Table S1. Tools for Neural Circuit Mapping

Selected techniques currently available for neural circuit mapping and covering a broad range of capabilities are summarized, with attention given both to major applications/advantages (particularly in terms of characterizing IODEs) and to major caveats. The terms IDE and ODE are defined only relative to the cell population of interest; hence transsynaptic markers are particularly useful in this regard for identifying the inputs to a genetically and anatomically specified starter cell population.

Method		Connectivity Information/ Tracing Directionality	Mechanism/ Marker	Properties Checklist						Species Compatibility	Major Applications/ Advantages	Major Caveats	References
				Long-range Connections	Cell-type specificity	Trans-synaptic	Mono-synaptic Restricted	Single Cell Resolution	Synapse Visualization				
Golgi staining		Detailed local cell morphology	Silver precipitate					✔		widely compatible	• Complete neuronal morphology and fine structure (e.g. spines) are visible • Sparse labeling allows single neurons to be distinguished	• Only sparse labeling is useful • Staining can only be applied to post-fixed samples • Difficult to establish connectivity patterns (esp. long-range)	Ranjan and Mallick, 2010 (modern updates)
Dyes	**DiX Lipophilic Tracers**	Non-specific membrane tracing	Fluorescent dye (variety of wavelengths available) incorporated into cell membranes								• Compatible with tracing in post-fixed brains as well as with live tissue imaging • Efficient transport via membrane diffusion	• No cell type specificity • No directional specificity for tracing	Honig and Hume, 1989
	Dextran Amines	Some anterograde vs retrograde specificity using different mW dextrans leading to preferential uptake by cell bodies vs axons	Fluorophore, biotin or other marker conjugated to the dextran amine.								• Wide variety of marker conjugates • Variety of MWs available to help achieve directional specificity • Can be used to identify ODEs	• No cell type specificity	Reiner et al., 2000
	FluoroGold	Retrograde (axonal uptake)	UV excitation gives gold or blue emission depending on pH	✔				✔ (sparse labeling can allow single cell tracing)		widely compatible	• Efficient uptake by axons • Can be used to identify ODEs • Visualization can be enhanced by immunostraining • Compatible with EM for ultrastructural studies	• No cell type specificity • One color option • High diffusibility can make local injections difficult	Naumann et al., 2000
	Retrobeads	Retrograde (axonal uptake)	Latex microbeads used to deliver red or green fluorescent dyes								• Limited local spread of beads allows local connectivity mapping or very precise ODE tracing • Beads are trafficked quickly, yet are non-toxic, allowing a very wide range of survival times post-injection	• No cell type specificity • Punctate appearance can make cell ID difficult • No labeling of cell morphology • Less efficient axonal uptake than other options (e.g. FluoroGold)	Katz et al., 1984 Katz and Iarovici, 1990

Table S1. Tools for Neural Circuit Mapping 2 of 5

	Method	Connectivity Information/ Tracing Directionality	Mechanism/ Marker	Properties Checklist						Species Compatibility	Major Applications/ Advantages	Major Caveats	References
				Long-range Connections	Cell-type specificity	Trans-synaptic	Mono-synaptic Restricted	Single Cell Resolution	Synapse Visualization				
Tracer Proteins	**HRP**	Retrograde (axonal uptake)	Diaminobenzidine (DAB) reaction								• One component system • Can be used to identify ODEs	• No cell type specificity • One staining option	LaVail and LaVail, 1972
	WGA	Retrograde (transsynaptic) and anterograde (transsynaptic): specific in some contexts	Fluorophore, biotin, HRP, cre or other marker conjugated to tracer protein	✔	✔ (optionally compatible with viral/genetic technqiues for cell specificity)	✔		✔ (sparse expression can allow single cell tracing)		widely compatible	• Transsynaptic labeling • Can be used to identify IDE or ODEs	• Transsynaptic labeling is not highly efficient • Direction of transsynaptic labeling can be mixed, variable, and circuit-dependent	Schwab et al., 1978
	PHA-L	Anterograde (transsynaptic)				✔					• Transsynaptic labeling • Can be used to identify IDEs	• Transsynaptic labeling is not highly efficient • Not strictly anterograde	Gerfen and Sawchenko, 1984
	CtB	Retrograde (axonal uptake)									• Retrograde labeling • Cell type specificity possible • Can be used to identify ODEs	• Not strictly retrograde	Conte et al., 2009
	TTC	Retrograde (transsynaptic)				✔					• Transsynaptic labeling • Can be used to identify IDE or ODEs	• Transsynaptic labeling is not highly efficient • Not strictly retrograde	Kissa et al., 2002
	AAV	Anterograde (axon tracing) Can also be used to express transsynaptic markers	XFP or cre expressed by virus	✔	✔	✔ (if encoded virus is engineered to express a transsynaptic tracer protein)		✔ (sparse expression can allow single cell tracing		mammals	• Versatile, relatively non-toxic package for delivery of numerous tracing components • Allows cell type specificity using specific promoters or when combined with recombinase expression strategies • Can be used to identify IDEs (e.g. when combined with transsynaptic tracer proteins) and/or ODEs (e.g. via axon tracing)	• Packaging size limited to ~5 kB • Inconsistent reports of retrograde transport, may require batch-by-batch characterization	Betley and Sternson, 2011 (review) Wang et al., 2014 (comparison with BDA) Oh et al., 2014 (Allen Mouse Connectivity Atlas)

