A whole-cell recording database of neuromodulatory action in the adult neocortex

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Background

The recent release of two large intracellular electrophysiological databases now allows high-dimensional systematic analysis of mechanisms of information processing in the neocortex. Here, to complement these efforts, we introduce a freely and publicly available database that provides a comparative insight into the role of various neuromodulatory transmitters in controlling neural information processing.

Findings

A database of *in vitro* whole-cell patch-clamp recordings from primary somatosensory and motor cortices (layers 2/3) of the adult mice (2-15 months old) from both sexes is introduced. A total of 464 current-clamp experiments from identified excitatory and inhibitory neurons are provided. Experiments include recordings with (i) Step-and-Hold protocol during which the current was transiently held at 10 steps, gradually increasing in amplitude, (ii) “Frozen Noise” injections that model the amplitude and time-varying nature of synaptic inputs to a neuron in biological networks. All experiments follow a within neuron across drug design which includes a vehicle control and a modulation of one of the following targets in the same neuron: dopamine and its receptors D1R, D2R, serotonin 5HT1f receptor, norepinephrine Alpha1, and acetylcholine M1 receptors.

Conclusions

This dataset is the first to provide a systematic and comparative insight into the role of the selected neuromodulators in controlling cellular excitability. The data will help to mechanistically address how bottom-up information processing can be modulated, providing a reference for studying neural coding characteristics and revealing the contribution of neuromodulation to information processing.

Data description

Any behaviorally relevant computation in the brain is mediated through a network of neurons. Individual neurons, which constitute the nodes in the network, have powerful information processing capabilities¹. The process is governed by (i) neuronal properties, e.g. cell class, type and density of calcium buffers^{2,3}, (ii) biophysical properties of the cell, e.g. membrane capacitance, ion channel type, and density^{4,5}, as well as (iii) the nature of (chemical) communication impinging onto the neuron^{6,7}. Because neurons primarily integrate information sent to them through ligand-gated neurotransmission, understanding how different neuromodulators alter information processing is crucial to uncover the mechanism of information coding in the brain.

Even though Recent large-scale studies^{8,9} now provide freely available datasets to biophysically and computationally study the mechanisms of information processing, they nonetheless do not address the contribution of different neurotransmitters, including neuromodulators, in this process. Neuromodulators, e.g. dopamine¹⁰, serotonin¹¹, acetylcholine¹², and norepinephrine¹³, as regulators of neuronal communication throughout the brain, control various neural, behavioural, and metabolic functions^{14,15}. The highly efficient and complex regulation of neuromodulators depends on their large family of receptor subtypes, receptor expression sites, ligands that are being synthesised and released, as well as the identity of the postsynaptic neurons^{7,16–18}. Here we provide a database collected from the neocortex of the mouse to help to contribute to these efforts. Focusing on the supragranular layers (Layers 2/3, L2/3) of the adult mouse, we intracellularly recorded from different types of neurons in sensory and motor cortices. Two protocols that mimic the sustained vs time-and-amplitude varying synaptic inputs were delivered to each identified neuron before and after pharmacological interventions targeting specific receptors. The Step-and-Hold protocol, i.e. a sustained depolarization of the membrane potential at 10 different depolarization steps, provides information regarding the active electrophysiological properties of the cell, including but not limited to the action potential threshold, spike timing, firing rate, and firing pattern, i.e. relative timing of action potentials in a spike train. The “frozen noise” protocol simulates the synaptic input impinging on a given postsynaptic cell, originating from 1000 synaptically connected presynaptic neurons^{1,3,19} and allows for the quantification of intracellular information transfer as time-and-amplitude varying somatic currents are translated into action potential sequences. Both protocols are repeated multiple times while controlling the pharmacological state of the intervention in the neuron (see Materials and Methods).

The database is freely available online (bit.ly/NeuromodulationDatabase) and will help address: (1) the regulation of neuronal activity by neuromodulators through specific receptors, (2) neuromodulatory control of information processing and transfer under sustained and acute changes in neuronal excitability, (3) Cell-type specific control over intracellular information processing by

neuromodulatory transmission. It will complement the recent efforts in the transcriptomic^{20,21}, proteomic²², cellular^{8,23}, and behavioural^{1,24–26} mapping of the sensory cortex to mechanistically study the neural information processing from molecules to behaviour.

Materials and Method

Experiments: Ethics statement

All experiments were conducted in accordance with the European Directive 2010/63/EU and have been approved by the local and national authorities prior to the start of experiments. Adult mice (Pvalbtm1(cre)Arb (RRID: MGI:5315557) or Ssttm2.1(cre)Zjh/J (RRID: IMSR_JAX:013044)) were backcrossed to C57BL6 and maintained on a 12-hour day-night cycle. They had ad libitum access to food and water and were kept in family cages until the day of the experiment.

