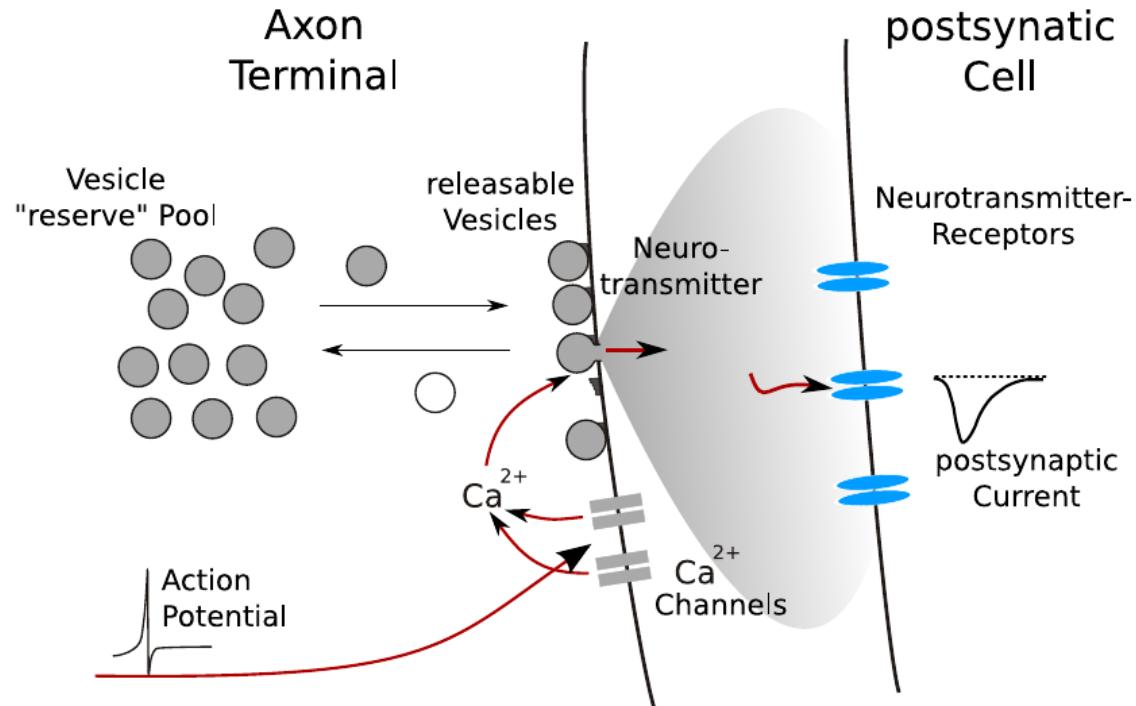
A Synaptic vesicle cycle



B Mechanisms for recycling synaptic vesicles



Short-time plasticity (presynaptic membrane)



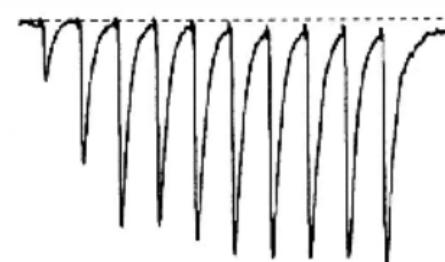
Types of short-time plasticity

Climbing Fibre to Purkinje Cell



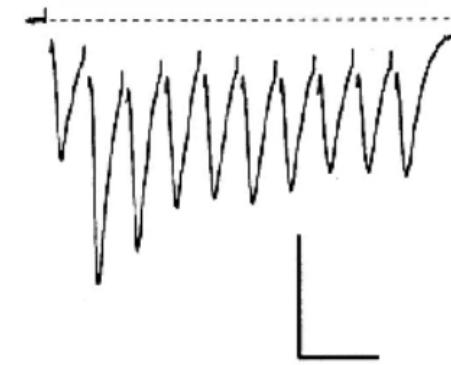
depression

Parallel Fibre to Purkinje Cell



facilitation

Schaffer Collateral



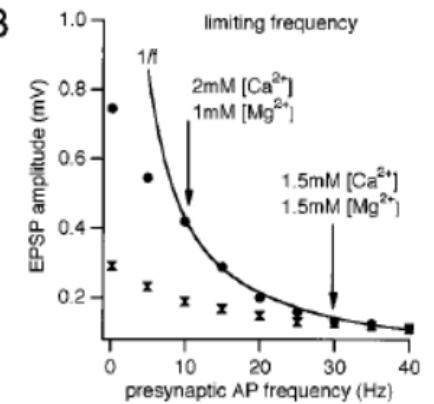
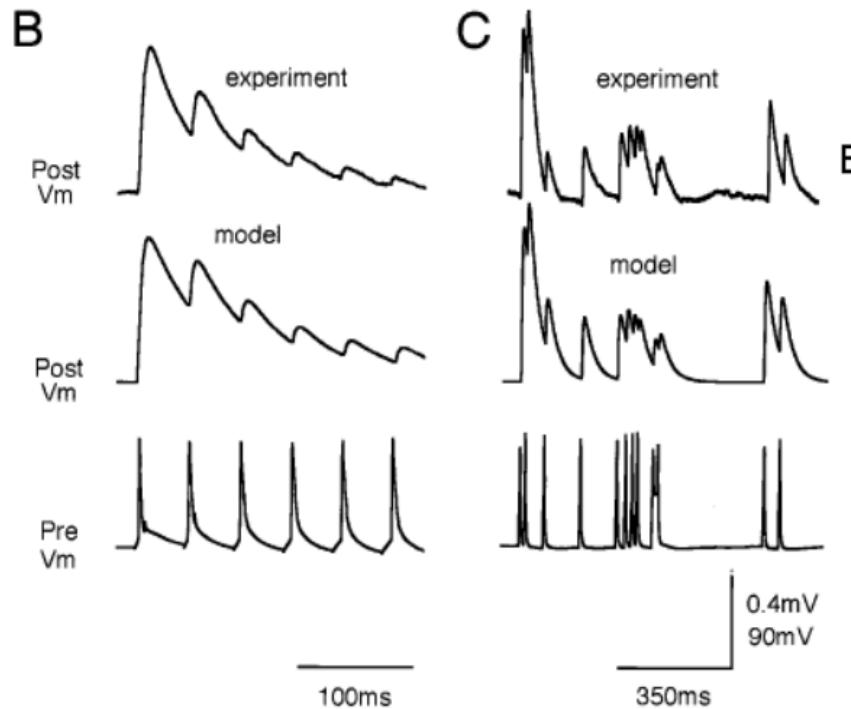
mixed

Dittman et al., 2000 (10 Stimuli at 50 Hz)

Depletion/facilitation model

$$\frac{dn(t)}{dt} = \underbrace{\frac{1 - n(t)}{\tau_r}}_{\text{refilling}} - \sum_j \delta(t - t_j) \cdot p \cdot n(t),$$

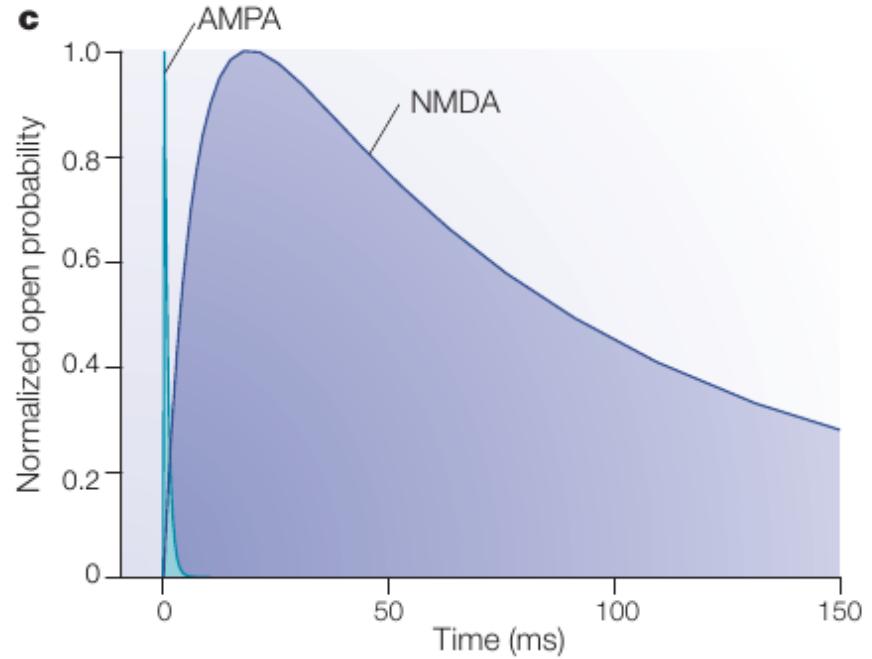
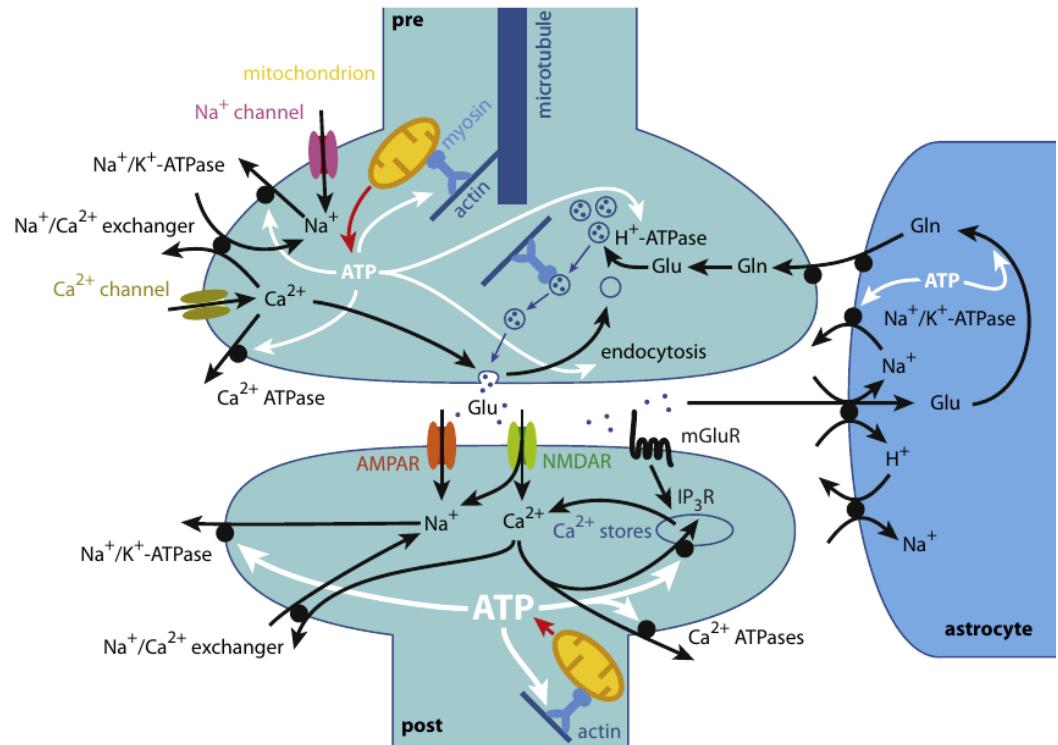
$$\frac{dp(t)}{dt} = \frac{p_0 - p}{\tau_f} + \sum_j \delta(t - t_j) \cdot f \cdot (1 - p(t)),$$



Tsodyks and Markram, 1997

Fig. 8: Modelling synaptic depression with a simple depletion model (neocortical pyramidal cells, compiled from Tsodyks and Markram 1997).

The Glu-ergic synapse



Glutamate receptors that make channels

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

- heterotetrameres
- pre- and post-translational modifications

Molecular structure of Glu-receptors

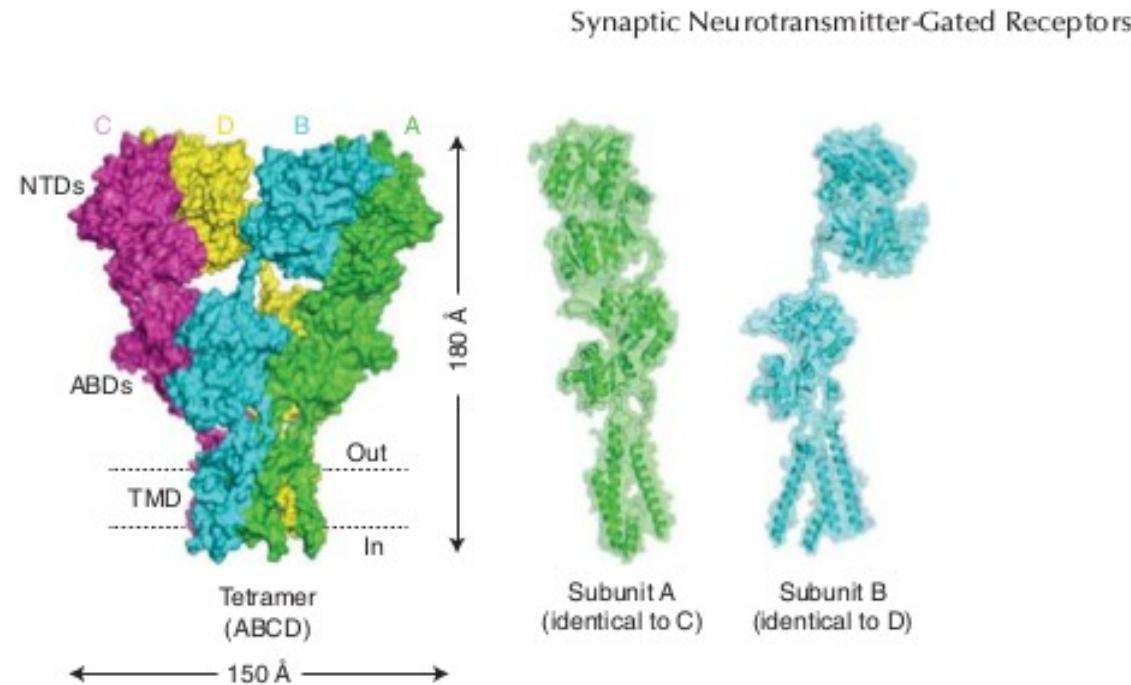
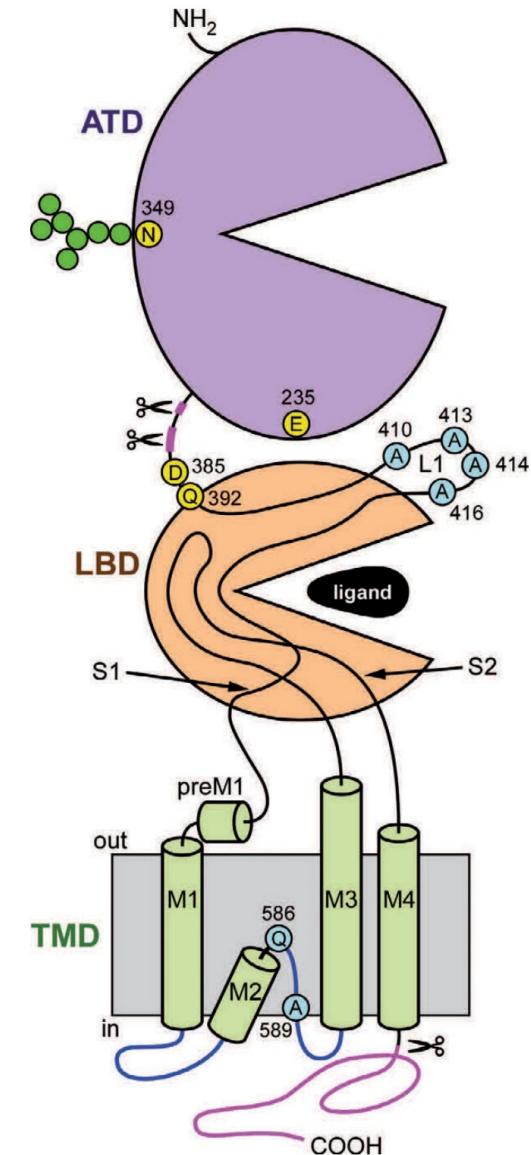