Table S1. Tools for Neural Circuit Mapping 3 of 5

	Method	Connectivity Information/ Tracing Directionality	Mechanism/ Marker	Properties Checklist: Long-range Connections	Cell-type specificity	Trans-synaptic	Mono-synaptic Restricted	Single Cell Resolution	Synapse Visualization	Species Compatibility	Major Applications/ Advantages	Major Caveats	References
alpha-herpesviruses	**HSV-1**	Retrograde (transsynaptic)	XFP or cre expressed by virus	✔	✔	✔	✔ (Ba2000 variant; see References)			mammals, some evidence for fish (see References)	• Efficient retrograde viral tracer • Transsynaptic labeling • Can be used to identify IDEs or ODEs (as in Fenno et al., 2014)	• Toxicity • Careful characterization required to assure that spread is restricted to synaptically connected cells • Only particular strains are specifically retrograde	Ugolini et al., 1987 Zemanick et al., 1991 (strain specificity) LaVail et al., 1997 (strain specificity) Fenno et al., 2014 (cell-type specific approaches) Zou et al., 2014 (fish)
	PRV Bartha									non-primate mammals	• Efficient retrograde viral tracer • Transsynaptic labeling • Monosynaptic restriction may be possible • Less toxic than other HSV strains • Can be used to identify IDEs or ODEs	• Toxicity	Enquist, 2002 Ekstrand et al., 2008 De Falco et al., 2001 (Ba2001 cell-type specific strain) Callaway, 2008 (see comment on Ba2000 for monosynaptic restriction)
	H129 strain	Anterograde (transsynaptic)								mammals	• Anterograde viral tracer • Transsynaptic labeling • Can be used to identify IDEs	• Toxicity	Sun et al., 1996 Lo and Anderson, 2011 (cre-dependent cell-type specificity)
	VSV	Anterograde (transsynaptic) or retrograde (transsynaptic): Directionality is glycoprotein dependent	XFP label expressed by virus	✔	✔	✔	✔			widely compatible	• Anterograde viral tracer • Transsynaptic labeling • Can be used to identify IDEs • Can be retricted to monosynaptic labeling using G deletion • Cell type specificity using EnvA pseudotyping	• Toxicity • Poorly understood batch variability, requires careful batch-by-batch characterization (see Correction to Beier et al., 2011)	Beier et al., 2011 Mundell et al., 2015
	CAV	Retrograde (axon transducing)	cre or GFP expressed by virus	✔	✔					mammals	• Relatively non-toxic retrograde viral tracer. The lack of toxicity makes this virus particularly appealing for examining functional circuit elements in vivo. • Can be used to identify ODEs	• Not transsynaptic	Soudais et al., 2001 Junyent and Kremer, 2015 also see TRIO references

