Supplementary Materials

From single cells and single columns to cortical networks: dendritic excitability, coincidence detection and synaptic transmission in brain slices and brains

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Supporting information

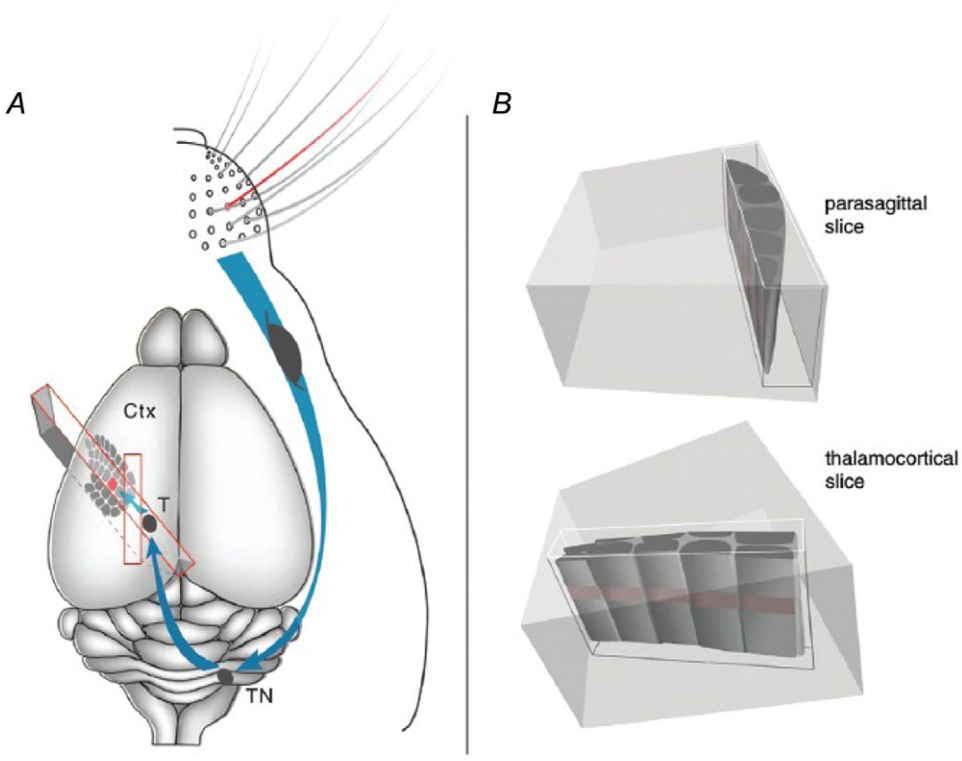

Figure S1. Rodent somatosensory cortex and brain slice preparations
A, Mechanoreceptors in the facial whisker pad excite neurons in the trigeminal nucleus (TN). These project to two thalamic subnuclei (T, *viz* VPM and POm). Thalamic nuclei project via thalamo-cortical (TC) projections to an array of cortical columns in the vibrissal area of cortex (Ctx), referred to as vS1 (S1: somatomotor cortex). Columns are specified as approximately caudo-rostrally oriented and alphabetically designated rows and as numbered arcs that are oriented medio-laterally. Whisker C2 (red) activates column C2 (red) of the vibrissal cortex. The dimensions of two types of brain slices, parasagittal and thalamocortical prepared from vS1 are outlined in red. Modified from Sakmann (2006) based on Knott et al. (2002). *B,* Parasagittal (upper panel) and a thalamocortical (lower panel) brain slice (Agmon & Connors, 1991) in a tissue block of vS1. In the examples shown the thalamocortical brain slice includes most of the C-row of columns.