Figure 6. The tetrameric structure of the AMPA GluA2 receptor. (Left) X-ray crystal structure of the AMPA GluA2 homotetrameric receptor (Sobolevsky et al. 2009). Each subunit is in a different color. The tetramer shows a typical layer organization with at the “top” the amino-terminal domains (ATDs or NTDs), at the “bottom” the transmembrane domain (TMD) where the ion channel sits, and sandwiched between the two the agonist-binding domains (ABDs or S1S2 domains) binding glutamate (or glycine/d-serine). (Right) Subunit non-equivalence. α -Carbon traces of subunit A and subunit B with the ABDs similarly oriented. Note the striking difference in overall domain orientation between the two subunits.

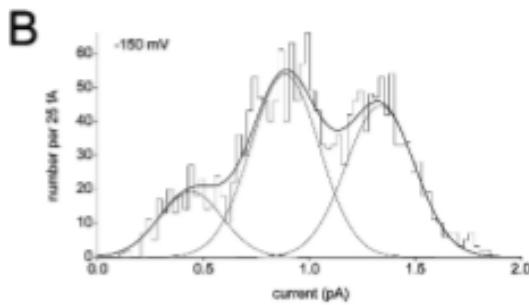
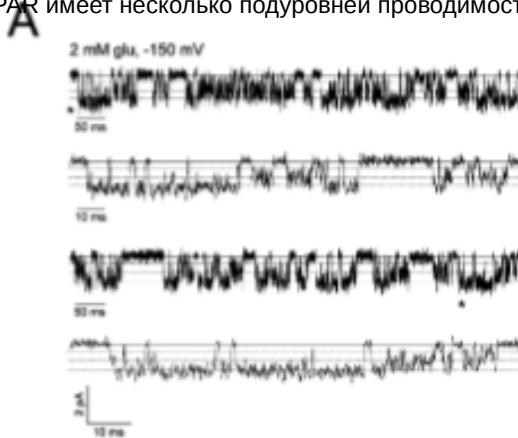


Conductivity and kinetics of AMPA receptors

AMPA Receptors

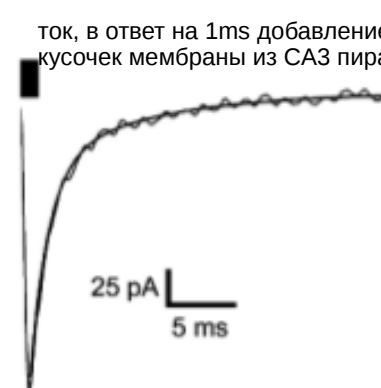
11

AMPAR имеет несколько подуровней проводимости

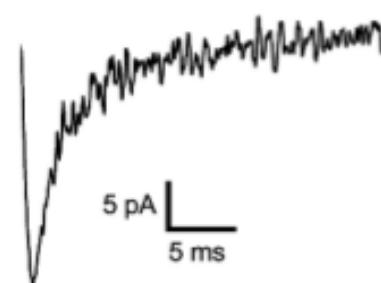


C

ток, в ответ на 1ms добавление Glu (пэтч-кламп),
кусочек мембранны из CA3 пирамид. нейрона



D



Миниатюрный постсинаптический ток в
интернейроне коры

AMPAR

- $\langle g \rangle \sim 12 \text{ pS}$
- $V_0 \sim 0 \text{ mV}$
- permeable to: Na, K, but not Ca^{2+} (in mature animals GluA₂)
- NB: QRN site: filter
- fast desensitizing
- main type of GluR

NMDAR

- well permeable to Ca^{2+} , 15% if all inward current
- involved in memory formation
- blocked by Mg^{2+} (voltage-dependent)
- need to bind 2 Glu and 2 {Gly | D-Ser}

From transmitter binding to opening to desensitization

T.G. Smart and P. Paoletti

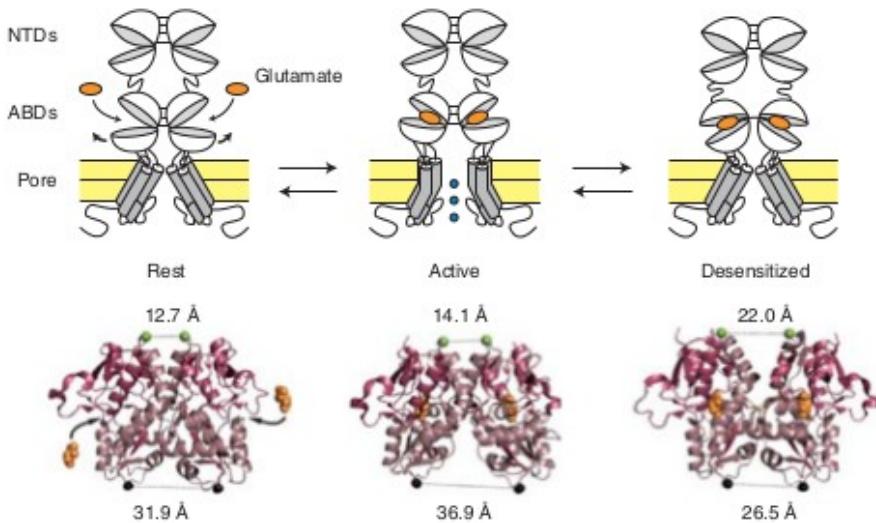


Figure 7. Structural mechanism of iGluR activation and desensitization. A single dimer is represented; a full receptor is a tetramer made of two such dimers. (Below) The crystal structures of the GluA2 ABD dimer in conformations that correspond to the resting state (no ligand bound; pdb code 1FT0), the active state (glutamate-bound; pdb code 1FTI), and the desensitized state (pdb code 2I3V). The distances between the two protomers, at the top of the upper lobes (green spheres; dimer interface) and at the bottom of the lower lobes (black spheres; connections to the transmembrane segments), are indicated (Armstrong et al. 2006).

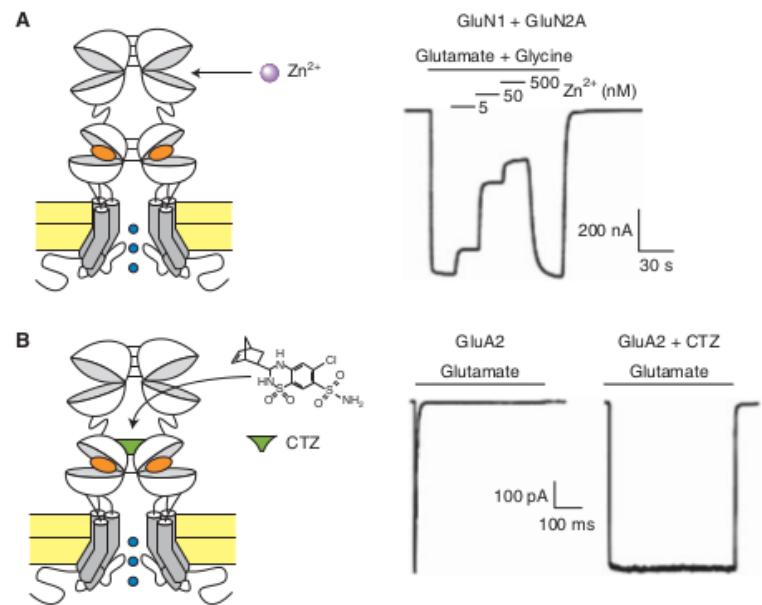
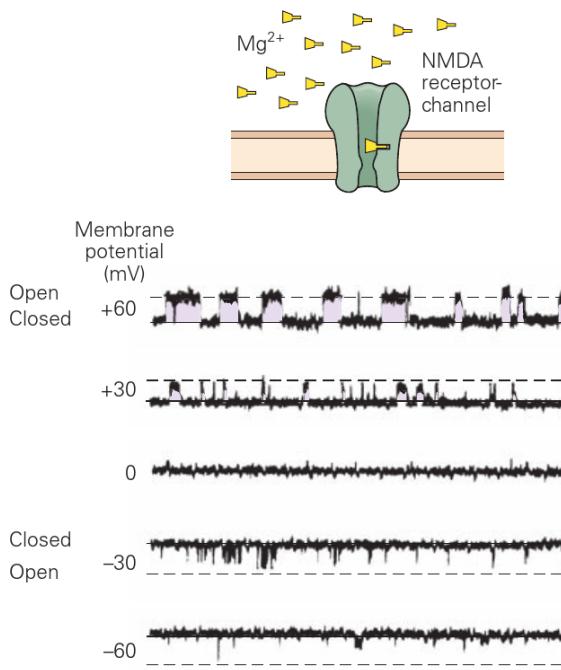


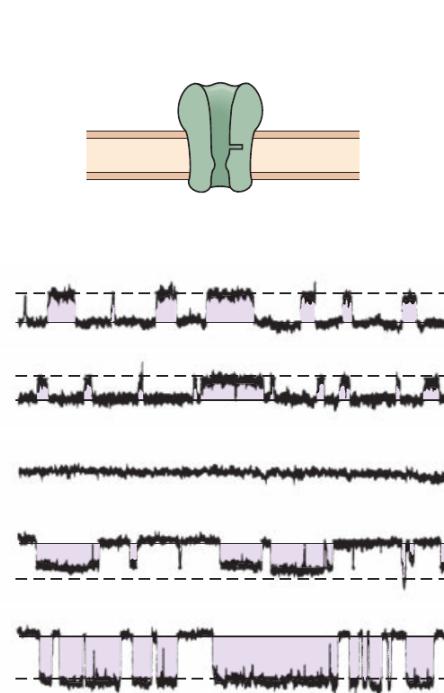
Figure 8. Allosteric modulation of iGluRs. (A) Negative allosteric modulation of NMDARs by extracellular zinc. The GluN2A and GluN2B NTDs form subunit-specific inhibitory zinc-binding sites. (Right) Inhibition by nanomolar zinc concentrations of GluN1/GluN2A responses (adapted from Paoletti et al. 2000). (B) Positive allosteric modulation of AMPARs by cyclothiazide (CTZ). CTZ binds and stabilizes the ABD dimer interface. (Right) CTZ blocks desensitization of GluA2 receptors (Sun et al. 2002).