Method	Connectivity Information/ Tracing Directionality	Mechanism/ Marker	Properties Checklist						Species Compatibility	Major Applications/ Advantages	Major Caveats	References
			Long-range Connections	Cell-type specificity	Trans-synaptic	Mono-synaptic Restricted	Single Cell Resolution	Synapse Visualization				
Rabies	Retrograde (transsynaptic and axon tranducing)	XFP label expressed by virus	✔	✔ (EnvA variants; see References)	✔	✔ (G-deleted variants; see References)			mammals	• Specific, efficient retrograde viral tracer • Transsynaptic labeling • Can be used to identify IDEs or ODEs • Can be retricted to monosynaptic labeling using G deletion • Cell type specificity using EnvA pseudotyping	• Toxicity • Down-regulation of host gene expression	Wickersham et al., 2007 Callaway and Luo, 2015 (review)
TRIO/cTRIO	Retrograde (axon transducing; CAV) and Retrograde (transsynaptic; rabies): Allows three steps of a circuit to be examined	XFP label expressed by virus	✔	✔ (cTRIO variant; see References)	✔	✔			demonstrated in mice, likely compatible with other mammalian systems	• Same advantages of rabies (above) • Specification of inputs based on output target, allowing visualization of the relationship between IDEs and ODEs (IODEs)	• Toxicity • Down-regulation of host gene expression	Schwarz et al., 2015 Beier et al., 2015 Lerner et al., 2015
GRASP/mGRASP	Synaptic partners	Split GFP reconstituted at synapses	✔	✔				✔	currently optimized for worms (GRASP) and mammals (mGRASP)	• Synapse visualization from defined partners • Can be used to further characterize the fine structure of IDEs or ODEs	• Possible bias for false positives in synapse detection	Feinberg et al., 2008 Kim et al., 2011
SynView	Synaptic partners	Split GFP reconstituted at synapses	✔	✔				✔	currently optimized for mammals	• Synapse visualization from defined partners • Can be used to further characterize the fine structure of IDEs or ODEs	• Currently limited to examining synaptic contacts initiated by specific adhesion molecules	Tsetsenis et al., 2014
Brainbow	Anterograde (axon tracing)	Stochastic expression of 3 XFPs	✔	✔			✔		widely compatible - currently adapted for worms, flies, fish, mice	• Combination of single cell resolution and dense labeling is possible (up to 100s of colors) • Can be used to identify ODEs	• Imaging is a major challenge (chromatic aberrations, bleaching, etc can make analysis difficult)	Livet et al., 2007 Pan et al., 2011 (fish) Hampel et al., 2011 (flies) Hadjieconomou et al., 2011 (flies) Cai et al., 2013
Electron Microscopy	Ultrastructural cell morphology	HRP/Diaminobenzidine (DAB) reaction, electron-dense membrane contrast agents, and/or heavy metal-conjugated antibody labeling	✔ (can be combined with long-range techniques e.g. FluoroGold, GESEM)	✔ (limited multifeature immunostaining)			✔	✔ (synapses can be identified by morphology and/or limited immunostaining)	widely compatible	• The most complete picture of neuronal morphology and circuit structure is obtained • Can be used to identify or further characterize the fine structure of IDEs or ODEs	• Extensive time and cost, even for imaging very small tissue volumes	Jurrus et al., 2009 Kleinfeld et al., 2011 Ward et al., 1975 Bock et al., 2011 Briggman et al., 2011 Atasoy et al., 2014 (GESEM)

Method	Connectivity Information/ Tracing Directionality	Mechanism/ Marker	Properties Checklist						Species Compatibility	Major Applications/ Advantages	Major Caveats	References
			Long-range Connections	Cell-type specificity	Trans-synaptic	Mono-synaptic Restricted	Single Cell Resolution	Synapse Visualization				
Functional Magnetic Resonance Imaging (fMRI)	Functional connectivity	BOLD signal (correlation)	(inference by correlation, need not be direct)						Human, non-human primate, rodent	• Whole brain functional connectivity visible in a live subject • Non-invasive, compatible with human studies	• Indirect (non-anatomical) measure of connectivity precludes IODE identification • No cell type specificity	Friston, 2011 (functional and effective connectivity review) Poldrack and Farah, 2015 (recent review of human imaging methods, with a focus on fMRI)
Diffusion Weighted Imaging (DWI)	White matter tract structure	Visualization of water diffusion preferentially along white matter tracts	(inference by diffusion, need not be direct)						Human, non-human primate, rodent	• Whole brain structural pathways visible in a live subject • Non-invasive, compatible with human studies	• Resolution limited to large white matter tracts • No functional information • No cell type specificity	Le Bihan and Johansen-Berg, 2012

Supplemental References

Acar, M., Kocherlakota, K.S., Murphy, M.M., Peyer, J.G., Oguro, H., Inra, C.N., Jaiyeola, C., Zhao, Z., Luby-Phelps, K., and Morrison, S.J. (2015). Deep imaging of bone marrow shows non-dividing stem cells are mainly perisinusoidal. Nature 526, 126–130.

Ando, K., Laborde, Q., Lazar, A., Godefroy, D., Youssef, I., Amar, M., Pooler, A., Potier, M.-C., Delatour, B., and Duyckaerts, C. (2014). Inside Alzheimer brain with CLARITY: senile plaques, neurofibrillary tangles and axons in 3-D. Acta Neuropathol. 128, 457–459.

Asai, H., Ikezu, S., Tsunoda, S., Medalla, M., Luebke, J., Haydar, T., Wolozin, B., Butovsky, O., Kügler, S., and Ikezu, T. (2015). Depletion of microglia and inhibition of exosome synthesis halt tau propagation. Nat. Neurosci. 18, 1584–1593.

Barth, A.L. (2007). Visualizing circuits and systems using transgenic reporters of neural activity. Curr. Opin. Neurobiol. 17, 567–571.

Beier, K.T., Saunders, A., Oldenburg, I.A., Miyamichi, K., Akhtar, N., Luo, L., Whelan, S.P.J., Sabatini, B., and Cepko, C.L. (2011). Anterograde or retrograde transsynaptic labeling of CNS neurons with vesicular stomatitis virus vectors. Proc. Natl. Acad. Sci. USA 108, 15414–15419.

Betley, J.N., and Sternson, S.M. (2011). Adeno-associated viral vectors for mapping, monitoring, and manipulating neural circuits. Hum. Gene Ther. 22, 669–677.