Experimental Physiology

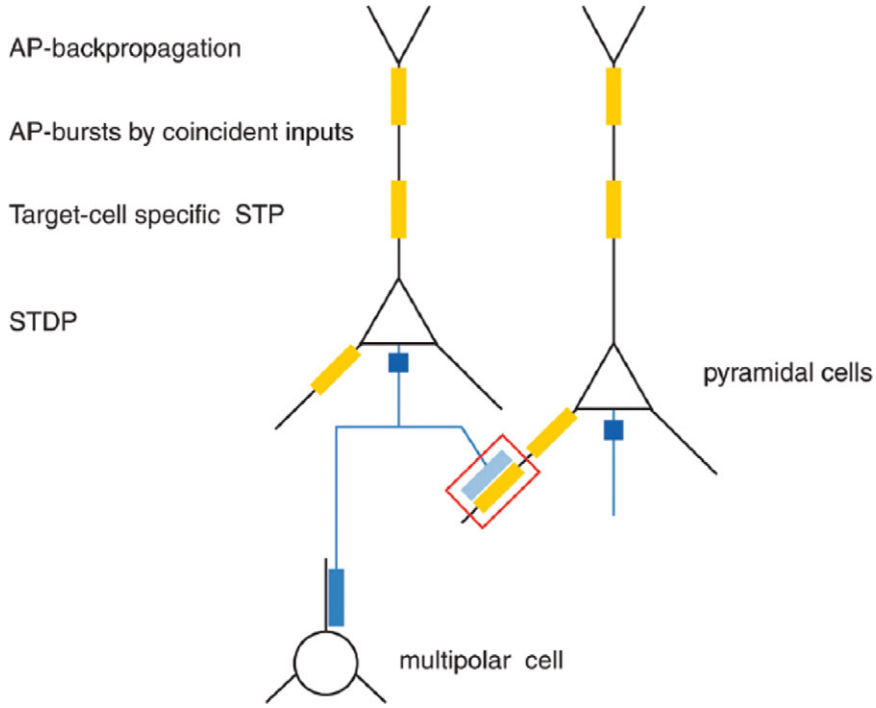

Figure S2. Subcellular structure elements of L5tt pyramids that are functionally relevant as shown in a simple cortical network consisting of two pyramidal cells and one (multipolar) non-pyramidal cell
Pyramidal cells (soma symbol: triangle) receive excitatory synaptic inputs via three dendritic zones (symbol: ochre rectangles). When evoked EPSPs are suprathreshold an AP is generated in the axon initial segment (symbol: blue square). The AP back-propagates into basal and propagates forward into axon and axon collaterals contacting different types of target cells (Stuart & Sakmann 1994). Coincident synaptic input to two or more spatially separate dendritic zones generate AP-bursts at the axon initial segment which also propagate backward into dendrites and forward into the main axon and its collaterals (Larkum et al. 1999b). The collaterals rout APs to different target cell-types (e.g. pyramidal cells, inhibitory cells or a POm cell). Depending on the target cell-type the release of transmitter from nerve terminals (dark and light blue rectangles) shows different forms of STP, either enhancing or depressing synaptic gain during repetitive APs (Reyes & Sakmann 1999; Groh et al. 2008). L5tt cells in the same cortical column can receive synchronous synaptic input and evoke AP-bursts are evoked in two connected cells. Such coincidences can increase or decrease synaptic gain (Markram et al.1997b) a mechanism referred to as spiking time dependent plasticity (STDP). The forward propagating APs in the upstream projecting cell (left pyramidal cell) evoke e.g. facilitating EPSPs in the downstream cell (right pyramidal cell). Near simultaneously the back-propagating dendritic APs in the downstream cell briefly depolarize the dendrites. Depolarisation can trigger an increase of intracellular calcium ions, via GluR channels and trigger post- (ochre rectangle) and presynaptic changes (light blue rectangle) in gain of synapses with coincident pre- and postsynaptic depolarisations (red frame).The modulated synapses in pairs of connected pyramidal cells are expected to be located mostly in the basal and apical oblique dendrites (Markram et al. 1997a).