NMDA-receptors (Glu-ergic synapses)

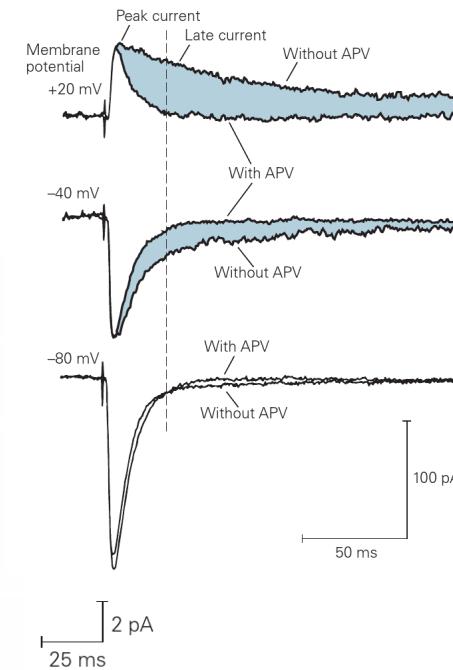
A Normal extracellular Mg^{2+}



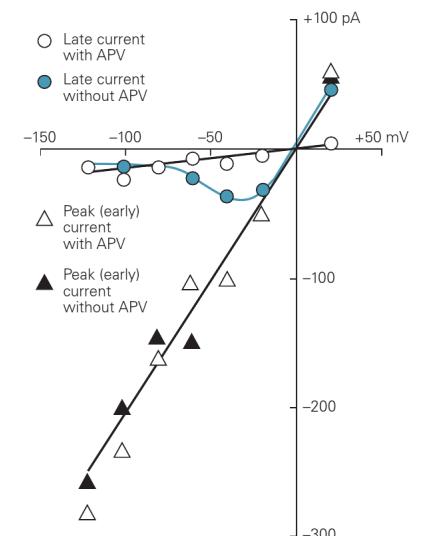
B No extracellular Mg^{2+}



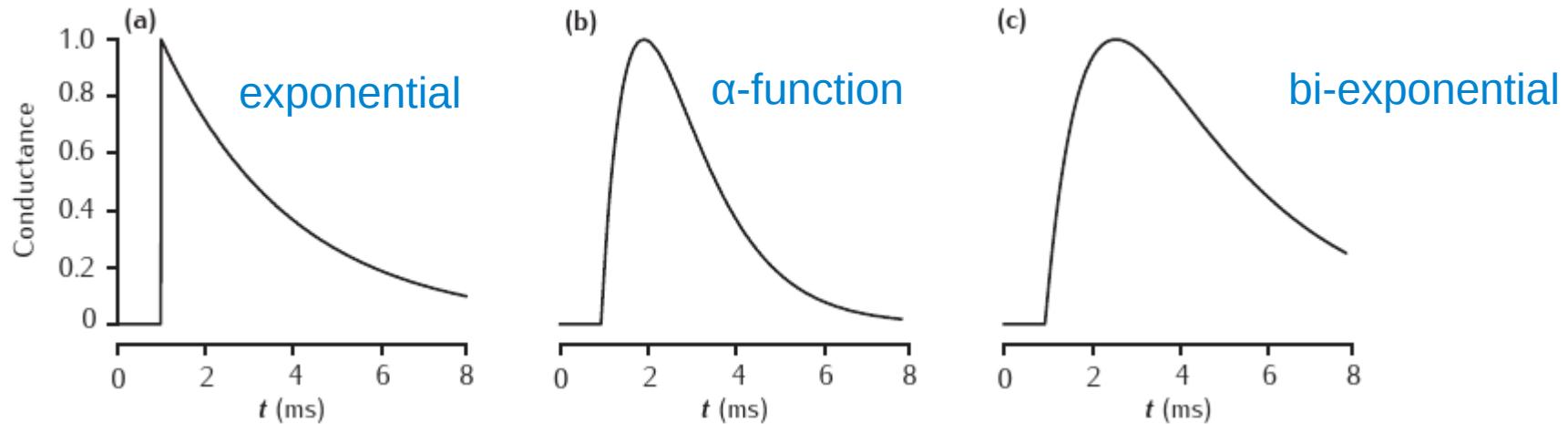
A Early and late components of synaptic current



B Current-voltage relationship of the synaptic current



Phenomenological models of postsynaptic conductance

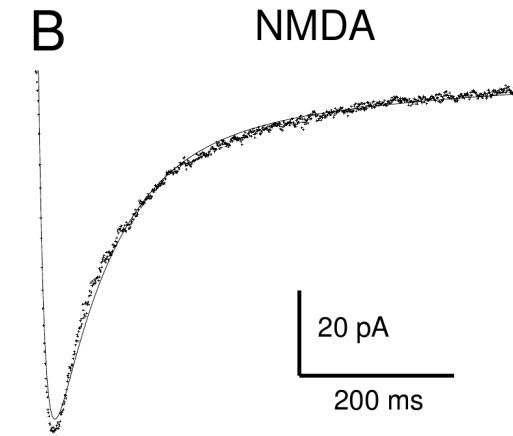
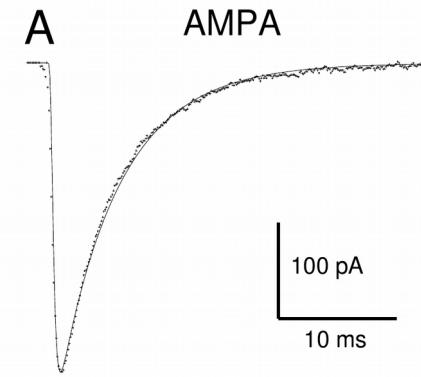
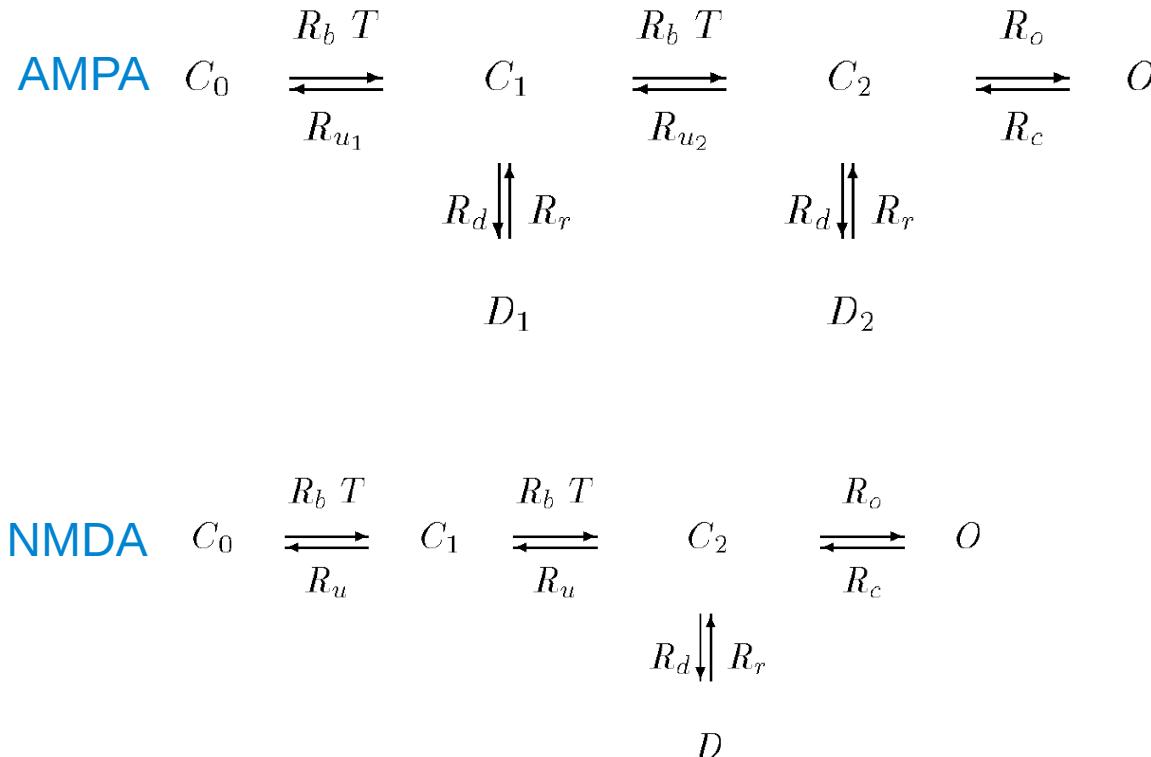


$$g_{\text{syn}}(t) = \bar{g}_{\text{syn}} \exp\left(-\frac{t - t_s}{\tau}\right) \quad (7.2)$$

$$g_{\text{syn}}(t) = \bar{g}_{\text{syn}} \frac{t - t_s}{\tau} \exp\left(-\frac{t - t_s}{\tau}\right) \quad (7.3)$$

$$g_{\text{syn}}(t) = \bar{g}_{\text{syn}} \frac{\tau_1 \tau_2}{\tau_1 - \tau_2} \left(\exp\left(-\frac{t - t_s}{\tau_1}\right) - \exp\left(-\frac{t - t_s}{\tau_2}\right) \right). \quad (7.4)$$

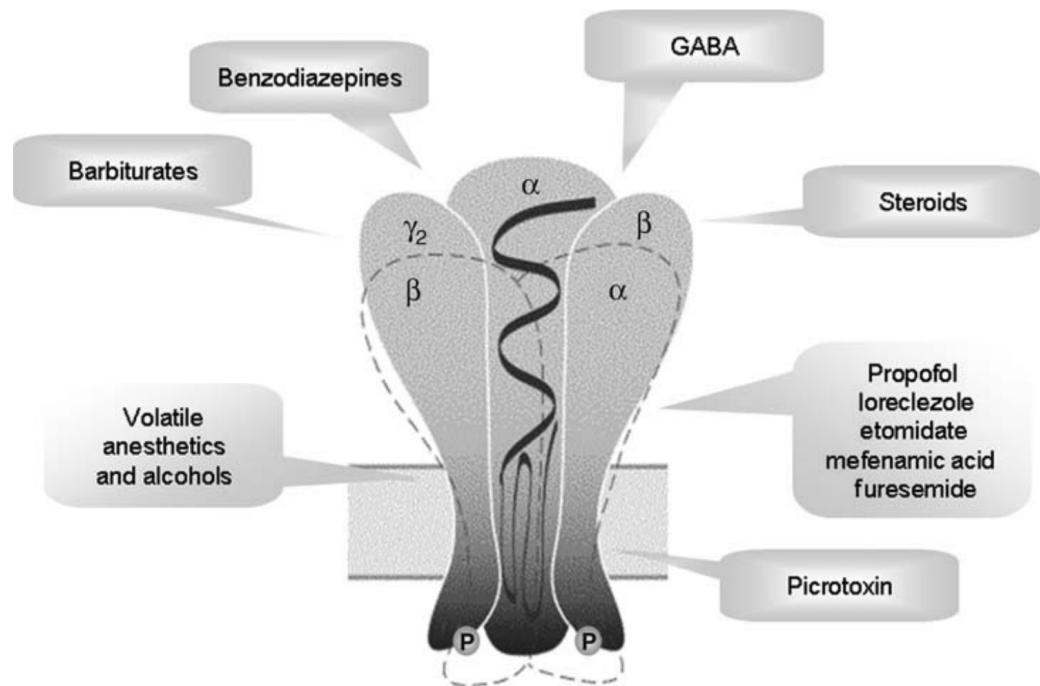
Kinetic model of AMPA receptors



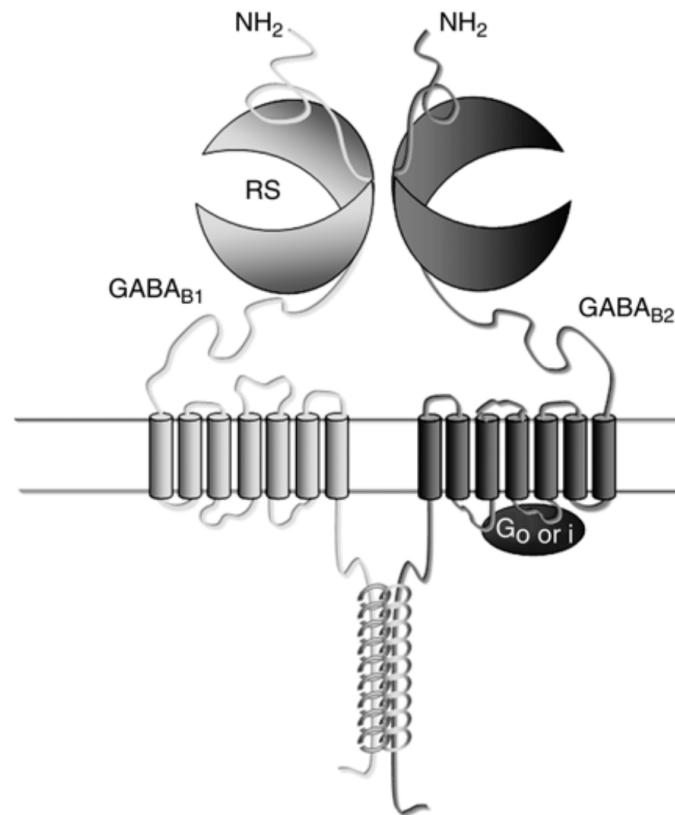
Destexhe, Mainen, Sejnowski. Synthesis of Models for Excitable Membranes,
Synaptic Transmission and Neuromodulation Using a Common Kinetic Formalism.
Journal of Computational Neuroscience, **1**, 195–230 (1994)

Receptor	Scheme	Receptor	Scheme	r_1 ($s^{-1} \mu M^{-1}$)	r_2 (s^{-1})	r_3 (s^{-1})	r_4 (s^{-1})	r_5 (s^{-1})	r_6 ($s^{-1} \mu M^{-1}$)	pulse (ms)
AMPA/kainate		GABA _B		16	4.7	—	—	—	—	84
				0	0	19	17	10	36	60
				18	4.4	1.4	1.7	0	0	97.5
				18	4.4	1.5	1.5	0.12	0.28	97
				38	12	18	17	2.3	2.4*	77
NMDA		Serotonin (5HT - 1)		2.4	1.1	—	—	—	—	100
		Acetylcholine (M2)		2.0	7.5	—	—	—	—	100
GABA _A		Noradrenaline (α2)		1.7	2.4	—	—	—	—	100
		Dopamine (D2), Adenosine (A1), Histamine, and peptides		2.0	1.5	—	—	—	—	100

GABA receptors



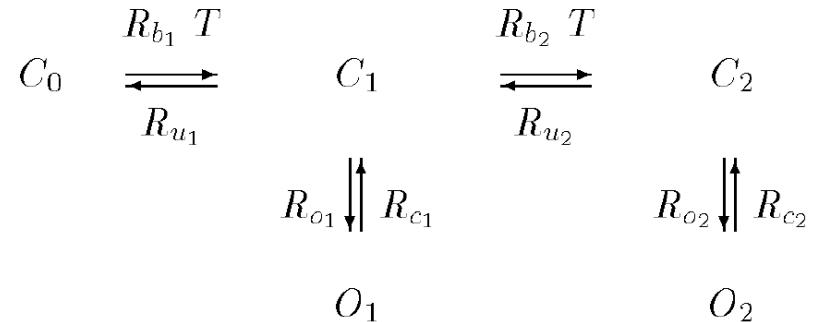
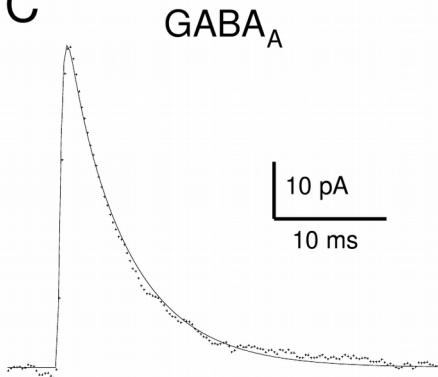
GABA-A receptors: channels