Bock, D.D., Lee, W.-C.A., Kerlin, A.M., Andermann, M.L., Hood, G., Wetzel, A.W., Yurgenson, S., Soucy, E.R., Kim, H.S., and Reid, R.C. (2011). Network anatomy and in vivo physiology of visual cortical neurons. Nature 471, 177–182.

Briggman, K.L., Helmstaedter, M., and Denk, W. (2011). Wiring specificity in the direction-selectivity circuit of the retina. Nature 471, 183–188.

Callaway, E.M. (2008). Transneuronal circuit tracing with neurotropic viruses. Curr. Opin. Neurobiol. 18, 617–623.

Callaway, E.M., and Luo, L. (2015). Monosynaptic Circuit Tracing with Glycoprotein-Deleted Rabies Viruses. J. Neurosci. 35, 8979–8985.

Cardin, J.A., Carlén, M., Meletis, K., Knoblich, U., Zhang, F., Deisseroth, K., Tsai, L.-H., and Moore, C.I. (2010). Targeted optogenetic stimulation and recording of neurons in vivo using cell-type-specific expression of Channelrhodopsin-2. Nat. Protoc. 5, 247–254.

Chabab, S., Lescroart, F., Rulands, S., Mathiah, N., Simons, B.D., and Blanpain, C. (2016). Uncovering the Number and Clonal Dynamics of Mesp1 Progenitors during Heart Morphogenesis. Cell Rep. 14, 1–10.

Chen, F., Tillberg, P.W., and Boyden, E.S. (2015). Expansion microscopy. Science 347, 543–548.

Chorev, E., Epsztein, J., Houweling, A.R., Lee, A.K., and Brecht, M. (2009). Electrophysiological recordings from behaving animals--going beyond spikes. Curr. Opin. Neurobiol. 19, 513–519.

Clairembault, T., Leclair-Visonneau, L., Coron, E., Bourreille, A., Le Dily, S., Vavasseur, F., Heymann, M.-F., Neunlist, M., and Derkinderen, P. (2015). Structural alterations of the intestinal epithelial barrier in Parkinson's disease. Acta Neuropathol. Commun. 3, 12.

DeFalco, J., Tomishima, M., Liu, H., Zhao, C., Cai, X., Marth, J.D., Enquist, L., and Friedman, J.M. (2001). Virus-assisted mapping of neural inputs to a feeding center in the hypothalamus. Science 291, 2608–2613.

Dorr, K.M., Amin, N.M., Kuchenbrod, L.M., Labiner, H., Charpentier, M.S., Pevny, L.H., Wessels, A., and Conlon, F.L. (2015). Casz1 is required for cardiomyocyte G1-to-S phase progression during mammalian cardiac development. Development 142, 2037–2047.

Ekstrand, M.I., Enquist, L.W., and Pomeranz, L.E. (2008). The alpha-herpesviruses: molecular pathfinders in nervous system circuits. Trends Mol. Med. 14, 134–140.

Enquist, L.W. (2002). Exploiting circuit-specific spread of pseudorabies virus in the central nervous system: insights to pathogenesis and circuit tracers. J. Infect. Dis. 186 (Suppl 2), S209–S214.

Epp, J.R., Niibori, Y., Liz Hsiang, H.L., Mercaldo, V., Deisseroth, K., Josselyn, S.A., and Frankland, P.W. (2015). Optimization of CLARITY for Clearing Whole-Brain and Other Intact Organs(1,2,3). eNeuro 2, pii: ENEURO.0087-15.2015.

Font-Burgada, J., Shalapour, S., Ramaswamy, S., Hsueh, B., Rossell, D., Umemura, A., Taniguchi, K., Nakagawa, H., Valasek, M.A., Ye, L., et al. (2015). Hybrid Periportal Hepatocytes Regenerate the Injured Liver without Giving Rise to Cancer. Cell 162, 766–779.

Botelho, J.F., Smith-Paredes, D., Soto-Acuña, S., Mpodozis, J., Palma, V., and Vargas, A.O. (2015). Skeletal plasticity in response to embryonic muscular activity underlies the development and evolution of the perching digit of birds. Sci. Rep. 5, 9840.

Friston, K.J. (2011). Functional and effective connectivity: a review. Brain Connect. 1, 13–36.

Garofalo, S., D'Alessandro, G., Chece, G., Brau, F., Maggi, L., Rosa, A., Porzia, A., Mainiero, F., Esposito, V., Lauro, C., et al. (2015). Enriched environment reduces glioma growth through immune and non-immune mechanisms in mice. Nat. Commun. 6, 6623.

Guo, Q., Zhou, J., Feng, Q., Lin, R., Gong, H., Luo, Q., Zeng, S., Luo, M., and Fu, L. (2015). Multi-channel fiber photometry for population neuronal activity recording. Biomed. Opt. Express 6, 3919–3931.