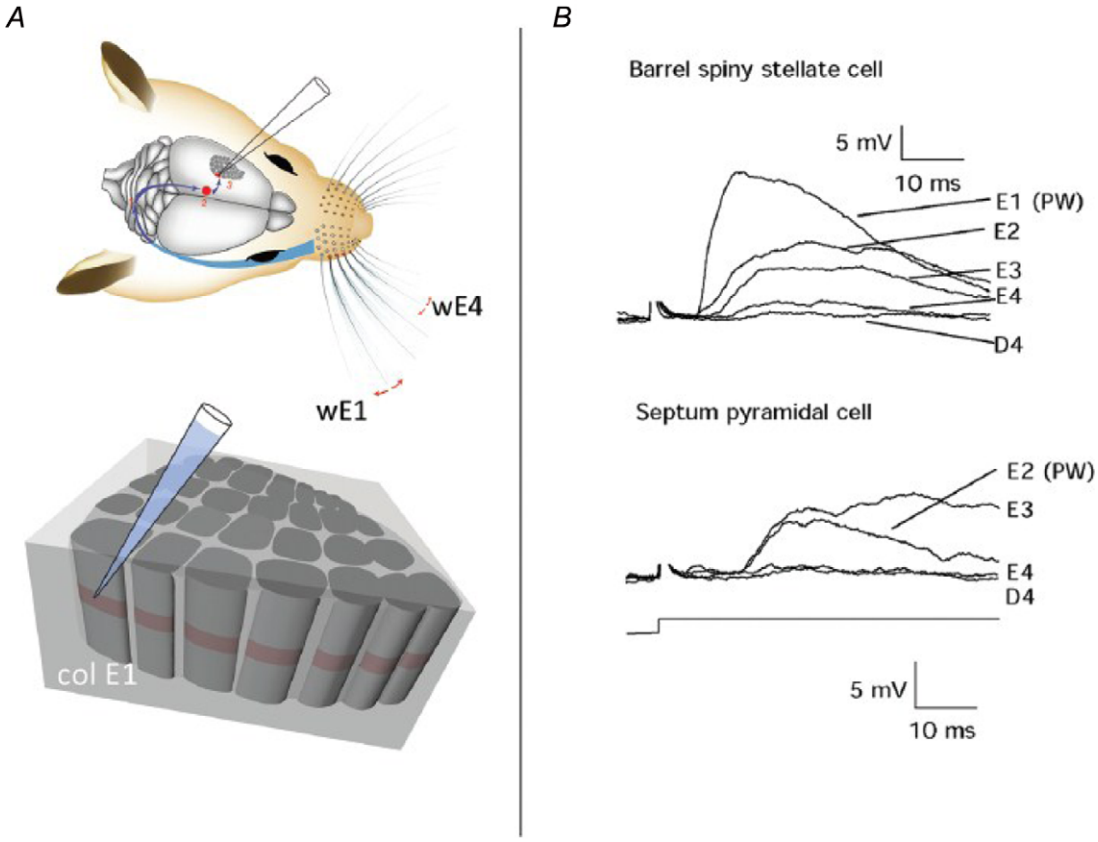

Figure S3. Whisker evoked subthreshold responses in granular layer 4
A, Whole-cell voltage recording from identified cells in a column of the whisker field and receptive field (RF) mapping of a *post hoc* identified cell. Individual deflections of different whiskers in the E-row (wE1 to wE4) while recording from a cell in in the granular layer in an identified column (col E1). Whisker E1 is the principal whisker, wE2 to wE4 are surround whiskers for cells located in column E1. *B,* Voltage responses (PSPs) to PW and individual SuW deflections (as indicated) recorded in granular layer from a spiny stellate cell located in the E1 PW-column (upper panel). Note longer PSP onset latency following SuW stimulation. Recordings from cells located in a septum between columns (lower panel) also show longer onset latencies. From Brecht & Sakmann (2002b).

