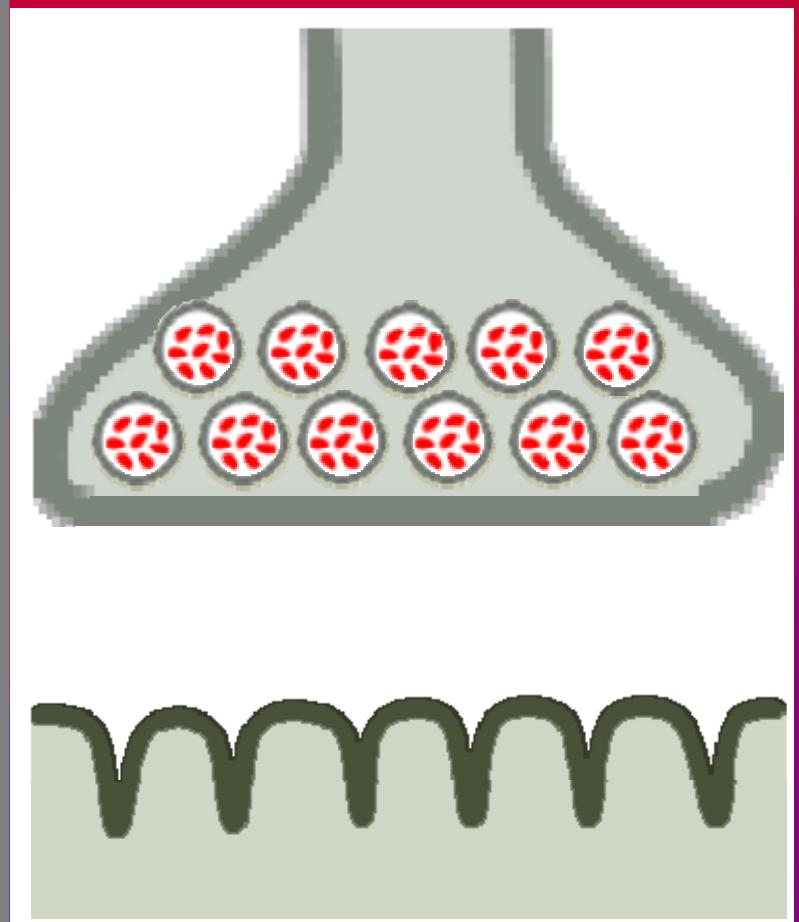
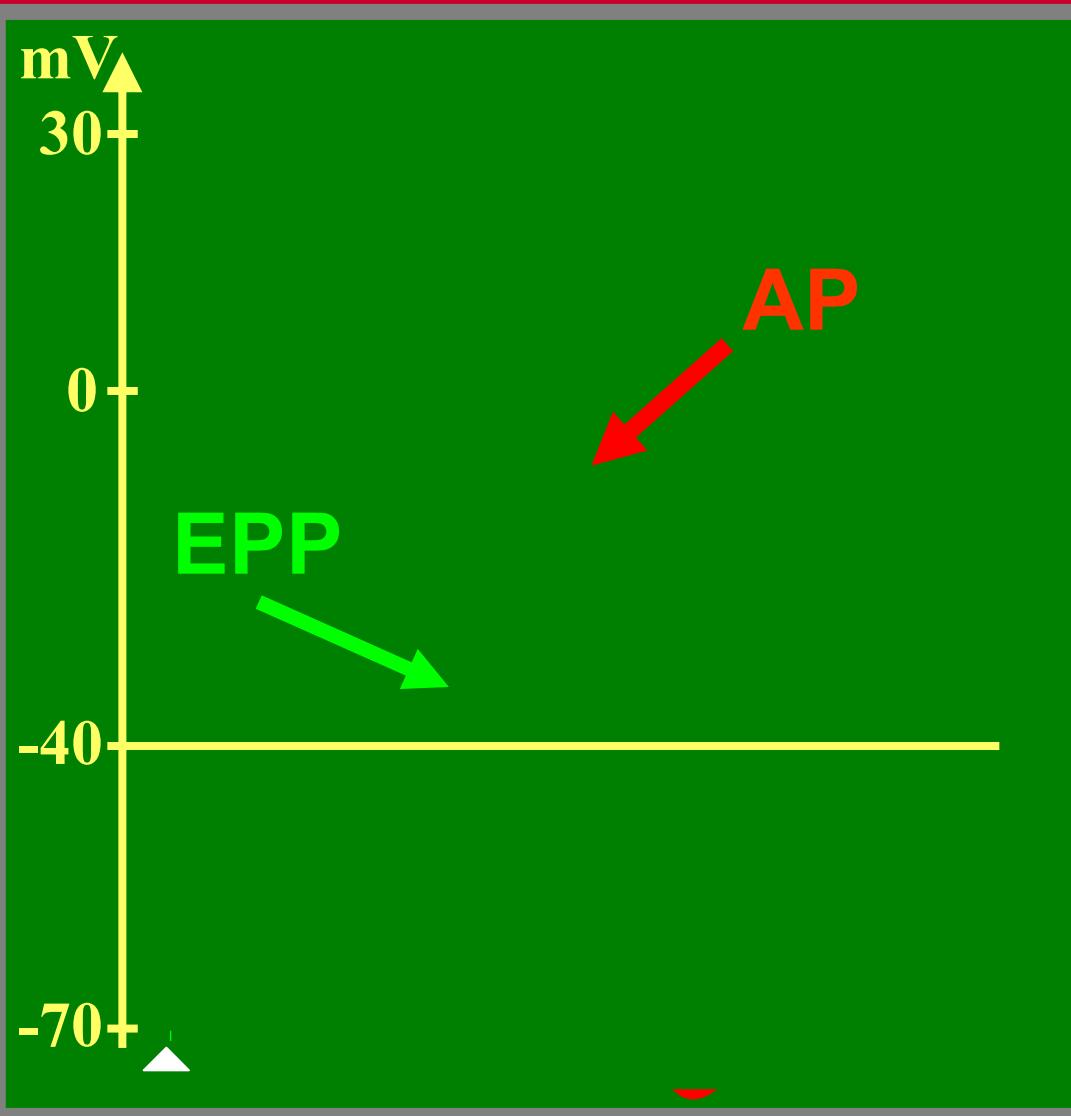


