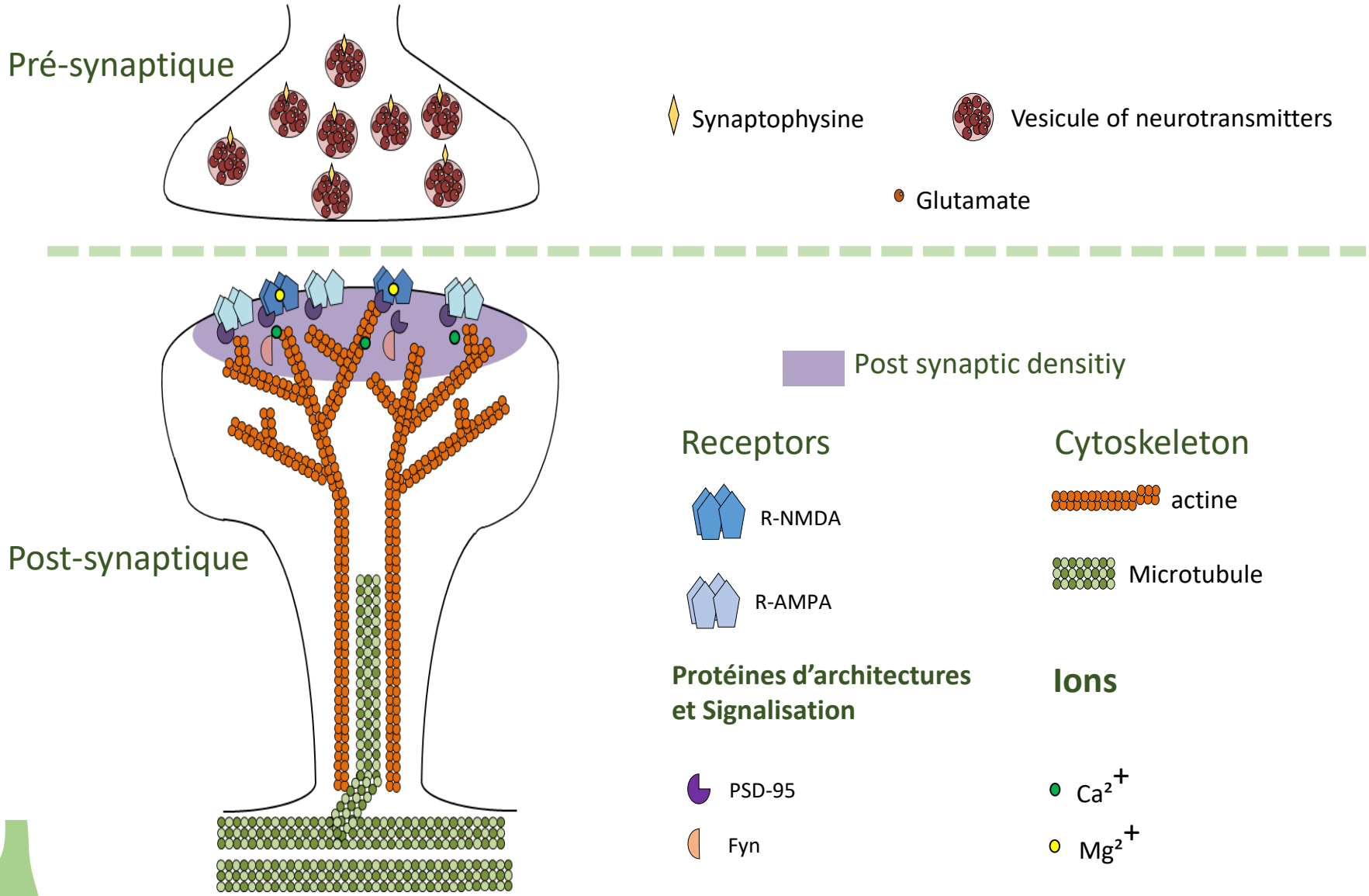
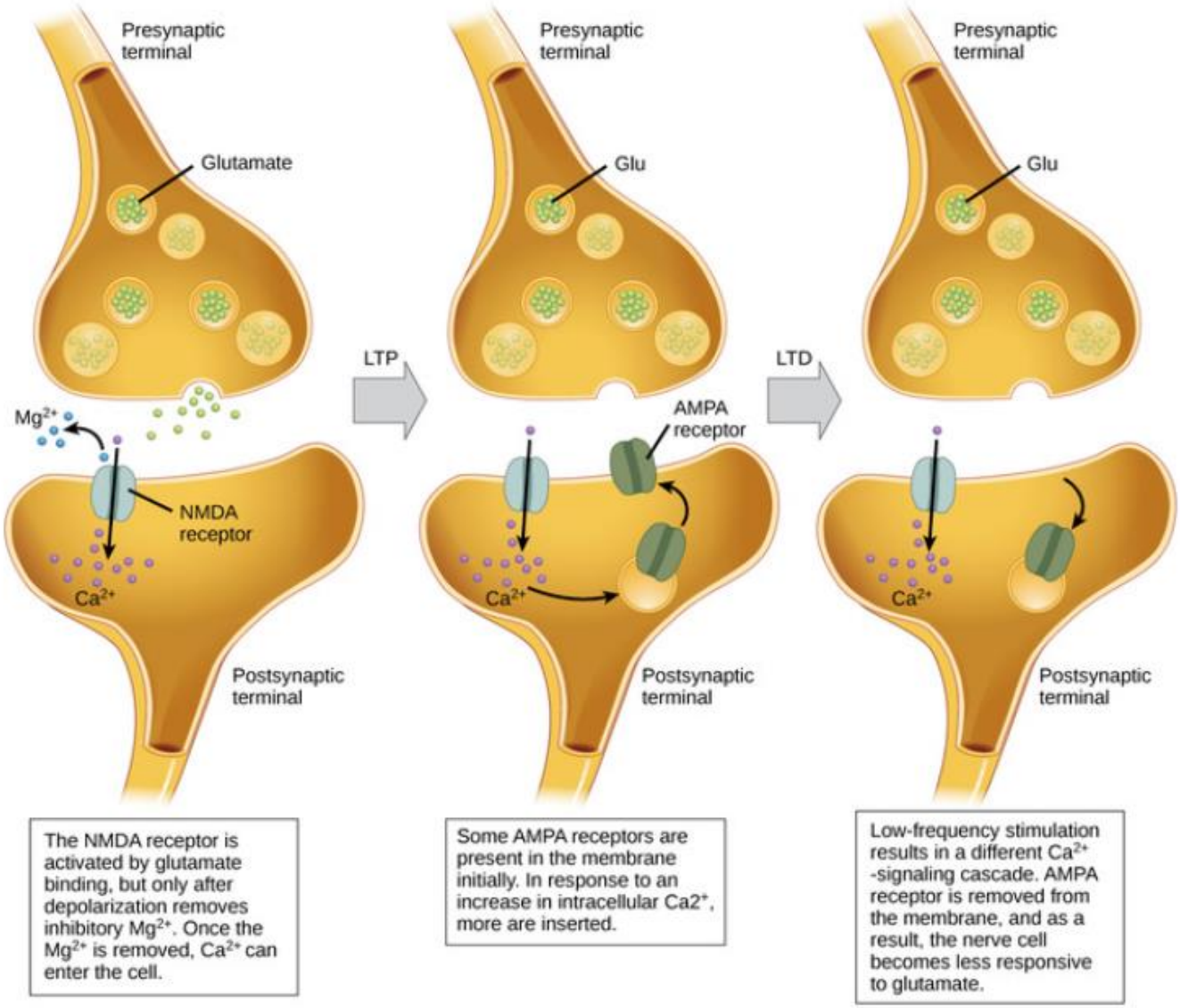
Excitatory synapses

