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 ($n = 5, ±sd$) 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 ($±$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:

|      | alxP | e1cb4a1 | e1cb4a5 | e4cb2a2 | e4cb3a1 | p19 | p20 | purk1 | purk2 | purk3 |
|------|------|---------|---------|---------|---------|-----|-----|-------|-------|-------|
| smooth | 72   | 57      | 56      | 58      | 56      | 82  | 49  | 81    | 56    | 74    |
| spiny  | 851  | 630     | 633     | 660     | 685     | 1055| 650 | 863   | 784   | 760   |
| S1     | 462  | 344     | 345     | 360     | 371     | 568 | 349 | 472   | 420   | 417   |
| S2     | 253  | 193     | 202     | 223     | 221     | 341 | 202 | 266   | 258   | 243   |
| S3     | 136  | 93      | 86      | 77      | 93      | 146 | 99  | 125   | 106   | 100   |
| S4     | 46   | 34      | 30      | 40      | 40      | 53  | 30  | 42    | 30    | 55    |
| S5     | 17   | 14      | 22      | 11      | 14      | 24  | 9   | 26    | 24    | 17    |
| S6     | 9    | 9       | 4       | 7       | 2       | 3   | 8   | 7     | 1     | 1     |
| S7     | 0    | 0       | 0       | 0       | 0       | 1   | 1   | 1     | 1     | 1     |
| S8     | 0    | 0       | 0       | 0       | 0       | 1   | 1   | 1     | 0     | 0     |
| S9     | 0    | 0       | 0       | 0       | 0       | 1   | 1   | 1     | 0     | 0     |
| R_{in, full} | 66 | 36      | 74      | 60      | 53      | 21  | 26  | 11    | 13    | 14    |
| tot. area | 9937 | 24303   | 10638   | 11130   | 9379    | 39834| 24867| 55628 | 39861 | 46586 |

3-comp

|      | R_{in, full} | 89 | 37 | 96 | 75 | 73 | 25 | 28 | 17 | 17 | 19 |
|------|--------------|----|----|----|----|----|----|----|----|----|----|
| soma | 553          | 922| 511| 990| 800| 730| 750| 1521| 1521| 1521| 1521|
| C 1  | 850          | 1787| 722| 847| 1356| 2719| 1892| 5395| 5101| 4107|
| C 2  | 586          | 1500| 723| 646| 480| 2114| 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 MΩ), and the total membrane area (in μm²). 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.
Supplementary Figure 1

| Mouse   | Rat   | Guinea-pig |
|---------|-------|------------|
| e1cb4a1 | alxP  | purk1      |
| e1cb4a5 | p19   | purk2      |
| e4cb2a2 | p20   | purk3      |
| e4cb3a1 |       |            |
loc.2
loc.1

both syn on loc.1
full
reduced
syn on loc.1 and 2

Supplementary Figure 4
Supplementary Figure 5
a) 140 synapses

b) With Strahler’s analysis (no maxStim) vs. previous method (with maxStim) vs. previous method (no maxStim)