BNN Course: Synaptic Plasticity

Abigail Morrison, Philipp Weidel

Institute of Neuroscience and Medicine (INM-6)
Jülich Research Center

Freiburg, 31th May 2018

Reminder:

- git pull (To access new changes to the repository)
- Handouts part 3 (www.nest-simulator.org/introduction-to-pynest/)

Synaptic plasticity

- considered to be the biological substrate of learning and memory

Synaptic changes can be induced by specific stimulation conditions:

- presynaptic firing rates
- spike timing

Detailed biophysical models

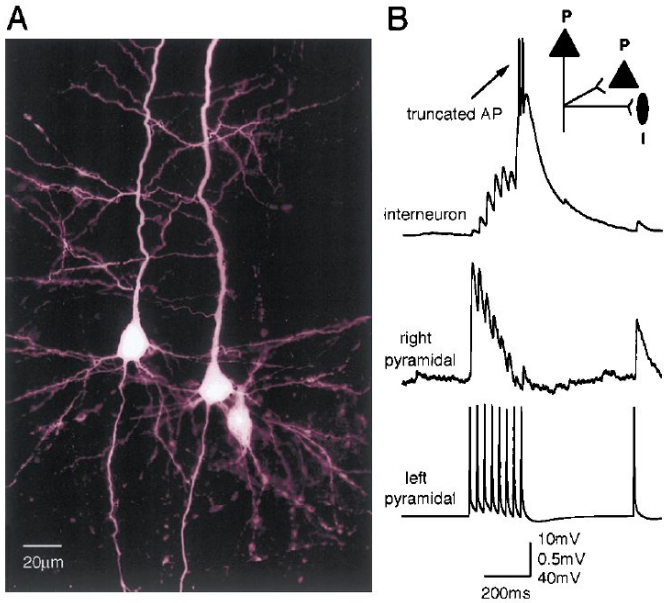
- crucial to understand undelying biological mechanisms

Phenomenological models

- describe synaptic changes without reference to mechanism
- generally more tractable and less computationally expensive

Outline

Short-term plasticity

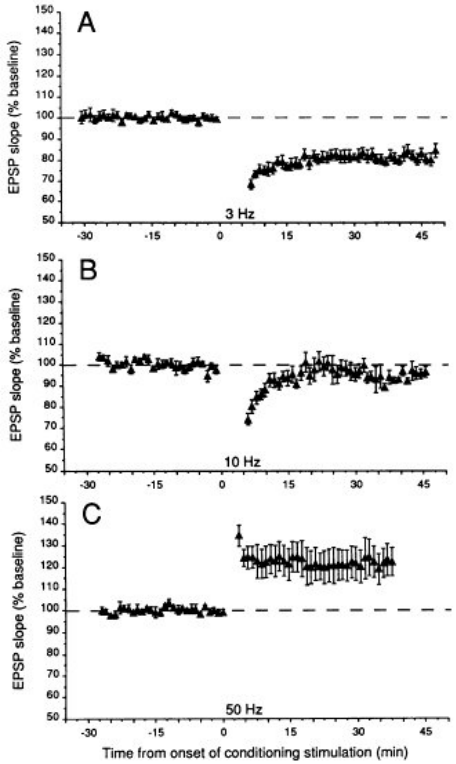


Markram et al. (1998)
Proc Natl Acad Sci USA. **95**(9):5323–5328

- sequence of eight presynaptic spikes at 20Hz evokes successively smaller (depression) or successively larger (facilitation) responses in postsynaptic cell
- same presynaptic neuron makes connections to different types of target neurons with different plasticity properties

- enables the synaptic efficacy to represent the history of presynaptic activity (e.g higher activity - faster depletion of resources - STD)
- change persists only for a few hundred milliseconds (amplitude of the postsynaptic response recovers to close-to-normal values within less than a second)

Long-term plasticity

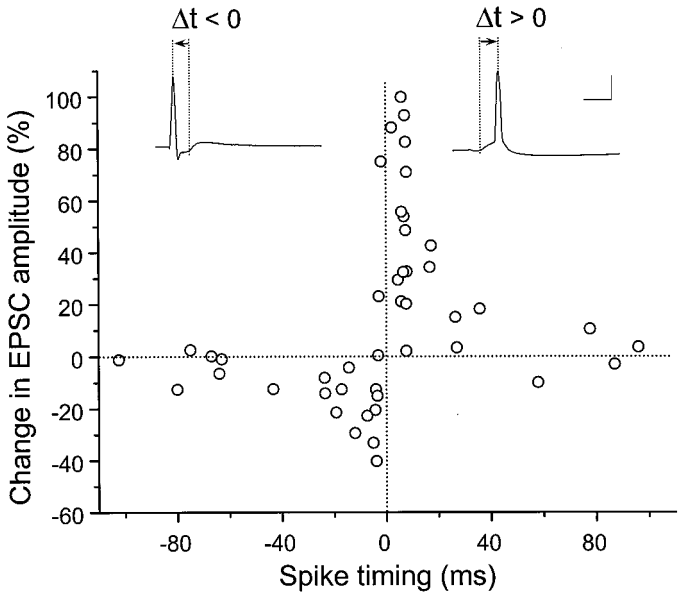


- 900 presynaptic stimulation pulses yield either persistent depression (LTD) or potentiation (LTP) depending on rate

Dudek & Bear (1992)
Proc Natl Acad Sci USA. **89**:4363–4367

- sensitive to the presynaptic firing rate over a time scale of tens or hundreds of seconds
- change can persist for more than one hour
- final stabilization on a time scale of hours
  (e.g. late phase of LTP reported by Frey & Morris, 1997)

