# Glossary

**Ablation** Permanent destruction of a cell or tissue.

**Absolute recovery** In microdialysis, the total amount of substance collected in the dialysate over a set amount of time.

**ACRs** See *Anion conducting channelrhodopsins*.

**Action potential** A rapid, all-or-none depolarization of the cell membrane of a neuron that causes an electrochemical impulse to travel down the length of an axon. These impulses allow a neuron to communicate with other cells over great distances.

**Acute culture** A primary cell or tissue culture used for short-term experiments, usually lasting less than a day. For example, a slice culture for patch clamping experiments.

**Adeno-associated virus (AAV)** A type of virus used as a DNA delivery tool that infects dividing and postmitotic cells.

**Affinity chromatography** A form of chromatography used to purify proteins that uses small molecules fixed to a porous column to bind to proteins with a high affinity, such as a substrate binding to an enzyme.

**Agarose gel electrophoresis** The process of using an electrical field to force DNA molecules through an agarose gel to identify, isolate, and/or purify DNA sequences of interest.

**Agonist** A compound that can bind and activate an endogenous receptor, thus mimicking an endogenous ligand.

**Allatostatin receptor (Alstr)** A ligand-gated receptor found in insects. In the presence of the insect hormone allatostatin, the receptor causes hyperpolarization of cells. This receptor can be used as a genetically encoded tool to inhibit neural activity.

**Alstr** See *Allatostatin receptor.*

**Amino acid** A category of molecule consisting of amine and carboxyl functional groups, as well as a variable side chain. Used as the monomeric building blocks of proteins, as well as intermediates in metabolism.

**Amperometry** A form of voltammetry that uses an electrode to detect neurochemicals in living tissue. Unlike other voltammetry techniques, the electrode is held at a specific, constant voltage.

**Amplifier** A device used in electrophysiology recordings to amplify the relatively weak electrical signals derived from a recording electrode.

**Anhedonia** The loss of motivation to pursue an activity that is normally rewarding.

**Anion conducting channelrhodopsins (ACRs)** Genetically encoded chloride channels capable of hyperpolarizing neurons upon illumination with blue light.

**Anisotropic** Describes a diffusion of substances that is not equal in all directions but instead tends to move along a single axis. The opposite of *Isotropic*.

**Antagonist** A compound that can bind to a receptor but does not cause activation, simultaneously preventing the endogenous ligand from binding and thereby blocking its biological activity.

**Anterograde** In the direction from the neural cell body toward the presynaptic terminal.

**Anterograde tracer** A chemical probe that labels efferent axon tracts from the cell body through the axon to the presynaptic terminal to determine afferent projections.

**Antibody** A specialized protein used by an animal's immune system to detect and bind to foreign proteins. Used by neuroscientists to bind, identify, and/or purify proteins of interest.

**Antigen** A substance (usually a protein) recognized by an antibody.

**Aptamer** An engineered nucleic acid or peptide-based molecule that binds to a specific target molecule. Used as an alternative to antibodies.

**Arch** See *Archaerhodopsin.*

**Archaerhodopsin (Arch)** A genetically encoded transmembrane proton pump that hyperpolarizes neurons upon illumination with yellow light.

**Archon** A genetically encoded voltage indicator.

**Array tomography** A technique used to create highly detailed three-dimensional images of protein expression by combining the collection of ultrathin, serial brain sections with immunohistochemistry techniques.

**Artificial chromosome** A large DNA molecule that contains the telomeric, centromeric, and replication origin sequences necessary for replication and preservation in yeast, bacteria, or phage. Useful to neuroscientists as a vector for cloning relatively large DNA fragments (50−350 kb).

**Ataxia** A neurological condition exhibited as a gross lack of coordination of muscle movements.

**Ataxin** A genetically encoded toxin used to ablate specific neurons of interest.

**Autoclave** A large device used to sterilize tools, glassware, and reagents.

**Autofluorescence** The natural ability of some structures to fluoresce, even without the addition of exogenous fluorescent tags or dyes.

