

## Supplementary Material for the paper:

*Using Strahler's analysis to reduce up to 200-fold the run time of realistic neuron models*

by

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**Supplementary Figure 1: The cells used in this paper and the four areas used for synaptic stimulations;** projection to the XY plane of 3D reconstructions of Purkinje cells from different animals, as indicated in the table. Colors indicate the different dendritic areas used to stimulate each cell.

**Supplementary Figure 2: I/O properties of a Purkinje cell model;** **a)** representation of the stimulation conditions; colored dendrites represent typical partial and segregated areas; **b)** (left) average ( $n = 5, \pm sd$ ) APs frequency and ISIs for 1000 synaptic inputs; (right) average firing frequency and ISIs with randomly activated synaptic inputs (Poisson) at 80 Hz; **c)** (left) raster plots of the spike trains (plots above traces), and somatic potential for cell *e4cb2a2* during simulations with 1000 synapses; grey areas in raster plots indicate regular spiking, with the first ISI of each pattern darker; blank areas indicate pauses; (right) normalized ISIs distribution. Average  $CV_2 = 0.38$  for full and partial, 0.37 for segregated stimulation.

**Supplementary Figure 3: The method is robust for perturbations of peak ionic conductances.**

(left) average trace accuracy for simulations using the original set of values,  $g_{peak}$ , for the 12 peak ionic conductances (black) or after 10 random perturbations (red) redrawn from a normal distribution with average  $g_{peak}$  and variance 10%  $g_{peak}$ , resulting in a maximum perturbation  $>20\%$  of  $g_{peak}$ ; different symbols indicate results obtained for full (circles), partial (triangles), and segregated (squares) stimulations; (right) percent of statistically indistinguishable ISIs from simulations using the realistic and the reduced model, compared pairwise (Wilcoxon Signed Rank test); all simulations were carried out using cell *e4cb3a1*.

**Supplementary Figure 4: The reduced model is able to reproduce the differential effect of two synaptic inputs colocalized or at two different locations.** (*left*) the full and the reduced morphologies of cell *p19*, and their somatic potential during simulations with two identical synapses targeting the same location (loc.1) or two different branches (loc 1 and 2).

**Supplementary Figure 5: The method is extremely accurate and quite robust for most morphologies and under all conditions of stimulation.** Average accuracy and percent of spikes times statistically indistinguishable for each cell as a function of the average synaptic stimulation frequency under different stimulation conditions; average results calculated from 550 (full), 500 (partial), and 600 (segregated) simulations. In all cases the dendrites were clustered using Strahler's order  $s = 5$  (see *Methods*), and statistics was calculated from pairwise comparison of the traces from each simulation.

**Supplementary Figure 6: In several cases, a 3-compartment reduction gave ISIs statistically different from the full model but still high overall trace accuracy.** **A)** Full and reduced model of cells *purk2* (*left*) and *p20* (*right*); **B)** (*top*) Somatic membrane potential of cell *purk2* during a simulation with 1000 synchronous synapses activating at a random (Poisson) average frequency of 120 Hz; (*bottom*) Somatic membrane potential of cell *p20* during a simulation with 1000 synchronous synapses activated by a random (Poisson) average frequency of 160 Hz. In both cases, we used a *full* stimulation protocol (see *Methods*) and the ISIs were statistically different between the full and reduced model (Wilcoxon Rank Sum test,  $p < 0.001$ ). The trace accuracy was 0.86 (*purk2*) and 0.89 (*p20*).