Guzowski, J.F., Timlin, J.A., Roysam, B., McNaughton, B.L., Worley, P.F., and Barnes, C.A. (2005). Mapping behaviorally relevant neural circuits with immediate-early gene expression. Curr. Opin. Neurobiol. 15, 599–606.

Hama, H., Hioki, H., Namiki, K., Hoshida, T., Kurokawa, H., Ishidate, F., Kaneko, T., Akagi, T., Saito, T., Saido, T., and Miyawaki, A. (2015). ScaleS: an optical clearing palette for biological imaging. Nat. Neurosci. 18, 1518–1529.

Hamel, E.J.O., Grewe, B.F., Parker, J.G., and Schnitzer, M.J. (2015). Cellular level brain imaging in behaving mammals: an engineering approach. Neuron 86, 140–159.

Hartman, B.H., Durruthy-Durruthy, R., Laske, R.D., Losorelli, S., and Heller, S. (2015). Identification and characterization of mouse otic sensory lineage genes. Front. Cell. Neurosci. 9, 79.

Higashiyama, H., Sumitomo, H., Ozawa, A., Igarashi, H., Tsunekawa, N., Kurohmaru, M., and Kanai, Y. (2016). Anatomy of the Murine Hepatobiliary System: A Whole-Organ-Level Analysis Using a Transparency Method. Anat. Rec. (Hoboken) 299, 161–172.

Hinckley, C.A., Alaynick, W.A., Gallarda, B.W., Hayashi, M., Hilde, K.L., Driscoll, S.P., Dekker, J.D., Tucker, H.O., Sharpee, T.O., and Pfaff, S.L. (2015). Spinal Locomotor Circuits Develop Using Hierarchical Rules Based on Motorneuron Position and Identity. Neuron 87, 1008–1021.

Hirashima, T., and Adachi, T. (2015). Procedures for the quantification of whole-tissue immunofluorescence images obtained at single-cell resolution during murine tubular organ development. PLoS ONE 10, e0135343.

Hoffmann, J., Marsh, L.M., Pieper, M., Stacher, E., Ghanim, B., Kovacs, G., König, P., Wilkens, H., Haitchi, H.M., Hoefler, G., et al. (2015). Compartment-specific expression of collagens and their processing enzymes in intrapulmonary arteries of IPAH patients. Am. J. Physiol. Lung Cell. Mol. Physiol. 308, L1002–L1013.

Hsiang, H.L., Epp, J.R., van den Oever, M.C., Yan, C., Rashid, A.J., Insel, N., Ye, L., Niibori, Y., Deisseroth, K., Frankland, P.W., and Josselyn, S.A. (2014). Manipulating a “cocaine engram” in mice. J. Neurosci. 34, 14115–14127.

Huang, A.H., Riordan, T.J., Pryce, B., Weibel, J.L., Watson, S.S., Long, F., Lefebvre, V., Harfe, B.D., Stadler, H.S., Akiyama, H., et al. (2015). Musculoskeletal integration at the wrist underlies the modular development of limb tendons. Development 142, 2431–2441.

Jafarnejad, M., Woodruff, M.C., Zawieja, D.C., Carroll, M.C., and Moore, J.E., Jr. (2015). Modeling Lymph Flow and Fluid Exchange with Blood Vessels in Lymph Nodes. Lymphat. Res. Biol. 13, 234–247.

Jain, R., Barkauskas, C.E., Takeda, N., Bowie, E.J., Aghajanian, H., Wang, Q., Padmanabhan, A., Manderfield, L.J., Gupta, M., Li, D., et al. (2015). Plasticity of Hopx(+) type I alveolar cells to regenerate type II cells in the lung. Nat. Commun. 6, 6727.

Joshi, N.S., Akama-Garren, E.H., Lu, Y., Lee, D.-Y., Chang, G.P., Li, A., DuPage, M., Tammela, T., Kerper, N.R., Farago, A.F., et al. (2015). Regulatory T Cells in Tumor-Associated Tertiary Lymphoid Structures Suppress Anti-tumor T Cell Responses. Immunity 43, 579–590.

Juang, J.-H., Kuo, C.-H., Peng, S.-J., and Tang, S.-C. (2015). 3-D Imaging Reveals Participation of Donor Islet Schwann Cells and Pericytes in Islet Transplantation and Graft Neurovascular Regeneration. EBioMedicine 2, 109–119.

Junyent, F., and Kremer, E.J. (2015). CAV-2-why a canine virus is a neurobiologist’s best friend. Curr. Opin. Pharmacol. 24, 86–93.

Jurrus, E., Hardy, M., Tasdizen, T., Fletcher, P.T., Koshevoy, P., Chien, C.-B., Denk, W., and Whitaker, R. (2009). Axon tracking in serial block-face scanning electron microscopy. Med. Image Anal. 13, 180–188.