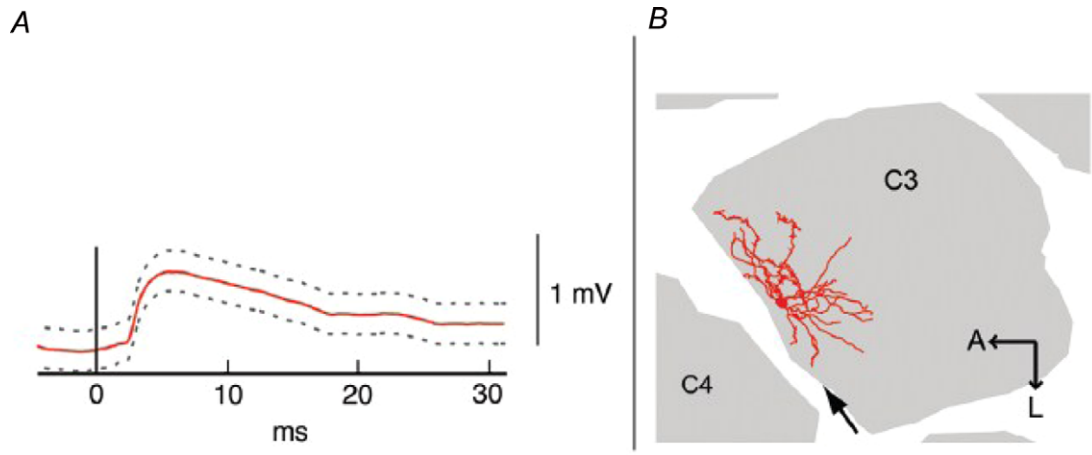

Figure S4. Average postsynaptic potential that a single thalamic AP evoked in a cortical L4 cell
A, Average postsynaptic potential (aPSP, or average unitary EPSP) recorded from a spiny stellate cell located in granular layer (L4) of the C3 column. Time of occurrence of the VPM action potential evoking a unitary EPSP is at 0 ms. *B,* Location of recorded spiny stellate cell in the granular layer of the C3 column. Tangential cross section of the C3 column (grey) and reconstructed soma and dendrites (red). A, anterior L, lateral direction. From Bruno & Sakmann (2006).

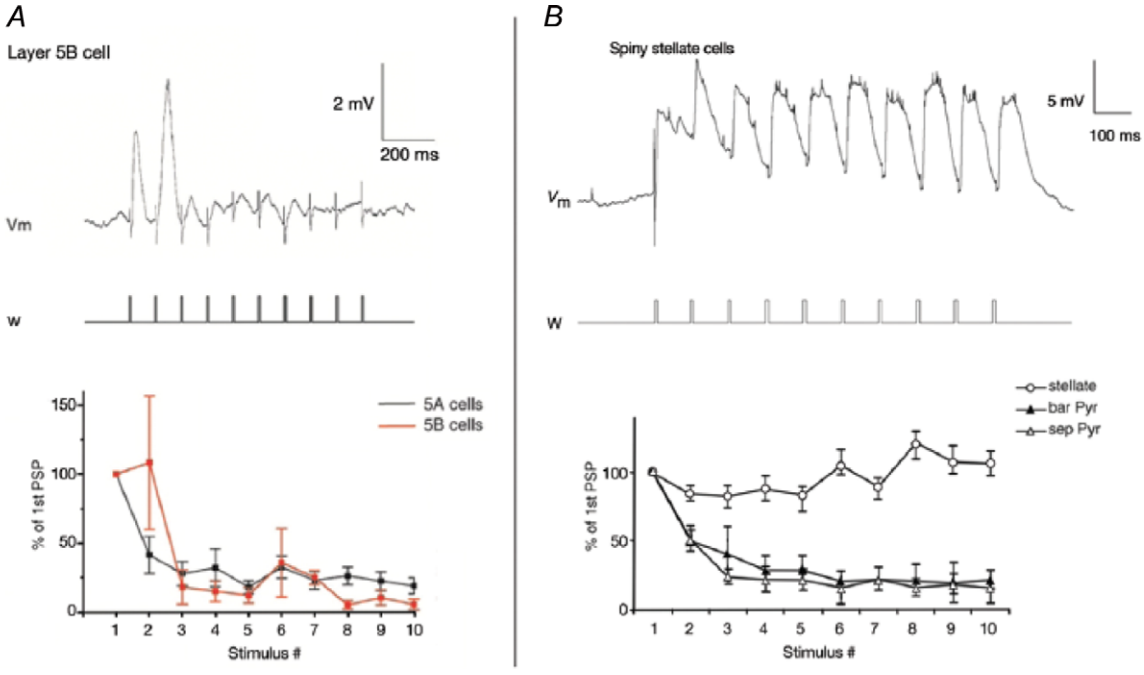

Figure S5. Response adaptation of whisker evoked PSPs in infragranular and granular layers during repetitive (10Hz) deflections of a principal whisker
A, Response adaptation of two cell-types located in L5 (L5A and L5B respectively). Recording from a L5tt cell located in L5B (upper panel) shows rapid average response (Vm) adaptation during repetitive whisker deflections (w). Lower graph: Rapid response adaptation of L5tt and L5st cell averaged responses located in layer 5B and L5A, respectively. *B,* Response amplitude is maintained in a spiny stellate cell located in the granular layer 4 (upper panel). Response adaptation of averaged responses in three different cell-types located in granular layer indicating cell-type specific differences (lower panel). From Brecht & Sakmann (2002b) & Manns et al. (2004).

