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Characterization of short-term synaptic plasticity in mouse primary visual cortex

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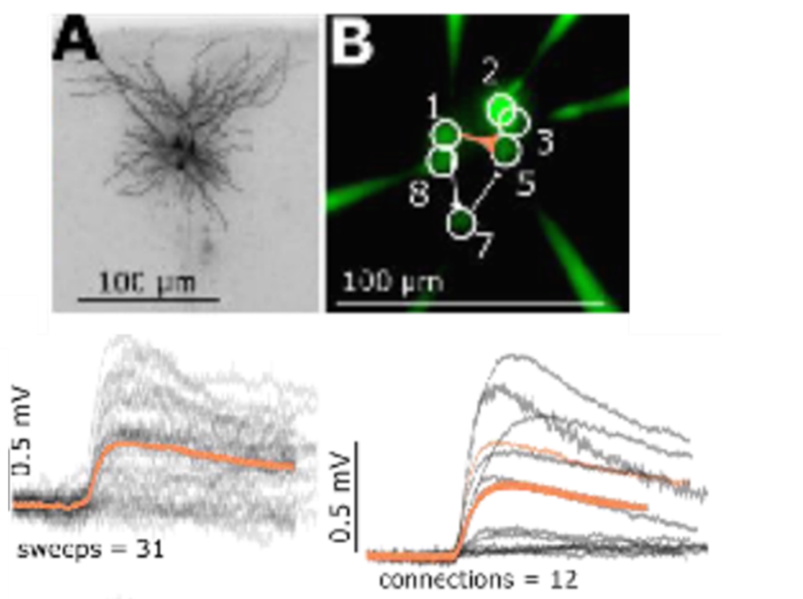
Background

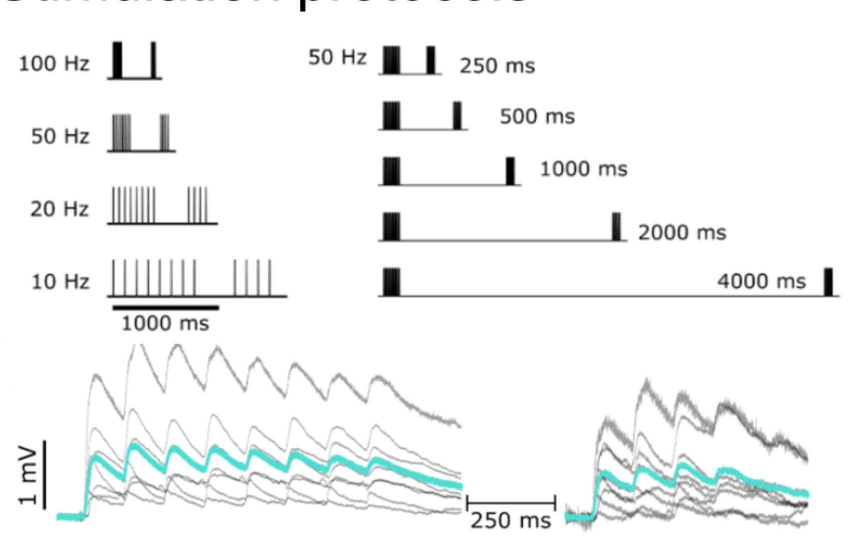
The exact functions of 'short-term synaptic plasticity' remain contentious partly due to its diversity. Thus, it is necessary to characterize short-term synaptic plasticity. To this end, we analyzed data from Allen Institute's large scale multi-patch pipeline project which focuses on synaptic connections in mouse primary visual cortex (V1). As short-term synaptic plasticity depends on both pre- and post-synaptic neuron classes (Beierlein et al., 2003; Blackman et al., 2013; Gibson et al., 1999; Hayut et al., 2011; Lefort and Petersen, 2017; Pala et al., 2015), we defined synapse classes using pre- and post-synaptic neuron classes and studied their properties.

Data collection

Synaptic dynamics were collected using the sub-millisecond sampling, high gain, and low noise of multipatch recordings (Seeman et al. , 2018).