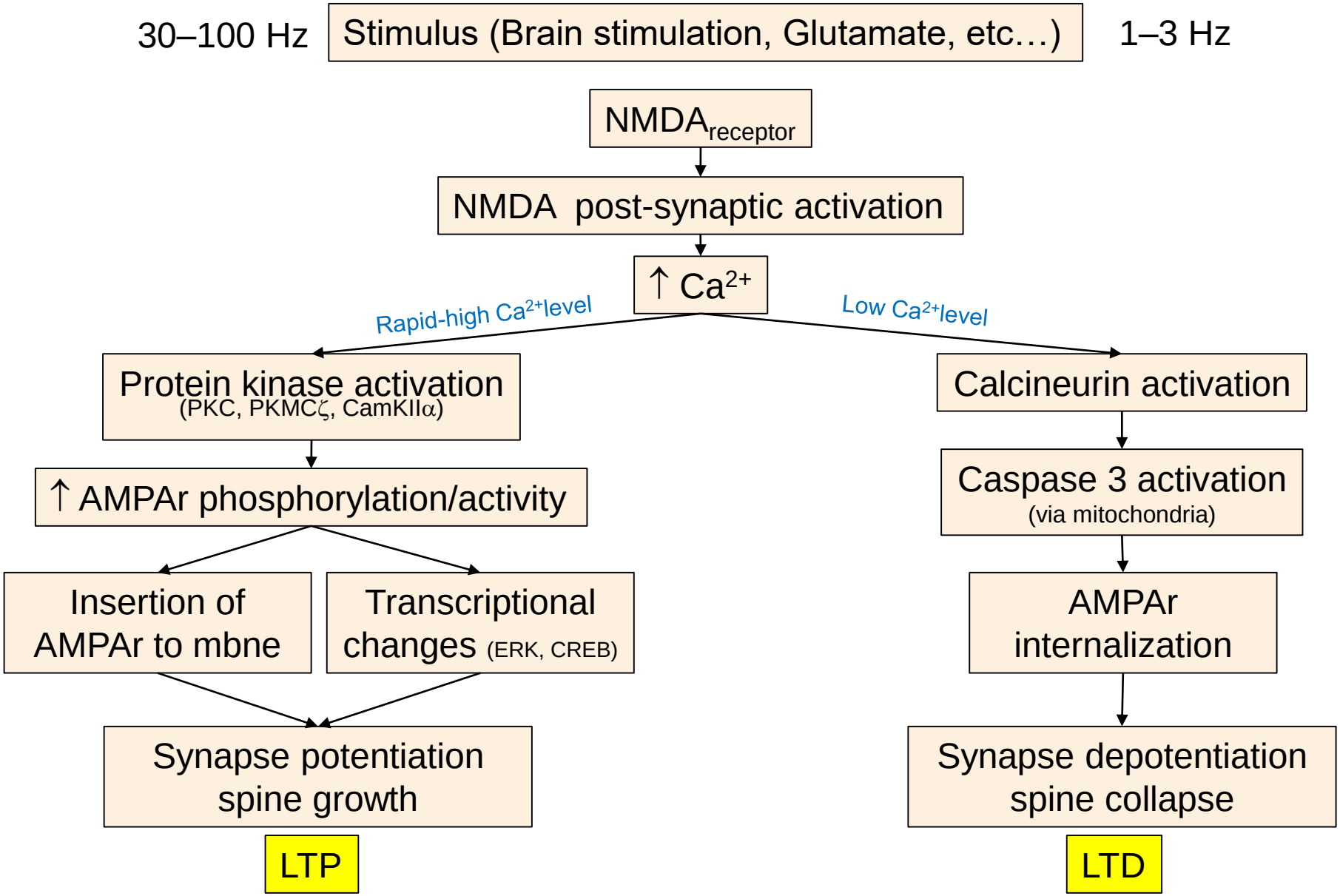


Slide from A. Buisson (Grenoble Institute of Neuroscience)