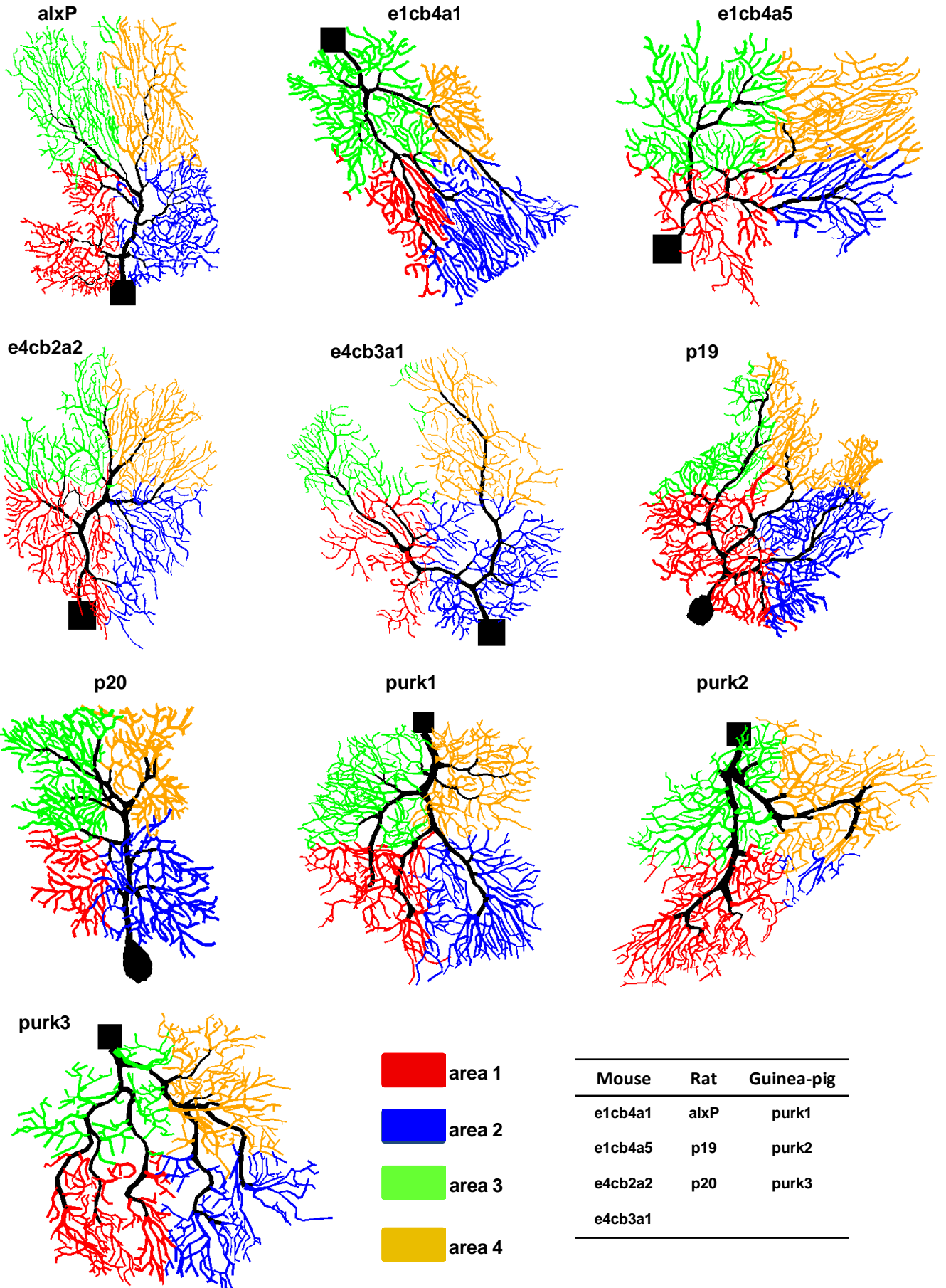
**Supplementary Figure 7: The method works also for CA1 pyramidal neurons.** **a)** somatic membrane potential for a full of a hippocampal pyramidal CA1 neuron (*blue* traces, cell *c70863* from Marasco et al., 2012) and the corresponding reduced model (*red* traces) during a simulation activating 140 (*left*) or 400 (*right*) randomly distributed synapses. **b)** Average number of APs ( $\pm$ sd) elicited in 500 ms long simulations as a function of the number of synaptic inputs activated in the full model (*blue* plots) or reduced (*red* plots) using the