**Autoradiography** A technique that uses the pattern of decay emissions produced from a radioactive substance to form an image on an X-ray film. Used in neuroscience to detect radioactive probes.

**Axial** The plane in space that divides the brain and body into superior and inferior sections (top to bottom).

**BAC** See *Bacterial artificial chromosome*.

**Bacterial artificial chromosome** A large (50−250 kb) DNA vector capable of replicating in bacteria. Useful for manipulating large sequences of DNA, such as in the generation of transgenic or knockout constructs.

**Bacteriophage** A virus that infects bacteria. Sometimes simply referred to as "phage."

**Barnes maze** A maze used to test spatial learning and memory in rodents. The animal must learn the location of a drop box on a large circular table using spatial cues placed around the maze.

**Base pair** Describes a single, complementary nucleotide−nucleotide match between two strands of DNA or RNA. These base pairs are formed by hydrogen bonds between adenine−thymine, adenine−uracil, or cytosine−guanine bases.

**Basic Local Alignment Search Tool (BLAST)** A free public access database used to identify and compare DNA and protein sequences.

**Basophilic stain** A histological stain used to visualize cell bodies.

**Bead sterilizer** A tabletop device that uses hot beads to quickly sterilize surgical instruments and other tools.

**Between-subjects study** A study that compares two or more different groups of human subjects or animals. Compare with *Within-subjects study.*

**Bicuculline** A GABA receptor antagonist that prevents the normal inhibitory effects of GABA signaling. Used as a pharmacological agent to increase neural excitability.

**BiFC** See *Bimolecular fluorescence complementation*.

**Bimolecular fluorescence complementation (BiFC)** A technique used to visualize the interaction between two proteins. Each protein is fused to half of a fluorescent protein. When the proteins interact, the two halves of the fluorescent protein can fold together to emit light and report the interaction.

**Binary expression system** A genetic targeting approach that uses two or more DNA constructs to express a transgene in cells. Used to refine the spatial or temporal properties of transgene expression.

**BioID** A proximity labeling technique used to label and identify proteins that come into close proximity with a protein of interest.

**Biolistics** A method of DNA delivery that uses a gene gun to physically discharge DNA into cells.

**Biotin** A small molecule with an extremely high affinity for another molecule called avidin. Used in various histology and biochemistry techniques to amplify signal and purify proteins.

**BLAST** See *Basic Local Alignment Search Tool.*

**Blastocyst** An early embryonic structure that follows the fertilization of an egg.

**Bleed-through** A phenomenon in fluorescence microscopy that occurs when the signal of one fluorophore appears when a scientist uses a filter designed to detect the signal of a separate fluorophore.

**Blocked design** A strategy for presenting stimuli to human subjects in functional imaging experiments. Stimuli of the same category are presented grouped together in blocks. An alternative to an *Event-related design*.

**Blood oxygen level–dependent (BOLD) effect** The phenomenon in which the brain microvasculature increases the flow of oxygen-rich blood to neurons following an increase in neural activity.

**Blunt ends** Ends of fragments of DNA cut with restriction enzymes that result in no 5′ or 3′ overhangs; both strands of DNA terminate at the same complementary base pair. Opposite of *Sticky ends*.

**BOLD effect** See *Blood oxygen level–dependent effect*.

**BoNT** See *Botulinum toxin*.

**Botulinum toxin** A genetically encoded toxin that abates neurons upon expression.

**Brain atlas** A tool that identifies and depicts brain anatomy in three-dimensional coordinates.

**Brain organoid** An artificially grown, three-dimensional cell culture model of brain-like tissue produced from pluripotent stem cells. Used to model complex tissues within the brain and study neurodegenerative diseases.

**BrdU** See *Bromodeoxyuridine*.

**Bregma** A landmark on the surface of the mammalian skull, defined as the intersection between the sagittal and coronal sutures.