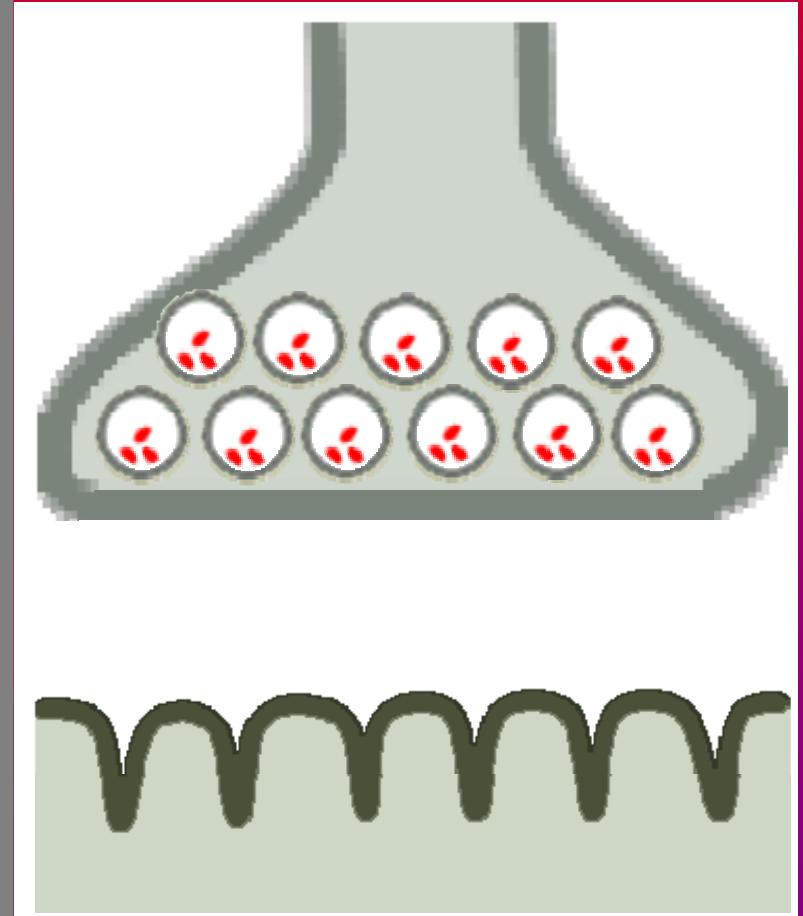
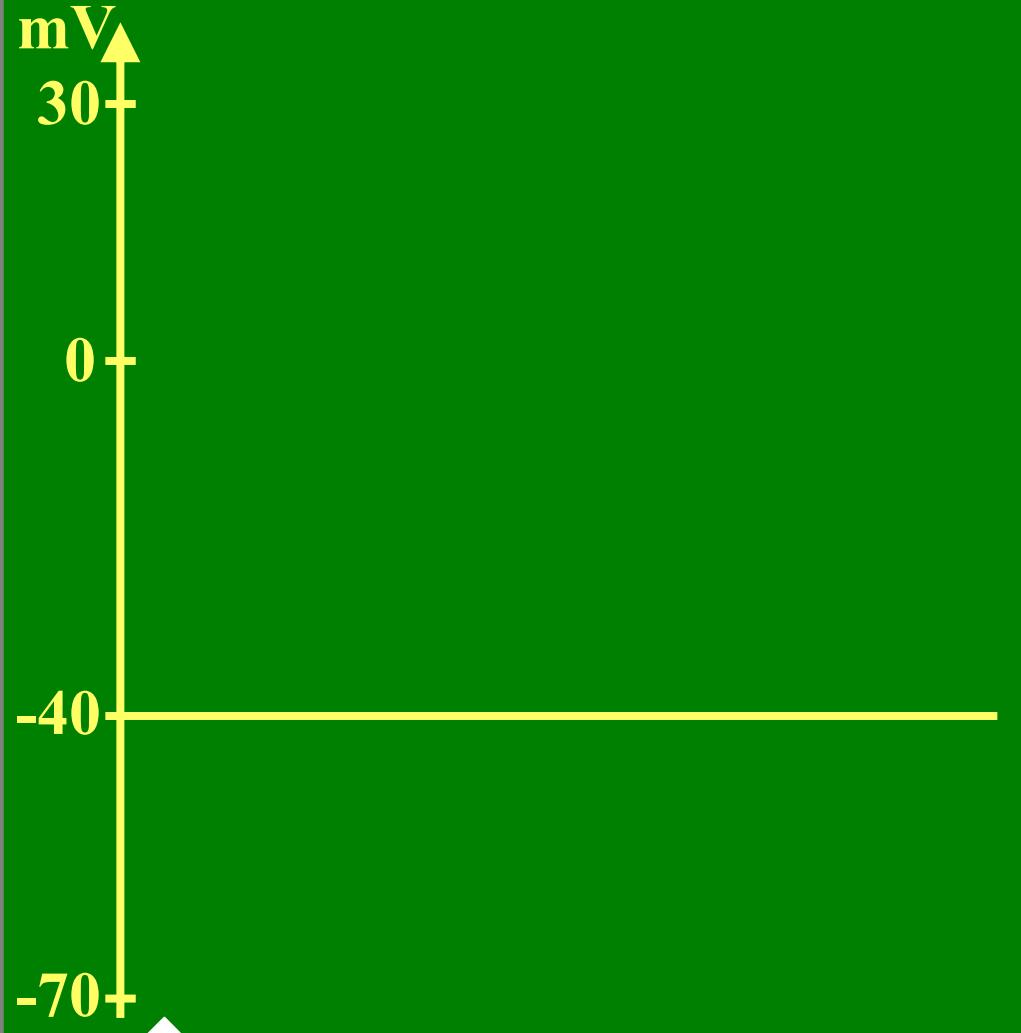
Adrenergic and cholinergic regulation of synaptic quanta release dispersion

Vyskočil, F, Bukharaeva E., Samigullin D., Nikolsky E.

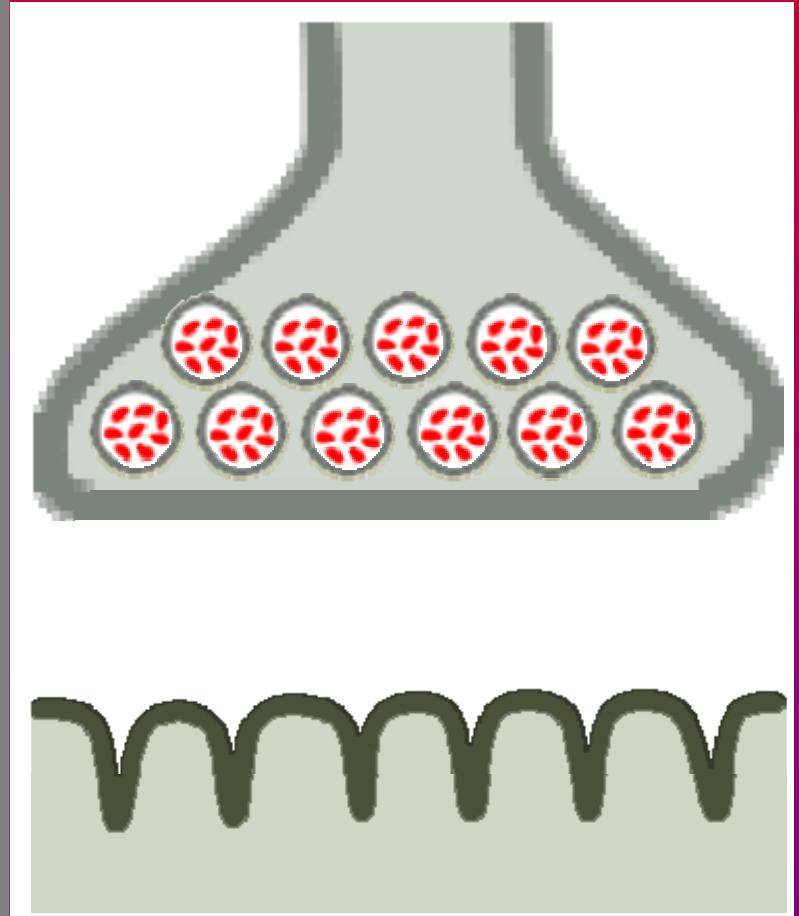
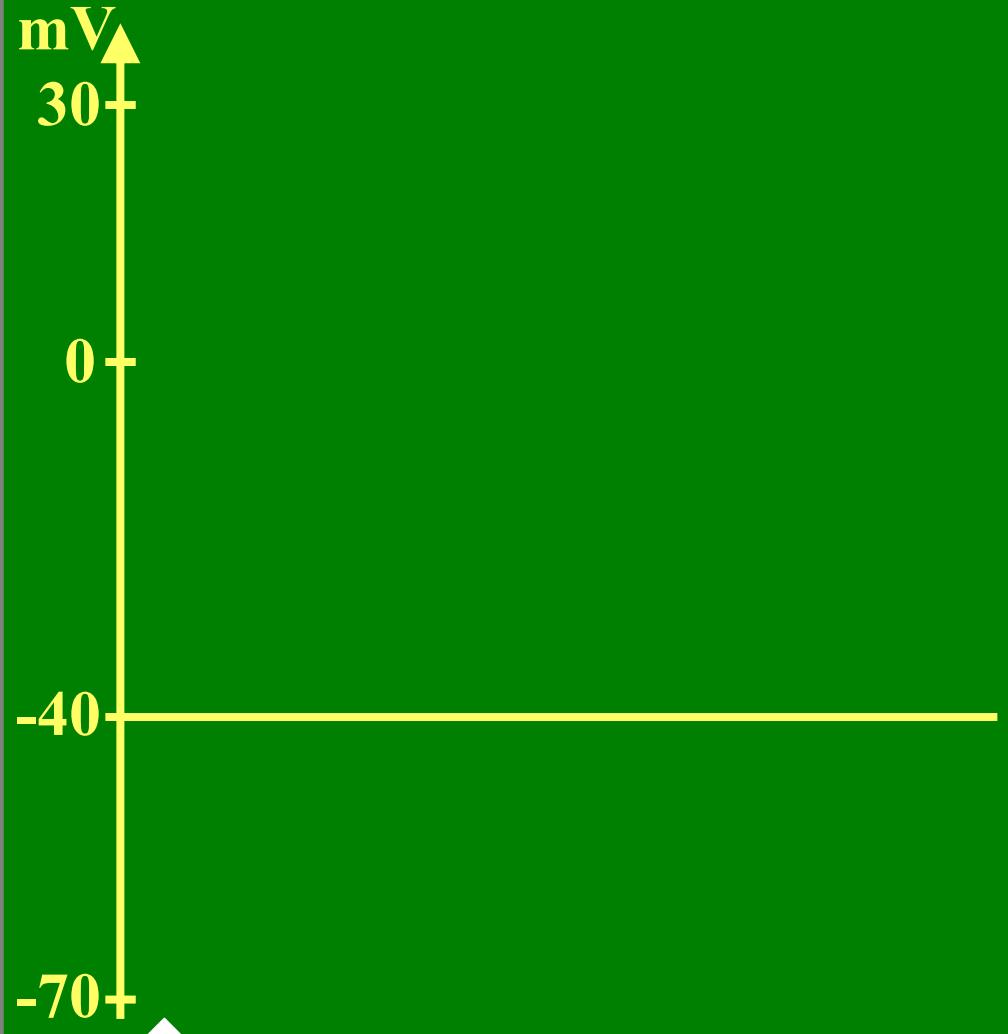
Institute of Physiology, Academy of Sciences, Dept. Anim. Physiology Charles University, Prague, Medical University, Kazan, Russia.