Stimulation protocols



Synapse model: definition

5 model variants were constructed by combining 5 temporal dynamics:

Dynamics	Mathematical description
Depression (Dep)	$\frac{dn}{dt} = \frac{1-n}{\tau_r} - Pn\delta(t-t_k)$
Facilitation (Fac)	$\frac{dP}{dt} = \frac{P_0 - P}{\tau_f} + P_0(1-P)\delta(t-t_k)$
Use-dependent replenishment (UR)	$\frac{d\tau_r}{dt} = \frac{\tau_{r0} - \tau_r}{\tau_{FDR}} - a_{FDR}\tau_r\delta(t-t_k)$
Desensitization (DSR)	$\frac{dS}{dt} = \frac{1-S}{\tau_D} - a_D nPS\delta(t-t_k)$
Slow modulation of rel. Prob. (SMR)	$\frac{dP_0}{dt} = \frac{\overline{P_0} - P_0}{\tau_i} - a_i P_0\delta(t-t_k)$
Synaptic weights	$w \propto n \cdot P \cdot S$

Model #	Dynamics
1	Dep
2	Dep +UR
3	Dep + UR+ DSR
4	Dep+ Fac
5	All five dynamics

Synapse model: parameter extraction

1. Defined synapse classes using pre- and post-synaptic neuron classes
2. Identified homogenous clusters in each synapse class by using x-means clustering (Pelleg and Moore, 2000)
3. Estimated post-synaptic potentials (PSPs) elicited by pre-synaptic spike trains
4. Tested whether Tsodyks-Markram model can account for PSPs time courses at individual stimulation frequencies
5. Fitted the dataset to the all 5 synapse models and determined the best model via adj. R^2

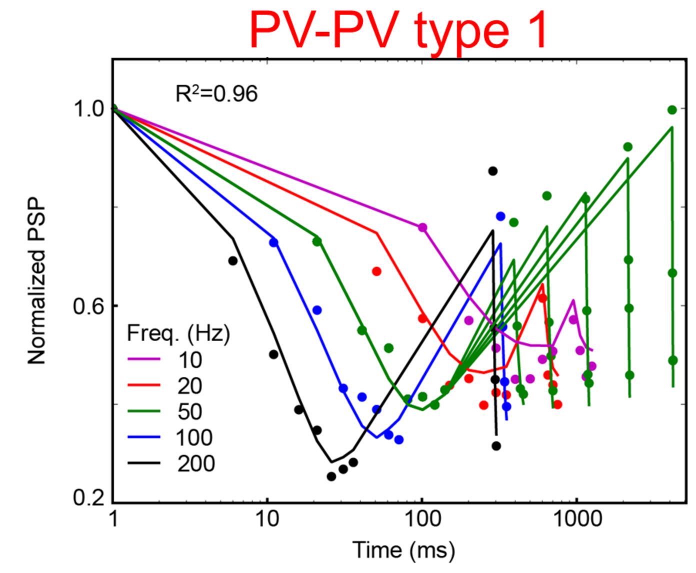
Examples of adj. R^2 across models

	M1	M2	M3	M4	M5
PV-PV	0.778	0.961	0.96	0.776	0.879
PV-Rorb	0.762	0.936	0.938	0.759	0.88

Synaptic parameters from fitting

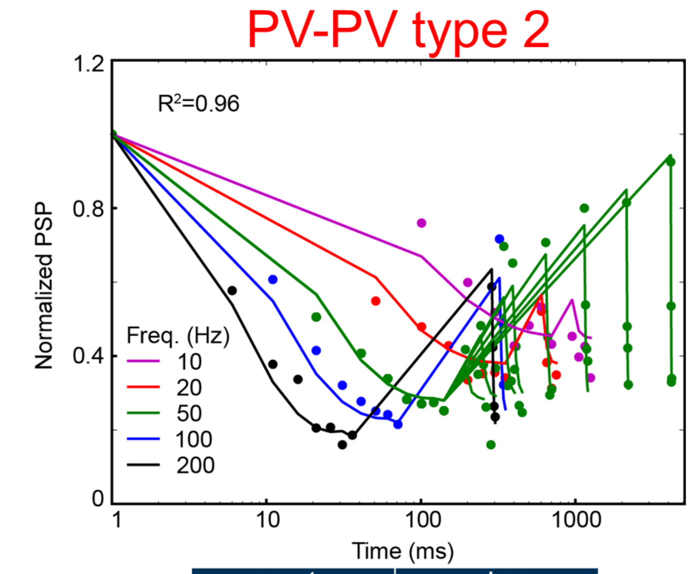
1. We defined pre- and post-synaptic neuron classes using cre-lines.
2. We display the synaptic parameters from the best model of each synapse class.