**Brightfield microscopy** A type of light microscopy in which white light passes directly through or is reflected off a specimen.

**Brodmann's areas** Divisions of the cerebral cortex defined by the cytoarchitecture of the cortical layers. Developed by Korbinian Brodmann in the early 20th century and still used today.

**Bromodeoxyuridine** A synthetic analog of the DNA nucleoside thymidine. Administered to an animal for use as a marker of cells in the DNA synthesis phase of mitosis; detected in subsequent histology experiments.

**Calcium phosphate transfection** A method of delivering DNA into cultured cells by using chemical reactions that form calcium phosphate precipitates.

**Canine adenovirus** A type of virus used as a DNA delivery tool that has retrograde properties (can be taken up at the synapse and transported back to projecting cell bodies).

**Cannula** A narrow, cylindrical tube implanted into the brain and through the skull for long-term access to deep brain structures in a living animal.

**Capsaicin receptor (TrpV1)** A genetically encoded, ligand-gated ion channel that depolarizes neurons in response to the capsaicin molecule. Can be used by neuroscientists to stimulate genetically defined populations of neurons.

**Cas9** See *CRISPR/Cas9*.

**Case study** An example of an event that happened to a subject (most often a human or group of humans) that retrospectively demonstrates an important finding about the nervous system.

**Cat scan** See *Computerized axial tomography.*

**cDNA** See *Complementary DNA*.

**cDNA library** A collection of hundreds or thousands of DNA plasmids, each containing a unique cDNA molecule. Used to collect and store DNA sequences that were actively expressed in a sample prior to exposure with the reverse transcriptase enzyme.

**Cell-attached mode** A patch-clamp electrophysiology technique in which a glass micropipette forms a tight gigaseal with the membrane of a cell, but the membrane is not punctured.

**Cell culture** An experimental approach in which cells or tissues are maintained outside of a living animal under carefully controlled conditions.

**Cell fractionation** A process in which a scientist centrifuges a sample multiple times at various speeds to divide the sample into different cellular components and organelles.

**Cell signaling** See *Intracellular signaling*.

**Central dogma of molecular biology** The overarching model of information flow in cells, briefly stated as "DNA codes for molecules of RNA and molecules of RNA code for proteins."

**Cerebral angiogram** A structural brain imaging technique that uses X-rays and radio-opaque dyes to produce images of the brain's vasculature.

**Cerebral organoid** See *Brain organoid*.

**Channelrhodopsin-2 (ChR2)** A genetically encoded cation channel capable of depolarizing a neuron upon illumination with blue light.

**Chemical gene delivery** The process by which a scientist uses a chemical reaction to deliver DNA into cells.

**Chemical mutagenesis** The use of chemical agents, such as EMS or ENU, to mutagenize hundreds or thousands of eggs/larvae for the purpose of performing a forward genetic screen.

**Chemogenetics** A method of manipulating neural activity by expressing genetically-encoded, engineered receptors on the cell membrane capable of being activated by a normally inert ligand. See also *DREADDS*.

**Chemosensory jump assay** A behavioral test in flies that exploits the tendency of flies to exhibit a startle response and jump when encountering a novel odor.

**ChETA** An engineered channelrhodopsin-2 variant that allows for higher stimulation frequencies.

**ChIP** See *Chromatin immunoprecipitation*.

**ChIP-seq** An assay in which chromatin immunoprecipitation is followed up with a high throughput sequencing assay to determine all of the genetic sequences that physically interact with a protein of interest.

**ChR2** See *Channelrhodopsin-2*.

**Chromatin immunoprecipitation (ChIP)** A technique used to determine whether a protein physically interacts with a specific DNA sequence.

**Chromatography** A category of biochemistry techniques used to separate proteins on a column based on their size, charge, substrates, or other properties.