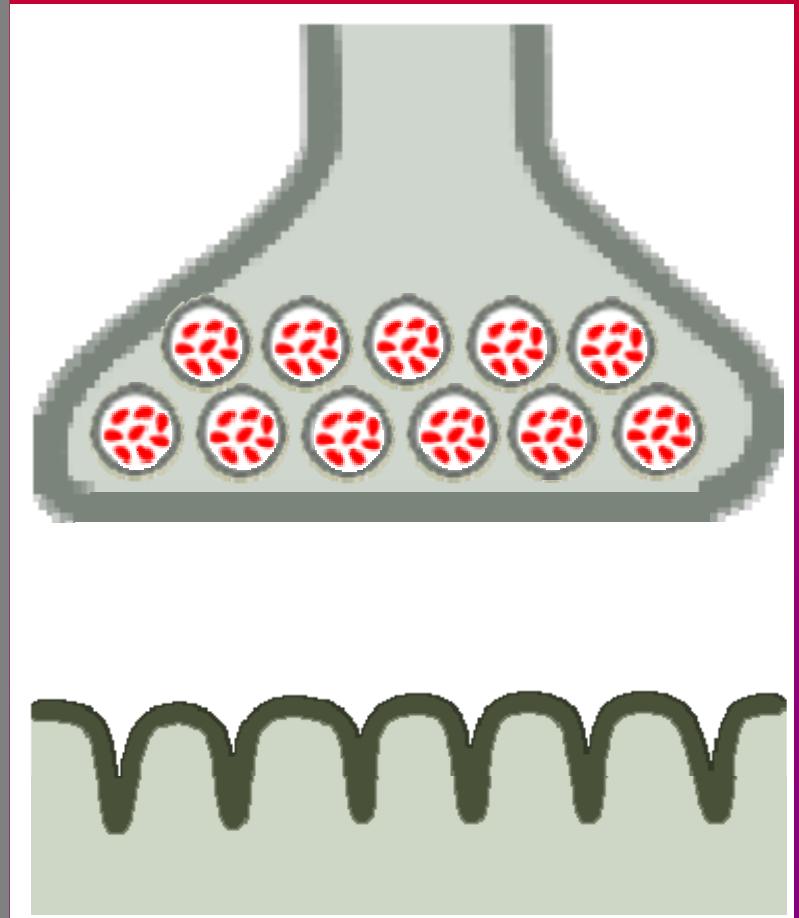
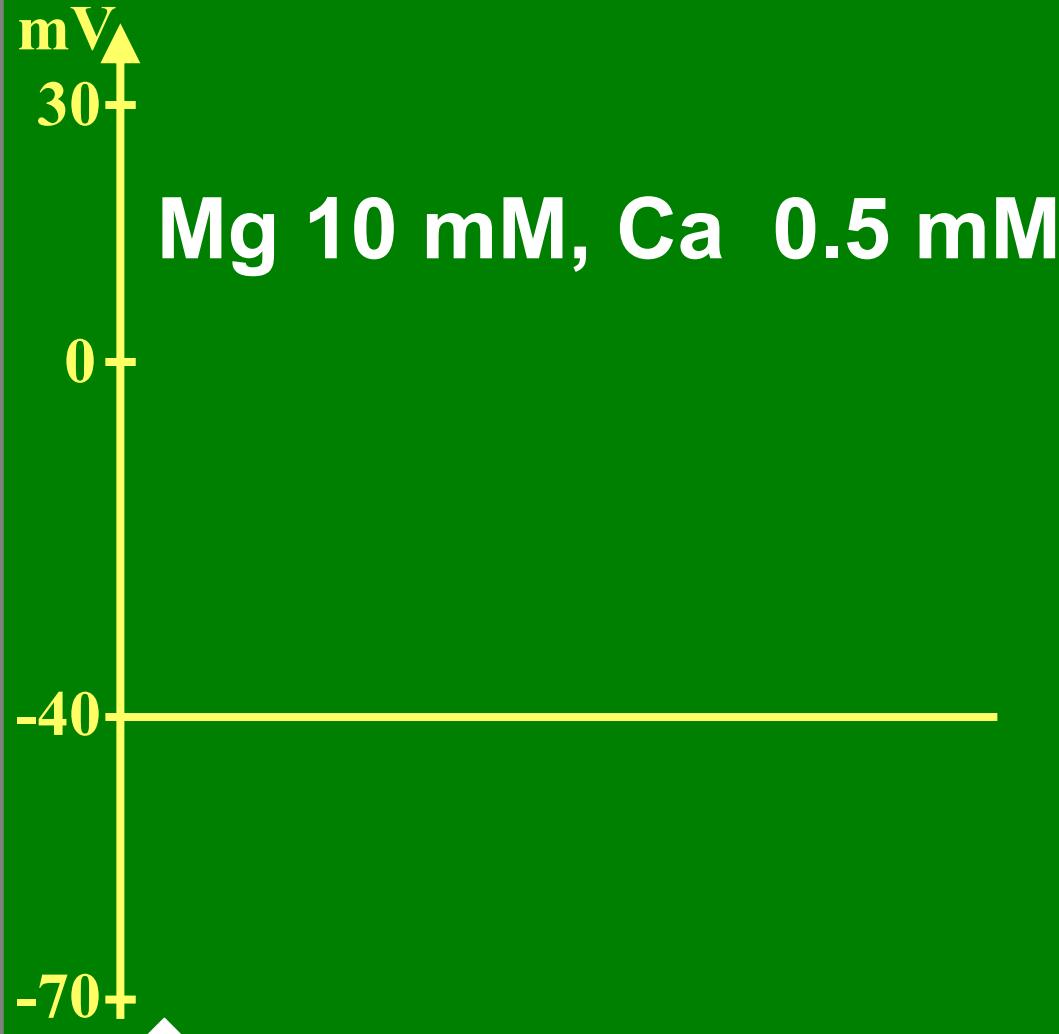
Synaptic transmission modulation by change of quantal size



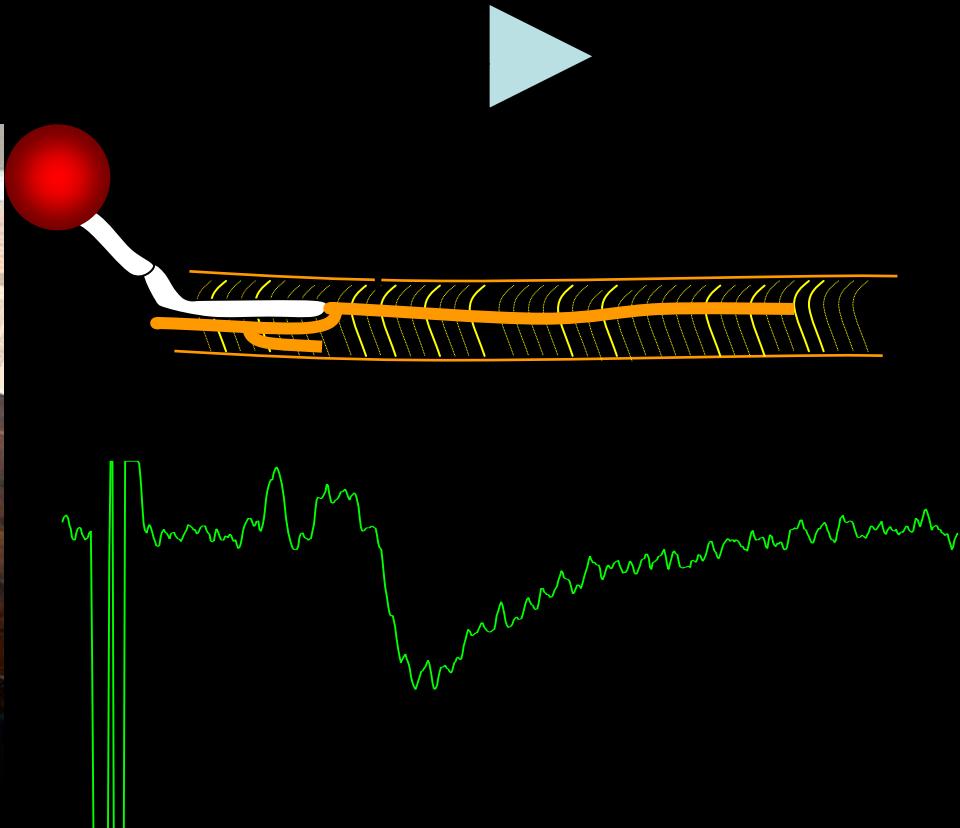
Synaptic transmission modulation by change of EPP quantal content