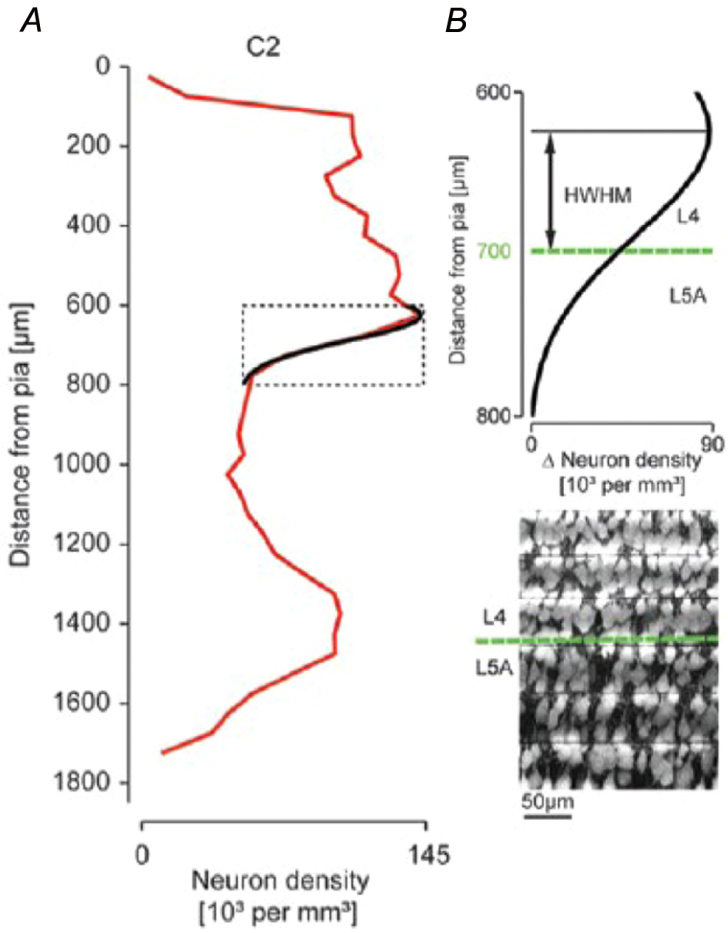

Figure S6. Density of cell bodies along a columns vertical axis
A, Cell body density profile (red line) between pia (top) and white matter (bottom). *B*. Definition of the border between the layers L4 and L5A at 700μm distance from the pia in a thalamocortical section graph). Density in the region of interest is indicated by the black segment of the density profile. Cell bodies in the transition zone between L4 and L5A are shown in the lower panel in a thalamocortical section (photomicrograph). From Meyer et al. (2010b).