**Chromogenic label** A label on a probe that allows a scientist to perform a simple biochemical reaction to produce a colored byproduct that can be visualized using light microscopy.

**Chronic mild stress** A series of mildly stressful events (periods of constant light, tilting an animal's cage, wetting the animal's bedding, etc.) used to create rodent models of depression and anxiety.

**Circadian rhythms** The regular, roughly 24-h cycle of stereotyped biochemical, physiological, and behavioral processes.

**CLARITY** A tissue clearing method used to make the brain transparent for visualizing fluorescent probes in intact specimens.

**Classical conditioning** A paradigm of animal learning in which a scientist couples an initially neutral stimulus, such as a tone or light, with a salient stimulus, such as food or an electric shock. An animal eventually associates the neutral stimulus with the salient stimulus.

**Cloning** A general term used to describe the processes of copying a gene from an organism's genome, storing the DNA sequence in a vector, and using recombinant DNA biology techniques to copy, manipulate, and/or sequence the DNA.

**Cloning vector** A DNA vector capable of storing DNA sequences for recombinant DNA techniques but lacking the necessary noncoding sequences that allow the DNA to be expressed in a host cell.

**Clozapine-n-oxide (CNO)** A synthetic ligand for many engineered DREADD receptors in chemogenetic stimulation/inhibition experiments.

**CNO** See *Clozapine-n-oxide*.

**Coculture system** A culture system in which two different cultured cell types or explants are cultured together in the same chamber, allowing a scientist to examine the effect of one type of cell or tissue on another.

**Coimmunoprecipitation (Co-IP)** A method used to determine whether a protein interacts with another protein.

**Co-IP** See *Coimmunoprecipitation*.

**Codon** A series of three nucleotides that code for a specific amino acid during translation.

**Cognitive neuroscience** The field of neuroscience dedicated to elucidating the neural basis of thought and perception.

**Cohesive ends** See *Sticky ends*.

**Colorimetric label** See *Chromogenic label*.

**Competent cell** A bacterial cell transiently capable of receiving DNA sequences through its cell wall.

**Complementary DNA (cDNA)** A fragment of DNA produced from an RNA template following reaction with the reverse transcriptase enzyme.

**Complementary strands** Refers to two strands of DNA that have complementary base pairs, allowing the two strands to hybridize into a double-stranded molecule.

**Complementation test** A test used to determine if a mutant animal with an abnormal phenotype has a mutation in the same gene as a different mutant animal with a similar abnormal phenotype.

**Compound microscope** A microscope in which two or more lenses are used in concert to enhance the magnification power to image a specimen.

**Computerized axial tomography (CAT/CT)** A structural imaging technique in which several X-rays are taken from multiple orientations around a single plane to produce an image of the brain.

**Computerized tomography** See *Computerized axial tomography.*

**Condenser** The part of a microscope that focuses light from a light source onto a specimen.

**Conditional knockout** An animal in which a gene is knocked out of the genome using gene targeting measures, but only in a specific cell type, and/or at a specific time.

**Conditioned place avoidance** A behavioral assay demonstrating a learned association between a specific environment and a negatively reinforcing stimulus.

**Conditioned place preference** A behavior assay demonstrating a learned association between a specific environment and a positively reinforcing stimulus.

**Conditioned stimulus (CS)** In classical conditioning, a neutral stimulus that eventually becomes associated with a salient, unconditioned stimulus.

**Confluence** The relative amount of space that a growing population of cultured cells takes up on the surface of a cell culture flask/plate.

**Confocal microscope** A specialized fluorescent microscope that can produce clear images of structures within specimens by using a spatial pinhole to block out-of-focus light during image formation.

**Construct** A recombinant DNA sequence capable of coding for a functional protein when properly expressed in host cells.

**Construct validity** A category of animal model validity in which an animal model and human model have the same underlying genetic or cellular mechanism that may result in a certain behavior or disease.