Experiments: Slicing preparations

All the procedures were as described before^{20,27–29}. Total of 232 cells were studied in vitro in coronal sections of the primary somatosensory and primary motor cortices of the mouse (Figure 1). On the day of the experiment, each animal was deeply anaesthetised with isoflurane before transcardially perfused using ice-cold physiological (slicing) solution containing (in mM) 108 choline chloride, 3 KCl, 26 NaHCO₃, 1.25 NaH₂PO₄ · H₂O, 25 glucose · H₂O, 1 CaCl₂ · 2H₂O, 6 MgSO₄ · 7H₂O. The brain was removed and placed in the same medium we used before. Coronal sections (300 micrometres) were cut from the barrel cortex subfield of the primary somatosensory cortex or the primary motor cortex while the brain was submerged in ice-cold slicing solution as described before²⁰. Sections were transferred to a recovery chamber filled with artificial cerebrospinal fluid (ACSF) containing (in mM) 120 NaCl, 3.5 KCl, 10 glucose · H₂O, 2.5 CaCl₂ · 2H₂O, 1.3 MgSO₄ · 7H₂O, 25 NaHCO₃, and 1.25 NaH₂PO₄ · H₂O at 37 °C. After an hour of incubation, the slices were transferred to room temperature and used for recording. All the solutions used were pre-oxygenated with 95% O₂ and 5% CO₂.

Experiments: Whole-cell recording

The slice was placed in a chamber filled with ACSF and was continuously oxygenated throughout recordings. The primary somatosensory or primary motor cortex was located under the 2.5X magnification and target neurons were visually identified at 40X. We use HEKA EPC10 amplifiers and Patch Master v2 x 90.2 software for recording. The glass capillaries (1.00 mm [external diameter], 0.50 mm [internal diameter], 75 mm [length], GC100FS-7.5, Harvard Apparatus) were used as the electrodes after they pulled using a P-2000 puller (Sutter Instrument, USA). The initial resistance was 5-9 MOhm. The intracellular solution contained (in mM) 130 K-Gluconate, 5 KCl, 1.5 MgCl₂ · 6H₂O, 0.4 Na₃GTP,

4 Na₂ATP, 10 HEPES, 10 Naphosphocreatine, and 0.6 EGTA, whose pH was set at 7.22 with KOH and was filled into the electrodes for patching.

Figure 1. Description of the experimental procedures and dataset. Acute slices from the primary somatosensory (barrel) cortex and primary motor cortex, which is located rostra-laterally to the primary somatosensory cortex, were prepared from adult mice. Whole-cell current clamp recordings from putative excitatory and inhibitory neurons were made using two different stimulation conditions (Step-and-Hold and Frozen Noise, see Materials and Methods for details), before and during administration of receptor specific agonists (see Materials and Methods for details). **(A)** Left: Coronal slices from the adult neocortex were prepared. Right: Representative examples of microscopic imaging of soma at 40x and the membrane potential recorded (inset). **(B-D)** The distribution of the number of cells recorded across sexes (B), drug conditions and (C) cell classes.

Step-and-Hold protocol: we performed current-clamp recordings before and after the receptor

activation to determine the basic biophysical and spiking properties of each neuron. The resting membrane potential was set at -70mV. Neurons whose resting membrane potential fluctuated >7mV throughout the experiment were excluded from the database. Current injections were delivered in 10 incremental steps of 20 or 40pA/step for 500 ms with an inter-sweep interval of 6.5s (see Figure 2).

Figure 2. The representative dataset collected with the Step-and-Hold protocol. The variables are provided as a hierarchical tree. Variables in bold are the data displays shown on the right side of each column. AP=action potential, AHP=afterhyperpolarization. “Latency compression” is the difference in delay between the first and last action potential during each stimulation period normalised to the stimulus duration. “Adaptation” is the relative change of the observed variable normalised to the first event. The membrane potential traces on the top-right show the spiking responses to different amplitudes of injected current, superimposed on each other. The data underneath represents the number of action

potentials and the intensity of current injected under 10 step-and-hold stimuli (Filename=asli_2-7-19-E2-CCSTEP-NODRUG; neuron class: excitatory).

Frozen Noise protocol: We established an artificial neural network composed of 1000 neurons, each firing Poisson spike trains in response to a ‘hidden state’, a binary signal switching between an ‘on’ and an ‘off’ state according to a Markov process¹⁹. For each recorded inhibitory or excitatory neuron, the same ‘frozen noise’ signal was used, although the switching speed of the hidden state and the firing rates of the artificial neurons differed across cell types (see Table 1). The fluctuating frozen noise current (amplitude: 700, 2100 pA, for excitatory and inhibitory neurons respectively) was injected in addition to a baseline current that kept resting membrane potential at -70mV, both before and after receptor activation. The resulting membrane potential and currents were recorded.

Table 1. Frozen noise parameters

Parameter	Excitatory cells	Inhibitory cells
Number of artificial neurons N	1000	1000
Hidden state time constant τ	250 ms	50 ms
Average firing rate artificial neurons μ_q	0.1 Hz	0.5 Hz

Pharmacology

We regulated the activation of serotonin 5HT1f receptors (LY334370: 5 μ M), norepinephrine Alpha1 (Cirazoline hydrochloride: 40 μ M), acetylcholine M1 (McA-N-343: 20 μ M), as well as dopamine D1 (SKF38393: 1 μ M) and D2 receptors (Quinpirole: 10 μ M) independently and simultaneously using dopamine (50 μ M). All chemicals were obtained from Sigma-Aldrich.

All experiments included were within cell controls. Recordings in ACSF served as vehicle control, as all drugs were dissolved in ACSF. Both recording protocols (i.e. Step-and-Hold and Frozen Noise) were repeated before and after drug administration. The recordings upon drug administration started 3 min after each drug was released into the circulating bath solution. After each experiment, the recording chamber was cleaned and the circulating bath solutions were kept in separate containers to ensure that there is no cross-drug contamination.