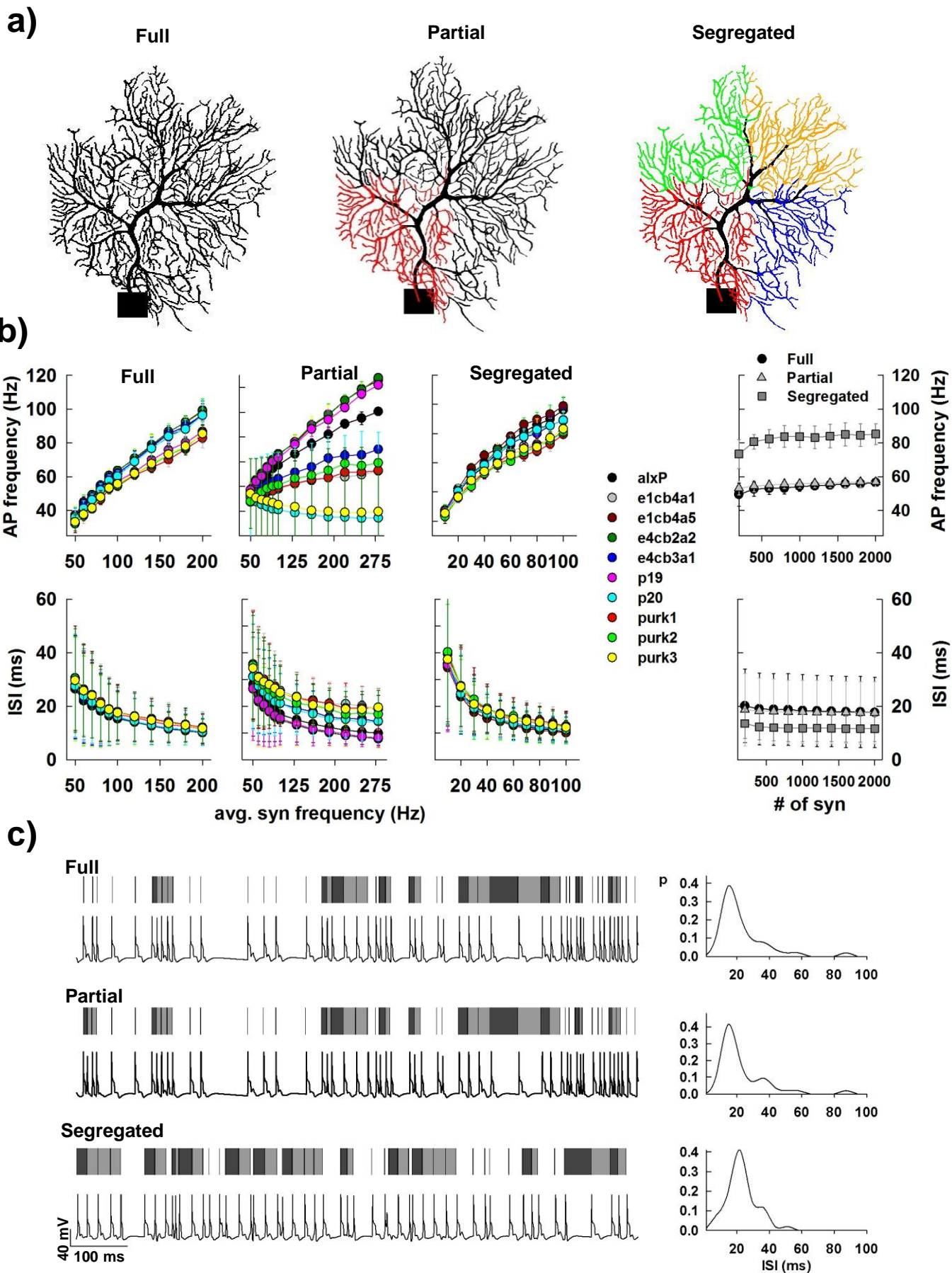
method discussed in this paper (*left*), or a previous method with (middle) or without (*right*) the calculation of the *max Stim* parameter (19); all simulations were carried out as in ref.(19).