PV-PV type 1



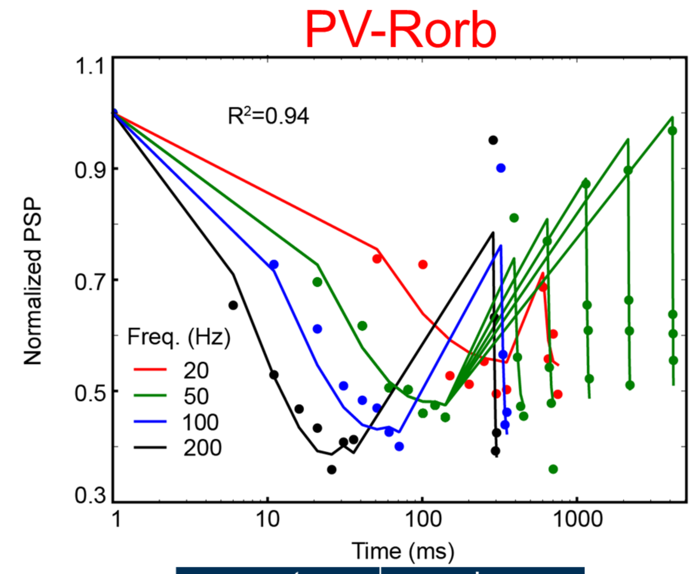
parameters	values
τ_{r0} (msec)	2059.8±437.7
τ_{FDR} (msec)	569.8±129.0
a_{FDR}	0.53±0.02
P_0	0.27±0.01

PV-PV type 2



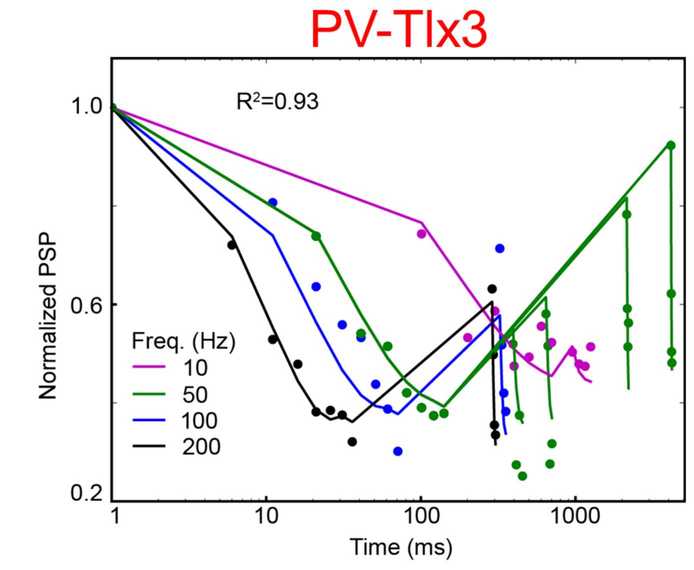
parameters	values
τ_{r0} (msec)	2037.8±555.2
τ_{FDR} (msec)	281.9±91.7
τ_D (msec)	113.6±24.6
a_{FDR}	0.76±0.05
a_D	0.87±0.14
P_0	0.29±0.02

PV-Rorb



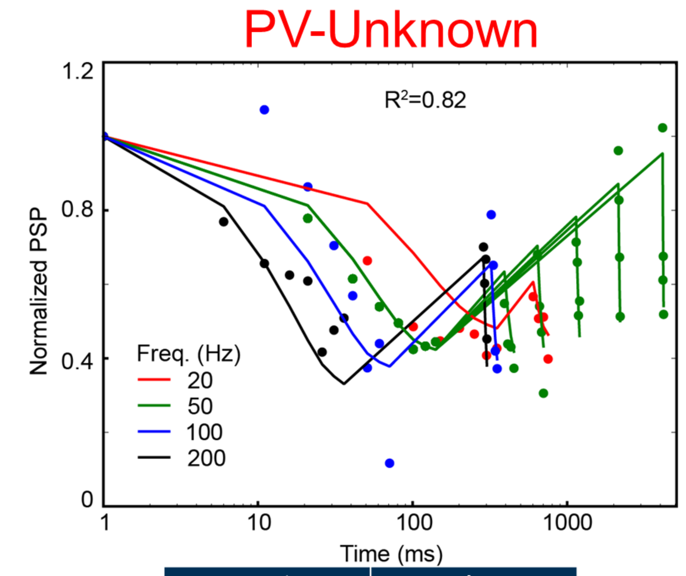
parameters	values
τ_{r0} (msec)	1093.1±373.4
τ_{FDR} (msec)	216.5±84.0
τ_D (msec)	94.5±51.8
a_{FDR}	0.70±0.05
a_D	0.33±0.14
P_0	0.24±0.02