Data organisation

The metadata contains information about the recorded animals, including the age, sex, strain, the date of the recording, the experiment number, and the target receptor (see Supplemental Table1). The experiments are named as prefix_date-experiment number-CCSTEP(or FN)-condition. All cells recorded from the same animal share the same experimental date. The current clamp data (CurrentClamp

folder) contains two subfolders, “Step-and-Hold protocol” and “Frozen Noise protocol”. Each cell has two files, they have the same name although the suffix depends on the stimulus condition. Similar to the “Step-and-Hold protocol”, the “FrozenNoise” subfolder contains all the recordings with the data recorded under the frozen noise protocol.

Data collected using the “Step-and-Hold protocol” includes the injected current, the recorded voltage, and the timestamps for each variable. The recordings are named similarly using a template, i.e “Trace_a_b_c_d” where (a) is the cell number, (b) sequence of recording, (c) sweep number, and (d) the channel, i.e 1 for current injected, 2 is for voltage observed.

The “Frozen Noise protocol” subfolder is organised similarly to the other one. Each datafile contains the cell response (i.e voltage recordings upon injected current), hidden state ¹⁹ (binary stimulus), the input current trace, and a Matlab structural variable named “settings”. These ‘settings’ include the following information: condition (ACSF or the specific agonist), experimenter, baseline current (in pA) that is injected to keep the resting membrane potential at -70 mV, amplitude_scaling ¹⁹ (to control spiking rate), tau (the time constant of the average switching speed of the hidden state), mean_firing_rate (the mean firing rate of the artificial neurons, in kHz), sampling_rate (the acquisition rate, in kHz), duration (in ms) and FLAG_convert_to_ampere (a binary value that is 1 if the output was converted into ampere) ⁸.

Cell type identification

We putatively classified neurons into excitatory and inhibitory subclasses based on the shape of soma and the pattern of spiking. The soma of excitatory neurons in acute slices appear more triangular and are larger than inhibitory neurons. This criterion is initially used to target neurons whose cell class was confirmed post-hoc using the spike patterns. The end-user can classify the neurons based on the active properties of the spiking to identify cellular classes of interest.

Re-use potential

The database provided herein contains sub- and suprathreshold voltage dynamics of adult cortical neurons upon sustained or time and amplitude modulated somatic depolarization with and without the activation of selected neuromodulatory receptors. It complements the dataset previously made available from our group⁸, which focused on the electrical characterization of sensory neocortical neurons in the adult brain as well as the community efforts to make electrophysiological data freely available ^{9,30}. The stimulus protocols provided in this dataset will help address fundamental questions like how the neuromodulators change action potential dynamics, shape and patterning (including adaptation), what are the cell type specific consequences of neuromodulation on cellular excitability,

and what are the contribution of neuromodulators to intracellular information transfer and communication in synaptically coupled networks.

Spike pattern adaptation to sustained current injection is often used to classify neuron types⁸. Excitatory neurons usually show a lower firing frequency than inhibitory neurons, rapidly adapting to prolonged stimulation. The data collected with the Step-and-Hold protocol provides means to systematically address how neuromodulators alter firing rate, relative and absolute action potential timing in a cell type specific manner (compare Figure 2 to Figure 3 for a representative case from excitatory and inhibitory neurons, respectively).

The way neurons encode and process information, among other things, depends on the features of action potentials and spiking patterns^{31,32} which reflect the activities of ion channels. While somatic depolarization is primarily regulated by calcium and sodium channels³³, repolarization is mediated by potassium and chloride channels³⁴. Neuromodulatory neurotransmitters could alter this process by phosphorylation of ion channels, thus controlling spiking patterns. The data provided herein will help address which neuromodulatory transmitters control action potential shape and its temporal dynamics, thus nominating receptor specific signalling pathways to explore the biophysical mechanism of neural information processing.

Spike patterns are the embodiment of information processing in the nervous system which is regulated by varying the rate and timing of action potentials¹. Quantification of intracellular information transfer from subthreshold to suprathreshold responses with and without the activation of neuromodulatory neurotransmitters will help shed light on the role of neuromodulation in information processing. The Frozen Noise protocol provides a systematic analysis of this process as time and amplitude varying somatic input is injected into the neuron while observing spike generation⁸. Researchers can analyse the changes between the input (current injected) and output (membrane potential recorded) to study information processing quantitatively. This approach ensures bias-free quantification of intracellular information transfer with a short (around 6 min) stimulation protocol¹⁹.

Given the bandwidth limited time and amplitude varying nature of the current injection in the Frozen Noise protocol, the observations will complement the observations made with the help of the Step-and-Hold protocol, as researchers can directly compare the action potential dynamics during sustained and fluctuating depolarization with and without receptor intervention.

Figure 3. Responses of a representative inhibitory neuron to sustained current injection. Stimulus protocol: Step-and-Hold. Variables quantified are shown as a hierarchical tree. Those that are in bold are used as data displays on the right columns. Labels and descriptions of definitions are as in Figure 2. (Filename=asli_12-7-19-E3-CCSTEP-NODRUG).

Application prospects

This database will contribute to multidisciplinary efforts, serving biologists, physiologists, computational and systems neuroscientists. It advances global efforts for the systematic analysis of neural responses across species^{8,35,36}. Because our experimental protocols are identical across the database provided herein and the one we previously published⁸, the user can benefit from a large dataset

of intracellular recordings with over 1500 experiments performed in the adult brain. Developing a unified description of information processing across different types of neurons and identifying the common mechanisms that regulate information transfer across (different classes of) neurons will be a significant contribution to many branches of neuroscience.