Long-term plasticity

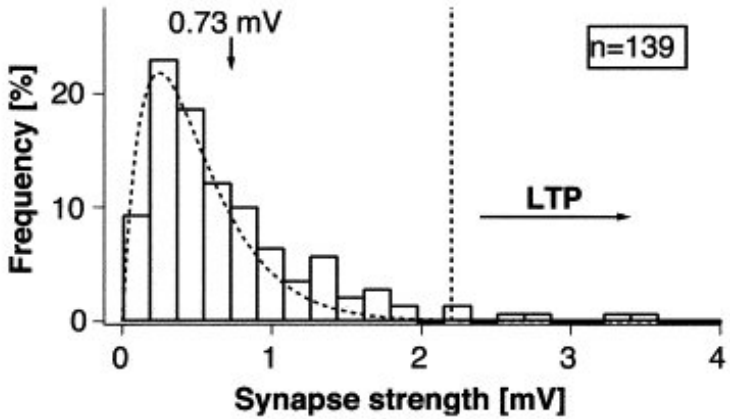


- LTP if presynaptic spike precedes postsynaptic spike by 10 ms
- LTD if order of spikes reversed
- repetitions of 60 pairs of spikes (single pair has no effect)

Bi & Poo (1998)
J Neurosci **18**:10464–10472

- depends on exact timing of pre- and postsynaptic spikes on time scale of milliseconds
- so called spike-timing dependent plasticity (STDP)

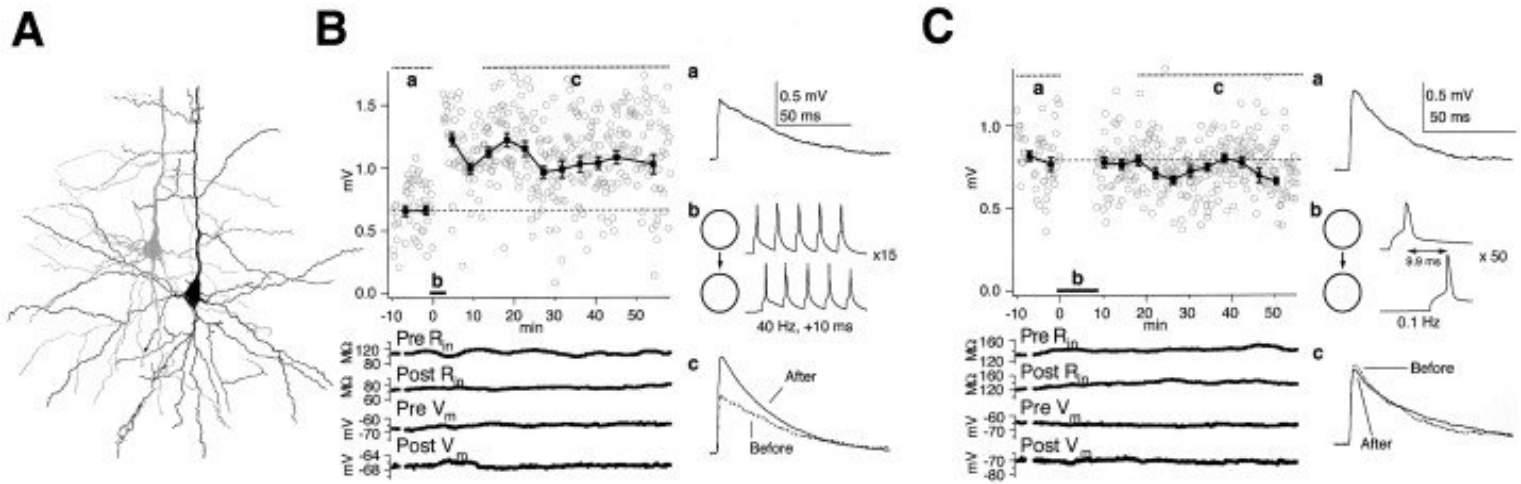
Spike-timing dependent plasticity (STDP)

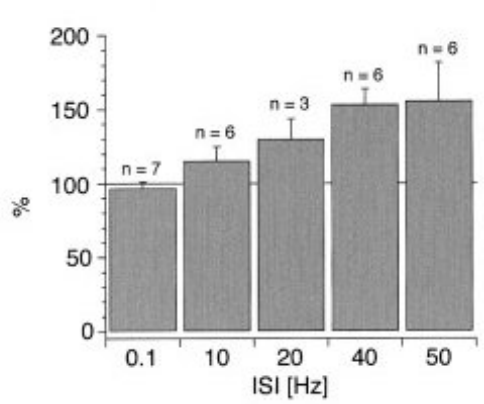


Sjostrom et al. (2001) *Neuron.* **32**(6):1149–64

- synaptic strength (e.g. EPSP amplitudes) in data collected across several pairs of neurons reported to be unimodal

Spike-timing dependent plasticity (STDP)



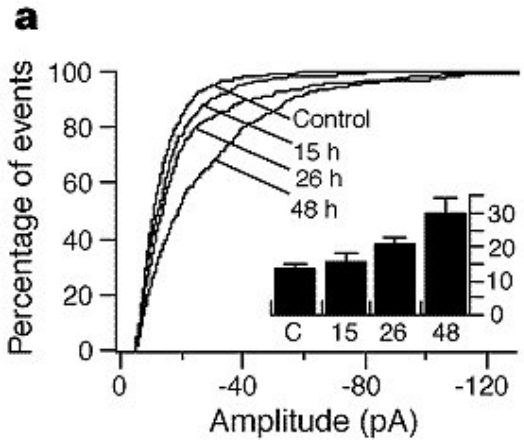


- 60 pre-post pairings at 0.1 Hz have no effect (C)
- same number of pairs at 40 Hz gives strong potentiation (B)