Synaptic transmission modulation by change of EPP quantal content



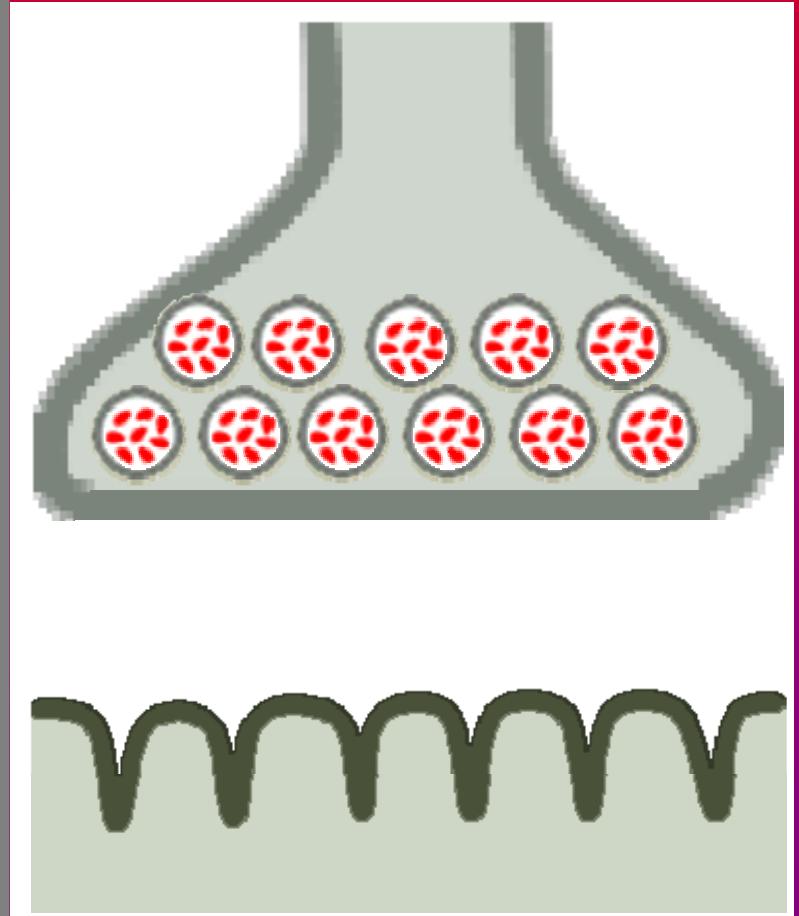
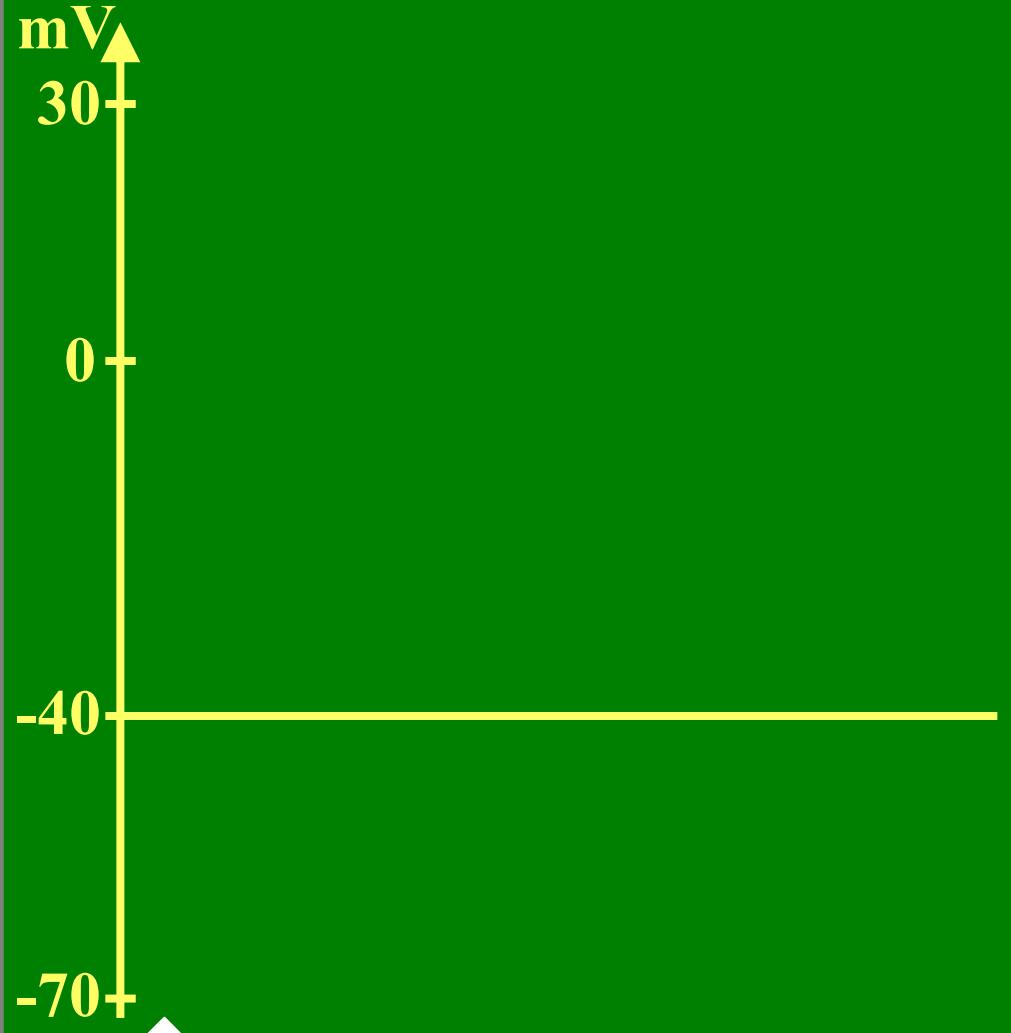
Demonstration of asynchrony of quantal release



Katz B., Miledi R. (1965) The measurement of synaptic delay, and the time course of acetylcholine release at the neuromuscular junction. Proc. R. Soc. B. 161: 483-495.