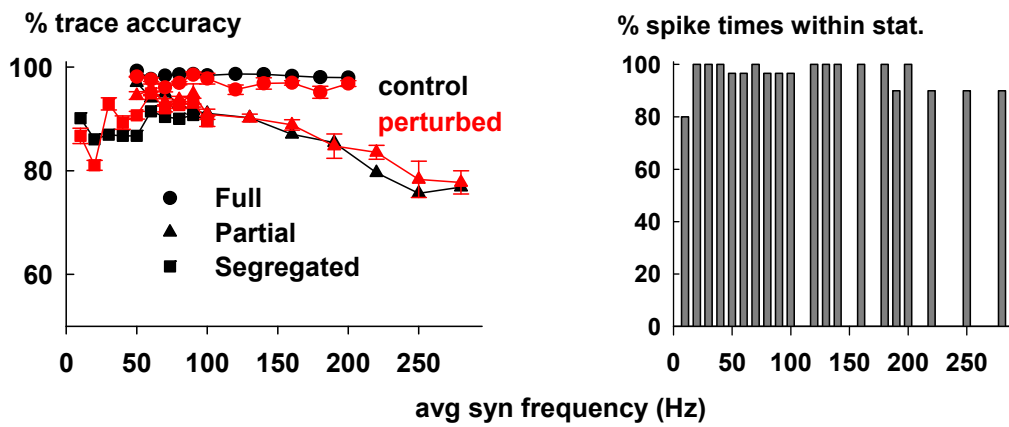
**Supplementary Table:**

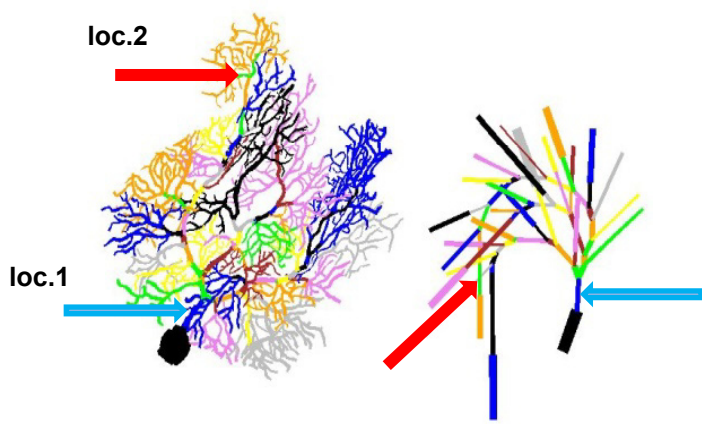
	<b>alxP</b>	<b>e1cb4a1</b>	e1cb4a5	e4cb2a2	e4cb3a1	<b>p19</b>	p20	purk1	purk2	purk3
smooth	<b>72</b>	<b>57</b>	56	58	56	<b>82</b>	49	81	56	74
spiny	<b>851</b>	<b>630</b>	633	660	685	<b>1055</b>	650	863	784	760
S1	<b>462</b>	<b>344</b>	345	360	371	<b>568</b>	349	472	420	417
S2	<b>253</b>	<b>193</b>	202	223	221	<b>341</b>	202	266	258	243
S3	<b>136</b>	<b>93</b>	86	77	93	<b>146</b>	99	125	106	100
S4	<b>46</b>	<b>34</b>	30	40	40	<b>53</b>	30	42	30	55
S5	<b>17</b>	<b>14</b>	22	11	14	<b>24</b>	9	26	24	17
S6	<b>9</b>	<b>9</b>	4	7	2	<b>3</b>	8	7	1	1
S7	<b>0</b>	<b>0</b>	0	0	0	<b>1</b>	1	5	1	1
S8	<b>0</b>	<b>0</b>	0	0	0	<b>1</b>	1	1	0	0
R <sub>in, full</sub>	<b>66</b>	<b>36</b>	74	60	53	<b>21</b>	26	11	13	14
tot. area	<b>9937</b>	<b>24303</b>	10638	11130	9379	<b>39834</b>	24867	55628	39861	46586
<b>3-comp</b>										
R <sub>in, 3comp</sub>	<b>89</b>	<b>37</b>	96	75	73	<b>25</b>	28	17	17	19
soma	<b>553</b>	<b>922</b>	511	990	800	<b>730</b>	750	1521	1521	1521
C 1	<b>850</b>	<b>1787</b>	722	847	1356	<b>2719</b>	1892	5395	5101	4107
C 2	<b>586</b>	<b>1500</b>	723	646	480	<b>2114</b>	1457	3300	2658	3251