**Contextual fear conditioning** A form of classical conditioning in which an animal associates a neutral stimulus with an aversive stimulus, and the animal subsequently displays a fearful behavior when placed back in the training chamber, even in the absence of the aversive stimulus.

**Continuous reinforcement schedule** In operant conditioning, a paradigm in which a subject receives reinforcement (such as a food reward) each time it produces an action (such as a lever press). Compare to *Fixed ratio reinforcement schedule* or *Progressive ratio reinforcement schedule*.

**Coomassie blue** A blue dye used to stain proteins in SDS-PAGE gels.

**Coronal plane** A neuroanatomical plane that divides the brain into anterior and posterior sections (from ear to ear).

**Cosmid** A large (30–50 kb) DNA plasmid capable of replicating in bacteria. Useful for engineering very large DNA constructs.

**Countercurrent apparatus** A device used to fractionate a population of flies based on their behavioral responses to a sensory stimulus.

**Cranial window** An implant or surgical preparation on the surface of a rodent's skull that allows for direct observation of fluorescent biosensors in vivo.

**Craniotomy** A procedure used to remove a small section of skull during a surgical procedure.

**Cre recombinase** A protein derived from bacteriophage that recognizes small 34-base pair sequences called lox sites as part of the Cre/lox system. Cre excises any DNA sequences between two lox sites oriented in the same direction and inverts any DNA sequences between two lox sites oriented in inverted directions.

**Cre-ER system** An enhancement of the Cre/lox binary transgenic system in which Cre recombinase is fused to the estrogen receptor (ER). The estrogen receptor (ER) is sequestered in the cytoplasm; however, in the presence of tamoxifen, ER translocates to the nucleus. A Cre-ER fusion protein allows for inducible translocation of Cre to the nucleus (where lox sites may be present), only when a scientist administers tamoxifen.

**Cre/lox system** A binary expression system used to control the spatial and/or temporal expression of a transgene.

**Cresyl violet** A basophilic Nissl stain that highlights RNA to visualize cell bodies.

**CRISPR/Cas9** A nuclease system used to introduce double-strand breaks at precise genomic locations for DNA editing.

**Cross-linked** Describes a specimen that has been preserved using a fixative.

**Cross-linking fixatives** Chemical fixatives that create covalent chemical bonds between proteins in tissue and cells.

**Cross-talk** See *Bleed-through*.

**Cryostat** A device used to freeze and cut tissue specimens into 10−50 μm sections.

**CT scan** See *Computerized axial tomography*.

**Cued fear conditioning** A form of classical conditioning in which an animal associates a neutral stimulus with an aversive stimulus, such as a foot shock, and then displays freezing behaviors in the presence of the formerly neutral stimulus, even in the absence of foot shock.

**Current (I)** The rate of flow of electrical charge over time.

**Current clamp** An electrophysiological technique in which a scientist injects current into a cell and measures the change in voltage over time.

**Cyclic voltammogram** The visualization of data following a fast-scan cyclic voltammetry experiment that plots the amount of measured current versus the applied voltage, useful for detecting the presence of various neurochemicals in neural tissue.

**Cyclotron** A large machine that produces positron-emitting isotopes, such as the kind used in positron emission tomography (PET) experiments.

**Cytokine** Extracellular signaling molecules used in intercellular communication.

**Darkfield microscopy** A form of light microscopy that uses an oblique light source to illuminate a specimen from the side so that only scattered light enters the objective lens, causing some organelles to stand out from a dark background.

**Darkground microscopy** See *Darkfield microscopy*.

**Deconvolution** A mathematical signal and image processing technique used to improve signal to noise ratio, reduce noise, and enhance contrast.

**Defensive marble burying assay** A behavioral paradigm used to assay anxiety in a rodent. Marbles are placed in an animal's cage, and a scientist measures how many marbles an animal buries in the cage bedding over a fixed amount of time. Animals that are more anxious typically bury more marbles than nonanxious animals.