Sjostrom et al. (2001)
Neuron. **32**(6):1149–64

- depends on repetition frequency of pre-post spike-pairings

Homeostasis of synaptic efficacies



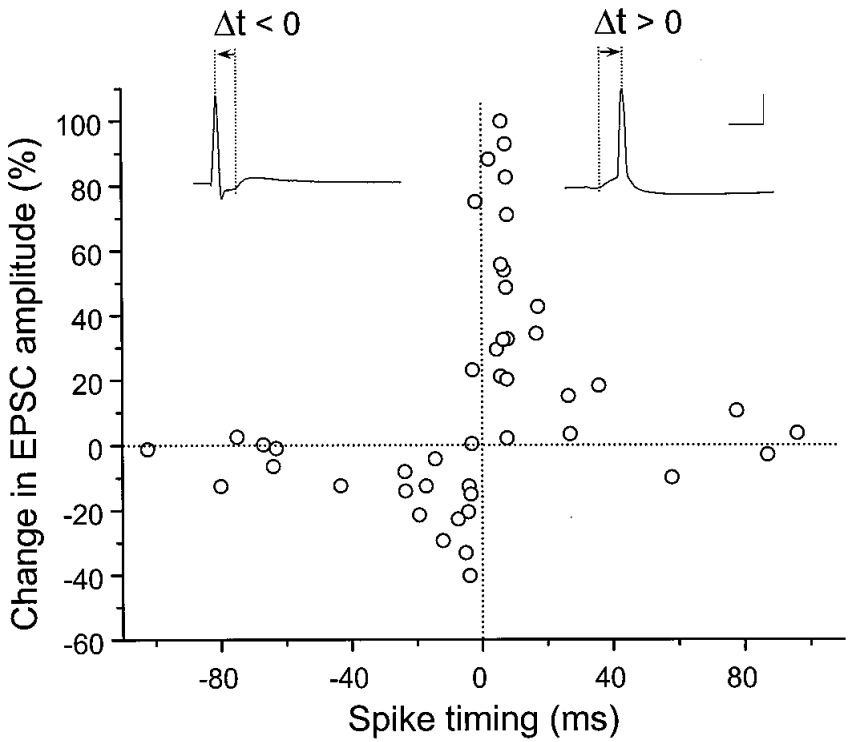
- chronic blockade of cortical culture activity increases amplitude of mEPSCs without changing their kinetics

Turrigiano et al. (1998)
Nature. **391**:892–896

- on a time scale of hours, rescaling of synaptic response amplitudes may occur
- useful to stabilize neuronal firing rates

Phenomenological models of spike-timing dependent plasticity

What do we need to specify a pair-based model of STDP?



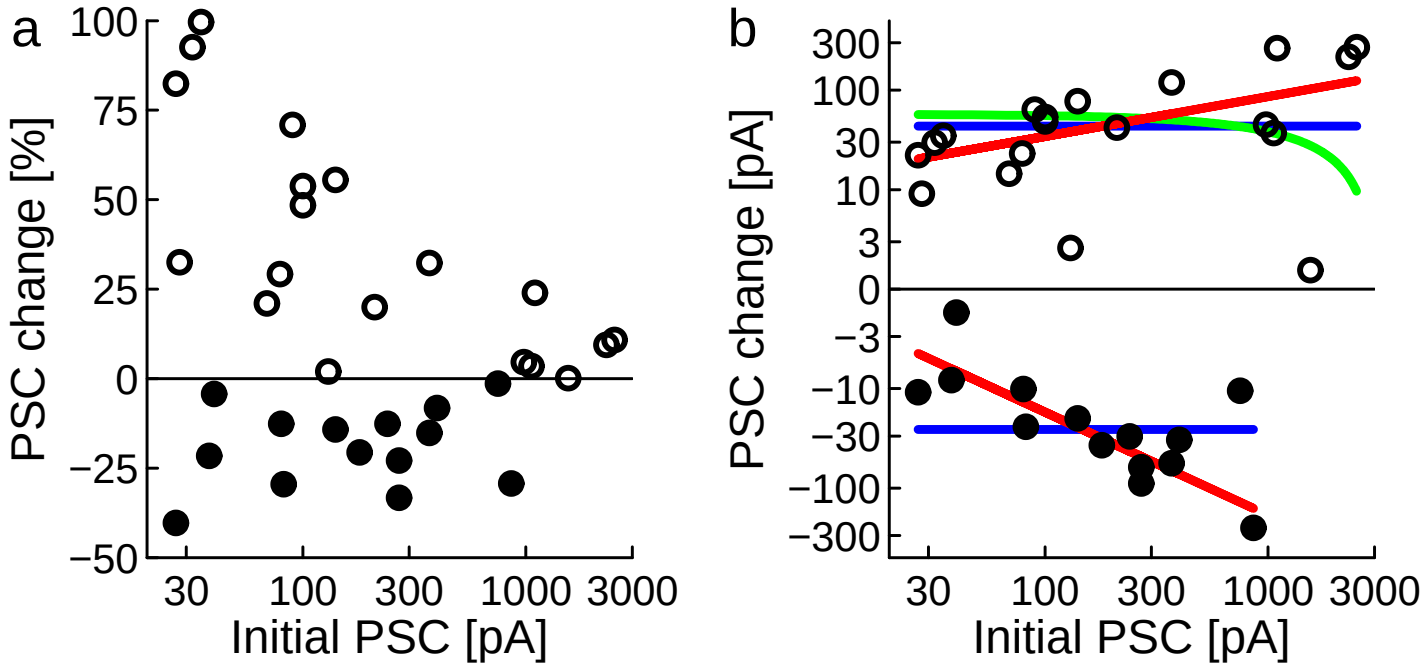
Bi & Poo (1998)
J Neurosci **18**:10464–10472

$$\begin{aligned} \Delta w_- &= -F_-(w)\exp(-|\Delta t|/\tau_-) \\ \Delta w_+ &= -F_+(w)\exp(-|\Delta t|/\tau_+) \end{aligned}$$

- weight dependence i.e. $F_\pm(w)$
- spike pairing scheme
- decomposition of synaptic delay into axonal and dendritic components
- asymmetry of STDP kernel $(\alpha = \frac{F_-}{F_+})$