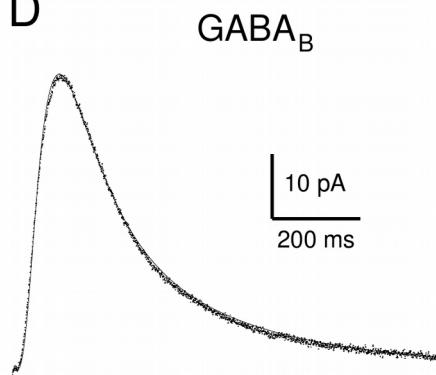
GABA-B receptors: G-protein coupled

Kinetic models of GABARs

C



D



$$I_{GABA_A} = \bar{g}_{GABA_A} ([O_1] + [O_2]) (V - E_{Cl})$$

$$\begin{aligned}
 \frac{d[R]}{dt} &= K_1 [T] (1 - [R] - [D]) - K_2 [R] + K_3 [D] \\
 \frac{d[D]}{dt} &= K_4 [R] - K_3 [D] \\
 \frac{d[G]}{dt} &= K_5 [R] - K_6 [G]
 \end{aligned}$$

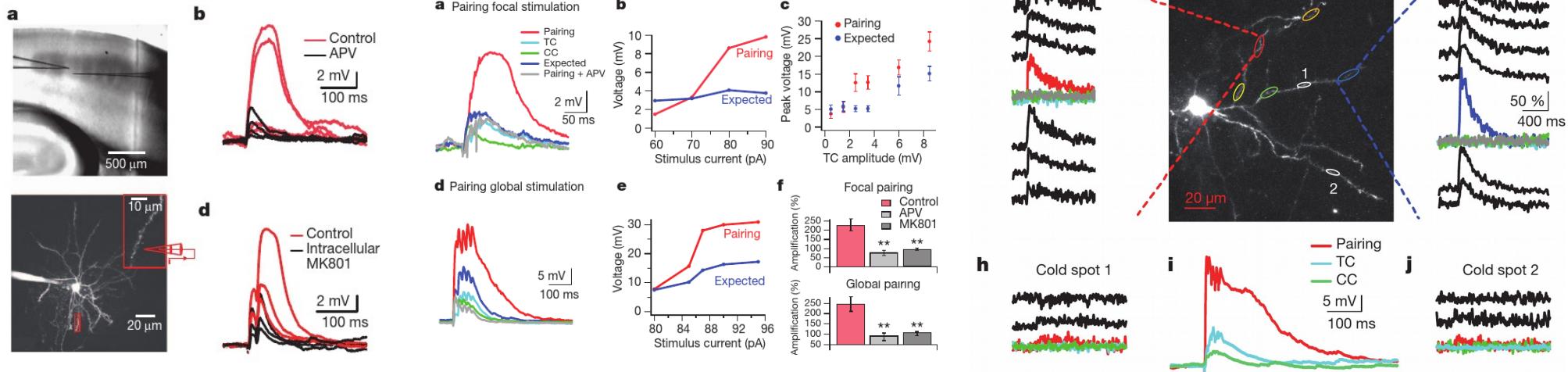
$$I_{GABA_B} = \bar{g}_{GABA_B} \frac{[G]^n}{[G]^n + K_d} (V - E_K)$$

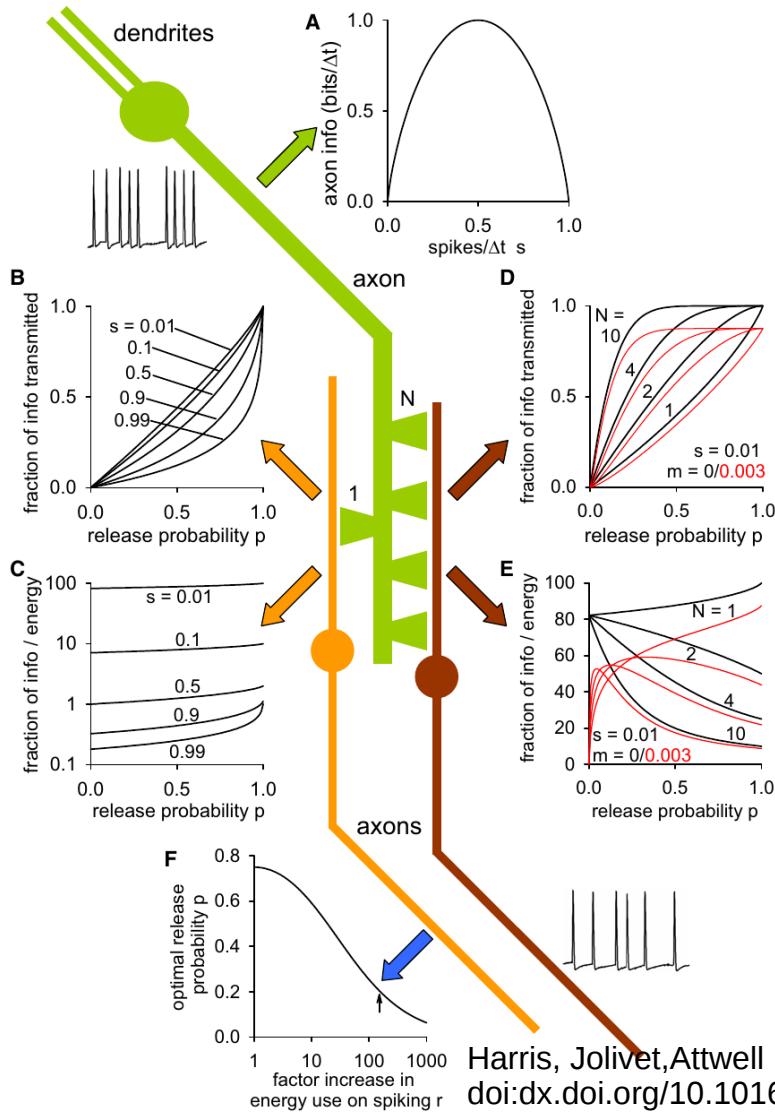
LETTER

doi:10.1038/nature11451

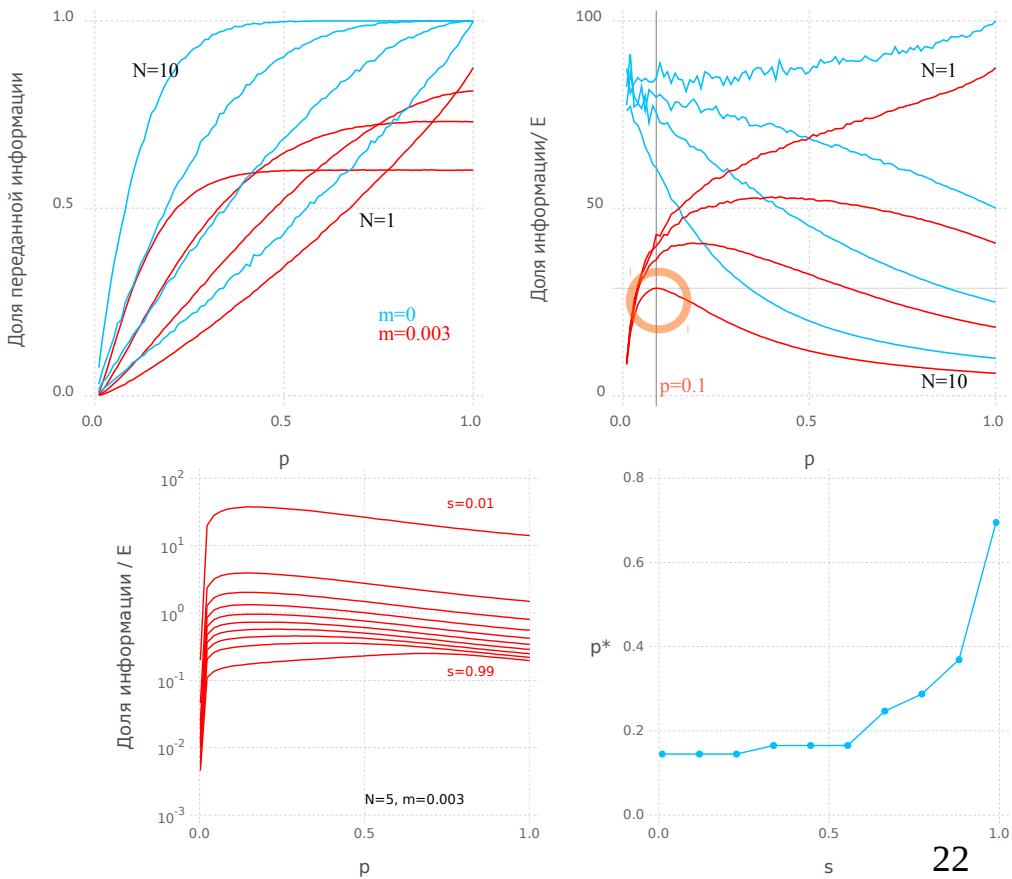
Nonlinear dendritic processing determines angular tuning of barrel cortex neurons *in vivo*

Maria Lavzin^{1*}, Sophia Rapoport^{1*}, Alon Polsky², Liora Garion¹ & Jackie Schiller¹





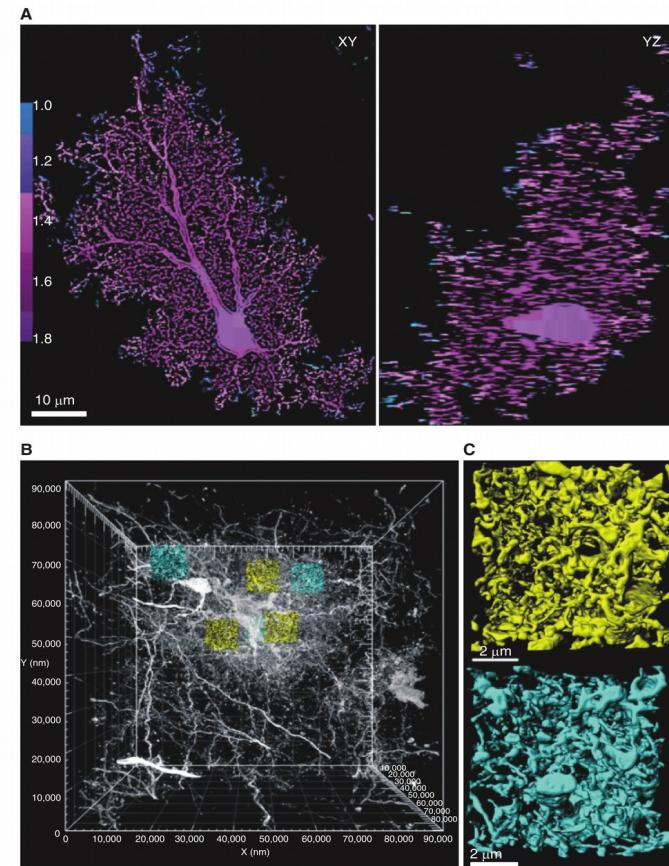
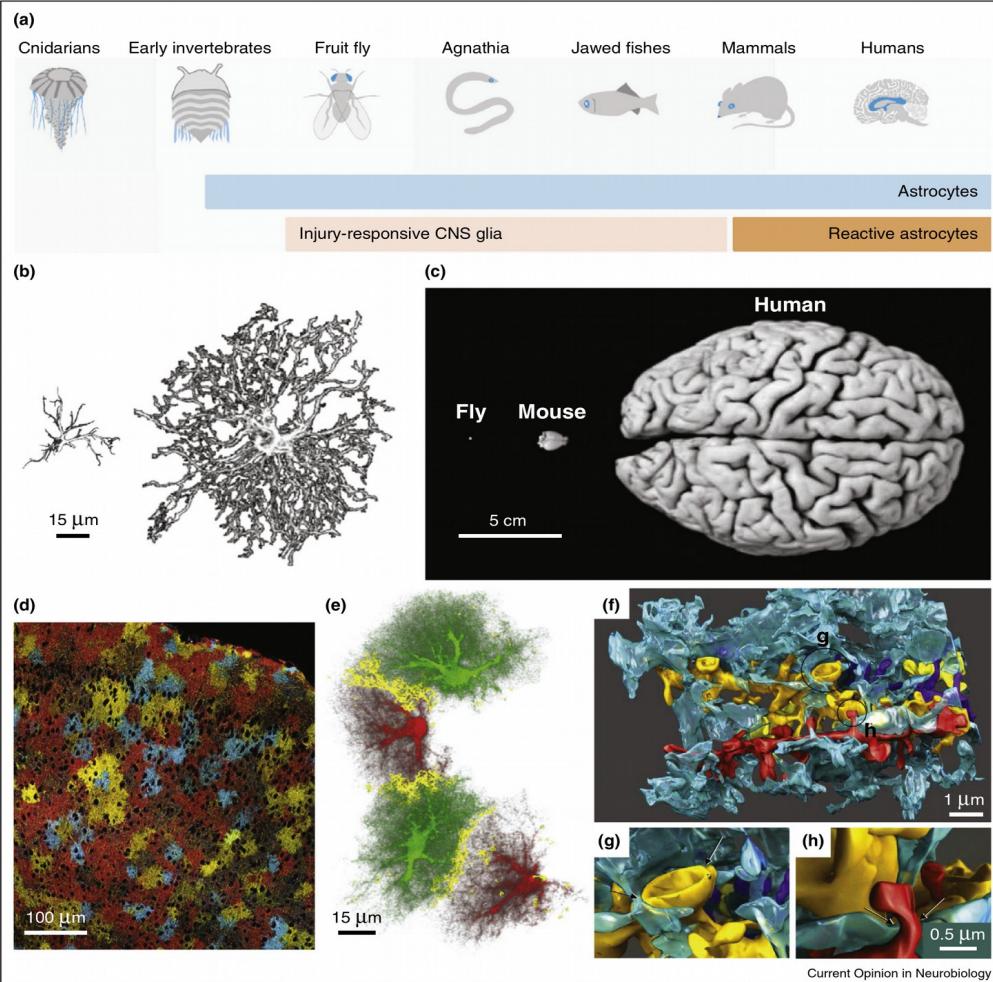
Transfer of information through the synapse: optimization of energy cost?