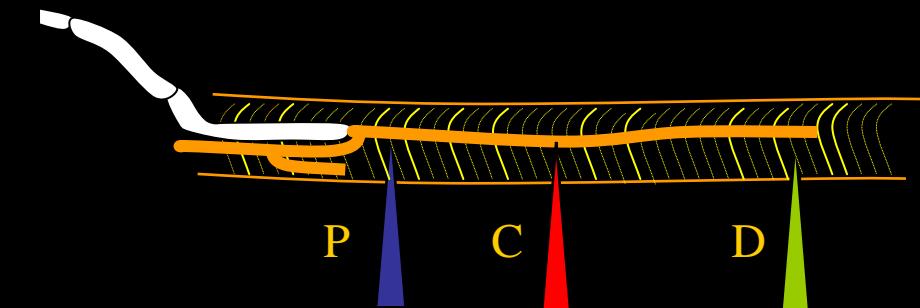
Synaptic delay

Synaptic transmission modulation by change of ACh secretion kinetics

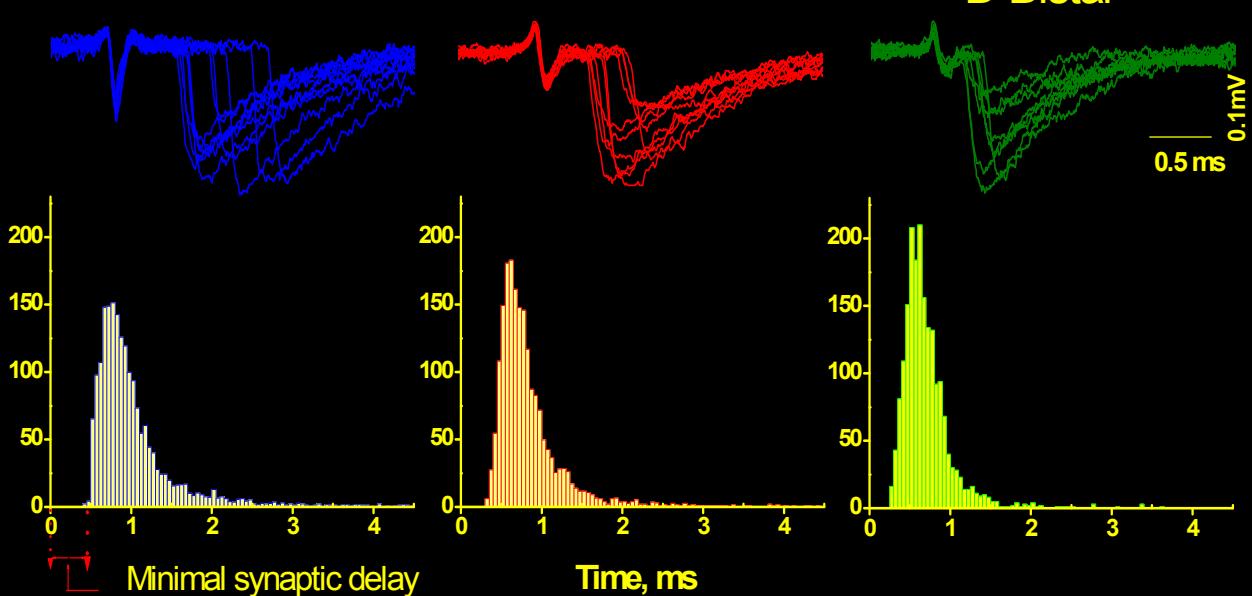




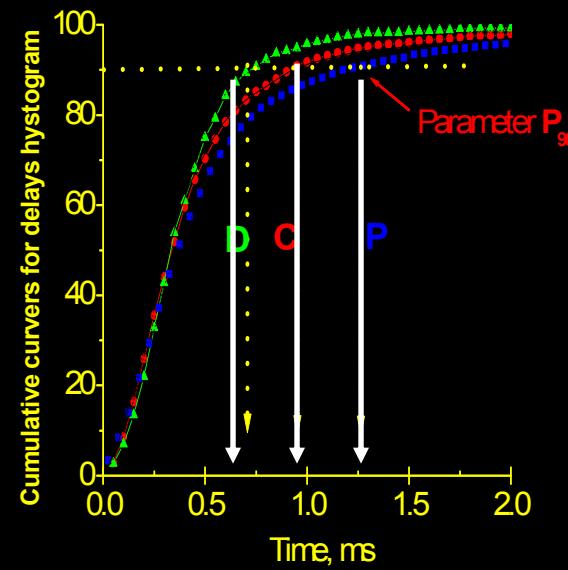
The scheme of experiment



P-Proximal



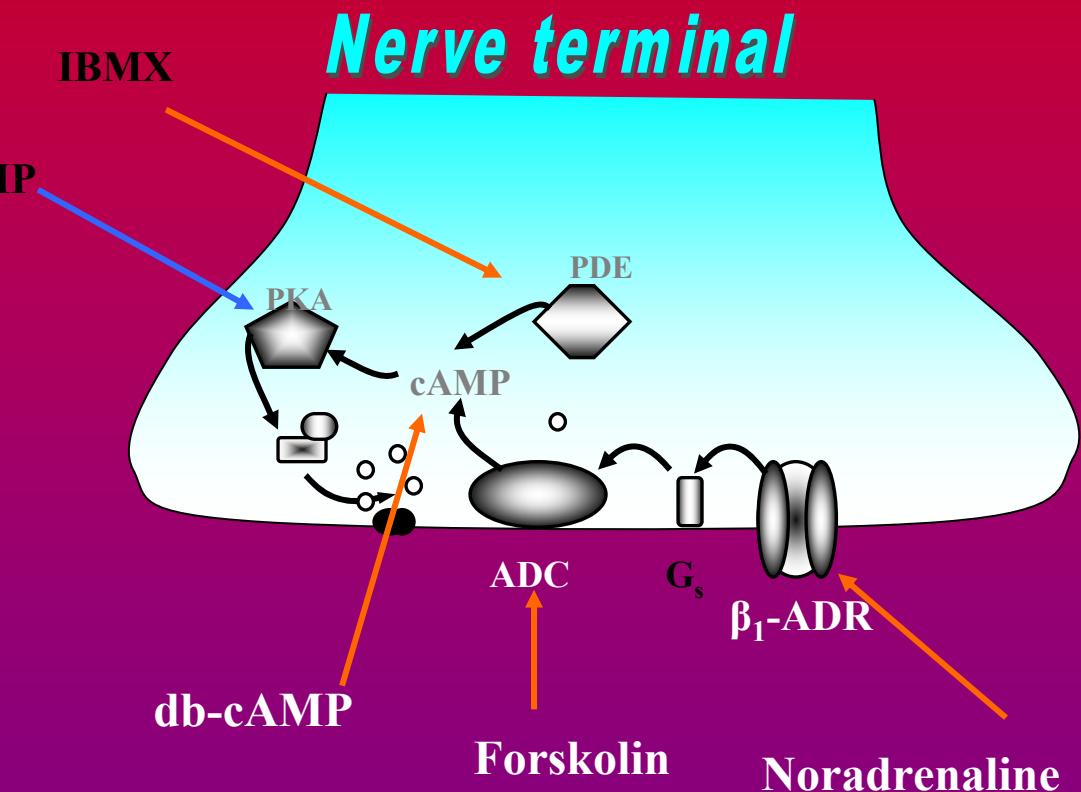
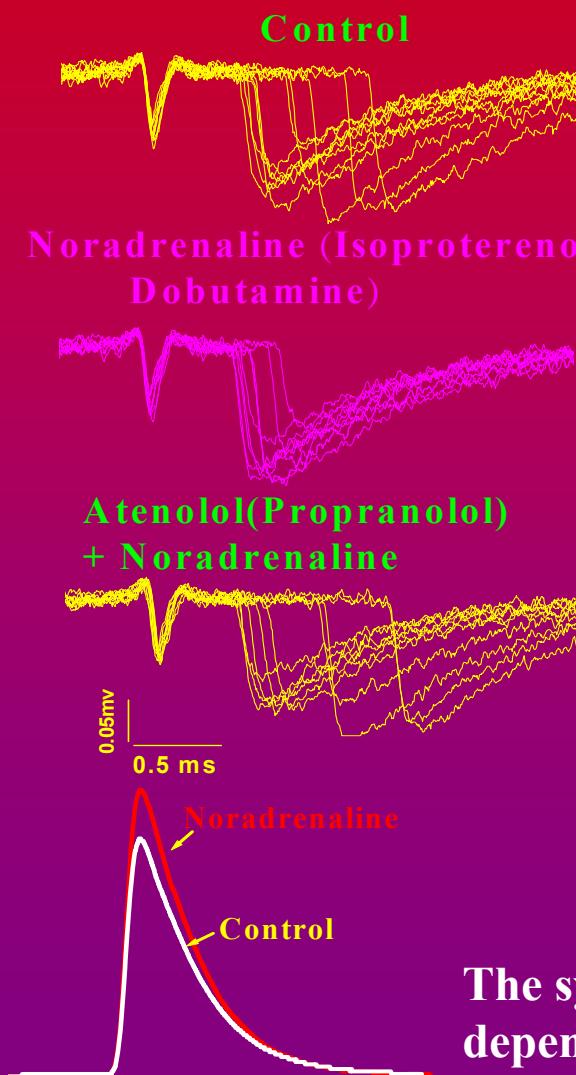
P-90



Possible mechanisms regulating the quanta secretion kinetics

1. The change of Ca^{2+} transients.
2. The change of the colocalization degree of Ca^{2+} -sensors and release sites.
3. The change of the biochemical status of the vesicles and proteins involved into exocytosis.
4. The change of the vesicles mobilization velocity.

Noradrenaline, β_1 -adrenomimetics and the increase of intracellular level of cAMP synchronize the release in the proximal regions where the secretion is originally the most dispersed



The synchronizing noradrenaline action is realized via cAMP-dependent phosphorylation and PKA activation. This synchronization of release leads to the increase of the size of postsynaptic response without changing the quantal content.

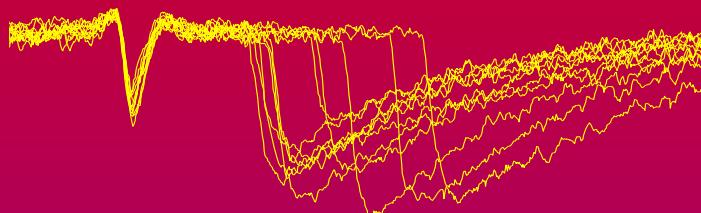
ZESI
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NÁŠ PŘÍKLAD - J.PHYSIOL.1999,
2002, 2004

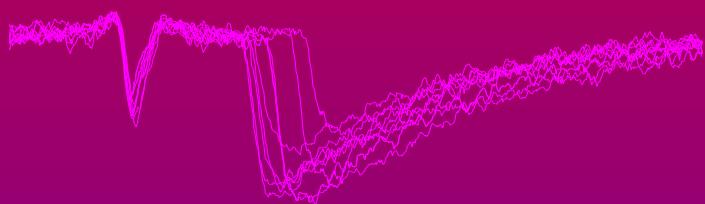
MIKROELEKTRODA



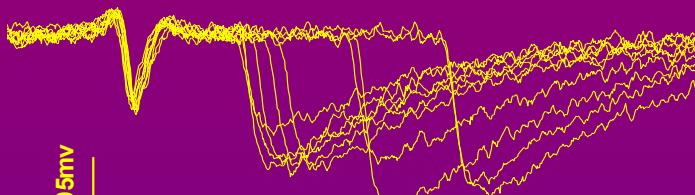
Control



Noradrenaline (Isoproterenol,
Dobutamine)