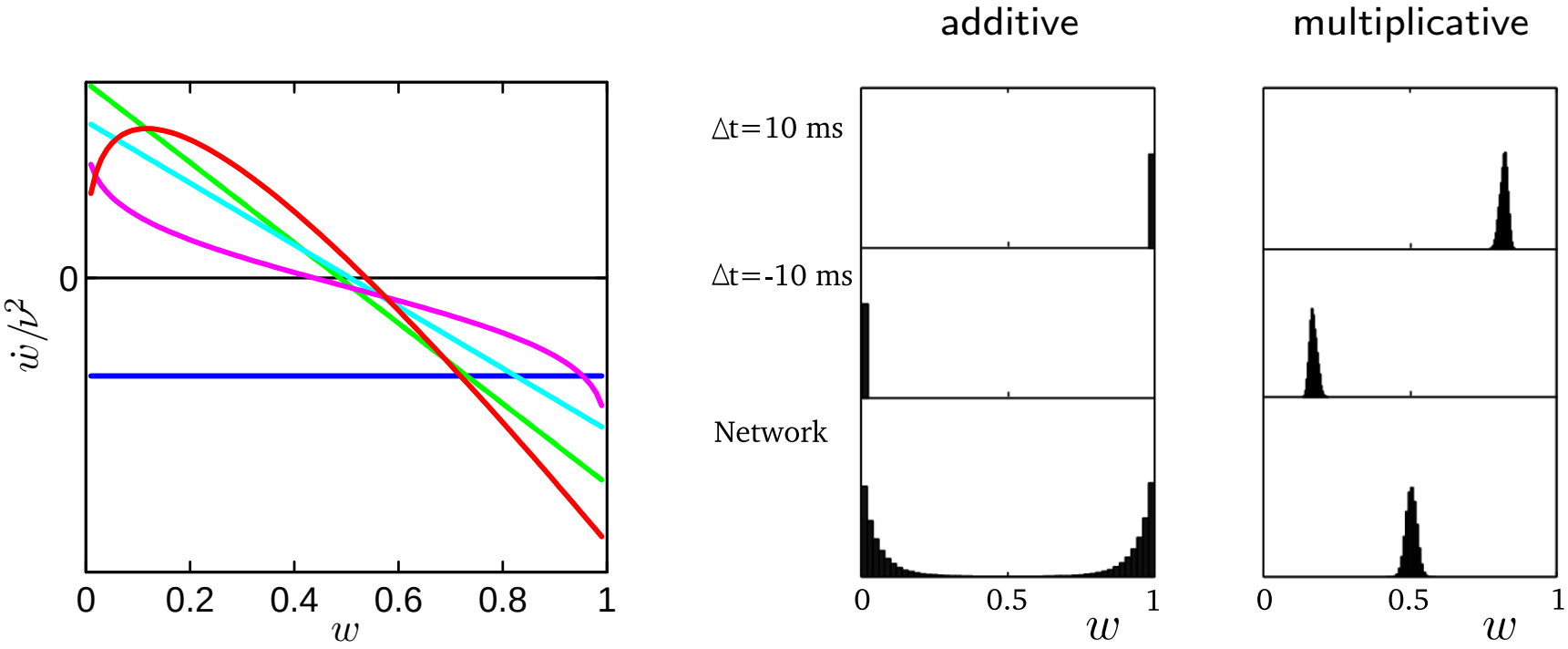
all of these aspects are important and should not be chosen arbitrarily

Models of STDP: Weight Dependence



- Reanalysis of Bi & Poo (1998) data shows that the commonly used additive model ($F_- = A_-, F_+ = A_+$) is not a good fit for the data.
- Depression data are best fit by a multiplicative/power law model ($F_- = A_- w^{-1}$)
- Potentiation data are best fit by a power law model ($F_+ = A_+ w^{\mu}$, $\mu = 0.4$)

Models of STDP: Distribution of synaptic weights



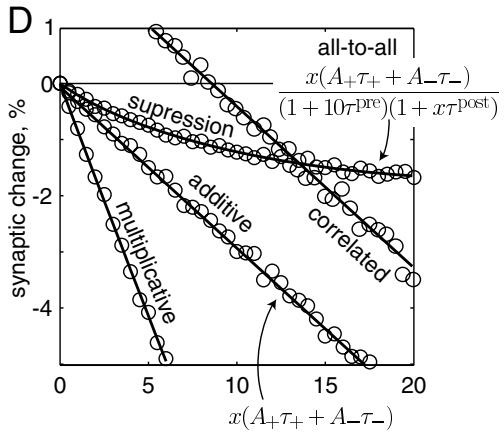
- all weight dependent models exhibit a stable fixed point and generate a unimodal distribution (multiplicative, power law, Gütig, Van Rossum)
- the additive model does not have a stable fixed point and produces a bimodal distribution

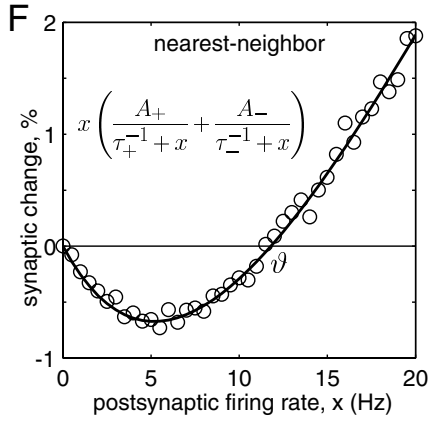
Models of STDP: Spike Pairing Scheme

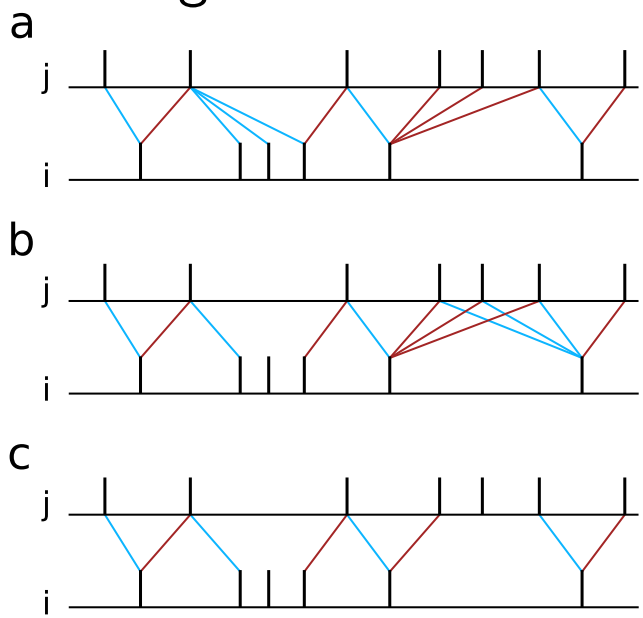
all-to-all...