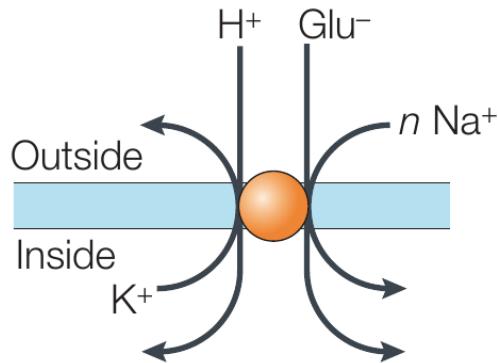
Optimization of ATP use by synaptic transmission

- Diameter of the spike ($\sim 1\mu$) is constrained by the timescale ($\sim 1\text{ms}$), as neurotransmitter has to diffuse to the fringe
- Number of postsynaptic receptors is constrained by signal-to-noise ratio **crowding and energy use**
- Low affinity of AMPA-receptors to glutamate is explained by the need for fast dissociation at 1 ms timescale

Astrocytes and the synapse



Glu⁻ uptake by astrocytes



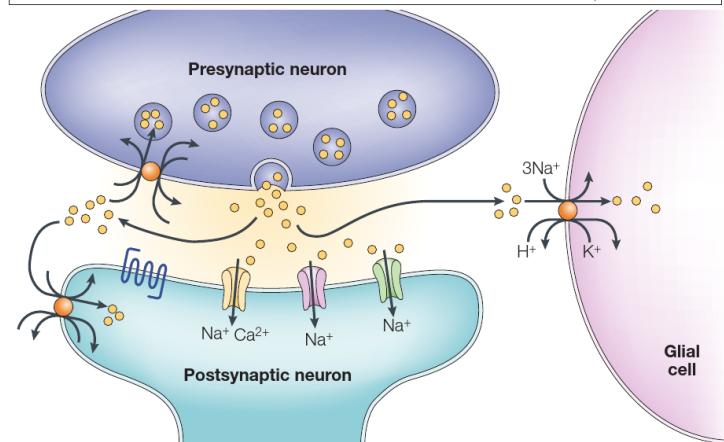
$$[\text{Glu}]_o = [\text{Glu}]_i (\text{Na}^+)_i / (\text{Na}^+)_o)^n ([\text{H}^+]_i / [\text{H}^+]_o) ([\text{K}^+]_o / [\text{K}^+]_i) e^{(n-1)VF/RT}$$

n	$[\text{Glu}]_o$	% of NMDA p_{\max} (steady state)
1	21 μM	99%
2	0.18 μM	13%
3	0.0016 μM	0.002%



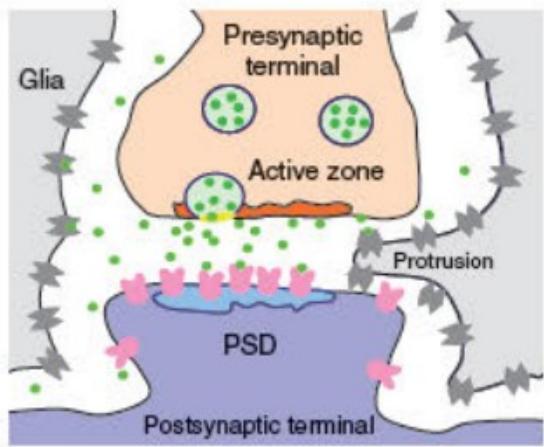
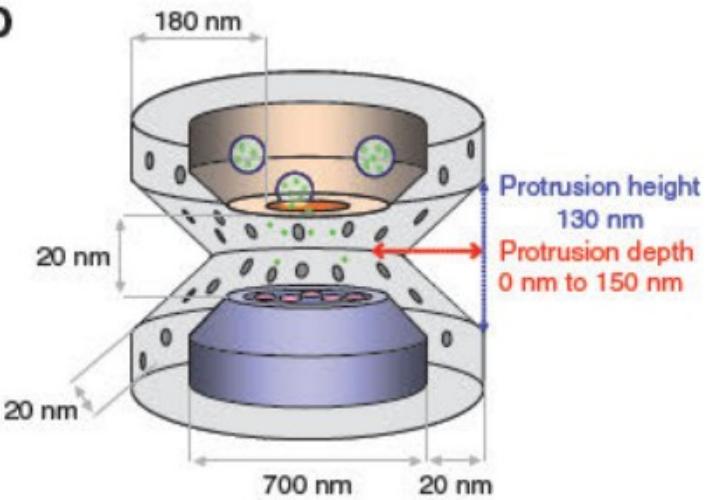
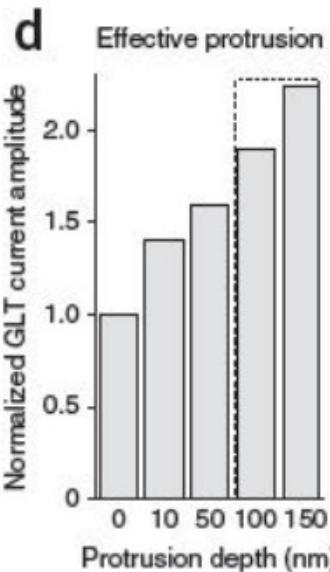
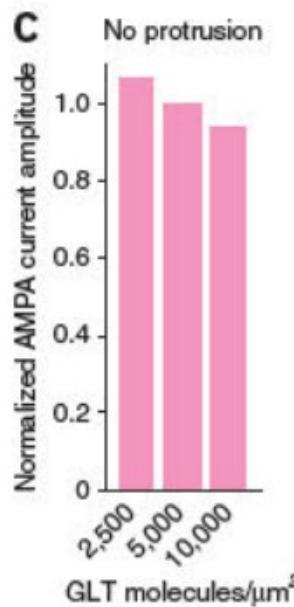
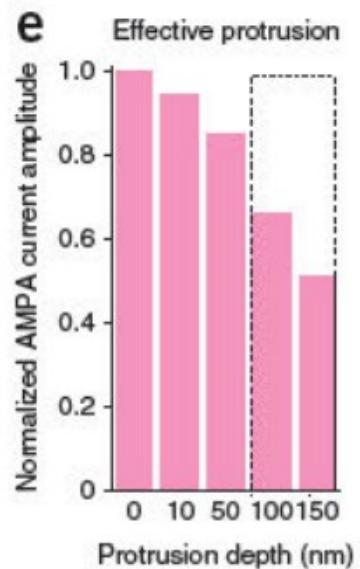
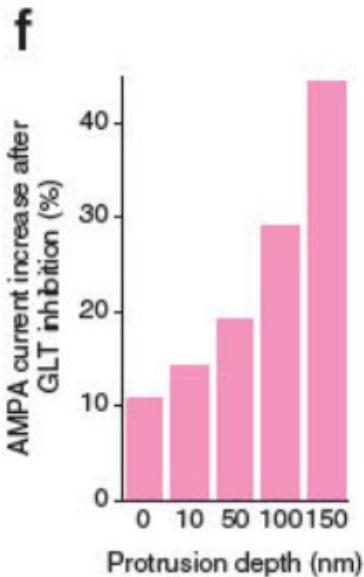
Перенос 3-х ионов Na^+ необходим
для достаточно полного удаления
Glu из синаптической щели

Перенос **каждого** из ионов, кроме Glu, энергетически выгоден



Connexin 30 sets synaptic strength by controlling astroglial synapse invasion

Ulrike Pannasch^{1,2,10}, Dominik Freche^{3,4,11}, Glenn Dallérac^{1,2,11}, Grégory Ghézali^{1,2}, Carole Escartin⁵,
Pascal Ezan^{1,2}, Martine Cohen-Salmon^{1,2}, Karim Benchenane⁶, Veronica Abudara^{1,2,10}, Amandine Dufour⁷,
Joachim H R Lübke^{7,8}, Nicole Déglon^{5,10}, Graham Knott⁹, David Holcman^{3,4} & Nathalie Rouach^{1,2}

a**b****c****e****f**

Astrocyte calcium signalling orchestrates neuronal synchronization in organotypic hippocampal slices

Takuya Sasaki¹, Tomoe Ishikawa¹, Reimi Abe¹, Ryota Nakayama¹, Akiko Asada¹, Norio Matsuki¹ and Yuji Ikegaya^{1,2}

¹Graduate School of Pharmaceutical Sciences, University of Tokyo, Tokyo, Japan

²Center for Information and Neural Networks, Saitama City, Osaka, Japan

Key points

- In the brain, astrocytes detect neuronal activity and regulate neuronal excitability and synaptic transmission.
- Recent studies show that calcium elevations that are localized within astrocyte processes upregulate endogenous neurotransmission at nearby synapses.
- We demonstrated that at the network level calcium buffering in astrocytes caused a significant reduction in the correlated activity of neurons in cultured hippocampal slices.
- In contrast, the uncaging of calcium in astrocytes triggered synchronized activity in neuronal populations.
- This study provides experimental support for the functional relevance of astrocyte signalling to the maintenance of collective neuronal dynamics.

Abstract Astrocytes are thought to detect neuronal activity in the form of intracellular calcium elevations; thereby, astrocytes can regulate neuronal excitability and synaptic transmission. Little is known, however, about how the astrocyte calcium signal regulates the activity of neuronal populations. In this study, we addressed this issue using functional multineuron calcium imaging in hippocampal slice cultures. Under normal conditions, CA3 neuronal networks exhibited temporally correlated activity patterns, occasionally generating large synchronization among



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Astrocytes contribute to gamma oscillations and recognition memory

Hosuk Sean Lee^{a,b,1}, Andrea Ghetti^{a,2}, António Pinto-Duarte^{c,d,e}, Xin Wang^f, Gustavo Dziewczapolski^a, Francesco Galimberti^g, Salvador Huitron-Resendiz^h, Juan C. Piña-Crespo^{a,3}, Amanda J. Roberts^h, Inder M. Vermaⁱ, Terrence J. Sejnowski^{c,i}, and Stephen F. Heinemann^{a,1}

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Contributed by Stephen F. Heinemann, June 15, 2014 sent for review March 10, 2014

Astrocytic regulation of cortical UP st

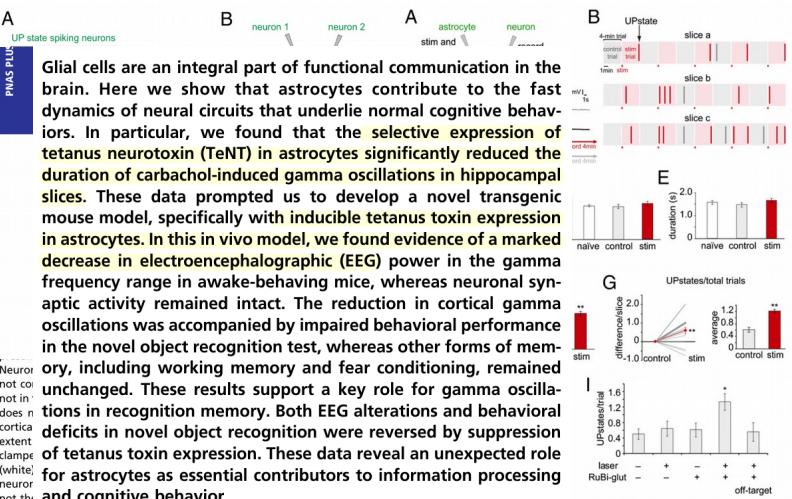
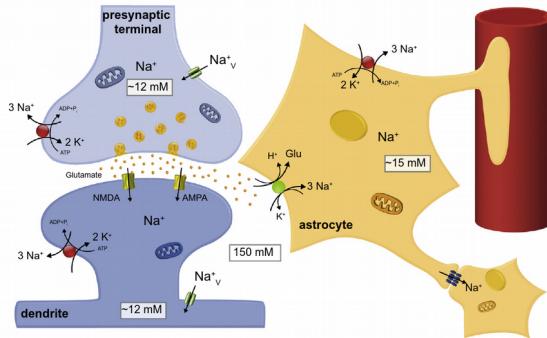
Kira E. Poskanzer¹ and Rafael Yuste¹

PNAS | November 8, 2011

Howard Hughes Medical Institute and Department of Biological Sciences, Columbia University, New York, NY
Edited* by Marcus E. Raichle, Washington University, St. Louis, MO, and approved September 27, 2011 (rec

The synchronization of neuronal assemblies during cortical UP states has been implicated in computational and homeostatic processes, but the mechanisms by which this occurs remain unknown. To investigate potential roles of astrocytes in synchronizing cortical circuits, we electrically activated astrocytes while monitoring the activity of the surrounding network with electrophysiological recordings and calcium imaging. Stimulating a single astrocyte activates other astrocytes in the local circuit and can trigger UP state synchronizations of neighboring neurons. Moreover, interfering with astrocytic activity with intracellular injections of a calcium chelator into individual astrocytes inhibits spontaneous and stimulated UP states. Finally, both astrocytic activity and neuronal UP states are regulated by purinergic signaling in the circuit. These results demonstrate that astroglia can play a causal role in regulating the synchronized activation of neuronal ensembles.

a spontaneous UP state, 35 slices). UP st lasted 1.59 ± 0.08 s and postsynaptic potentials and action potentials by kinetics (Fig. 1*A*). To establish the extent of synchronization during UP states, we performed calcium imaging of hundreds of neurons in the circuit, and observed that many neurons fired action potentials simultaneously during UP states (Fig. 1*B*) (6). Next, we patched two layer 2/3 pyramidal neurons 400–600- μ m apart and recorded spontaneous activity. UP states recorded from one neuron were always observed in the other neuron ($n = 8$ slices, 92 UP states), although UP state depolarizations were often subthreshold (Fig. 1*B*). Thus, most, if not all, pyramidal neurons in a cortical region undergo spontaneous UP states together, and recording from individual neurons reflects this.