**Dehydrating fixatives** Histological fixatives that disrupt lipids and reduce the solubility of protein molecules, precipitating them out of the cytoplasmic and extracellular solutions.

**Dependent variable** The variable in an experiment that is measured and dependent upon the value of an independent variable.

**Depolarization** A decrease in the absolute value of a cell's membrane potential.

**Descriptive science** A way of performing science by observing a subject or specimen of interest without any manipulation or perturbation.

**Designer Receptors Exclusively Activated by Designer Drugs (DREADDs)** Artificially engineered membrane-bound receptors capable of stimulating or inhibiting neural activity upon binding to a normally inert ligand.

**DIC microscopy** See *Differential interference contrast microscopy.*

**Dicer** An enzyme that recognizes double-stranded RNA and cleaves it into fragments about 23 bp long (siRNA). This siRNA-dicer complex then recruits additional cellular proteins to form an RNA-induced silencing complex (RISC), which mediates the phenomenon of RNA interference (RNAi).

**Differential interference contrast (DIC) microscopy** A type of brightfield microscopy that uses optical modifications within the microscope to exaggerate changes in the light-scattering properties of cellular structures, producing a three-dimensional, textured appearance.

**Diffuse optical imaging (DOI)** A type of noninvasive optical imaging method in which light is reflected off neural structures through the scalp.

**Diffusion** The passive movement of molecules from a region of higher concentration to a region of lower concentration caused by random molecular interaction.

**Diffusion MRI** A technique used to image fiber tracts in the brain by measuring the anisotropic diffusion of water molecules along fiber bundles.

**Diffusion tensor imaging (DTI)** A diffusion MRI method that measures the anisotropic diffusion of water molecules along fiber tracts in the brain to image connections between different brain regions.

**Digoxigenin** A steroid molecule used to tag molecular probes in histology experiments.

**DIO construct** See *Double-inverse orientation construct*.

**Diphtheria toxin receptor** A genetically encoded receptor that kills expressing cells in the presence of the diphtheria toxin, which is normally harmless to rodent mammalian neurons.

**Dipstick assay** See *Olfactory avoidance assay.*

**Direct IHC** A category of immunohistochemistry experiments in which the primary antibody is directly conjugated to a fluorescent or chromogenic label.

**Dissecting microscope** See *Stereomicroscope*.

**Dissociated cell culture** A primary cell culture method in which tissue removed directly from an animal is separated into individual cells.

**dLight** A genetically encoded fluorescent biosensor that reports the presence of dopamine in a synapse.

**DNA construct** An engineered sequence of DNA created using recombinant DNA technology.

**DNA ladder** A sample of various DNA fragments of known sizes, run on an agarose gel next to experimental DNA samples to determine the size of fragments in the samples.

**DNA library** A comprehensive collection of hundreds or thousands of cloned DNA fragments from a biological sample, stored in expression vectors or artificial chromosomes.

**DNA vector** See *vector.*

**DOI** See *Diffuse optical imaging*.

**Dominant negative** A mutated protein that interferes with the function of a wild-type protein.

**Double helix** The "twisted ladder" shape of a double-stranded DNA molecule.

**Double inverse orientation (DIO) construct** A recombinant DNA construct that allows Cre-dependent expression of a transgene due to the presence of two pairs of lox sites. See also *Flex construct*.

**Doxycycline** A drug that binds to the tetracycline transactivator protein (tTA) or reversed transactivator protein (rtTA) in Tet-off/Tet-on binary transgenic systems. This drug allows scientists to gain inducible control of the Tet-off/Tet-on system, allowing temporal control of transgene activity.

**DREADD** See *Designer Receptors Exclusively Activated by Designer Drugs*.

**DTI** See *Diffusion tensor imaging*.

**DTR** See *Diphtheria toxin receptor.*

**Dynamic clamp** An electrophysiological method that uses computer simulation to model artificial membrane or synaptic conductance in living cells.