The data provided herein can contribute to molecular physiology pipelines. Users can identify co-regulation networks in the transcriptome^{21,23,37} and proteome^{22,38} of the somatosensory cortex that we provided freely to the community; the data can be visualised online at barrelomics.science.ru.nl. By molecular analysis of transcription and translation for the neuromodulatory receptors regulated herein, the user can identify mechanisms of action that are coupled to action potential dynamics controlled by neuromodulation, and can study key genes and proteins that affect the coding and transmission of neuronal information.

The aforementioned molecular datasets include additional groups with experience dependent changes in the transcriptome and proteome after the altered sensory experience which ultimately control action potential dynamics as shown before^{25,27–29,39,40}. Differential transcriptome analysis (between sensory deprived and control conditions) for the downstream targets of the receptors modulated herein will help to identify the neuromodulatory mechanisms that contribute to adaptive changes in information processing.

Quantification of information transfer is traditionally performed using methods borrowed from signal processing literature. These methods are developed with different constraints than the experimental realities of intracellular recordings *in vitro*. Because neural recording quality is limited in duration, e.g. due to fluctuations in the membrane potential, drift, and change in the health of the cell in acute slices, electrophysiological recordings from individual neurons result in relatively short (<60 min) recording epochs that allow a limited number of synaptic input patterns to be studied in a given neuron. The Frozen Noise dataset provided in the current database as well as the one we made available previously⁸ offer a solution.

Limitations

The neurons in this database mainly come from neurons in the L2/3 layer of the sensory and motor cortices, thus the sample does not represent the spiking dynamics of neurons across all layers in distinct nuclei of the neocortex. We target neurons “blindly”, without any knowledge regarding their molecular cell type. Expanding these experiments with molecularly targeted cell populations will improve further classification of the neurons.

Due to the within cell, repeated measure design we cannot randomise the order of vehicle and drug conditions. Thus, in all experiments, vehicle control was delivered first. To control for this order bias, we have also provided experiments where the vehicle was delivered sequentially multiple times.

The analyses of both protocols (data not shown) show that the order bias does not impact the quality of recordings and the neural responses. Because we used each slice only once and the set-up was thoroughly cleaned in between recordings, there was no cross-drug contamination.

Declarations

The authors declare that they have no competing interests.

Funding

This work was supported by a doctoral fellowship from the Chinese Scholarship Council (CSC) to X.Y.; grants from the European Commission (Horizon2020, nr. 660328), European Regional Development Fund (MIND, nr. 122035), and the Netherlands Organisation for Scientific Research (NWO-ALW Open Competition, nr. 824.14.022) to T.C.; and by the Netherlands Organisation for Scientific Research (NWO Veni Research Grant, nr. 863.150.25) to F.Z.

Supplemental Table1: Metadata

<i>date</i> (DD.MM. YY)	<i>Experiment</i> <i>number</i>	<i>Animal</i> <i>number</i>	<i>prefix</i>	<i>Age(p)</i>	<i>sex</i>	<i>Experiment</i> <i>protocol</i>	<i>Classification</i>	<i>Agonist</i>
30719	E1	A1	xuan	241	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
30719	E2	A1	xuan	241	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
30719	E3	A1	xuan	241	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
30719	E4	A1	xuan	241	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
70619	E1	A2	xuan	229	F	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
70619	E2	A2	xuan	229	F	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
70619	E5	A2	xuan	229	F	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
120619	E1	A3	xuan	145	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
120619	E3	A3	xuan	145	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
130619	E4	A4	xuan	146	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
140619	E2	A5	xuan	147	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
140619	E3	A5	xuan	147	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
140619	E4	A5	xuan	147	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
50619	E4	A6	xuan	227	F	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
260619	E4	A7	xuan	201	M	Step-and-Hold, Frozen Noise	Excitatory	5HT-1f(S1 cortex)
50619	E3	A6	xuan	227	F	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
70619	E4	A2	xuan	229	F	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
90719	E3	A8	xuan	215	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
90719	E4	A8	xuan	215	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
130619	E1	A4	xuan	146	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)

130619	E2	A4	xuan	146	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
130619	E3	A4	xuan	146	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
240619	E1	A9	xuan	199	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
260619	E2	A7	xuan	201	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
260619	E6	A7	xuan	201	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
260619	E5	A7	xuan	201	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT-1f(S1 cortex)
30419	E2	A10	xuan	236	F	Step-and-Hold, Frozen Noise	Excitatory	D2
30419	E3	A10	xuan	236	F	Step-and-Hold, Frozen Noise	Excitatory	D2
60319	E1	A11	xuan	230	M	Step-and-Hold, Frozen Noise	Excitatory	D2
60319	E2	A11	xuan	230	M	Step-and-Hold, Frozen Noise	Excitatory	D2
70319	E2	A12	xuan	231	M	Step-and-Hold, Frozen Noise	Excitatory	D2
70319	E3	A12	xuan	231	M	Step-and-Hold, Frozen Noise	Excitatory	D2
80119	E2	A13	xuan	47	M	Step-and-Hold, Frozen Noise	Excitatory	D2
80119	E3	A13	xuan	47	M	Step-and-Hold, Frozen Noise	Excitatory	D2
90119	E3	A14	xuan	48	M	Step-and-Hold, Frozen Noise	Excitatory	D2
101018	E2	A15	xuan	115	F	Step-and-Hold, Frozen Noise	Excitatory	D2
121018	E1	A16	xuan	117	F	Step-and-Hold, Frozen Noise	Excitatory	D2
121018	E2	A16	xuan	117	F	Step-and-Hold, Frozen Noise	Excitatory	D2
140319	E2	A17	xuan	238	M	Step-and-Hold, Frozen Noise	Excitatory	D2
151018	E2	A18	xuan	162	M	Step-and-Hold, Frozen Noise	Excitatory	D2
170119	E2	A19	xuan	140	M	Step-and-Hold, Frozen Noise	Excitatory	D2
170119	E3	A19	xuan	140	M	Step-and-Hold, Frozen Noise	Excitatory	D2