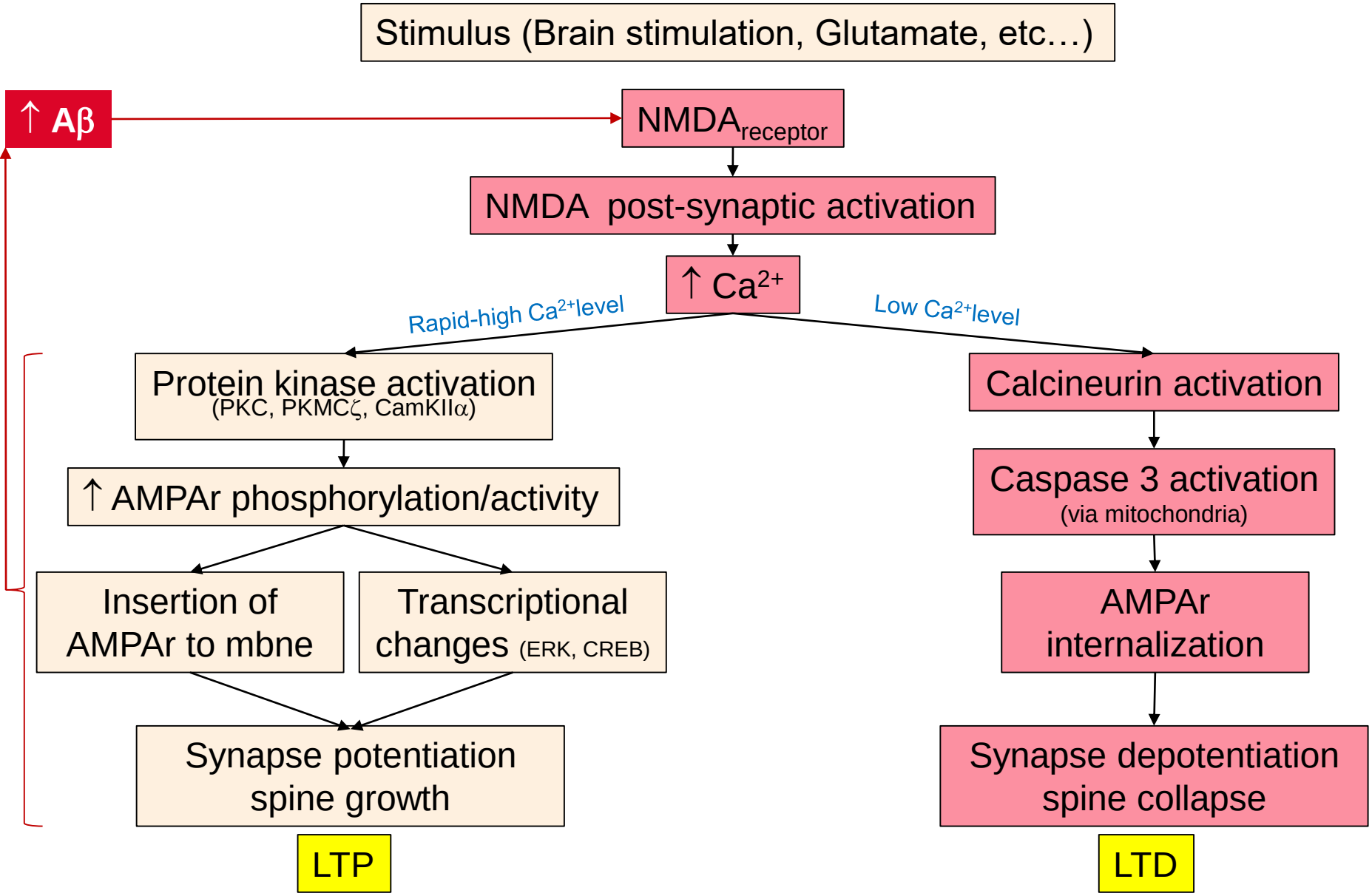
MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY
Long term depression (LTD)



MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY
Equilibrium between LTP and LTD



MECHANISMS ASSOCIATED TO THE PHYSIOLOGY OF MEMORY
Equilibrium between LTP and LTD - Regulation by Aβ



FACTORS SUGGESTING REGULATION OF LTP/LTD BY Aβ

- Neuronal activity increase Aβ production
- Aβ link to NMDAr
- Aβ modulates intracell Ca^{2+} (through many different mechanisms)

  (Demuro et al., 2005; Hudry et al., 2012; Mattson et al., 1992; Wu et al., 2010; Zempel et al., 2010)
- Aβ modulates calcineurin (Wu et al., 2012)
- Aβ induces caspase-3 activation (Chen et al., 2013; D'Amelio et al., 2011; Liu et al., 2010)
- Aβ causes internalization of AMPAr and NMDAr

  (Hsieh et al., 2006; Koffie et al., 2011; Snyder et al., 2005; Wang et al., 2004)

Tau → regulates synaptic function

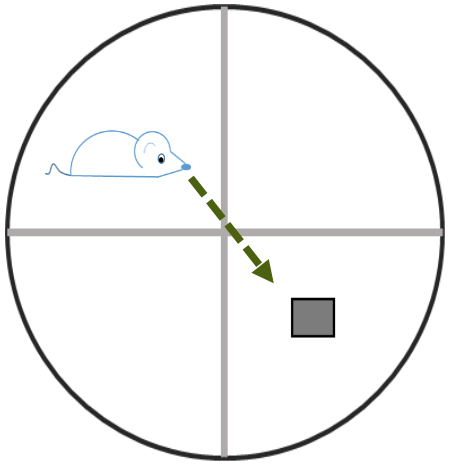
Aβ → regulate the ability of Tau to regulate synaptic function