**EEG** See *Electroencephalography.*

**Electrical potential** The difference in voltage between two sides of a membrane.

**Electroencephalography (EEG)** A noninvasive technique used to measure the gross electrical activity of superficial (cortical) regions of the brain.

**Electrolytic lesion** A physical lesion in the brain caused by injection of current.

**Electromyogram** A recording of the electrical potential generated by muscle cells that can be used to report motor activity.

**Electron microscope (EM)** A microscope that uses a beam of electrons rather than a beam of photons to image a specimen, greatly enhancing the resolving power.

**Electron microscope tomography** See *Electron tomography.*

**Electron tomography (ET)** A procedure used to collect and combine several transmission electron microscope images from the same specimen, allowing scientists to image the three-dimensional ultrastructure of organelles and macromolecules.

**Electrophoretic mobility shift assay (EMSA)** A technique used to determine if a protein is capable of directly binding to a short sequence of DNA.

**Electrophysiology** A branch of neuroscience and classical neuroscience method that studies the electrical activity of whole brain regions, single cells, and single ion channels.

**Electroporation** The process of using an electric field to deliver DNA constructs into cells.

**Elevated plus maze** A behavioral assay used to assay anxiety in rodents.

**ELISA** See *Enzyme-linked immunosorbent assay.*

**Embedding** The process of surrounding a brain or tissue section with a substance that infiltrates and forms a hard shell around the tissue.

**Embryonic lethal** A phenotype caused by the manipulation of an organism's genome (e.g., a loss-of-function mutation of a gene) that causes the death of an animal during gestation.

**Embryonic stem cell** A pluripotent cell capable of giving rise to any tissue in an organism.

**Emission filter** A filter on a fluorescent microscope that blocks extraneous wavelengths of light, including the light used to illuminate the specimen, but allows emitted light wavelengths to pass through to a detector.

**EMSA** See *Electrophoretic mobility shift assay.*

**Ensembl** A public genomic database, useful for looking up genomic sequences and genetic information for a variety of organisms.

**Enzymatic histochemistry** A histochemical procedure used to visualize the presence of an enzyme by using the enzyme's endogenous activity to create a visible reaction product.

**Enzyme-linked immunosorbent assay (ELISA)** A technique used to quantify the amount of protein in a sample.

**Epifluorescent microscopy** Standard fluorescent microscopy. Specimens labeled with fluorescent probes are illuminated by light with a specific excitation wavelength. The specimen is then viewed using a second filter that is opaque to the excitation wavelength but transmits the longer wavelength of the emitted light. Both the illuminated and emitted light travel through the same objective lens.

**Epitope** The specific region of an antigen where an antibody binds.

**EPSP** See *Excitatory postsynaptic potential.*

**ERF** See *Event-related field.*

**ERP** See *Event-related potential.*

**Estrogen receptor** An endogenous receptor that resides in the cytoplasm until binding with its ligand, at which point it translocates to the nucleus.

**Ethidium bromide** A chemical that intercalates with DNA and fluoresces when illuminated with ultraviolet light. Used to visualize bands of DNA following agarose gel electrophoresis.

**Ethology** The study of natural animal behaviors.

**Event-related design** A strategy for presenting stimuli to human subjects in functional imaging experiments in which stimuli are presented as isolated, individual events of short duration. An alternative to a *Blocked design*.

**Event-related field** A distinct, stereotyped waveform in magnetoencephalography (MEG) recordings that corresponds to a specific sensory, cognitive, or motor event.

**Event-related potential** A distinct, stereotyped waveform in electroencephalography (EEG) recordings that corresponds to a specific sensory, cognitive, or motor event.

**Excitation filter** A filter on a fluorescent microscope that allows only light in a specific range of wavelengths to pass through to an objective to illuminate a specimen.

**Excitatory postsynaptic potential (EPSP)** A localized potential change in a small region of a neuron that causes the membrane potential to depolarize, bringing the membrane potential closer to the threshold to generate an action potential.