Kim, S.-Y., Cho, J.H., Murray, E., Bakh, N., Choi, H., Ohn, K., Ruelas, L., Hubbert, A., McCue, M., Vassallo, S.L., et al. (2015a). Stochastic electrotransport selectively enhances the transport of highly electromobile molecules. Proc. Natl. Acad. Sci. USA 112, E6274–E6283.

Kitamura, K., Judkewitz, B., Kano, M., Denk, W., and Häusser, M. (2008). Targeted patch-clamp recordings and single-cell electroporation of unlabeled neurons in vivo. Nat. Methods 5, 61–67.

Kleinfeld, D., Bharioke, A., Blinder, P., Bock, D.D., Briggman, K.L., Chklovskii, D.B., Denk, W., Helmstaedter, M., Kaufhold, J.P., Lee, W.-C.A., et al. (2011). Large-scale automated histology in the pursuit of connectomes. J. Neurosci. 31, 16125–16138.

Knöpfel, T. (2012). Genetically encoded optical indicators for the analysis of neuronal circuits. Nat. Rev. Neurosci. 13, 687–700.

Kodandaramaiah, S.B., Franzesi, G.T., Chow, B.Y., Boyden, E.S., and Forest, C.R. (2012). Automated whole-cell patch-clamp electrophysiology of neurons in vivo. Nat. Methods 9, 585–587.

LaVail, J.H., Topp, K.S., Giblin, P.A., and Garner, J.A. (1997). Factors that contribute to the transneuronal spread of herpes simplex virus. J. Neurosci. Res. 49, 485–496.

Le Bihan, D., and Johansen-Berg, H. (2012). Diffusion MRI at 25: exploring brain tissue structure and function. Neuroimage 61, 324–341.

Lee, A.K., Manns, I.D., Sakmann, B., and Brecht, M. (2006). Whole-cell recordings in freely moving rats. Neuron 51, 399–407.

Lee, E., Choi, J., Jo, Y., Kim, J.Y., Jang, Y.J., Lee, H.M., Kim, S.Y., Lee, H.-J., Cho, K., Jung, N., et al. (2016). ACT-PRESTO: Rapid and consistent tissue clearing and labeling method for 3-dimensional (3D) imaging. Sci. Rep. 6, 18631.

Lima, S.Q., Hromádka, T., Znamenskiy, P., and Zador, A.M. (2009). PINP: a new method of tagging neuronal populations for identification during in vivo electrophysiological recording. PLoS ONE 4, e6099.

Lipski, J. (1981). Antidromic activation of neurones as an analytic tool in the study of the central nervous system. J. Neurosci. Methods 4, 1–32.

Liu, A.K.L., Hurry, M.E., Ng, O.T.-W., DeFelice, J., Lai, H.M., Pearce, R.K., Wong, G.T.-C., Chang, R.C.-C., and Gentleman, S.M. (2015a). Bringing CLARITY to the human brain: visualisation of Lewy pathology in three-dimensions. Neuropathol. Appl. Neurobiol. 10.1111/nan.12293.

Liu, C.Y., Dubé, P.E., Girish, N., Reddy, A.T., and Polk, D.B. (2015b). Optical reconstruction of murine colorectal mucosa at cellular resolution. Am. J. Physiol. Gastrointest. Liver Physiol. 308, G721–G735.

Liu, Z., Gerner, M.Y., Van Panhuys, N., Levine, A.G., Rudensky, A.Y., and Germain, R.N. (2015c). Immune homeostasis enforced by co-localized effector and regulatory T cells. Nature 528, 225–230.

Lo, L., and Anderson, D.J. (2011). A Cre-dependent, anterograde transsynaptic viral tracer for mapping output pathways of genetically marked neurons. Neuron 72, 938–950.

Machon, O., Masek, J., Machonova, O., Krauss, S., and Kozmik, Z. (2015). Meis2 is essential for cranial and cardiac neural crest development. BMC Dev. Biol. 15, 40.

Maksimovic, S., Nakatani, M., Baba, Y., Nelson, A.M., Marshall, K.L., Wellnitz, S.A., Firozi, P., Woo, S.-H., Ranade, S., Patapoutian, A., and Lumpkin, E.A. (2014). Epidermal Merkel cells are mechanosensory cells that tune mammalian touch receptors. Nature 509, 617–621.

Moalli, F., Proulx, S.T., Schwendener, R., Detmar, M., Schlapbach, C., and Stein, J.V. (2015). Intravital and whole-organ imaging reveals capture of melanoma-derived antigen by lymph node subcapsular macrophages leading to widespread deposition on follicular dendritic cells. Front. Immunol. 6, 114.

Mundell, N.A., Beier, K.T., Pan, Y.A., Lapan, S.W., Göz Aytürk, D., Berezovskii, V.K., Wark, A.R., Drokhlyansky, E., Bielecki, J., Born, R.T., et al. (2015). Vesicular stomatitis virus enables gene transfer and transsynaptic tracing in a wide range of organisms. J. Comp. Neurol. 523, 1639–1663.