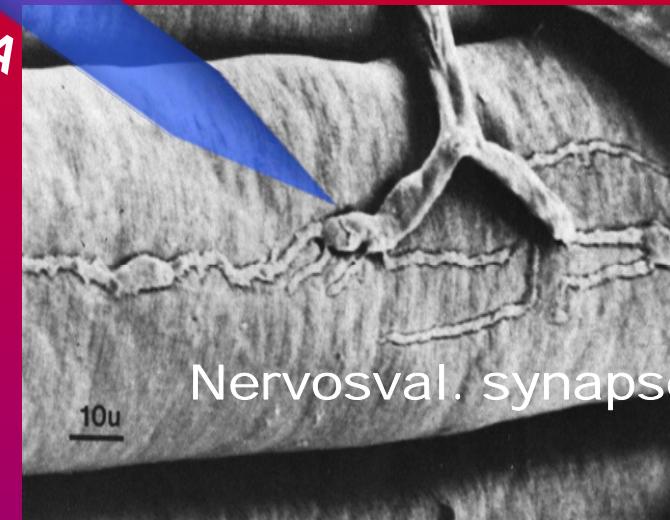
Atenolol(Propranolol)
+ Noradrenaline



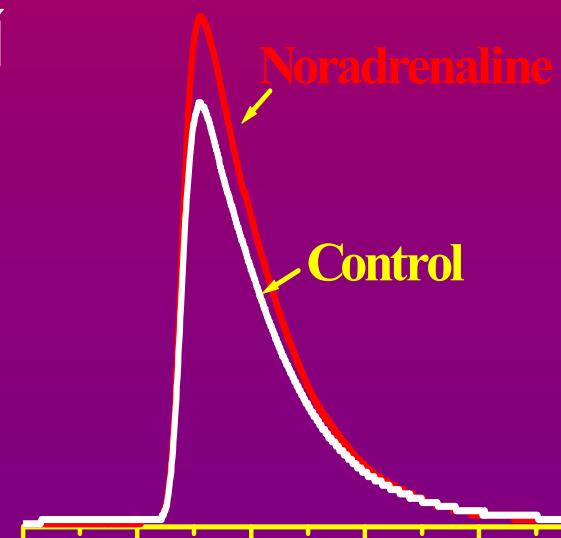
0.05mV
0.5 ms

β

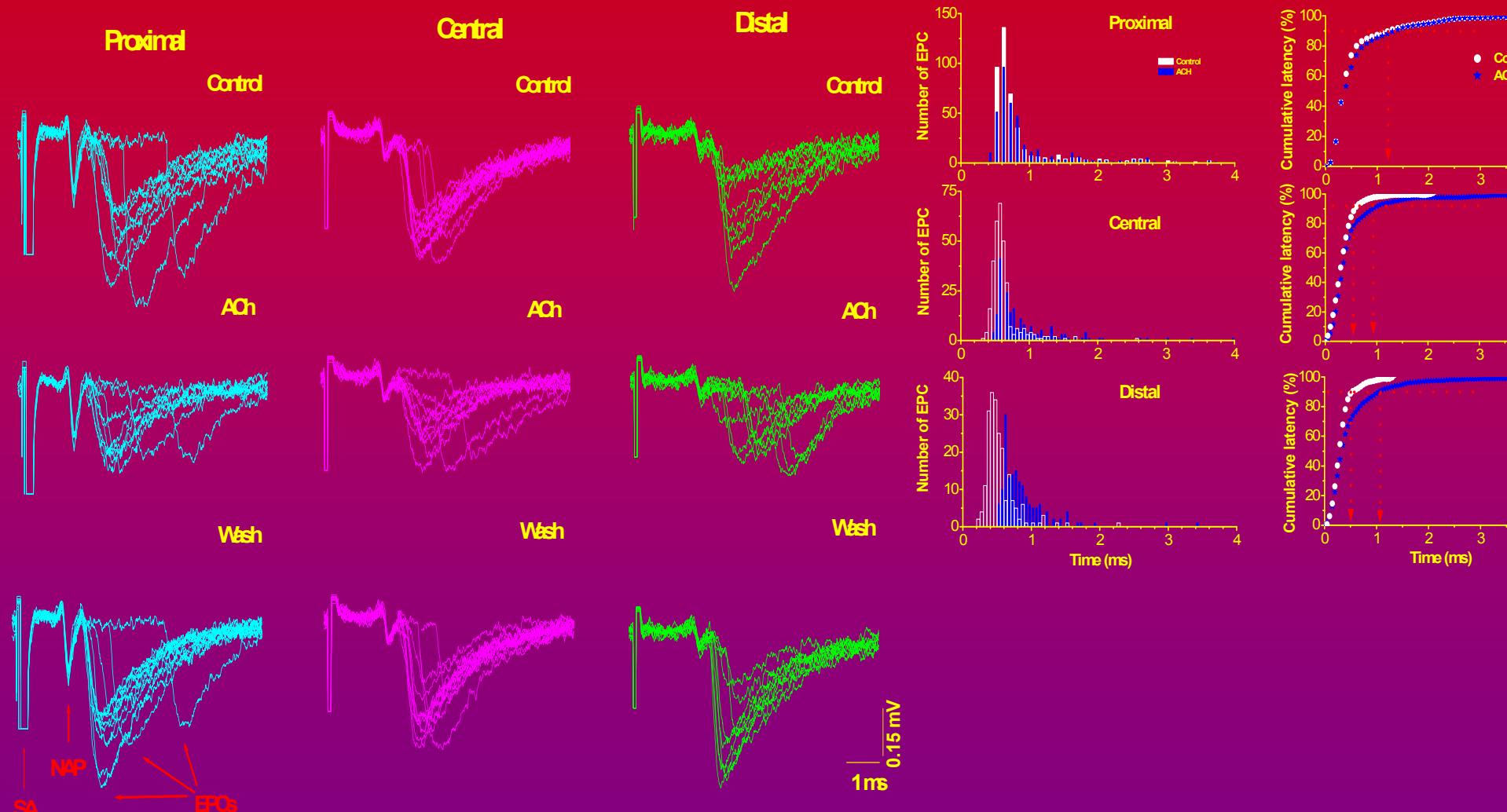
ADRENERGNÍ
RECEPTOR



Nervosval. synapse

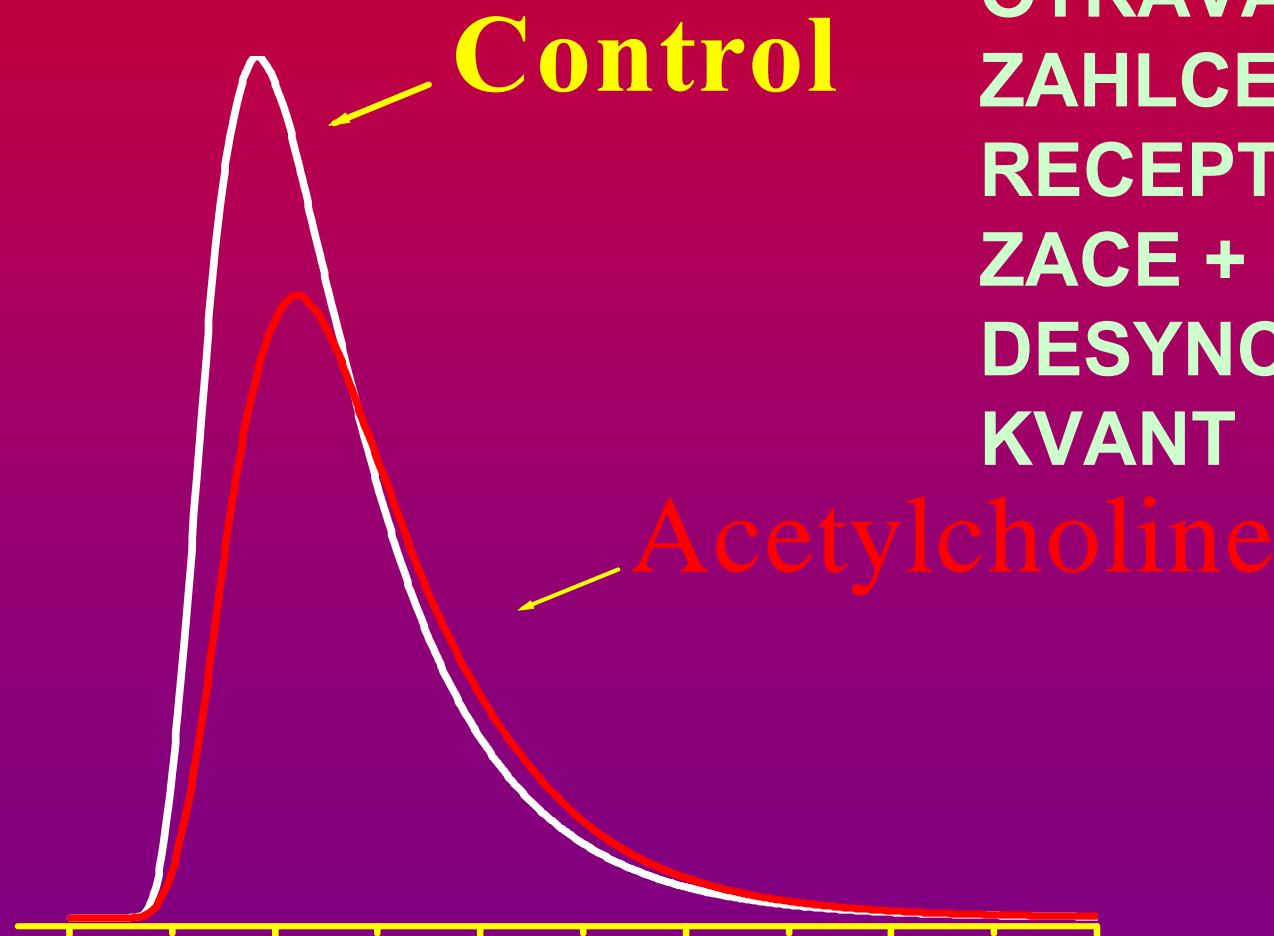


Acetylcholine, carbacholine and nicotine decrease the degree of release synchrony mainly in distal region of synapse



Acetylcholine, carbacholine or nicotine increased the numbers of EPSCs with long release latencies mainly in