190319	E4	A20	xuan	211	M	Step-and-Hold, Frozen Noise	Excitatory	D2
200319	E3	A21	xuan	213	F	Step-and-Hold, Frozen Noise	Excitatory	D2
210119	E1	A22	xuan	152	M	Step-and-Hold, Frozen Noise	Excitatory	D2
210319	E3	A23	xuan	211	M	Step-and-Hold, Frozen Noise	Excitatory	D2
210319	E4	A23	xuan	211	M	Step-and-Hold, Frozen Noise	Excitatory	D2
221018	E1	A24	xuan	92	F	Step-and-Hold, Frozen Noise	Excitatory	D2
231018	E1	A25	xuan	93	F	Step-and-Hold, Frozen Noise	Excitatory	D2
231018	E2	A25	xuan	93	F	Step-and-Hold, Frozen Noise	Excitatory	D2
231118	E2	A26	xuan	128	M	Step-and-Hold, Frozen Noise	Excitatory	D2
240119	E2	A27	xuan	147	M	Step-and-Hold, Frozen Noise	Excitatory	D2
260319	E2	A28	xuan	185	M	Step-and-Hold, Frozen Noise	Excitatory	D2
260319	E4	A28	xuan	185	M	Step-and-Hold, Frozen Noise	Excitatory	D2
270319	E2	A29	xuan	186	M	Step-and-Hold, Frozen Noise	Excitatory	D2
280319	E3	A30	xuan	187	M	Step-and-Hold, Frozen Noise	Excitatory	D2
280319	E4	A30	xuan	187	M	Step-and-Hold, Frozen Noise	Excitatory	D2
290319	E1	A31	xuan	188	M	Step-and-Hold, Frozen Noise	Excitatory	D2
210119	E5	A22	xuan	152	M	Step-and-Hold, Frozen Noise	Inhibitory	D2
220119	E1	A32	xuan	153	M	Step-and-Hold, Frozen Noise	Inhibitory	D2
220119	E2	A32	xuan	153	M	Step-and-Hold, Frozen Noise	Inhibitory	D2
230119	E1	A33	xuan	146	F	Step-and-Hold, Frozen Noise	Inhibitory	D2
190319	E1	A20	xuan	211	M	Step-and-Hold, Frozen Noise	Inhibitory	D2
220319	E2	A34	xuan	212	M	Step-and-Hold, Frozen Noise	Inhibitory	D2

290319	E2	A31	xuan	188	F	Step-and-Hold, Frozen Noise	Inhibitory	D2
20719	E2	A35	asli	105	M	Step-and-Hold, Frozen Noise	Excitatory	M1
20819	E1	A36	asli	162	M	Step-and-Hold, Frozen Noise	Excitatory	M1
50719	E3	A37	asli	173	M	Step-and-Hold, Frozen Noise	Excitatory	M1
50719	E4	A37	asli	173	M	Step-and-Hold, Frozen Noise	Excitatory	M1
50819	E1	A38	asli	163	F	Step-and-Hold, Frozen Noise	Excitatory	M1
50819	E2	A38	asli	163	F	Step-and-Hold, Frozen Noise	Excitatory	M1
50819	E3	A38	asli	163	F	Step-and-Hold, Frozen Noise	Excitatory	M1
50819	E7	A38	asli	163	F	Step-and-Hold, Frozen Noise	Excitatory	M1
60819	E2	A39	asli	164	F	Step-and-Hold, Frozen Noise	Excitatory	M1
60819	E5	A39	asli	164	F	Step-and-Hold, Frozen Noise	Excitatory	M1
80719	E2	A40	asli	176	M	Step-and-Hold, Frozen Noise	Excitatory	M1
120719	E2	A41	asli	178	M	Step-and-Hold, Frozen Noise	Excitatory	M1
170619	E2	A42	asli	113	F	Step-and-Hold, Frozen Noise	Excitatory	M1
230719	E2	A44	asli	136	M	Step-and-Hold, Frozen Noise	Excitatory	M1
230719	E3	A44	asli	136	M	Step-and-Hold, Frozen Noise	Excitatory	M1
230719	E5	A44	asli	136	M	Step-and-Hold, Frozen Noise	Excitatory	M1
240719	E5	A45	asli	137	M	Step-and-Hold, Frozen Noise	Excitatory	M1
270619	E1	A46	asli	132	M	Step-and-Hold, Frozen Noise	Excitatory	M1
270619	E2	A46	asli	132	M	Step-and-Hold, Frozen Noise	Excitatory	M1
300719	E1	A47	asli	141	M	Step-and-Hold, Frozen Noise	Excitatory	M1
160719	E1	A48	xuan	144	M	Step-and-Hold, Frozen Noise	Excitatory	M1