Astroglial networks scale synaptic activity and plasticity

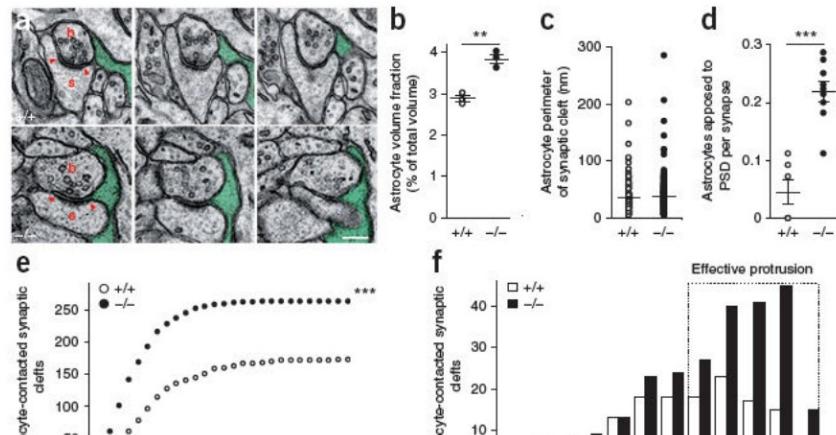
Ulrike Pannasch^a, Lydia Vargová^{b,c}, Jürgen Reingruber^d, Pascal Ezan^a, David Holcman^d, Christian Giaume^a, Eva Syková^{b,c}, and Nathalie Rouach^{a,1}

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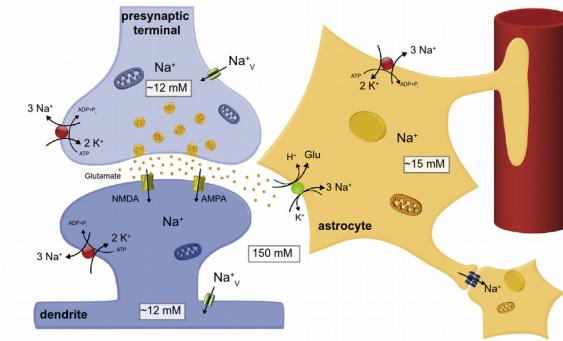
Edited* by Roger A. Nicoll, University of California, San Francisco, CA, and approved April 11, 2011 (received for review November 1, 2010)

Astrocytes dynamically interact with neurons to regulate synaptic transmission. Although the gap junction proteins connexin 30 (Cx30) and connexin 43 (Cx43) mediate the extensive network organization of astrocytes, their role in synaptic physiology is unknown. Here we show, by inactivating Cx30 and Cx43 genes, that astroglial networks tone down hippocampal synaptic transmission in CA1 pyramidal neurons. Gap junctional networking facilitates extracellular glutamate and potassium removal during synaptic activity through modulation of astroglial clearance rate and extracellular space volume. This regulation limits neuronal excitability, release probability, and insertion of postsynaptic AMPA receptors, silencing synapses. By controlling synaptic strength, connexins play an important role in synaptic plasticity. Altogether, these results establish connexins as critical proteins for extracellular homeostasis, important for the formation of functional synapses.

Figure 6 Astrocytes deficient in Cx30 invade synaptic clefts. (a) Serial electron microscopy images showing astroglial processes (green) penetrating the synaptic cleft in the stratum radiatum of *Cx30*^{-/-} mice. PSD, arrowhead; axonal bouton, b; dendritic spine, s. Scale bar, 0.2 μm. (b) Astrocytes from *Cx30*^{-/-} mice (*n* = 3 tissue samples) occupied a larger volume of the neuropil than those from *Cx30*^{+/+} mice (*n* = 3 tissue samples, *P* = 0.0024, *t*(4) = 6.798, unpaired *t* test), (c) Astrocyte perimeter of the synaptic cleft was comparable (*P* = 0.2864, *U* = 21671, Mann-Whitney) in *Cx30*^{+/+} (*n* = 176 synapses) and *Cx30*^{-/-} mice (*n* = 262 synapses). (d) Number of astroglial protrusions apposed to PSDs per synapse in defined volume fractions was increased in *Cx30*^{-/-} mice (*P* < 0.0001, *t*(13) = 6.323, *n* = 9 tissue samples).



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Connexin 30 sets synaptic strength by controlling astroglial synapse invasion

Ulrike Pannasch^{1,2,10}, Dominik Freche^{3,4,11}, Glenn Dallérac^{1,2,11}, Grégory Ghézali^{1,2}, Carole Escartin⁵, Pascal Ezan^{1,2}, Martine Cohen-Salmon^{1,2}, Karim Benchenane⁶, Veronica Abudara^{1,2,10}, Amandine Dufour⁷, Joachim H R Lübke^{7,8}, Nicole Déglon^{5,10}, Graham Knott⁹, David Holcman^{3,4} & Nathalie Rouach^{1,2}

Astrocytes play active roles in brain physiology by dynamic interactions with neurons. Connexin 30, one of the two main astroglial gap-junction subunits, is thought to be involved in behavioral and basic cognitive processes. However, the underlying cellular and molecular mechanisms are unknown.

show here in mice that connexin 30 controls hippocampal excitatory synaptic glutamate transport, which directly alters synaptic glutamate levels. Unexpectedly, deletion of connexin 30 and migration and that connexin 30 modulation of glutamate transport, in, was mediated by morphological changes controlling insertion of astroglial excitatory synaptic strength, connexin 30 plays an important role in long-term synaptic memory. Taken together, these results establish connexin 30 as a critical synaptic location of astroglial processes.

I disruption of connexin-43 impairs in mouse barrel cortex

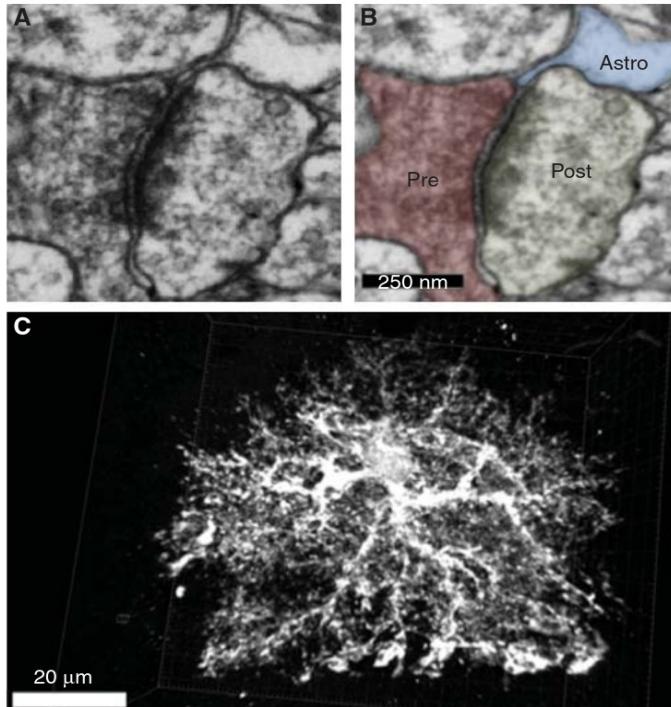
, Yiner Wang, Wang Xi and Yan-qin Yu

of the Ministry of Health of China, Zhejiang Province Key Laboratory of Neurobiology, Zhejiang University School of Medicine, Hangzhou, Zhejiang 310058 China

Astrocytes Control Synapse Formation, Function, and Elimination

Won-Suk Chung¹, Nicola J. Allen², and Cagla Eroglu³

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W.-S. Chung et al.

- Astrocytes
1. Silent "structural" synapses
 2. Postsynaptically active "functional" synapses
 3. Presynaptic function

TSPs ↑
SPARCL1/Hevin ↑
SPARC ↓

Glycans 4/6 ↑
TSPs ↓
SPARC ↓

ApoE/cholesterol ↑
TSPs x
SPARC ↓

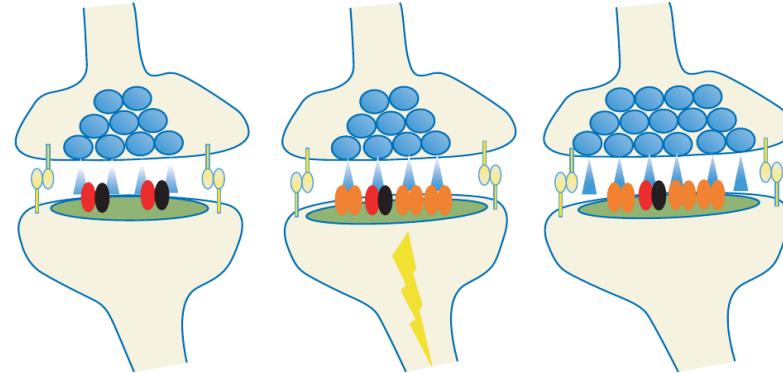


Figure 3. Astrocyte-secreted factors control different aspects of excitatory synaptic development. (1) Astrocytes increase the number of structural synapses. These synapses have normal morphology and contain N-methyl-D-aspartate (NMDA) receptors (red and black). However, they lack AMPA-type glutamate receptors (orange). (2) Astrocytes increase postsynaptic activity by inducing AMPA receptor localization to the postsynaptic density. (3) Astrocytes enhance presynaptic release by increasing release probabilities.

Astroglial cradle in the life of the synapse

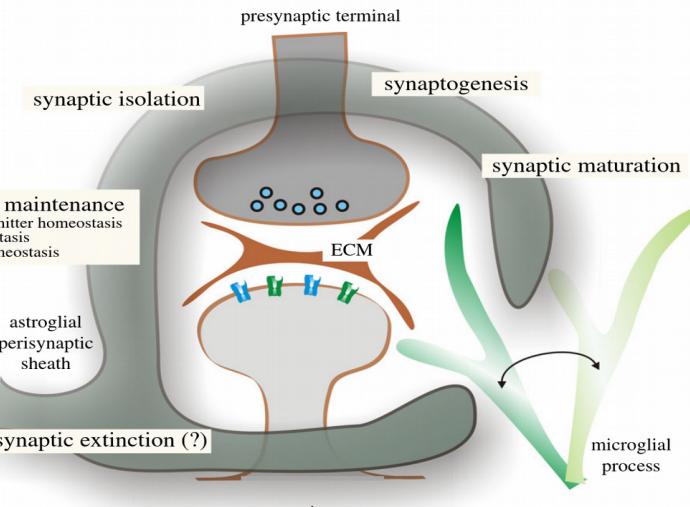
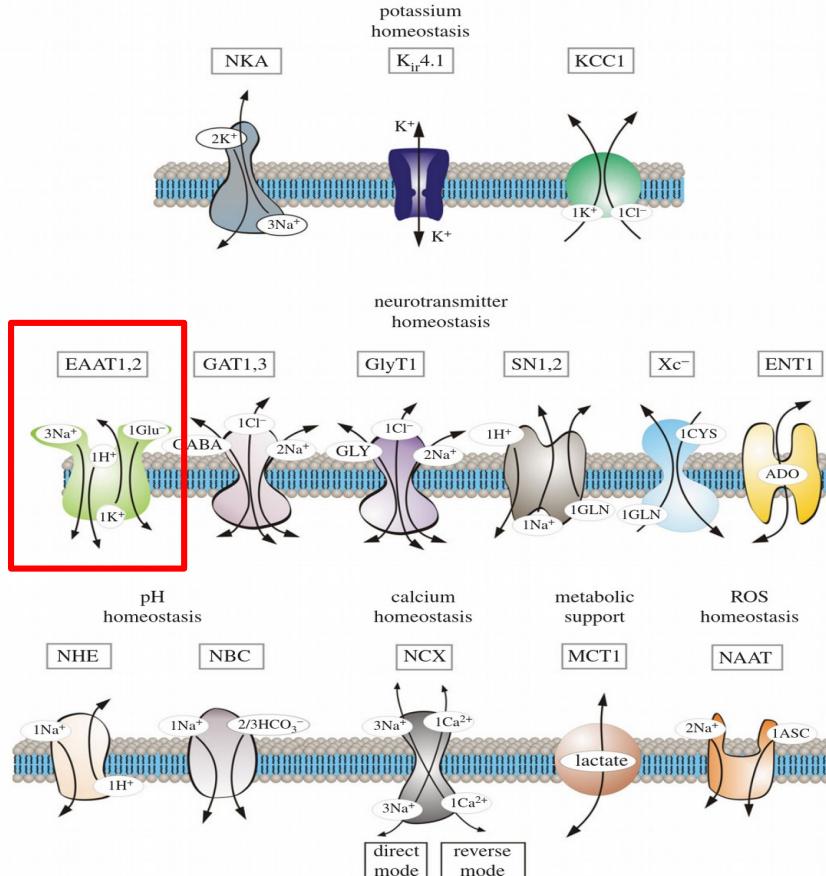
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⁴Division of Glia Disease and Therapeutics, Center for Translational Neuromedicine, University of Rochester Medical School, Rochester, NY 14580, USA