PV-Tlx3



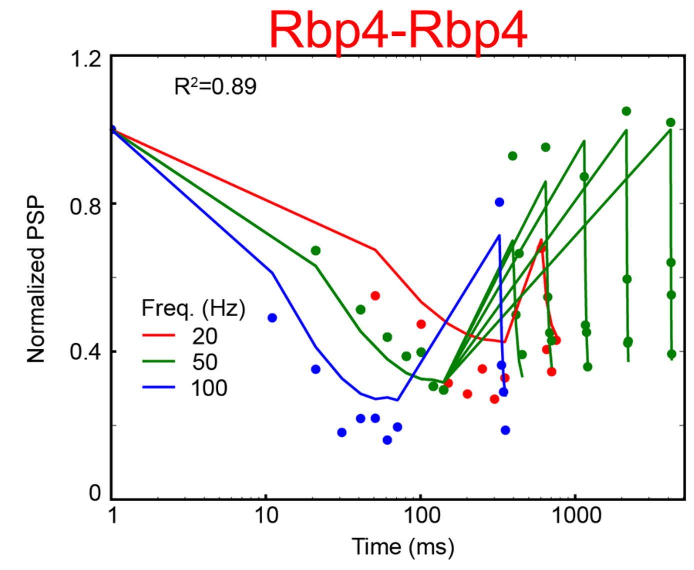
parameters	values
τ_{r0} (msec)	2052.8±373.5
τ_{FDR} (msec)	224.95±59.30
a_{FDR}	0.72±0.05
P_0	0.26±0.01

PV-Unknown



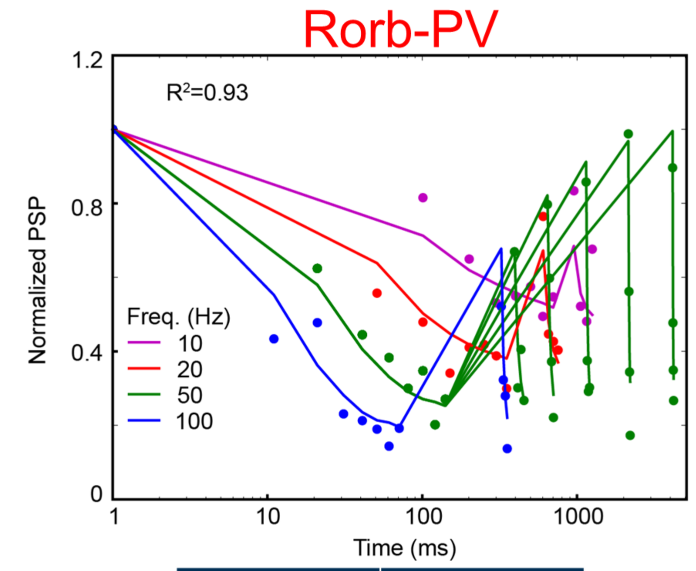
parameters	values
τ_{r0} (msec)	1962.5±834.4
τ_{FDR} (msec)	420.2±235.6
a_{FDR}	0.45±0.06
P_0	0.19±0.01