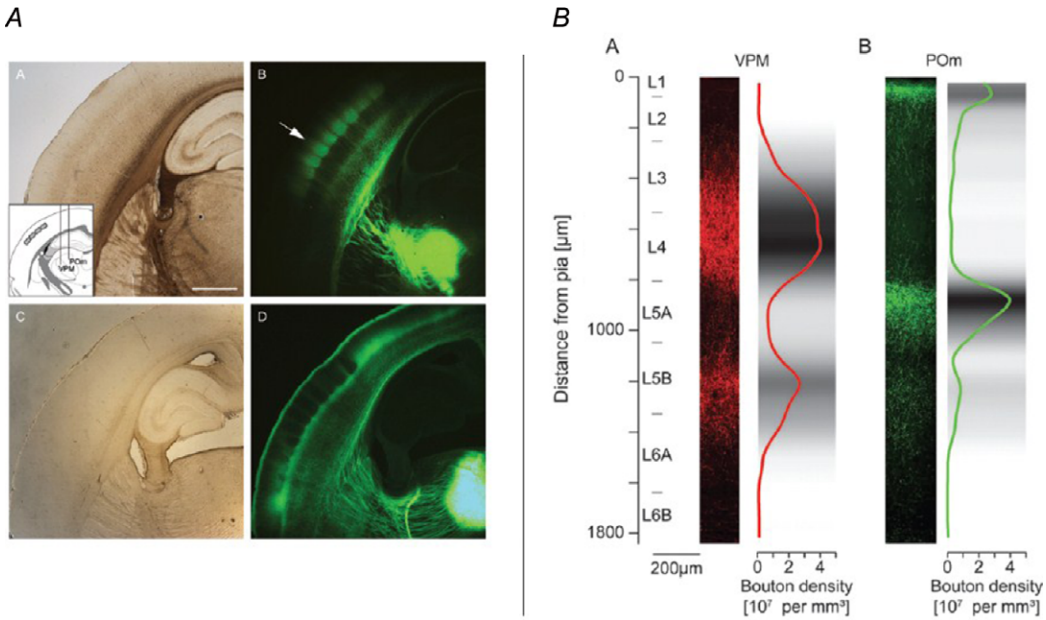

Figure S7. Thalamocortical innervation of vS1
A, Innervation domains of vS1 visualized by labeling thalamic VPM (upper right panel) and thalamic POm projection (lower right panel boutons with a fluorescent marker demonstrating the differences in projection density to different layers and the septa between columns of vS1. Left panels show the same sections as bright field photomicrographs for topographical orientation. *B,* Fluorescence density and calculated bouton density profile of VPM projections (A: red fluorescence and red line) and POm projections (B: green fluorescence and green line). Lines indicate complementary and overlapping innervation domains in different cortical layers. The ordinate shows the cortical depth measured from the pia and the location and width of cortical layers. From Wimmer et al. (2010) & Meyer et al. (2010a).

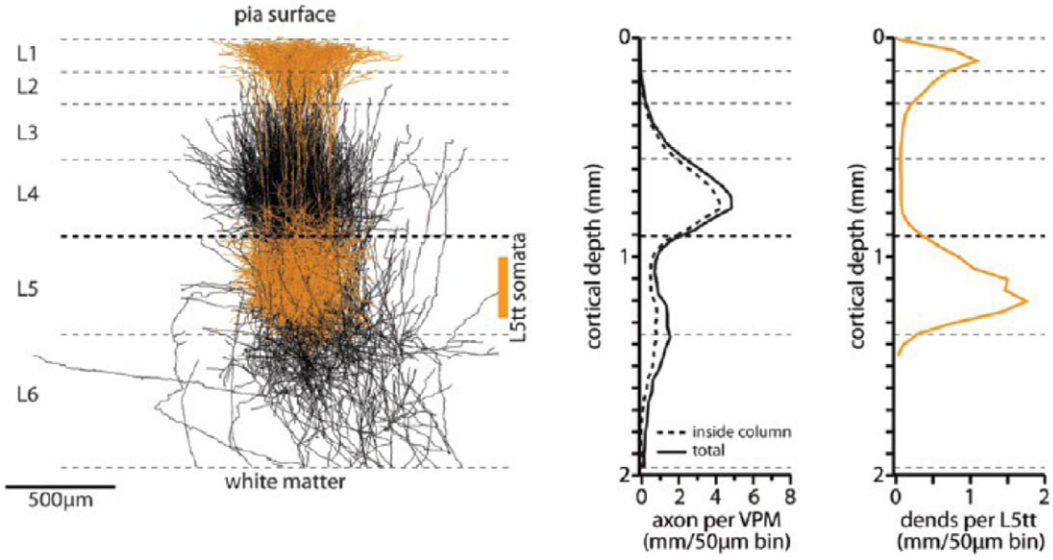

Figure S8. Thalamo-cortical (VPM) axon overlap with L5tt dendrites
Left, Overlay of projections of 3D VPM axon reconstructions (black) and 3D L5tt dendrite reconstructions (ochre), projected onto a thalamocortical plane. *Middle & Right,* 1D Vertical axon density profile (black) and dendrite density profile (ochre) suggesting potential VPM innervation on basal and L4 domain dendrite zones. From Narayanan et al. (2015).