... or nearest neighbour?

...but which nearest neighbour?



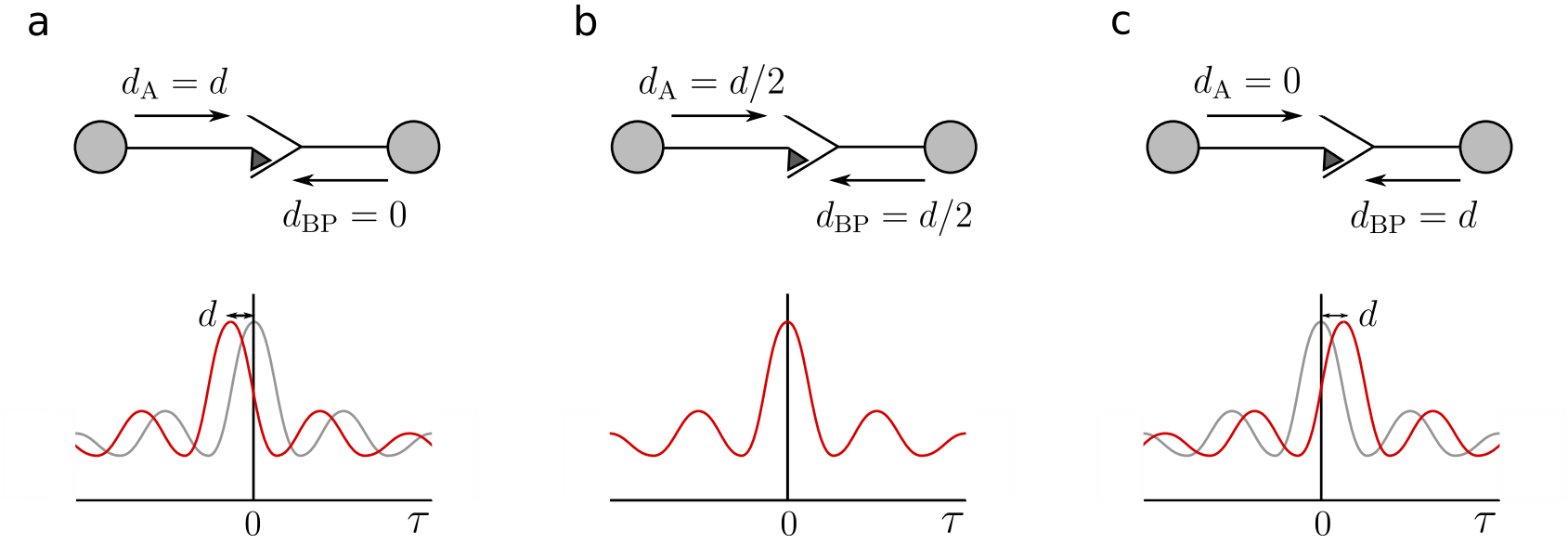




Izhikevich & Desai (2003) *Neural Comput* **15**:1511–1523

- there are many possible spike pairing schemes
- they can give qualitatively different results (e.g. Kempter et al. 2001; Morrison et al. 2007)
- see Burkitt et al (2004) for copious analysis

Models of STDP: Synaptic Delays

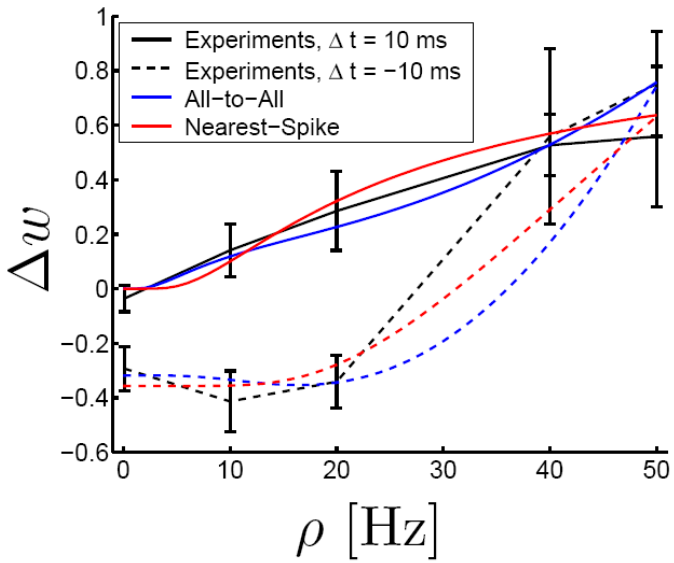


- The synaptic drift depends on the cross-correlation with respect to the synapse
- This is shifted from to the left or right of the (measurable) cross-correlation with respect to the soma depending on whether the synaptic delay is largely axonal (a) or dendritic (c)
- Therefore the same STDP rule coupled with the same network dynamics can give rise to either net depression, no change, or net potentiation