Rbp4-Rbp4



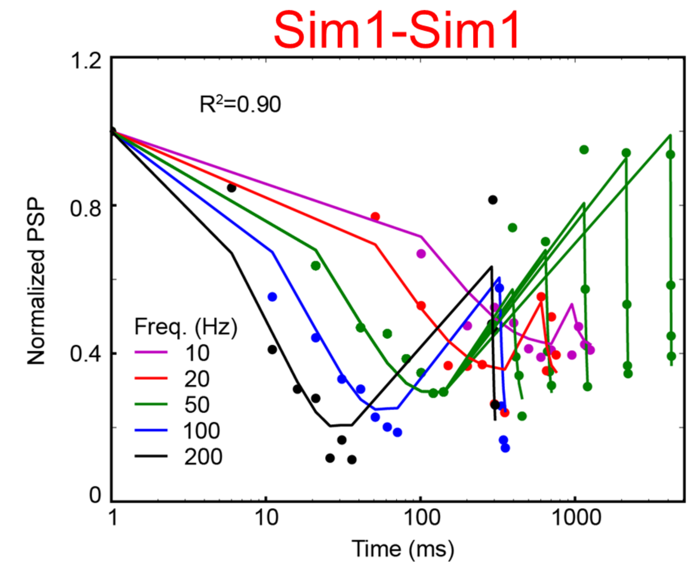
parameters	values
τ_{r0} (msec)	330.1±72.3
τ_{FDR} (msec)	52.4±42.9
a_{FDR}	0.51±0.21
P_0	0.41±0.03

Rorb-PV



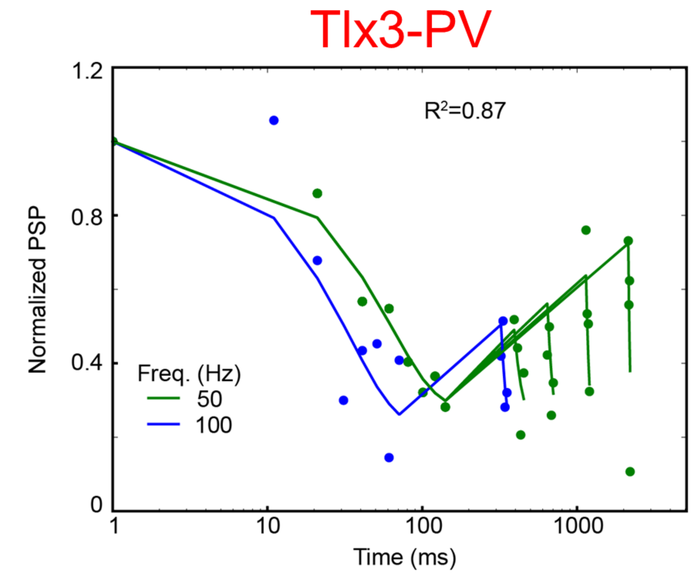
parameters	values
τ_{r0} (msec)	177.6±74.0
τ_{FDR} (msec)	13.26±37.45
τ_D (msec)	998.13±908.76
a_{FDR}	0.66±0.94
a_D	0.17±0.15
P_0	0.45±0.004

Sim1-Sim1



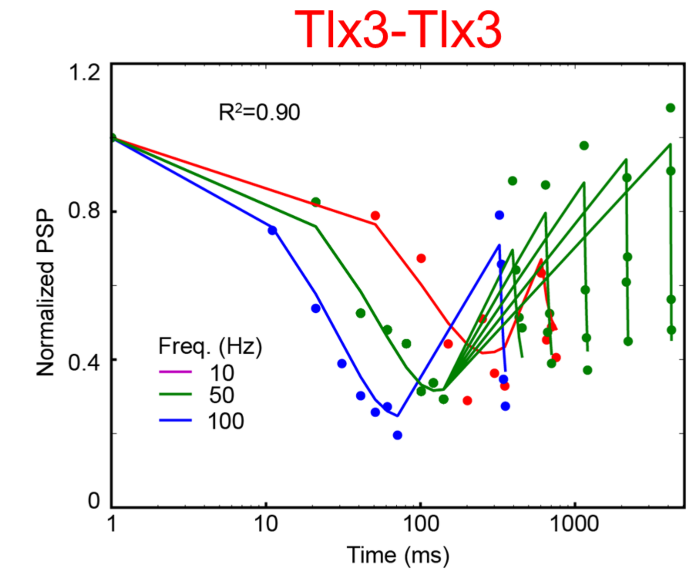
parameters	values
τ_{r0} (msec)	1020.7±262.7
τ_{FDR} (msec)	198.0±82.9
a_{FDR}	0.45±0.05
P_0	0.33±0.02