the distal region of endplate, where the synchronization of transmitter release was the most pronounced.

The reconstruction of integral EPC under normalized quantal content has shown that the pronounced desynchronization of the quantal release under ACh, CCh and nicotine resulted in the decrease of the multiquantal EPC amplitude.

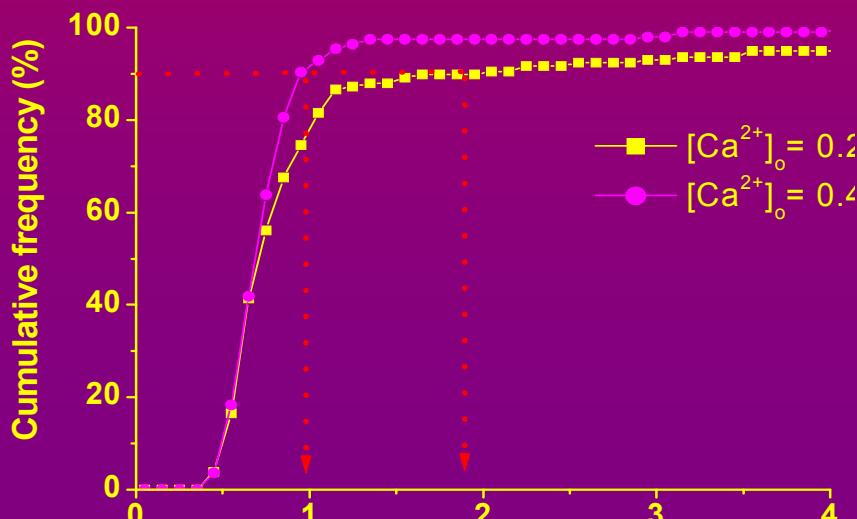
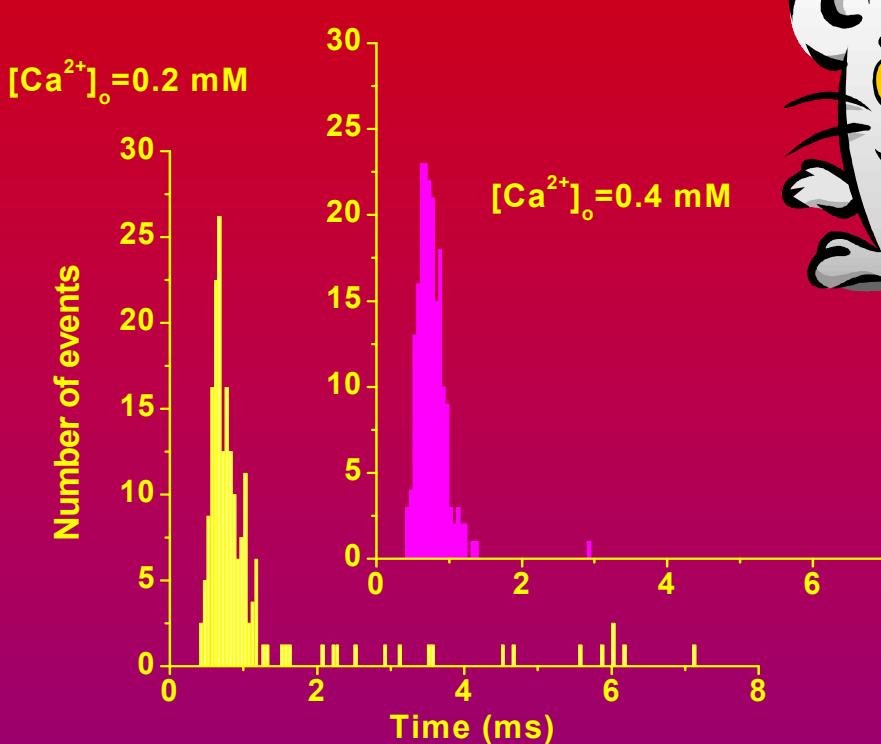
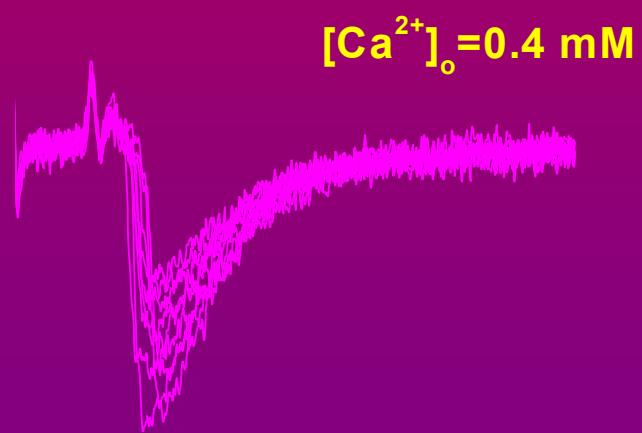
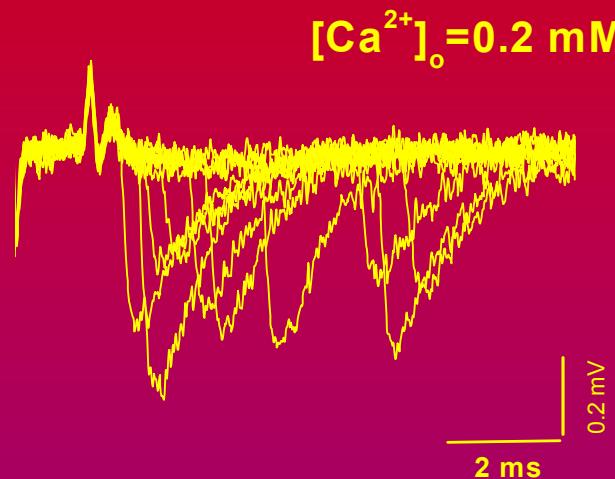