Models of STDP: Beyond Pair Effects

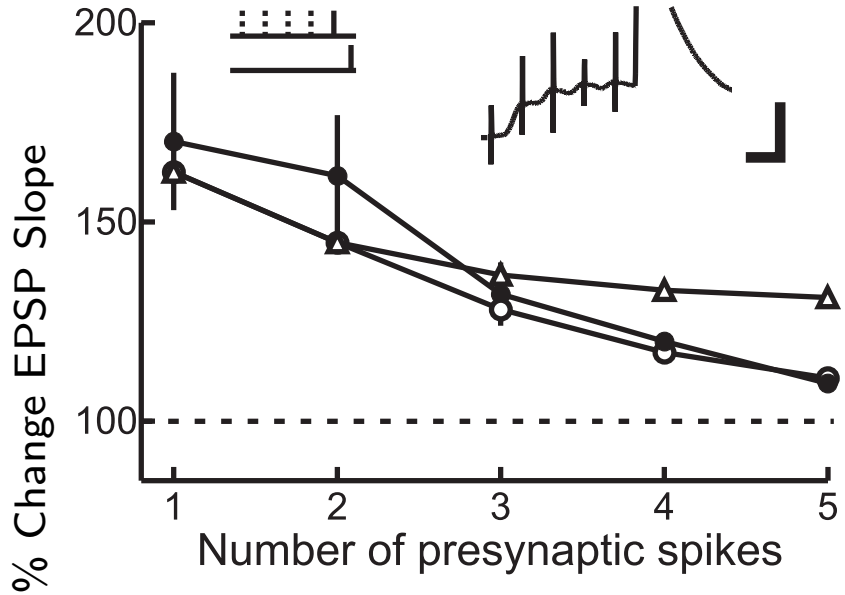
Many features of STDP cannot be explained by pair-based rules:

Frequency dependence



Data: Sjostrom et al. (2001) *Neuron* **32**:1149–1164
Modelling: Pfister et al. (2006) *J Neurosci* **26**:9673–9682
Modelling: Also see Clopath et. al (2010) *Front.Synap Neurosci.*, Shouval et. al (2010) *Front. Comp. Neurosci.*, Costa et al. (2015) *eLife*

Burst dependence



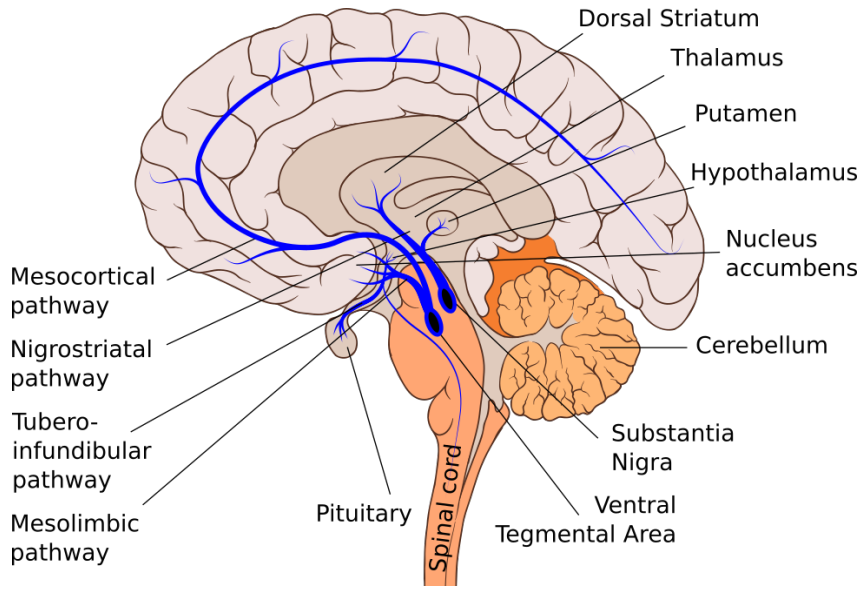
Data and modelling: Froemke et al. (2006) *J Neurophysiol* **95**:1620–1629

There is generally no cross-compatibility between models accounting for these features

Is pre- and post-spike timings enough to model learning?

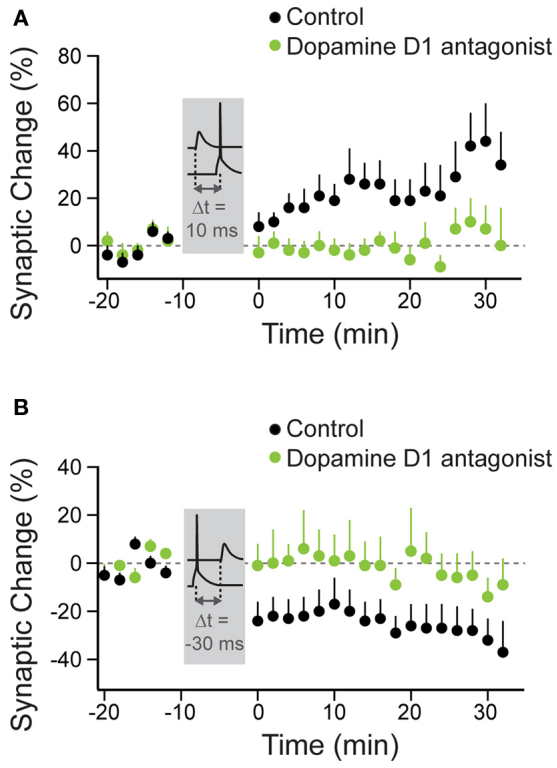
- Neuromodulators are neurotransmitter which are thought influence more that just one synapse but diffuse in larger cortical areas
- Therefore considered to be non-locallly modulating synaptic transmission
- I.e. Dopamine, Serotonine, Acetylcholine, ...