Muñoz, W., Tremblay, R., and Rudy, B. (2014). Channelrhodopsin-assisted patching: in vivo recording of genetically and morphologically identified neurons throughout the brain. Cell Rep. 9, 2304–2316.

Murray, E., Cho, J.H., Goodwin, D., Ku, T., Swaney, J., Kim, S.-Y., Choi, H., Park, Y.-G., Park, J.-Y., Hubbert, A., et al. (2015). Simple, Scalable Proteomic Imaging for High-Dimensional Profiling of Intact Systems. Cell 163, 1500–1514.

Noguchi, M., Sumiyama, K., and Morimoto, M. (2015). Directed Migration of Pulmonary Neuroendocrine Cells toward Airway Branches Organizes the Stereotypic Location of Neuroepithelial Bodies. Cell Rep. 13, 2679–2686.

Oshimori, N., Oristian, D., and Fuchs, E. (2015). TGF-Beta promotes heterogeneity and drug resistance in squamous cell carcinoma. Cell 160, 963–976.

Palmer, W.M., Martin, A.P., Flynn, J.R., Reed, S.L., White, R.G., Furbank, R.T., and Grof, C.P.L. (2015). PEA-CLARITY: 3D molecular imaging of whole plant organs. Sci. Rep. 5, 13492.

Papa, S., Caron, I., Erba, E., Panini, N., De Paola, M., Mariani, A., Colombo, C., Ferrari, R., Pozzer, D., Zanier, E.R., et al. (2016). Early modulation of pro-inflammatory microglia by minocycline loaded nanoparticles confers long lasting protection after spinal cord injury. Biomaterials 75, 13–24.

Pascoli, V., Turiault, M., and Lüscher, C. (2012). Reversal of cocaine-evoked synaptic potentiation resets drug-induced adaptive behaviour. Nature 481, 71–75.

Peng, T., Frank, D.B., Kadzik, R.S., Morley, M.P., Rathi, K.S., Wang, T., Zhou, S., Cheng, L., Lu, M.M., and Morrisey, E.E. (2015). Hedgehog actively maintains adult lung quiescence and regulates repair and regeneration. Nature 526, 578–582.

Plummer, N.W., Evsyukova, I.Y., Robertson, S.D., de Marchena, J., Tucker, C.J., and Jensen, P. (2015). Expanding the power of recombinase-based labeling to uncover cellular diversity. Development 142, 4385–4393.

Poldrack, R.A., and Farah, M.J. (2015). Progress and challenges in probing the human brain. Nature 526, 371–379

Ranjan, A., and Mallick, B.N. (2010). A modified method for consistent and reliable Golgi-cox staining in significantly reduced time. Front. Neurol. 1, 157.

Roccaro, A.M., Mishima, Y., Sacco, A., Moschetta, M., Tai, Y.-T., Shi, J., Zhang, Y., Reagan, M.R., Huynh, D., Kawano, Y., et al. (2015). CXCR4 Regulates Extra-Medullary Myeloma through Epithelial-Mesenchymal-Transition-like Transcriptional Activation. Cell Rep. 12, 622–635.

Saboor, F., Reckmann, A.N., Tomczyk, C.U.M., Peters, D.M., Weissmann, N., Kaschtanow, A., Schermuly, R.T., Michurina, T.V., Enikolopov, G., Müller, D., et al. (2015). Nestin-expressing vascular wall cells drive development of pulmonary hypertension. Eur. Respir. J. ERJ–00574–ERJ–02015.

Soderblom, C., Lee, D.-H., Dawood, A., Carballosa, M., Jimena Santamaria, A., Benavides, F.D., Jergova, S., Grumbles, R.M., Thomas, C.K., Park, K.K., et al. (2015). 3D Imaging of Axons in Transparent Spinal Cords from Rodents and Nonhuman Primates. eNeuro 2.

Spence, R.D., Kurth, F., Itoh, N., Mongerson, C.R.L., Wailes, S.H., Peng, M.S., and MacKenzie-Graham, A.J. (2014). Bringing CLARITY to gray matter atrophy. Neuroimage 101, 625–632.

St-Pierre, F., Marshall, J.D., Yang, Y., Gong, Y., Schnitzer, M.J., and Lin, M.Z. (2014). High-fidelity optical reporting of neuronal electrical activity with an ultrafast fluorescent voltage sensor. Nat. Neurosci. 17, 884–889.

Sun, N., Cassell, M.D., and Perlman, S. (1996). Anterograde, transneuronal transport of herpes simplex virus type 1 strain H129 in the murine visual system. J. Virol. 70, 5405–5413.

Sylwestrak, E.L., Rajasethupathy, P., Wright, M.A., Jaffe, A., and Deisseroth, K. (2016). Multiplexed intact-tissue transcriptional analysis at cellular resolution. Cell 164, 792–804.