Tlx3-PV



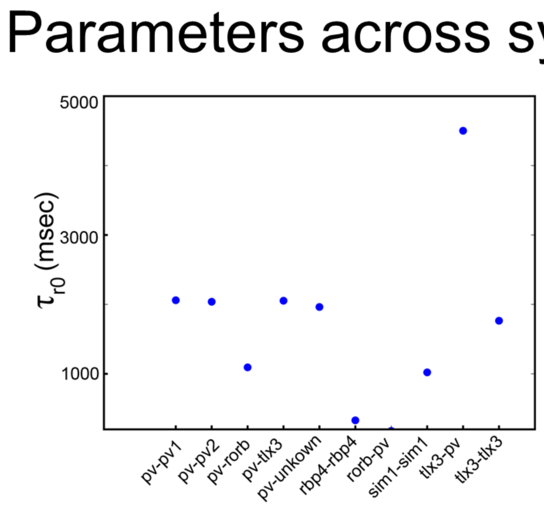
parameters	values
τ_{r0} (msec)	4501.4±4210
τ_{FDR} (msec)	874.1±1060
a_{FDR}	0.39±0.1
P_0	0.21±0.01

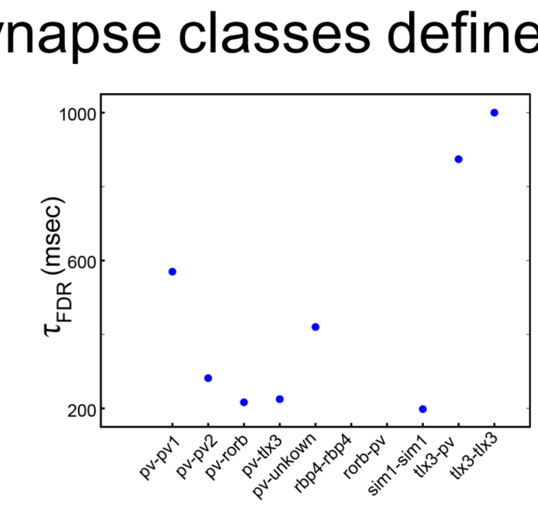
Tlx3-Tlx3

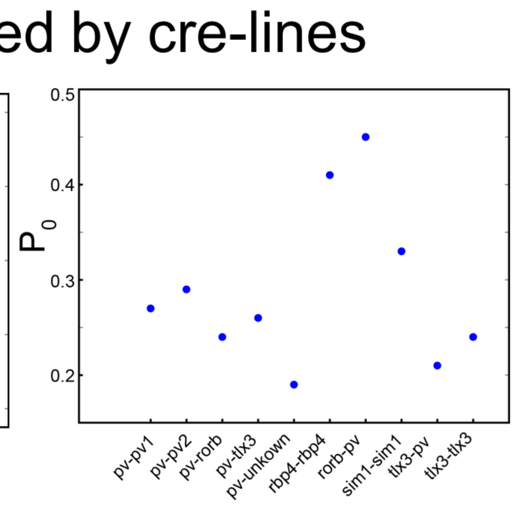


parameters	values
τ_{r0} (msec)	1764.5±1210
τ_{FDR} (msec)	1000.0±34.2
a_{FDR}	0.33±0.08
P_0	0.24±0.01