Dopaminergic pathway

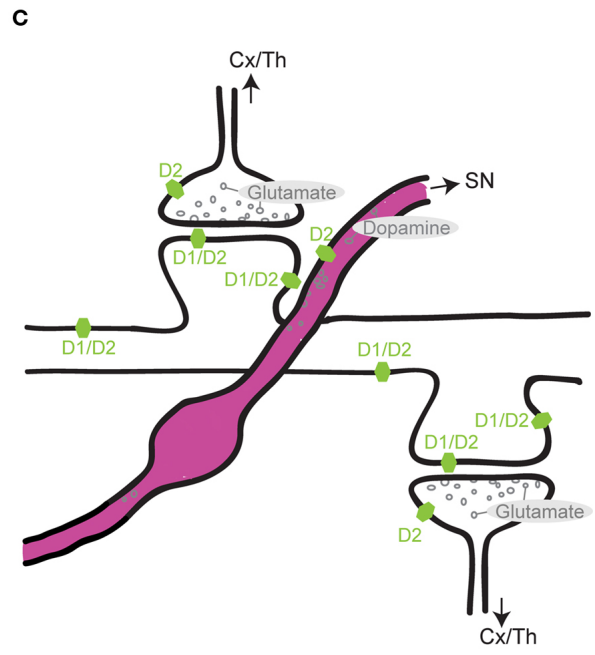


Effects of Neuromodulators on STDP

- Dopamine permits induction of LTP and LTD in striatal neuron
- If dopamine is blocked, no plasticity is induced

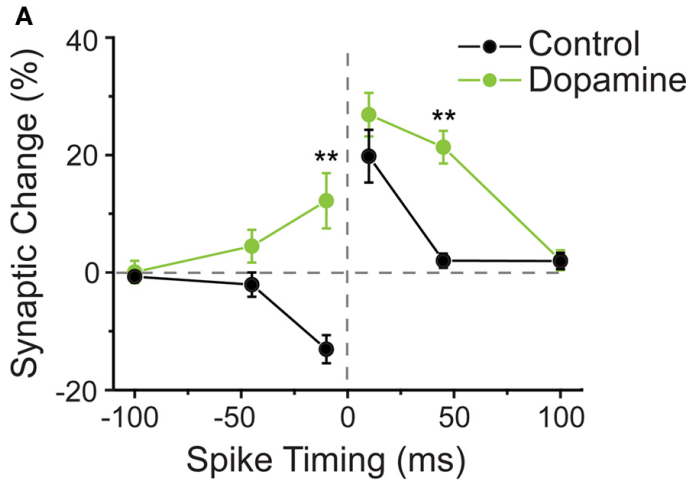


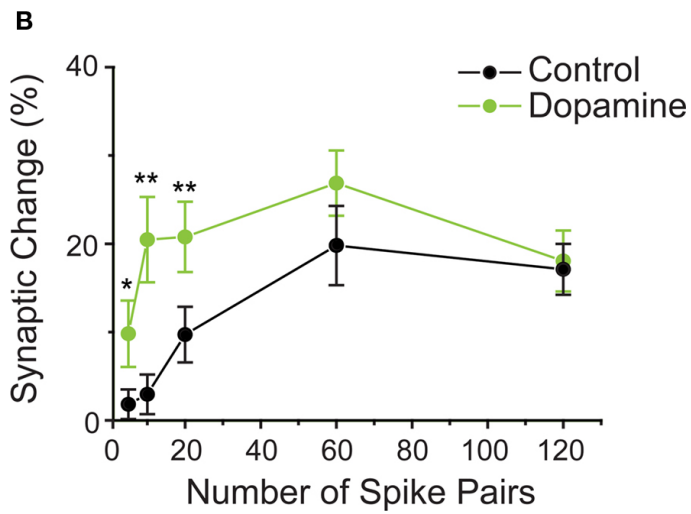
Pawlak and Kerr, 2008 / 2010



Effects of Neuromodulators on STDP

- Dopamine can switch the STDP window in hippocampus
- Less spikes are necessary to induce STDP under the influence of dopamine





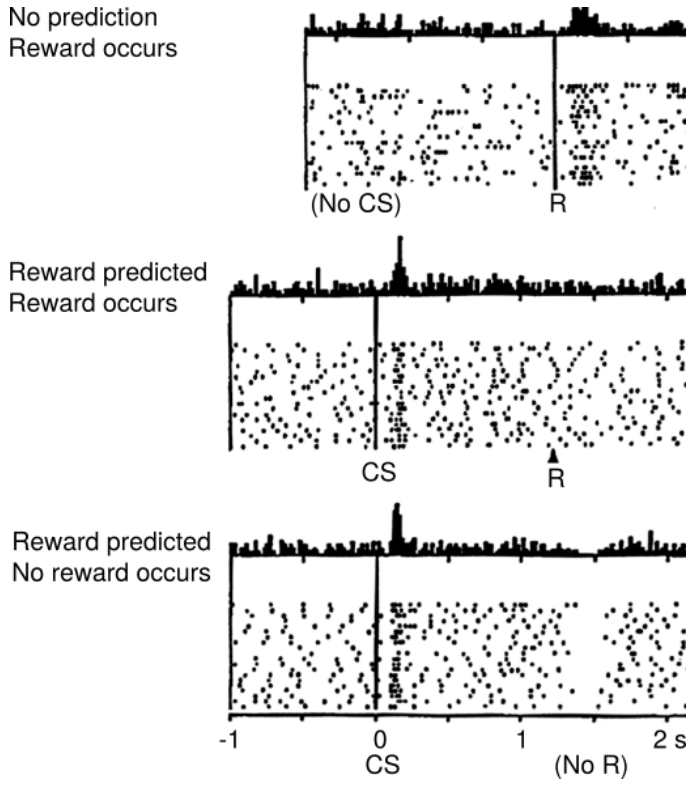
Zhang et al., 2009, Pawlak and Kerr, 2010