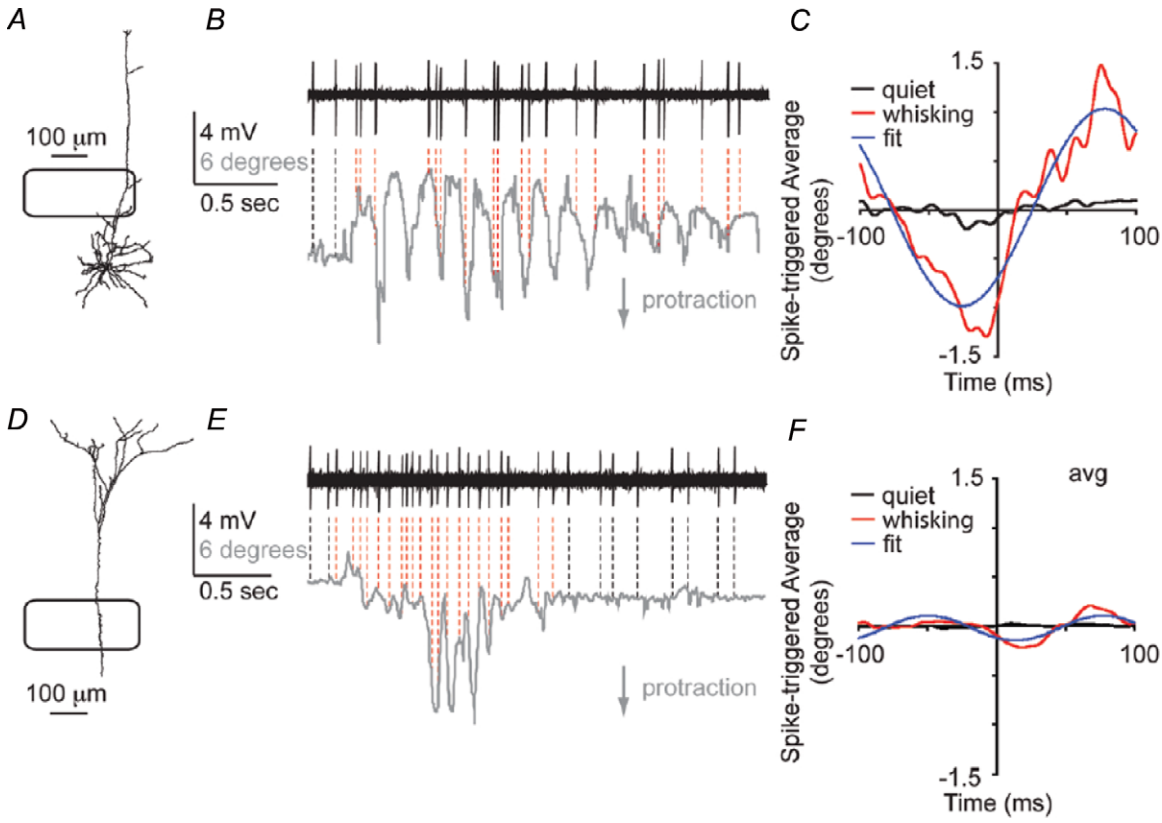

Figure S9. Unit AP-activity of L5st and L5tt cells during free whisking in awake animals
A, B, C, Layer 5st cell recording of unit AP-activity (black trace) before, during and after whisker movement (grey trace below). Graph shows that during whisking the unit activity is phase locked to whisker movement. *D, E, F,* Layer 5tt cell recording with only weak phase locking of unit AP-activity before, during and after whisker movements. From DeKock & Sakmann (2009).