Tainaka, K., Kubota, S.I., Suyama, T.Q., Susaki, E.A., Perrin, D., Ukai-Tadenuma, M., Ukai, H., and Ueda, H.R. (2014). Whole-body imaging with single-cell resolution by tissue decolorization. Cell 159, 911–924.

Theofilas, P., Polichiso, L., Wang, X., Lima, L.C., Alho, A.T.L., Leite, R.E.P., Suemoto, C.K., Pasqualucci, C.A., Jacob-Filho, W., Heinsen, H., and Grinberg, L.T.; Brazilian Aging Brain Study Group (2014). A novel approach for integrative studies on neurodegenerative diseases in human brains. J. Neurosci. Methods 226, 171–183.

Tsujioka, H., Kunieda, T., Katou, Y., Shirahige, K., and Kubo, T. (2015). Unique gene expression profile of the proliferating Xenopus tadpole tail blastema cells deciphered by RNA-sequencing analysis. PLoS ONE 10, e0111655.

Ugolini, G., Kuypers, H.G., and Simmons, A. (1987). Retrograde transneuronal transfer of herpes simplex virus type 1 (HSV 1) from motoneurones. Brain Res. 422, 242–256.

Unal, G., Joshi, A., Viney, T.J., Kis, V., and Somogyi, P. (2015). Synaptic Targets of Medial Septal Projections in the Hippocampus and Extrahippocampal Cortices of the Mouse. J. Neurosci. 35, 15812–15826.

Walz, W., Boulton, A., and Baker, G. (2002). Patch-Clamp Analysis (New Jersey: Humana Press).

Wang, Q., Henry, A.M., Harris, J.A., Oh, S.W., Joines, K.M., Nyhus, J., Hirokawa, K.E., Dee, N., Mortrud, M., Parry, S., et al. (2014). Systematic comparison of adeno-associated virus and biotinylated dextran amine reveals equivalent sensitivity between tracers and novel projection targets in the mouse brain. J. Comp. Neurol. 522, 1989–2012.

Ward, S., Thomson, N., White, J.G., and Brenner, S. (1975). Electron microscopical reconstruction of the anterior sensory anatomy of the nematode Caenorhabditis elegans.?2UU. J. Comp. Neurol. 160, 313–337.

Weber, T.G., Osl, F., Renner, A., Pöschinger, T., Galbán, S., Rehemtulla, A., and Scheuer, W. (2014). Apoptosis imaging for monitoring DR5 antibody accumulation and pharmacodynamics in brain tumors noninvasively. Cancer Res. 74, 1913–1923.

Yang, B., Treweek, J.B., Kulkarni, R.P., Deverman, B.E., Chen, C.-K., Lubeck, E., Shah, S., Cai, L., and Gradinaru, V. (2014). Single-cell phenotyping within transparent intact tissue through whole-body clearing. Cell 158, 945–958.

Zapiec, B., and Mombaerts, P. (2015). Multiplex assessment of the positions of odorant receptor-specific glomeruli in the mouse olfactory bulb by serial two-photon tomography. Proc. Natl. Acad. Sci. USA 112, E5873–E5882.

Zemanick, M.C., Strick, P.L., and Dix, R.D. (1991). Direction of transneuronal transport of herpes simplex virus 1 in the primate motor system is strain-dependent. Proc. Natl. Acad. Sci. USA 88, 8048–8051.

Zhang, M.D., Tortoriello, G., Hsueh, B., Tomer, R., Ye, L., Mitsios, N., Borgius, L., Grant, G., Kiehn, O., Watanabe, M., et al. (2014). Neuronal calcium-binding proteins 1/2 localize to dorsal root ganglia and excitatory spinal neurons and are regulated by nerve injury. Proc. Natl. Acad. Sci. USA 111, E1149–E1158.

Zheng, H., and Rinaman, L. (2015). Simplified CLARITY for visualizing immunofluorescence labeling in the developing rat brain. Brain Struct. Funct. Published online March 14, 2015. 10.1007/s00429-015-1020-0.

Zhu, Y., Soderblom, C., Krishnan, V., Ashbaugh, J., Bethea, J.R., and Lee, J.K. (2015). Hematogenous macrophage depletion reduces the fibrotic scar and increases axonal growth after spinal cord injury. Neurobiol. Dis. 74, 114–125.

Ziętara, N., Łyszkiewicz, M., Puchałka, J., Witzlau, K., Reinhardt, A., Förster, R., Pabst, O., Prinz, I., and Krueger, A. (2015). Multicongenic fate mapping quantification of dynamics of thymus colonization. J. Exp. Med. 212, 1589–1601.

Zou, M., De Koninck, P., Neve, R.L., and Friedrich, R.W. (2014). Fast gene transfer into the adult zebrafish brain by herpes simplex virus 1 (HSV-1) and electroporation: methods and optogenetic applications. Front. Neural Circuits 8, 41.