Parameters across synapse classes defined by cre-lines





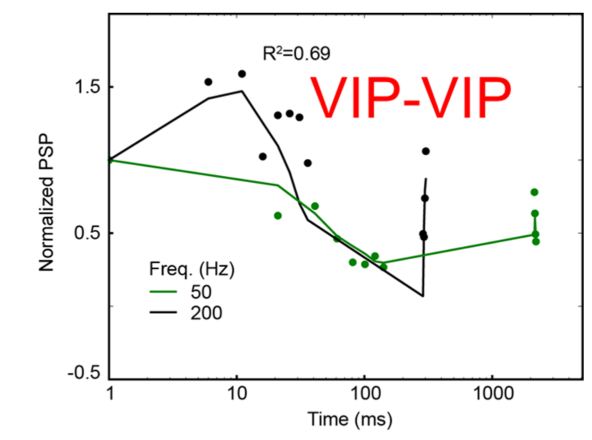


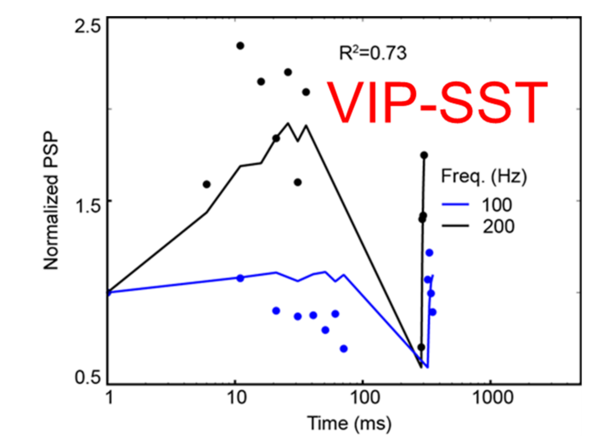
Results Summary

1. Models with depression, use dependent replenishment and desensitization of receptors (models 2 and 3) can account for a large fraction of depressing synapses in V1.
2. Synapse classes with distinct parameters are observed.

Facilitating synapses

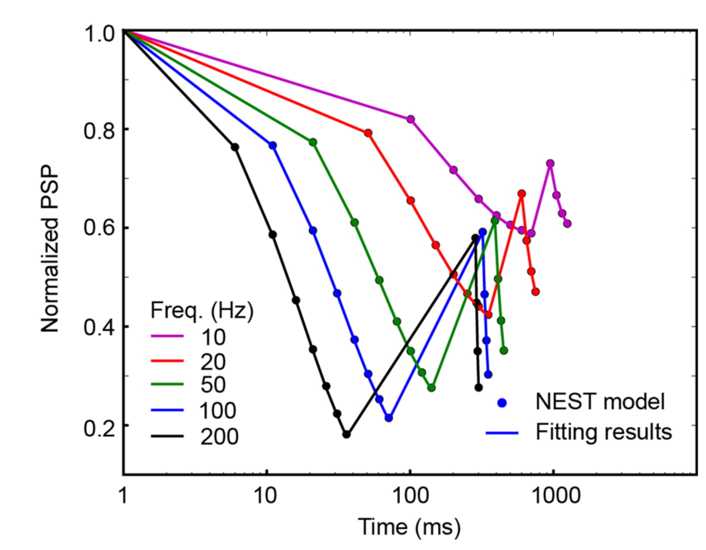
The inhibitory connections from VIP cells appear to be facilitating.





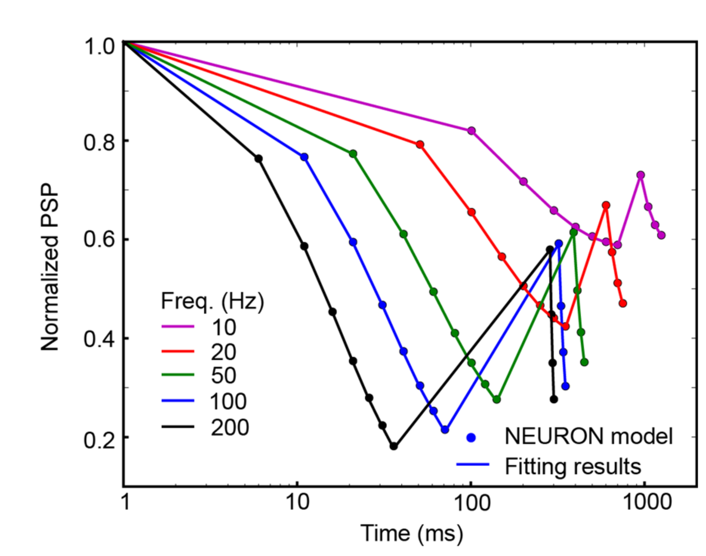
Synapse model implementation for NEST

Currently, the synapse models are implemented as extension models of NEST (http://nest.github.io/nest-simulator/extension_modules). Contact Jung Lee (jungl@alleninstitute.org) if interested.



Synapse model implementation for NEURON

The current mod file 'aisyn.mod' was written by Sergey Gratiy (sergeyg@alleninstitute.org). Contact Jung Lee (jungl@alleninstitute.org) if interested.



Discussion

So far, we constructed ~10 synapse models in V1 that can capture short-term synaptic plasticity observed in V1. These models suggest that most synapse classes depress in V1 and that short-term synaptic plasticity depends mainly on presynaptic neurons.

These synapse modules in NEST and NEURON can help us study the functional roles of short-term synaptic plasticity in cortical functions, and we will use them to study short-term synaptic plasticity's contribution to detection of changes in visual scenes.

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