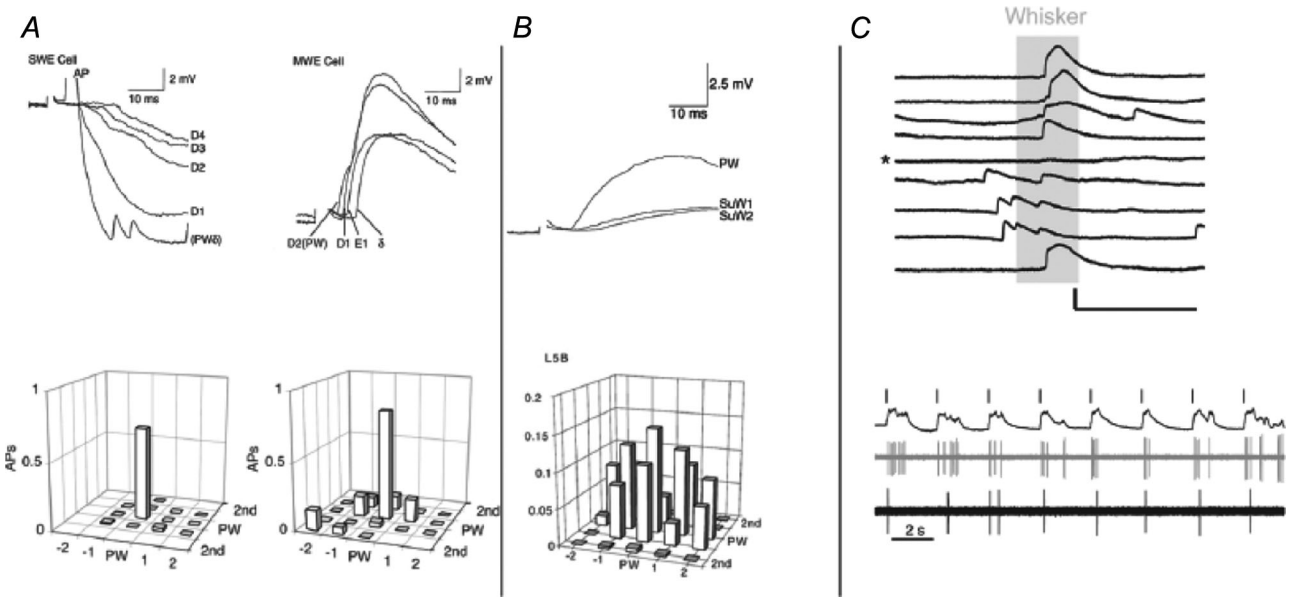

Figure S10. Principal whisker and surround whisker evoked PSP inputs (upper panels) and AP outputs (lower panels) in three (VPM, deep cortical layers of columns and POm) sequentially stacked modules of the vS1 network
A, VPM cells. Input PSP to single whisker (SWE) and multiwhisker (MWE) cells (upper graphs). The output AP response amplitudes are shown as bar histograms of AP-RF maps (lower graphs). Note narrow AP-map. From Brecht & Sakmann (2002a). *B,* L5tt cells. Input PSP-output AP comparison. Evoked input PSPs are shown in the upper graph and multiwhisker L5tt AP output is shown in the lower graph. Note broad AP-map. From Manns et al. (2004). *C,* POm cells. Input PSP-output AP comparison. Evoked (grey area) input PSPs are shown in the upper panel. Giant evoked PSP amplitude is decreased by previous spontaneous PSPs. Calibration bars: 10 mV and 100 ms. Lower panel: Simultaneous recording of whisker deflection evoked (vertical bars), local field potential (top trace), L5tt cell unit activity (middle trace) and thalamic POm cell unit activity (bottom trace) illustrating the sparsity of successful CT spike transmissions in the L5tt-to-POm pathway. For details see Mease et al. (2016b,c).

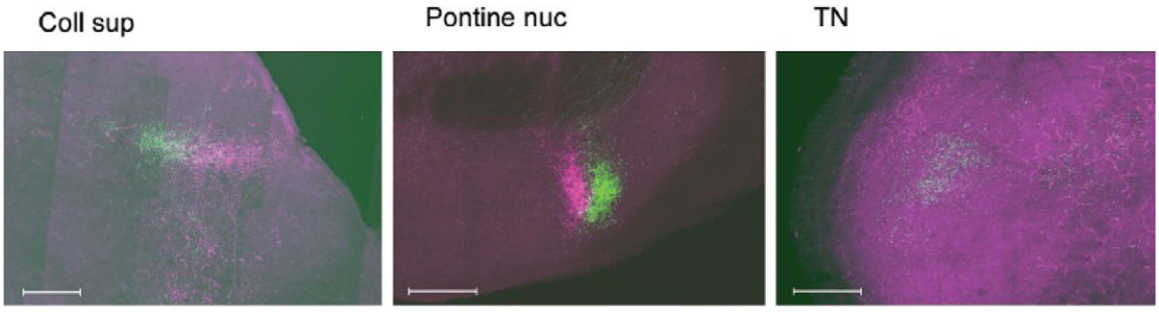

Figure S11. Whisker specific projection fields of fluorescent boutons of bulk labeled L5tt cells located in two separated columns
Virus encoding either of two different fluorescent markers labelling boutons was deposited in the lower stratum of two columns. Bouton projection domains of L5tt cells in are shown for the ipsilateral superior colliculus (Coll sup) and Pontine nuclei (Pontine nuc) and for contralateral trigeminal nucleus (TN). Coronal sections of colliculus superior (left panel), indicate that the label is located mostly in *stratum griseum intermedialis* (SGI). Sections of Pontine nuclei (middle panel) and of Sp5 of the trigeminal nucleus (right panel) show patial separation of L5tt projection terminals. Scale bar represents 200 μm. Unpublished results of A.Sumser and B.Sakmann.