Effects of neuromodulators on STDP

Study	Brain region	Cell type investigated	Neuromodulator involved (via receptor subtype)	STDP induction protocol	Neuromodulator effect on STDP	Main method of neuromodulatory system manipulation	Mechanism mediating neuromodulator effect on STDP
Bissiere et al. (2003)	Lateral amygdala (mouse)	Projection neurons	Dopamine via D2 Rs	t-LTP: 3 EPSPs timed to 3 APs	Permitted t-LTP	Application of dopamine (100 μM) and receptor agonists	Suppression of feedforward inhibition
Pawlak and Kerr (2008)	Dorsal striatum (rat)	Spiny projection neurons (SPNs)	Dopamine via D1/D5 Rs	t-LTP: 1 EPSP – 1 AP; t-LTD: 1 AP – 1 EPSP	Permitted t-LTP and t-LTD	Application of dopamine receptor antagonists	?
Shen et al. (2008)	Dorsal striatum (mouse)	Spiny projection neurons	Dopamine via D1/D5 and D2 Rs	t-LTP: 3 EPSPs timed to 3 APs; t-LTD: 3 APs timed to 1 EPSP	Permitted t-LTP and t-LTD in specific SPN subgroups	Application of dopamine receptor antagonists	?
Couey et al. (2007)	Prefrontal cortex (mouse)	Layer 5 pyramidal neurons	Nicotine via nAChRs	t-LTP: 1 EPSP – 1 AP	Block of t-LTP; instead, induction of small amount of LTD (only 10 μM)	Application of nicotine (300 nM; 10 μM)	Increase in inhibition; note: stronger protocol (1 EPSP – 2 or 3 APs) still induces t-LTP in nicotine
Zhang et al. (2009)	Hippocampus (rat, dissociated culture)	Glutamatergic (presumably pyramidal) neurons	Dopamine via D1/D5 Rs	t-LTP: 1 pre-AP – 1 post-AP; t-LTD: 1 post-AP – 1 pre-AP	"Wider" range of spike timings induces t-LTP, less spike pairings required to induce t-LTP	Application of dopamine (20 μM)	?
Lin et al. (2003)	Hippocampus (rat)	CA1 pyramidal neurons	Noradrenaline via β-adrenergic Rs	t-LTP: 1 EPSP – 1 AP	"Wider" range of spike timings induces t-LTP	Application of agonists	Modulation of PKA or ERK/MAPK signaling??
Seol et al. (2007)	Visual cortex (rat)	Layer 2/3 pyramidal neurons	Acetylcholine via M1 muscarinic Rs; noradrenaline via β-adrenergic Rs	t-LTP: 1 EPSP timed to 4 APs; t-LTD: 4 APs timed to 1 EPSP	Cooperation between cholinergic and adrenergic	Application of agonists	Promotion of AMPA receptor phosphorylation at sites implicated in

Functional aspects of dopamine

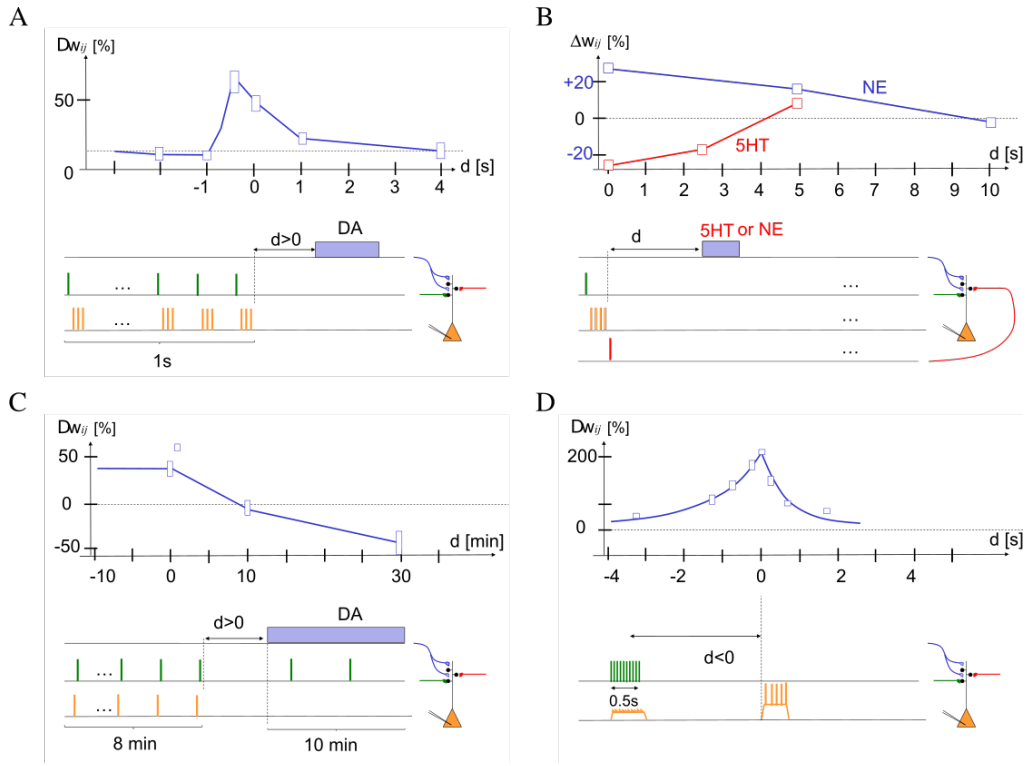
- Dopamine is probably the most studied neuromodulator
- Invovled in conditioning as reward and punishment signal
- Credit assignment problem
- Theoretical prediction of 'eligibility traces'



Schultz et al. 1997

Effective timescales of dopamine

- In different regions neuromodulators effect STDP with different timescales
- A) Striatum ($\sim$ 1s)
- B) Cortex ($\sim$ 5s)
- C) Hippocampus ($\sim$ min)



Gerstner et al. 2018, Yagishita et al. 2014, He et al. 2015, Bittner et al. 2017

Conclusions

- A modeller needs to specify a complete model despite lack of clear experimental evidence
- These choices can have profound consequences
- Almost all network modelling papers fail to consider whether the effects shown are artifacts of their specific choices
- There is so far no phenomenological model which accounts for all the nonlinearites exhibited by STDP
- For those who want to know more...

Biol Cybern (2008) 98:459–478
DOI 10.1007/s00422-008-0233-1

REVIEW

Biological Cybernetics

Phenomenological models of synaptic plasticity based on spike timing

Abigail Morrison · Markus Diesmann · Wulfram Gerstner