160719	E5	A48	xuan	144	M	Step-and-Hold, Frozen Noise	Excitatory	M1
20819	E2	A36	asli	162	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
20819	E3	A36	asli	162	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
50819	E4	A38	asli	163	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
60819	E1	A39	asli	164	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
60819	E3	A39	asli	164	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
60819	E4	A39	asli	164	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
120719	E3	A41	asli	178	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
170619	E1	A42	asli	113	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
180719	E1	A43	asli	180	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
240719	E4	A45	asli	137	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
250719	E1	A49	asli	138	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
250719	E2	A49	asli	138	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
250719	E3	A49	asli	138	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
250719	E4	A49	asli	138	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
310719	E1	A50	asli	119	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
310719	E2	A50	asli	119	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
310719	E3	A50	asli	119	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
310719	E4	A50	asli	119	F	Step-and-Hold, Frozen Noise	Inhibitory	M1
160719	E2	A48	xuan	144	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
160719	E3	A48	xuan	144	M	Step-and-Hold, Frozen Noise	Inhibitory	M1
120919	E4	A60	payam	148	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1

260919	E1	A61	payam	113	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
260919	E2	A61	payam	113	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
21019	E2	A62	payam	90	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
21019	E3	A62	payam	90	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
31019	E1	A63	payam	91	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
31019	E3	A63	payam	91	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
31019	E4	A63	payam	91	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
31019	E5	A63	payam	91	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
101019	E3	A64	payam	128	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
161019	E4	A65	payam	115	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
120919	E1	A60	payam	148	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
90919	E2	A67	xuan	366	M	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
160919	E2	A68	xuan	376	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
200919	E2	A69	xuan	377	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
200919	E3	A69	xuan	377	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
270919	E1	A70	xuan	271	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
111019	E3	A71	xuan	211	F	Step-and-Hold, Frozen Noise	Excitatory	Alpha1
120919	E3	A60	payam	148	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
50919	E1	A72	payam	363	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
50919	E2	A72	payam	363	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
50919	E3	A72	payam	363	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
240919	E1	A73	payam	348	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1

250919	E1	A74	payam	349	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
250919	E2	A74	payam	349	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
21019	E1	A62	payam	90	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
21019	E6	A62	payam	90	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
101019	E2	A64	payam	128	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
101019	E4	A64	payam	128	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
101019	E5	A64	payam	128	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
161019	E3	A65	payam	115	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
161019	E5	A65	payam	115	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
90919	E1	A67	xuan	366	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
90919	E3	A67	xuan	366	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
90919	E4	A67	xuan	366	M	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
160919	E4	A68	xuan	376	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
200919	E1	A69	xuan	377	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
270919	E2	A70	xuan	271	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
270919	E3	A70	xuan	272	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
111019	E1	A71	xuan	211	F	Step-and-Hold, Frozen Noise	Inhibitory	Alpha1
260520	E2	A75	xuan	358	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
260520	E3	A75	xuan	358	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
270520	E3	A76	xuan	359	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
280520	E2	A77	xuan	340	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
10620	E3	A78	xuan	291	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)

20620	E1	A79	xuan	292	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
20620	E5	A79	xuan	292	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
30620	E1	A80	xuan	293	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
30620	E2	A80	xuan	293	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
30620	E3	A80	xuan	293	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
30620	E4	A80	xuan	293	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
90620	E2	A81	xuan	313	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
100620	E4	A82	xuan	314	F	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
110620	E3	A83	xuan	324	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
140620	E1	A84	xuan	327	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
140620	E3	A84	xuan	327	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
300620	E1	A85	xuan	343	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
30720	E2	A86	xuan	364	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
20720	E3	A87	xuan	363	M	Step-and-Hold, Frozen Noise	Excitatory	5HT1f(M1 cortex)
250520	E2	A88	xuan	357	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
260520	E4	A75	xuan	358	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
260520	E5	A75	xuan	358	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
280520	E1	A77	xuan	358	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
10620	E4	A78	xuan	291	F	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
10620	E5	A78	xuan	291	F	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
20620	E3	A79	xuan	292	F	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)

40620	E2	A89	xuan	308	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
40620	E5	A89	xuan	308	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
50620	E2	A90	xuan	310	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
110620	E1	A83	xuan	324	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
110620	E2	A83	xuan	324	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
300620	E4	A85	xuan	343	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
10720	E1	A91	xuan	362	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
10720	E2	A91	xuan	362	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
10720	E3	A91	xuan	362	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
10720	E4	A91	xuan	362	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
20720	E1	A87	xuan	363	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
30720	E1	A86	xuan	364	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
30720	E3	A86	xuan	364	M	Step-and-Hold, Frozen Noise	Inhibitory	5HT1f(M1 cortex)
100519	E1	A51	xuan	259	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
100519	E2	A51	xuan	259	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
100519	E3	A51	xuan	259	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
100519	E4	A51	xuan	259	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
140519	E2	A52	xuan	339	M	Step-and-Hold, Frozen Noise	Excitatory	dopamine
140519	E4	A52	xuan	339	M	Step-and-Hold, Frozen Noise	Excitatory	dopamine
150519	E2	A54	xuan	340	M	Step-and-Hold, Frozen Noise	Excitatory	dopamine
160519	E3	A55	xuan	307	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine

160519	E5	A55	xuan	307	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
240519	E1	A56	xuan	312	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
70519	E1	A57	xuan	281	M	Step-and-Hold, Frozen Noise	Excitatory	dopamine
80519	E4	A58	xuan	282	M	Step-and-Hold, Frozen Noise	Excitatory	dopamine
80519	E5	A58	xuan	282	M	Step-and-Hold, Frozen Noise	Excitatory	dopamine
90519	E4	A59	xuan	258	F	Step-and-Hold, Frozen Noise	Excitatory	dopamine
100519	E5	A51	xuan	258	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
100519	E6	A51	xuan	259	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
140519	E1	A52	xuan	339	M	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
150519	E1	A54	xuan	340	M	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
160519	E1	A55	xuan	307	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
160519	E2	A55	xuan	307	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
240519	E4	A56	xuan	312	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
90519	E3	A59	xuan	258	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
90519	E1	A59	xuan	258	F	Step-and-Hold, Frozen Noise	Inhibitory	dopamine
110717	E4	A92	NC	89	M	Step-and-Hold, Frozen Noise	Excitatory	D1
120717	E2	A93	NC	84	F	Step-and-Hold, Frozen Noise	Excitatory	D1
150817	E4	A94	NC	118	F	Step-and-Hold, Frozen Noise	Excitatory	D1
210817	E3	A95	NC	84	F	Step-and-Hold, Frozen Noise	Excitatory	D1
300817	E3	A96	NC	285	F	Step-and-Hold, Frozen Noise	Excitatory	D1
101017	E4	A97	NC	335	M	Step-and-Hold, Frozen Noise	Excitatory	D1
101017	E5	A97	NC	335	M	Step-and-Hold, Frozen Noise	Excitatory	D1

111017	E1	A98	NC	372	M	Step-and-Hold, Frozen Noise	Excitatory	D1
111017	E3	A98	NC	372	M	Step-and-Hold, Frozen Noise	Excitatory	D1
111017	E4	A98	NC	372	M	Step-and-Hold, Frozen Noise	Excitatory	D1
121017	E6	A99	NC	373	M	Step-and-Hold, Frozen Noise	Excitatory	D1
171017	E2	A100	NC	154	F	Step-and-Hold, Frozen Noise	Excitatory	D1
171017	E4	A100	NC	154	F	Step-and-Hold, Frozen Noise	Excitatory	D1
201217	E4	A101	NC	218	F	Step-and-Hold, Frozen Noise	Excitatory	D1
300817	E6	A96	KK	285	F	Step-and-Hold, Frozen Noise	Inhibitory	D1
260617	E1	A102	NC	113	M	Step-and-Hold, Frozen Noise	Inhibitory	D1
260617	E2	A102	NC	113	M	Step-and-Hold, Frozen Noise	Inhibitory	D1
150817	E1	A94	NC	118	F	Step-and-Hold, Frozen Noise	Inhibitory	D1
150817	E3	A94	NC	118	F	Step-and-Hold, Frozen Noise	Inhibitory	D1
160817	E1	A103	NC	79	F	Step-and-Hold, Frozen Noise	Inhibitory	D1
160817	E2	A103	NC	79	F	Step-and-Hold, Frozen Noise	Inhibitory	D1
300817	E1	A96	NC	285	F	Step-and-Hold, Frozen Noise	Inhibitory	D1
140917	E1	A104	NC	309	F	Step-and-Hold, Frozen Noise	Inhibitory	D1

Bibliography

1. Azarfar, A., Calcini, N., Huang, C., Zeldenrust, F. & Celikel, T. Neural coding: A single neuron's perspective. *Neurosci. Biobehav. Rev.* **94**, 238–247 (2018).
2. Saftenku, E. E. & Friel, D. D. Combined computational and experimental approaches to understanding the Ca(2+) regulatory network in neurons. *Adv. Exp. Med. Biol.* **740**, 569–601 (2012).
3. Zeldenrust, F., Calcini, N., Yan, X., Bijlsma, A. & Celikel, T. Cell type specific information transfer for sparse coding. *BioRxiv* (2020) doi:10.1101/2020.11.06.371658.
4. Goillard, J.-M. & Marder, E. Ion channel degeneracy, variability, and covariation in neuron and circuit resilience. *Annu. Rev. Neurosci.* **44**, 335–357 (2021).
5. Nusser, Z. Differential subcellular distribution of ion channels and the diversity of neuronal function. *Curr. Opin. Neurobiol.* **22**, 366–371 (2012).
6. Miller, M. W. GABA as a neurotransmitter in gastropod molluscs. *Biol. Bull.* **236**, 144–156 (2019).
7. Picciotto, M. R., Higley, M. J. & Mineur, Y. S. Acetylcholine as a neuromodulator: cholinergic signaling shapes nervous system function and behavior. *Neuron* **76**, 116–129 (2012).
8. da Silva Lantyer, A. *et al.* A databank for intracellular electrophysiological mapping of the adult somatosensory cortex. *Gigascience* **7**, (2018).
9. Allen Institute Cell Types database. <http://celltypes.brain-map.org>.
10. Friston, K. J. *et al.* Dopamine, affordance and active inference. *PLoS Comput. Biol.* **8**, e1002327 (2012).
11. Rao, B. D., Sarkar, P. & Chattopadhyay, A. Selectivity in agonist and antagonist binding to Serotonin1A receptors via G-protein coupling. *Biochim. Biophys. Acta Biomembr.* **1862**, 183265 (2020).