**Supplementary Table:** For each full morphology the following are reported: the number of smooth and spiny dendrites, the number of compartments with different Strahler's number ( $S$ ), the input resistance ( $R_{in}$ , in  $M\Omega$ ), and the total membrane area (in  $\mu m^2$ ). The bottom part of the Table reports parameters (input resistance, and membrane area) for the 3-compartment reduction for all morphologies; C1 and C2 are the compartments used to implement the smooth and spiny dendrites, respectively, whereas the soma is the same as in the full morphology; highlighted in red are the cells for which a 3-compartment reduction gave the best results.



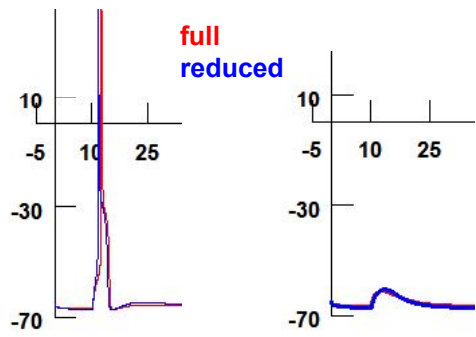






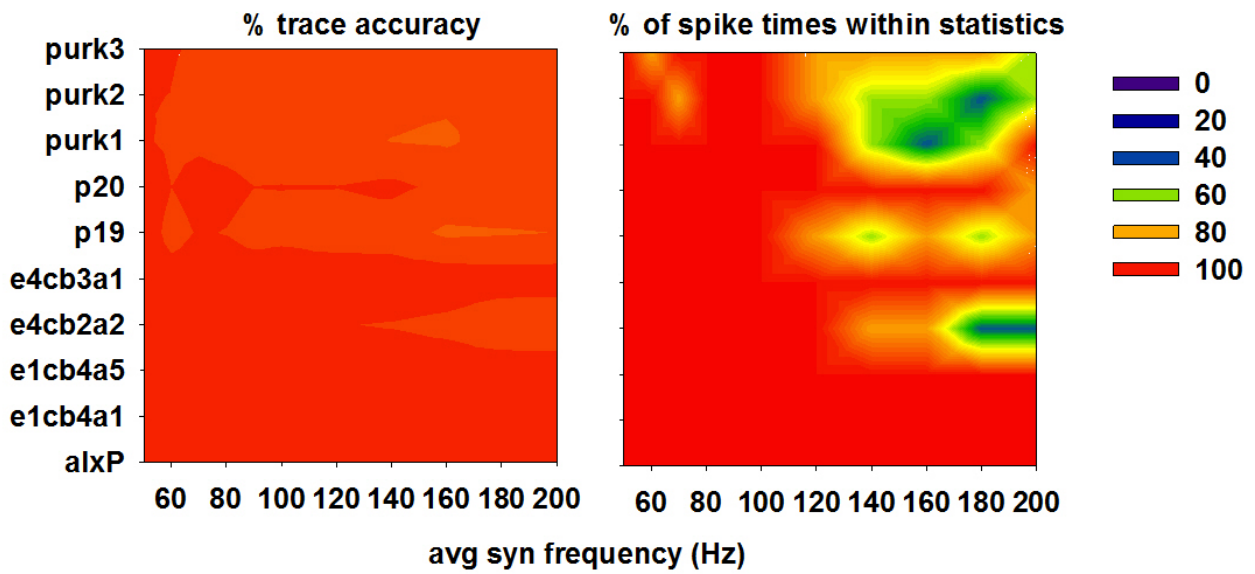