DALŠÍ KOMPLIKACE PŘI
OTRAVÁCH ANTI-ChE:
ZAHLCENÍ, OBSAZENÍ
RECEPTORŮ, DESENSITI
ZACE +
DESYNCHRONIZACE
KVANT

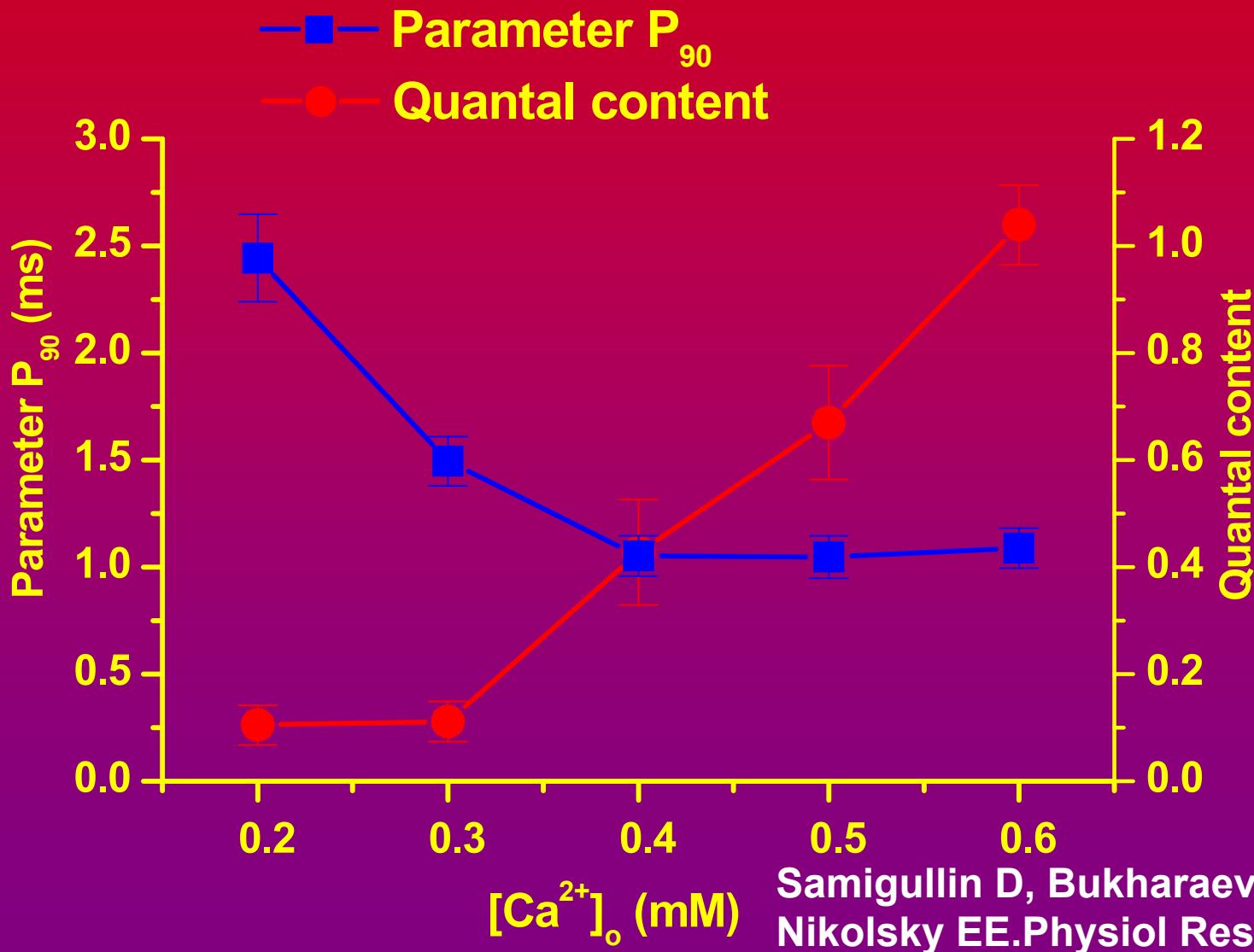
Possible mechanisms regulating the quanta secretion kinetics

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- 2. The change of the colocalization degree of Ca^{2+} -sensors and release sites.**
- 3. The change of the biochemical status of the vesicles and proteins involved into exocytosis.**
- 4. The change of the vesicles mobilization velocity.**

Asynchronous quanta release in low Ca^{2+} at the mouse endplate



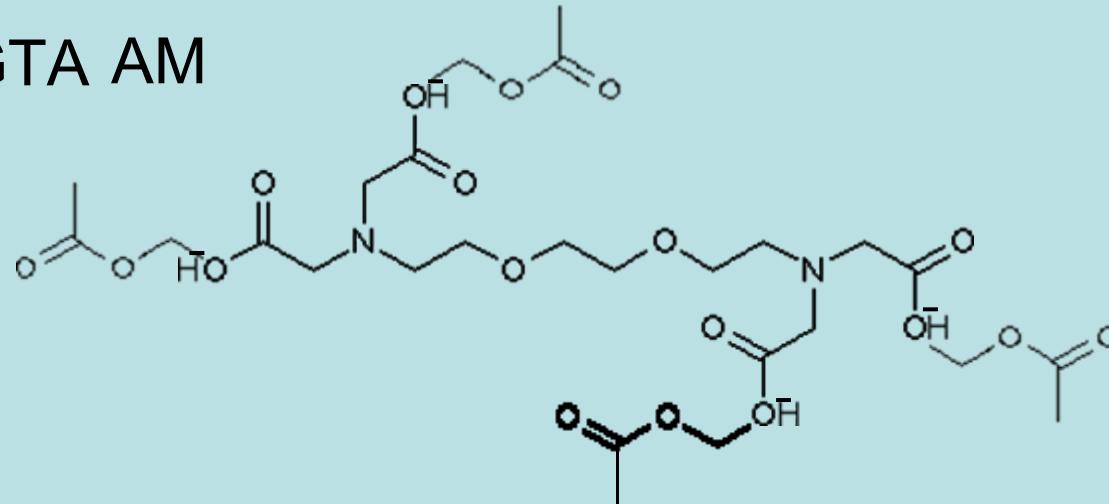
The change of quantal content and secretion synchrony degree



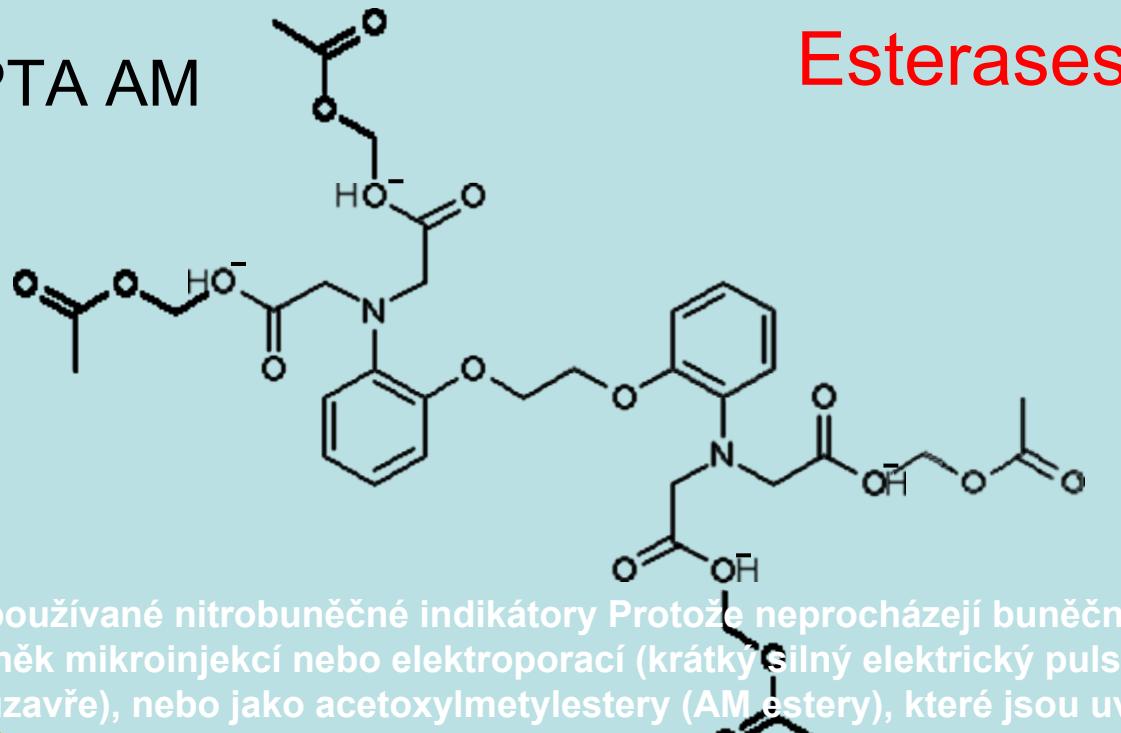
Samigullin D, Bukharaeva EA, Vyskocil F,
Nikolsky EE. Physiol Res. 2005

Slow and fast calcium buffers

EGTA AM



BAPTA AM



Esterases

Ca²⁺

Kalciové sondy jsou nejčastěji používané nitrobuněčné indikátory Protože neprocházejí buněčnou membránou, dostávají se do buněk mikroinjekcí nebo elektroporací (krátký silný elektrický puls na ms otevře membránu a ta se hned uzavře), nebo jako acetoxymetylestery (AM estery), které jsou uvnitř buňky štěpeny nitrobuněčnými esterázami za vzniku negativně nabitéch sond, uzavřených v buňce.

Possible mechanisms regulating the quanta secretion kinetics

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Skorinkin AI, Shaihutdinova AR, Vyskocil F.

Model of concentration changes across the synaptic cleft during a single quantum release.

Gen Physiol Biophys. 2008 Mar;27(1):19-24.

Gilmanov IR, Samigullin DV, Vyskočil F, Nikolsky EE, Bukharaeva EA.

Modeling of quantal neurotransmitter release kinetics in the presence of fixed and mobile calcium buffers.

J Comput Neurosci. 2008 Apr 22.