12. Parikh, V. & Bangasser, D. A. Cholinergic signaling dynamics and cognitive control of attention. *Curr. Top. Behav. Neurosci.* **45**, 71–87 (2020).
13. Langer, S. Z. α 2-Adrenoceptors in the treatment of major neuropsychiatric disorders. *Trends Pharmacol. Sci.* **36**, 196–202 (2015).
14. Palacios-Filardo, J. & Mellor, J. R. Neuromodulation of hippocampal long-term synaptic plasticity. *Curr. Opin. Neurobiol.* **54**, 37–43 (2019).
15. Likhtik, E. & Johansen, J. P. Neuromodulation in circuits of aversive emotional learning. *Nat. Neurosci.* **22**, 1586–1597 (2019).
16. Missale, C., Nash, S. R., Robinson, S. W., Jaber, M. & Caron, M. G. Dopamine receptors: from structure to function. *Physiol. Rev.* **78**, 189–225 (1998).
17. McCorvy, J. D. & Roth, B. L. Structure and function of serotonin G protein-coupled receptors. *Pharmacol. Ther.* **150**, 129–142 (2015).
18. Salgado, H., Treviño, M. & Atzori, M. Layer- and area-specific actions of norepinephrine on cortical synaptic transmission. *Brain Res.* **1641**, 163–176 (2016).
19. Zeldenrust, F., de Knecht, S., Wadman, W. J., Denève, S. & Gutkin, B. Estimating the Information Extracted by a Single Spiking Neuron from a Continuous Input Time Series. *Front. Comput. Neurosci.* **11**, 49 (2017).
20. Kole, K. & Celikel, T. Neocortical microdissection at columnar and laminar resolution for molecular interrogation. *Curr. Protoc. Neurosci.* **86**, e55 (2019).
21. Kole, K. *et al.* Transcriptional mapping of the primary somatosensory cortex upon sensory deprivation. *Gigascience* **6**, 1–6 (2017).
22. Kole, K. *et al.* Proteomic landscape of the primary somatosensory cortex upon sensory deprivation. *Gigascience* **6**, 1–10 (2017).
23. Kole, K., Scheenen, W., Tiesinga, P. & Celikel, T. Cellular diversity of the somatosensory cortical map plasticity. *Neurosci. Biobehav. Rev.* **84**, 100–115 (2018).
24. Azarfar, A. *et al.* An open-source high-speed infrared videography database to study the

- principles of active sensing in freely navigating rodents. *Gigascience* **7**, (2018).
25. Miceli, S. *et al.* Reduced Inhibition within Layer IV of Sert Knockout Rat Barrel Cortex is Associated with Faster Sensory Integration. *Cereb. Cortex* **27**, 933–949 (2017).
 26. Kole, K. *et al.* Assessing the utility of Magneto to control neuronal excitability in the somatosensory cortex. *Nat. Neurosci.* **23**, 1044–1046 (2020).
 27. Celikel, T., Szostak, V. A. & Feldman, D. E. Modulation of spike timing by sensory deprivation during induction of cortical map plasticity. *Nat. Neurosci.* **7**, 534–541 (2004).
 28. Allen, C. B., Celikel, T. & Feldman, D. E. Long-term depression induced by sensory deprivation during cortical map plasticity in vivo. *Nat. Neurosci.* **6**, 291–299 (2003).
 29. Clem, R. L., Celikel, T. & Barth, A. L. Ongoing in vivo experience triggers synaptic metaplasticity in the neocortex. *Science* **319**, 101–104 (2008).
 30. Neurodata without borders. <https://www.nwb.org>.
 31. Naundorf, B., Wolf, F. & Volgushev, M. Unique features of action potential initiation in cortical neurons. *Nature* **440**, 1060–1063 (2006).
 32. Yao, C., He, Z., Nakano, T. & Shuai, J. Spiking patterns of a neuron model to stimulus: Rich dynamics and oxygen's role. *Chaos* **28**, 083112 (2018).
 33. Catterall, W. A., Hulme, J. T., Jiang, X. & Few, W. P. Regulation of sodium and calcium channels by signaling complexes. *J. Recept. Signal Transduct. Res.* **26**, 577–598 (2006).
 34. Carmeliet, E. Mechanisms and control of repolarization. *Eur. Heart J.* **14 Suppl H**, 3–13 (1993).
 35. Eglén, S. J. *et al.* A data repository and analysis framework for spontaneous neural activity recordings in developing retina. *Gigascience* **3**, 3 (2014).
 36. Hawrylycz, M. J. *et al.* An anatomically comprehensive atlas of the adult human brain transcriptome. *Nature* **489**, 391–399 (2012).
 37. Kole, K. *et al.* Supporting data for “Transcriptional mapping of the primary somatosensory cortex upon sensory deprivation.” *GigaScience Database* (2017) doi:10.5524/100296.
 38. Kole, K. *et al.* Supporting data for “Proteomic landscape of the primary somatosensory cortex

upon sensory deprivation.” *GigaScience Database* (2017) doi:10.5524/100336.

39. Foeller, E., Celikel, T. & Feldman, D. E. Inhibitory sharpening of receptive fields contributes to whisker map plasticity in rat somatosensory cortex. *J. Neurophysiol.* **94**, 4387–4400 (2005).
40. Juczewski, K. *et al.* Somatosensory map expansion and altered processing of tactile inputs in a mouse model of fragile X syndrome. *Neurobiol. Dis.* **96**, 201–215 (2016).