both syn on loc.1

syn on loc.1 and 2

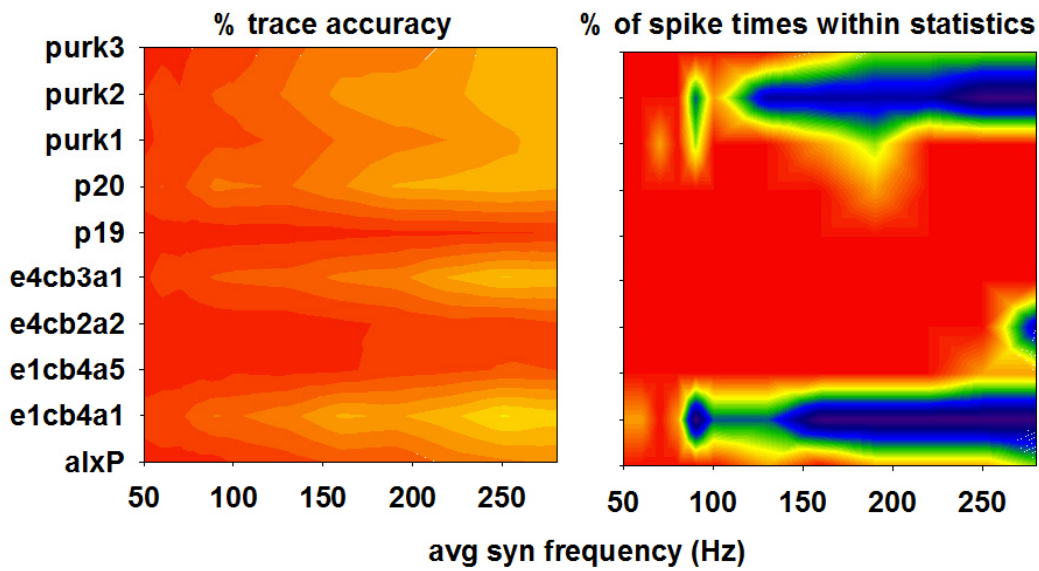




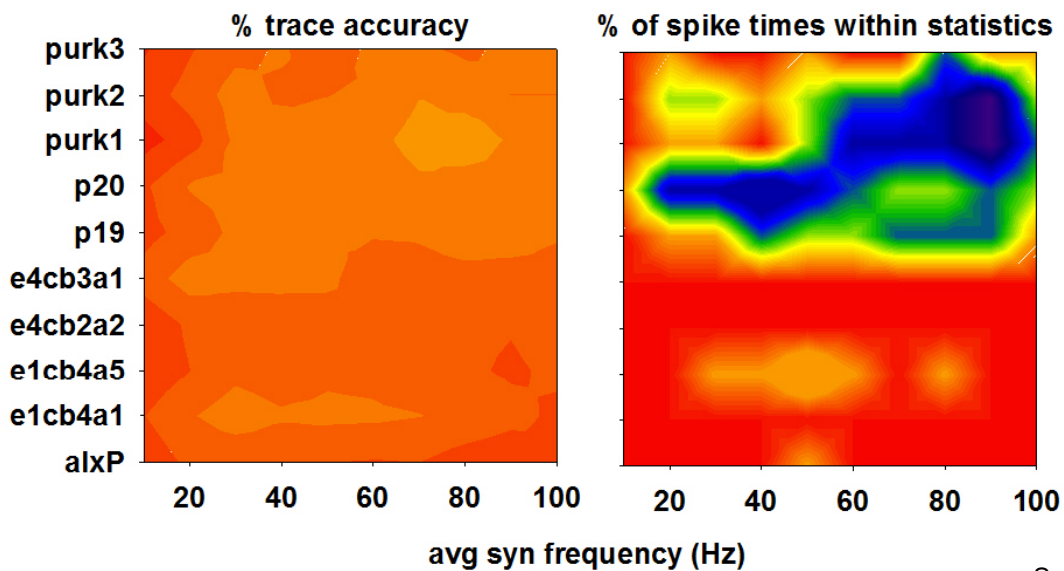
### Full

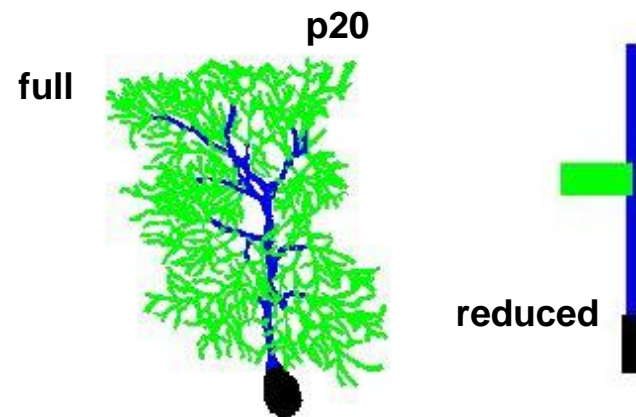
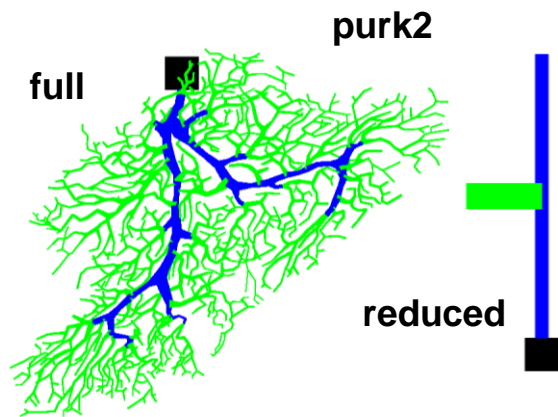


### Partial

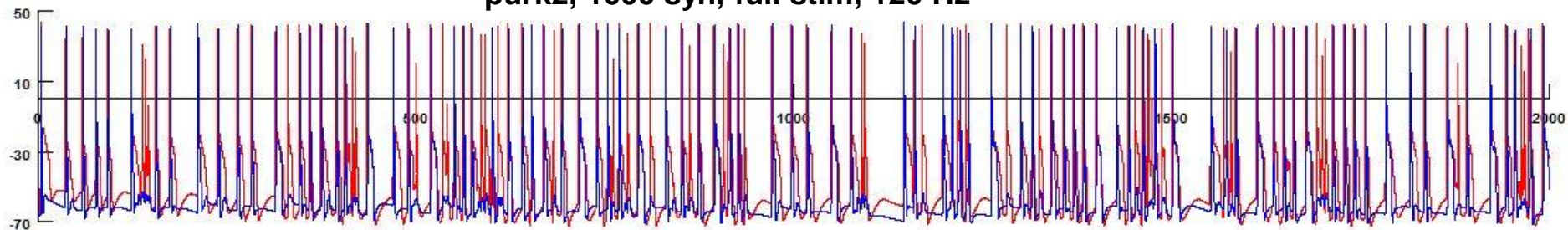


### Segregated





**purk2, 1000 syn, full stim, 120 Hz**



**full reduced**

**p20, 1000 syn, full stim, 160 Hz**