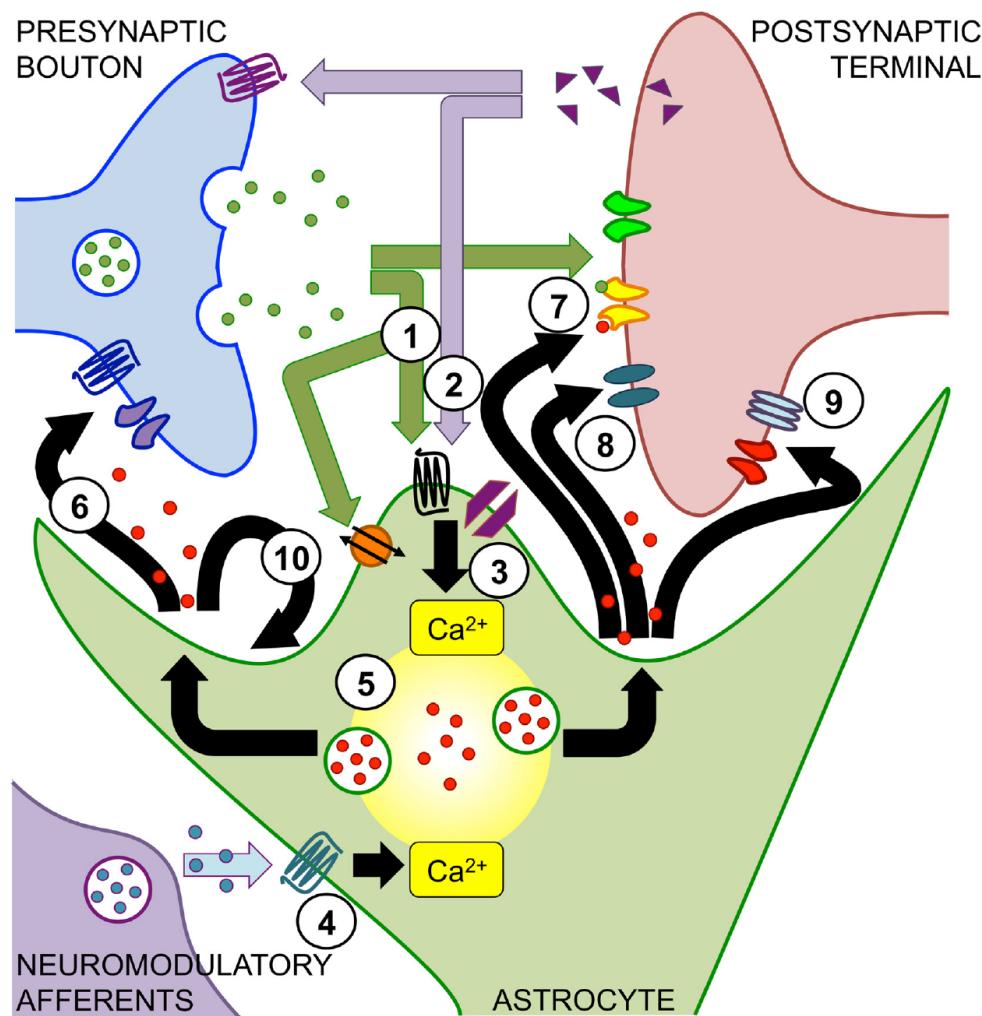
Astroglial perisynaptic sheath covers the majority of synapses in the central nervous system. This glial coverage evolved as a part of the synaptic structure in which elements directly responsible for neurotransmission (exocytotic machinery and appropriate receptors) concentrate in neuronal membranes, whereas multiple molecules imperative for homeostatic maintenance of the synapse (transporters for neurotransmitters, ions, amino acids, etc.) are shifted to glial membranes that have substantially larger surface area. The astrocytic perisynaptic processes act as an 'astroglial cradle' essential for synaptogenesis, maturation, isolation and maintenance of synapses, representing the fundamental mechanism contributing to synaptic connectivity, synaptic plasticity and information processing in the nervous system.

REVIEW

ASTROCYTES: ORCHESTRATING SYNAPTIC PLASTICITY?

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Modeling box: conditions for astrocyte regulation of short-term synaptic plasticity	55
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Astrocytes contribute to gamma oscillations and recognition memory

Hosuk Sean Lee^{a,b,1}, Andrea Ghetti^{a,2}, António Pinto-Duarte^{c,d,e}, Xin Wang^c, Gustavo Dziewczapolski^a, Francesco Galimberti^{f,g}, Salvador Huitron-Resendiz^h, Juan C. Piña-Crespo^{a,3}, Amanda J. Roberts^h, Inder M. Verma^f, Terrence J. Sejnowski^{c,i}, and Stephen F. Heinemann^{a,1}

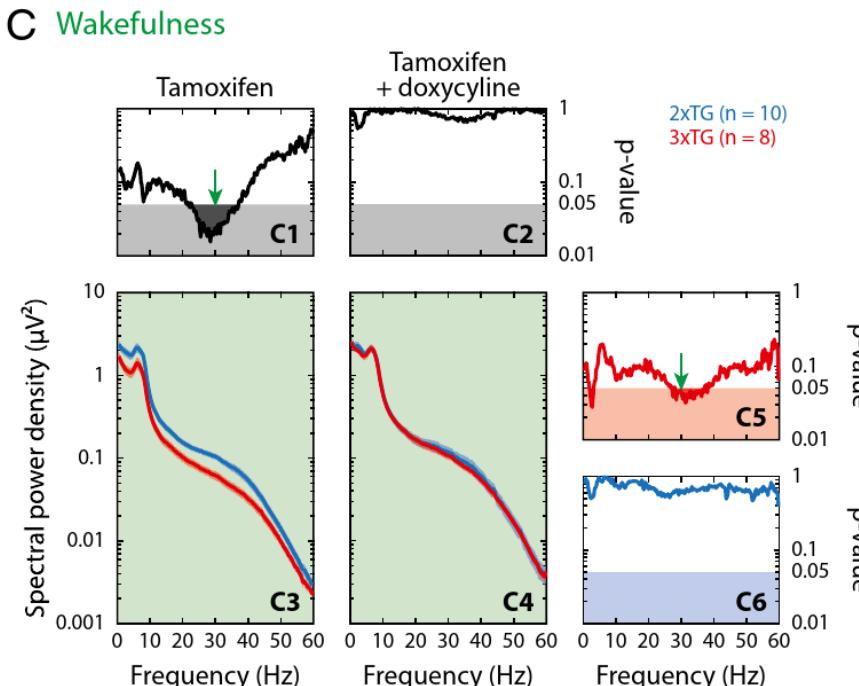
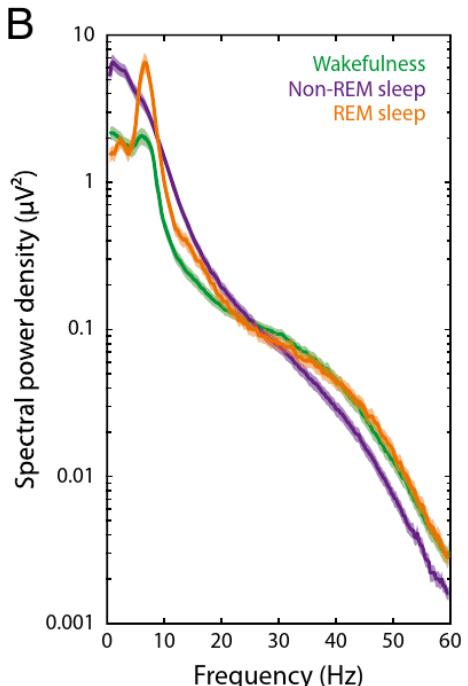
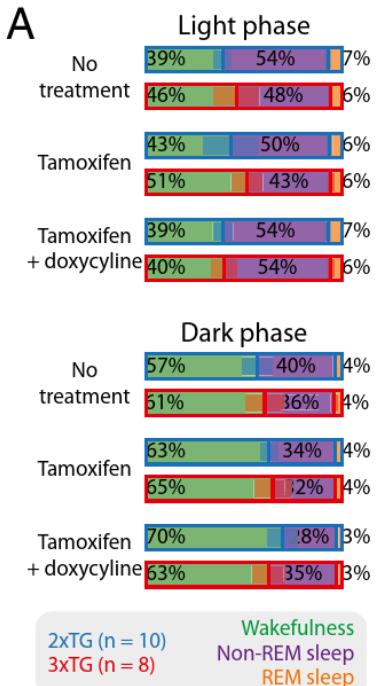
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Contributed by Stephen F. Heinemann, June 15, 2014 (sent for review March 10, 2014)

CROSSMARK

PNAS PLUS

Glial cells are an integral part of functional communication in the brain. Here we show that astrocytes contribute to the fast dynamics of neural circuits that underlie normal cognitive behaviors. In particular, we found that the selective expression of tetanus neurotoxin (TeNT) in astrocytes significantly reduced the duration of carbachol-induced gamma oscillations in hippocampal slices. These data prompted us to develop a novel transgenic mouse model, specifically with inducible tetanus toxin expression in astrocytes. In this in vivo model, we found evidence of a marked decrease in electroencephalographic (EEG) power in the gamma frequency range in awake-behaving mice, whereas neuronal synaptic activity remained intact. The reduction in cortical gamma oscillations was accompanied by impaired behavioral performance in the novel object recognition test, whereas other forms of memory, remained intact. Our results support a critical role for gamma oscillations in memory processing.



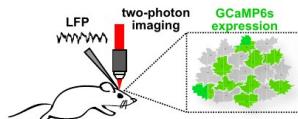
Astrocytes regulate cortical state switching in vivo

Kira E. Poskanzer^{a,1,2} and Rafael Yuste^a

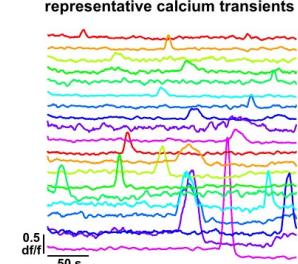
^aDepartment of Biological Sciences, Columbia University, New York, NY 10027

Edited by Charles F. Stevens, The Salk Institute for Biological Studies, La Jolla, CA, and approved March 18, 2016 (received for review October 20, 2015)

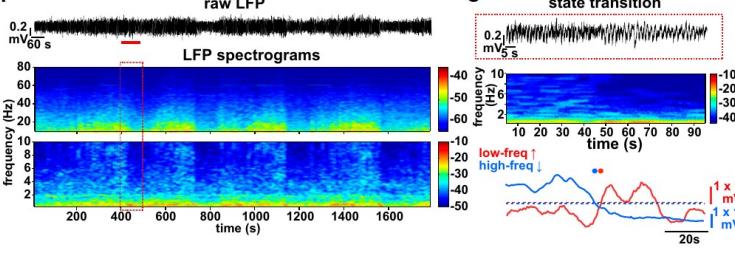
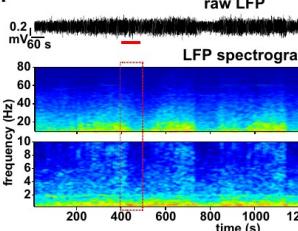
A astrocytic calcium imaging and LFP



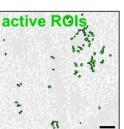
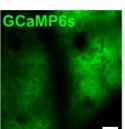
D representative calcium transients



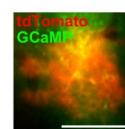
I raw LFP



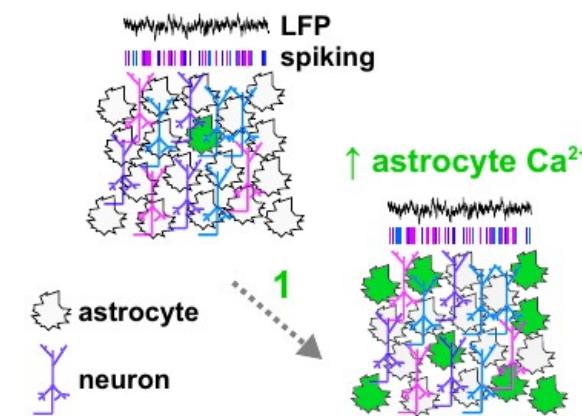
B



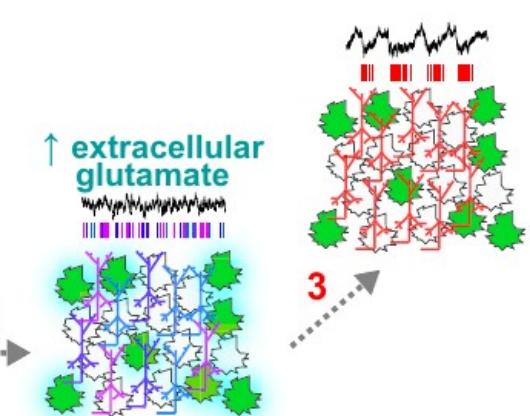
C



desynchronized state

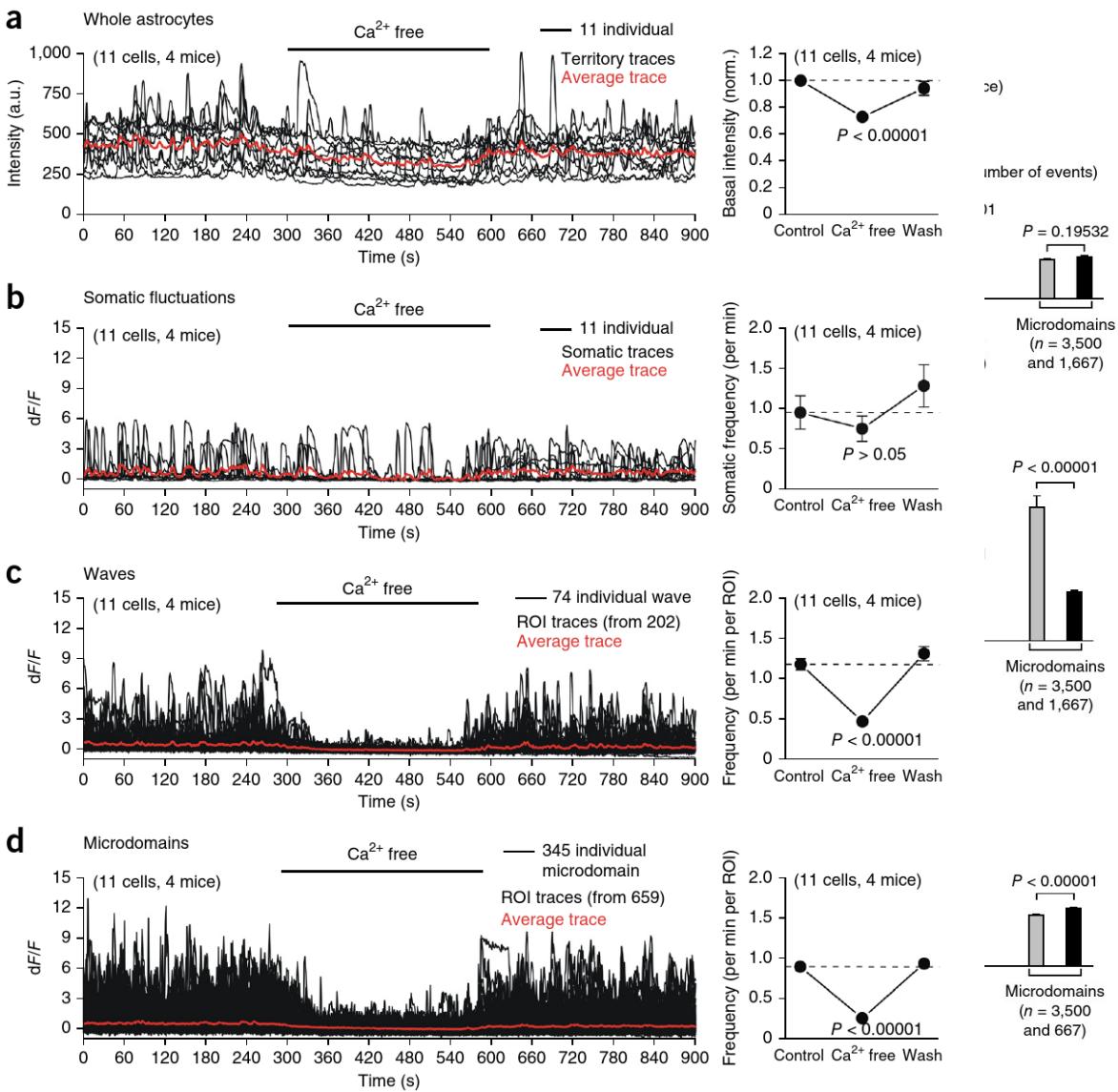
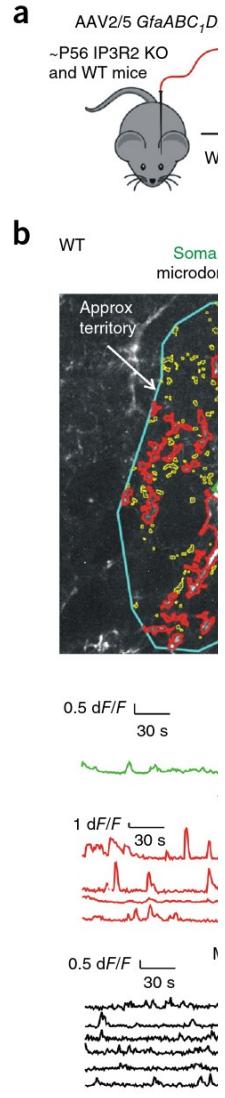