General publications

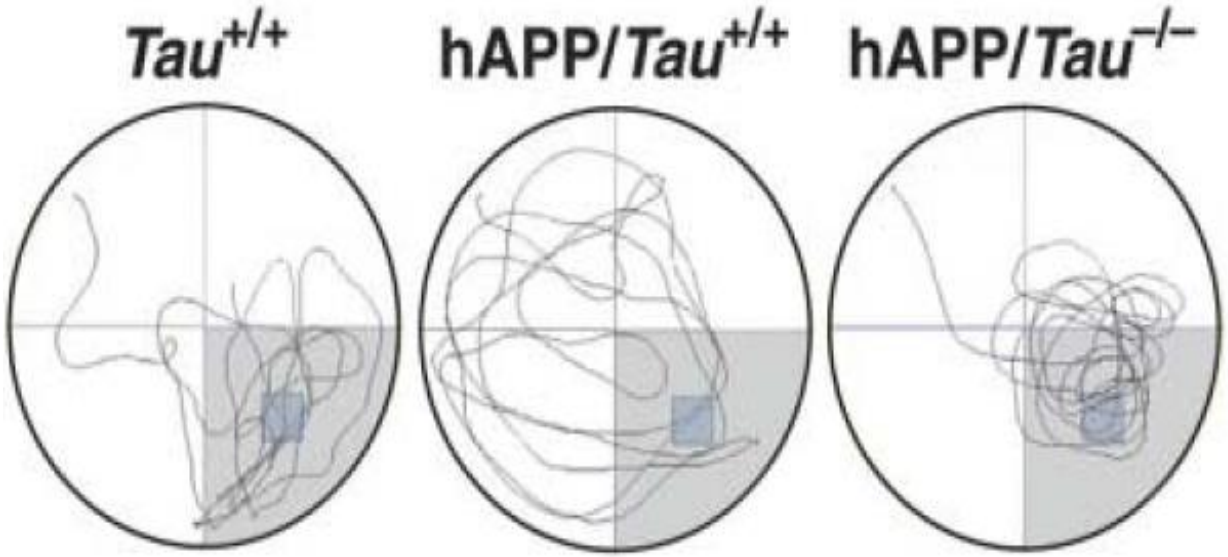
(Christie et al., 2001; Li et al., 2009; Shankar et al., 2008)

INTERACTION OF Aβ AND TAU AT POST-SYNAPTIC LEVEL

Tau mediates Aβ toxicity



Roberson et al., 2007, Science

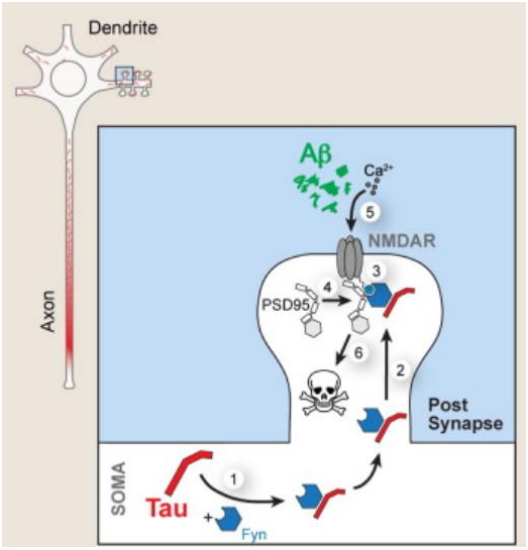


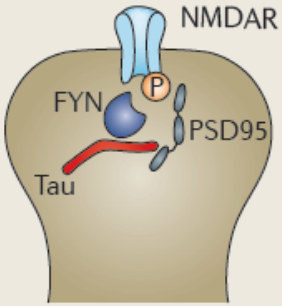
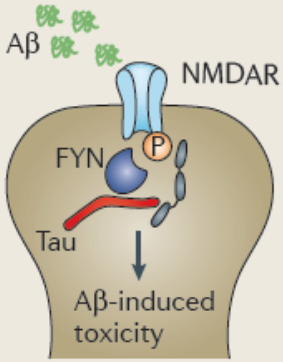
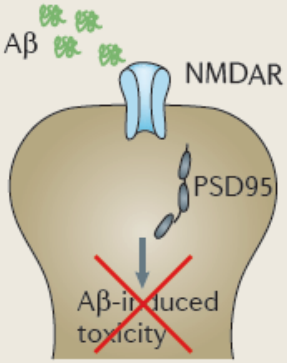
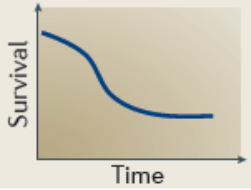
- **hAPP: mutations swe/ind**

Disruption of spatial memory induced by hAPP expression is dependent of tau.

INTERACTION OF Aβ AND TAU AT POST-SYNAPTIC LEVEL
Interaction through the fyn/PSD95/NMDA$_r$

Tau mediates Aβ toxicity



	Healthy control	APP^{tg}	APP^{tg}/*tau*$^{-/-}$
Postsynapse			
Dendrite			
Soma			
Axon			
Excitotoxicity		Increased	Decreased
Memory		Decreased	Increased
Mortality			

Ittner, 2010. Cell 142(3), 387-397. DOI: 10.1016/j.cell.2010.06.036.
Ittner, L.M., Gotz, J., 2011. Nat. Rev. Neurosci. 12(2), 65-72. DOI: 10.1038/nrn2967.