slow oscillation state



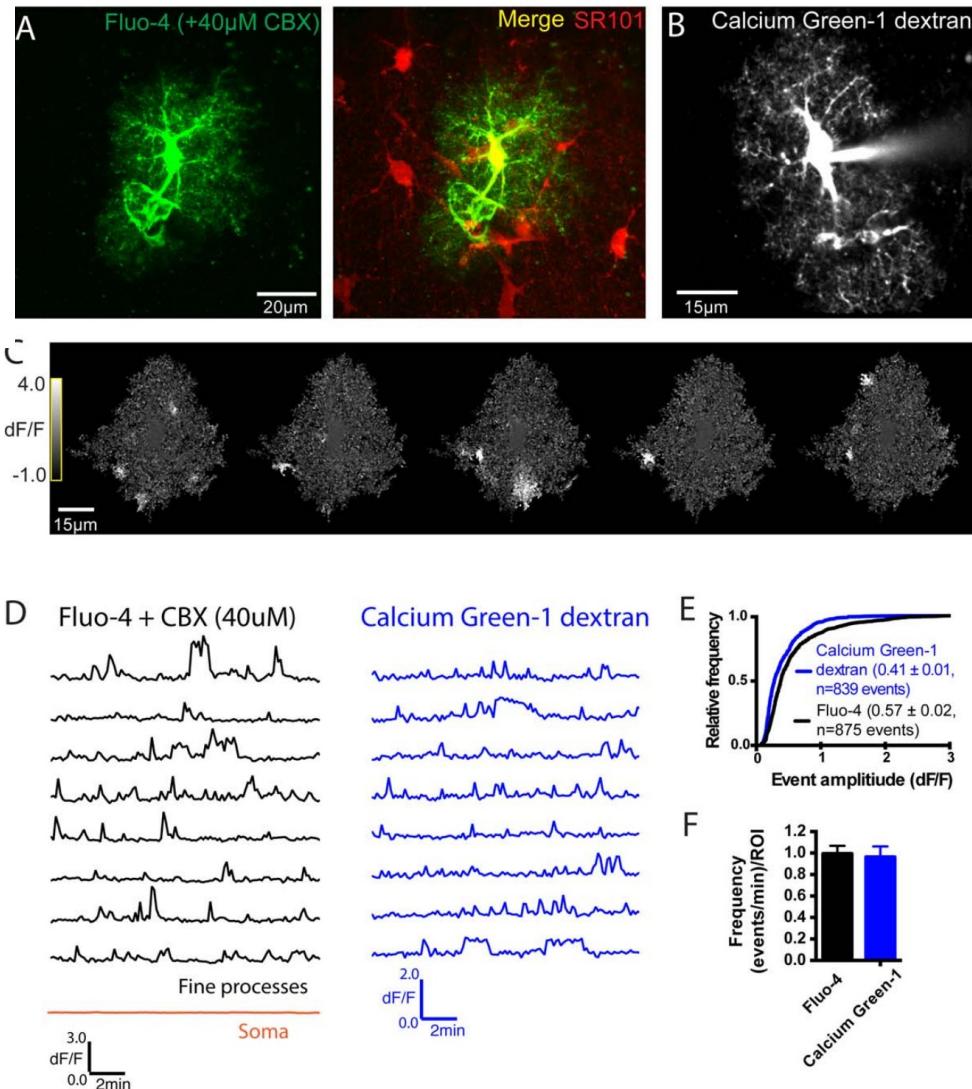
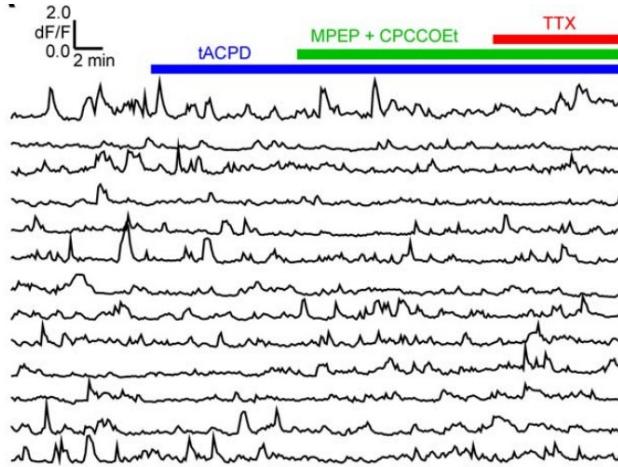
Ca^{2+} signalling in astrocytes from *Ip3r2*^{-/-} mice in brain slices and during startle responses *in vivo*

Rahul Srinivasan^{1,7}, Ben S Huang^{2,7}, Sharmini Venugopal¹, April D Johnston¹, Hua Chai¹, Hongkui Zeng³, Peyman Golshani^{2,4,5} & Baljit S Khakh^{1,6}



Ca^{2+} Transients in Astrocyte Fine Processes Occur Via Ca^{2+} Influx in the Adult Mouse Hippocampus

Ravi L. Rungta, Louis-Philippe Bernier, Lasse Dissing-Olesen, Christopher J. Grotewiel,
Jeffrey M. LeDue, Rebecca Ko, Sibyl Drissler, and Brian A. MacVicar



Synaptically induced sodium signals in hippocampal astrocytes *in situ*

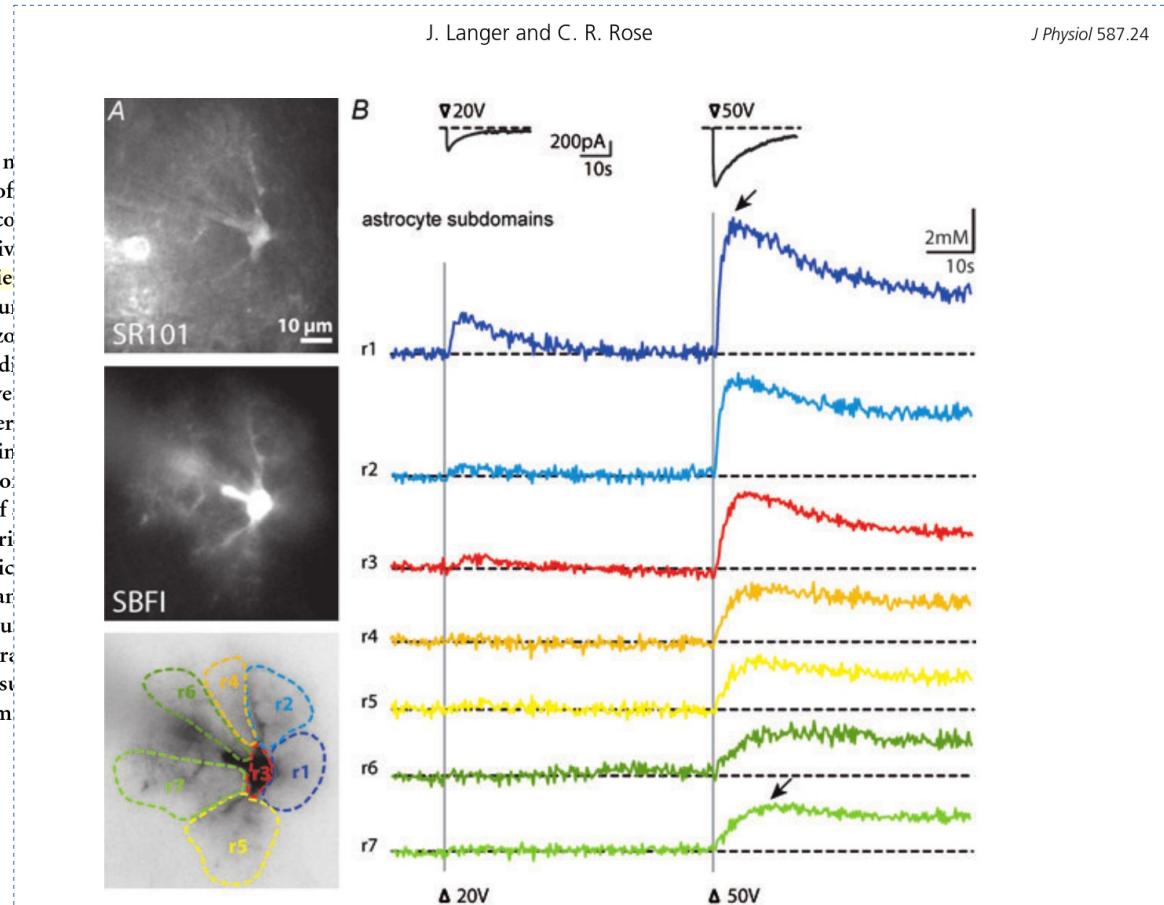
Julia Langer and Christine R. Rose

Institute for Neurobiology, Heinrich-Heine-University Duesseldorf, Universitaetsstrasse 1, 40225 Duesseldorf, Germany

Astrocytes are in close contact to excitatory synapses and express transporters which regulate sodium-dependent uptake of glutamate. In cultured astrocytes, selective activation of transport results in sodium elevations which stimulate Na^+/K^+ -ATPase and glucose metabolism, indicating that synaptic release of glutamate might couple excitatory neuronal activity to sodium homeostasis and metabolism. Here, we analysed intracellular sodium transients by synaptic stimulation in acute mouse hippocampal slices using quantitative sodium imaging with the sodium-sensitive fluorescent indicator dye SBFI (sodium-binding benzophenone phthalate). We found that short bursts of Schaffer collateral stimulation evoke sodium transients in the millimolar range in both CA1 pyramidal neurons and in SR101-positive cells of the stratum radiatum. At low stimulation intensities, glial sodium transients were limited to one to two primary branches and adjacent fine processes and only weakly in the soma. Increasing the number of activated afferent fibres by increasing the stimulation intensity elicited global sodium transients detectable in the processes as well as the somata of SR101-positive cells. Pharmacological analysis revealed that neuronal sodium signals were mainly attributed to sodium influx through ionotropic glutamate receptors. Activation of ionotropic glutamate receptors also contributed to glial sodium transients, while TBOA-sensitive glutamate transporters were the major pathway responsible for sodium influx into astrocytes. Our results thus demonstrate that glutamatergic synaptic transmission in the hippocampus results in sodium transients in SR101-positive cells of the stratum radiatum that are mainly mediated by activation of glutamate transport. They support the proposed link between excitatory synaptic activity, glutamate uptake and sodium transients in hippocampal astrocytes.

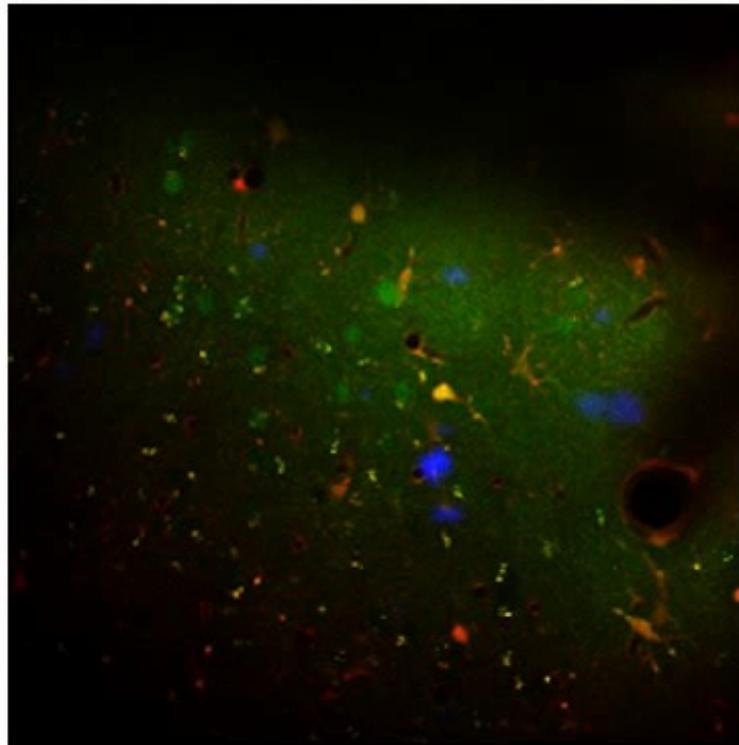
J. Langer and C. R. Rose

J Physiol 587.24



In vivo

frame 0072, time: 35.894 s



Experimental data from lab of
M. Lauritzen, CphU