**Exon** A sequence of a newly synthesized RNA molecule that remains in the final mRNA sequence after splicing occurs.

**Explant culture** A primary cell culture method in which intact chunks of tissue are removed from a living organism and kept alive in culture conditions.

**Expression vector** A DNA vector containing all of the necessary noncoding sequences necessary (e.g., a promoter sequence) for a host cell to express a coding DNA sequence as a protein.

**Extracellular recording** An electrophysiological recording in which the recording electrode is placed outside neurons in the extracellular environment.

**Eye coil** A wire loop implanted around the outer circumference of a primate's eye, used to ensure that the monkey correctly fixes its gaze during a visual task.

**Face validity** A category of animal model validity in which an animal's physiology or behavior is similar to a human's physiology or behavior.

**Fast-scan cyclic voltammetry** A technique used to measure neurochemicals capable of undergoing oxidation reactions (e.g., dopamine) by varying the voltage of an oxidizing electrode back and forth from a nonoxidizing potential to an oxidizing potential. The resulting current measurements can be used to identify and measure neurochemicals present in the extracellular environment.

**FDG** See *Fluorodeoxyglucose*.

**Feeding acceptance assay** A *Drosophila* assay that examines taste preferences. Slightly starved flies are offered a choice of appetitive, aversive, or neutral stimuli, each dyed a different color. The amount of each stimulus can be scored by examining the color of the fly's stomach.

**Fiber photometry** A technique for recording bulk fluorescence from a population of neurons expressing a genetically encoded calcium indicator. This bulk fluorescence is used as a readout of net population activity.

**Fiber stain** A histological stain used to mark the presence of fiber tracts in the nervous system.

**FISH** See *Fluorescent in situ hybridization*.

**Five choice serial reaction time task** A rodent behavioral assay used to study attention and impulsivity.

**Fixation** The process of using chemical methods to preserve, stabilize, and strengthen a biological specimen for subsequent histological procedures and microscopic analysis.

**Fixed ratio reinforcement schedule** In operant conditioning, a paradigm in which a subject receives reinforcement (such as a food reward) each time it produces a set number of actions (such as a set number of lever presses). Compare to *Continuous reinforcement schedule* or *Progressive ratio reinforcement schedule*.

**Flat skull position** The placement of an animal on a stereotaxic frame such that the top of the skull is perfectly level, at the same height along the rostral−caudal axis.

**Flex construct** A recombinant DNA construct that allows Cre-dependent expression of a transgene due to the presence of two pairs of lox sites. See also *DIO construct*.

**Flight simulator** Specialized chamber that suspends a fly from a thin pin and projects visual stimuli on a screen, depicting the external, visual environment. Used to determine the effect of visual stimuli on flying behavior.

**FLIM** See *Fluorescence-lifetime imaging microscopy.*

**Flippase recognition target (FRT)** A 34 bp sequence recognized by the flippase recombinase (Flp) enzyme.

**Flippase recombinase (Flp)** A protein that recognizes flippase recognition target (FRT) sites. Flp excises any DNA sequences between Frt sites oriented in the same direction and inverts any DNA sequences between two Frt sites oriented in inverted directions.

**Floxed** Term used to describe any DNA sequence flanked by two lox sites.

**Flp/FRT system** A binary expression system used to control the spatial and temporal expression of a transgene.

**Fluorescence-lifetime imaging microscopy (FLIM)** A technique used to visualize if and when two proteins interact.

**Fluorescence microscopy** Any form of microscopy that images fluorescent molecules within a specimen by illuminating the specimen with specific wavelengths of light.

**Fluorescence recovery after photobleaching (FRAP)** A protein visualization technique in which a scientist uses strong laser illumination to bleach fluorescently tagged proteins in a particular region of a cell and then measures the time course of fluorescence that returns to the bleached region.

**Fluorescence resonance energy transfer (FRET)** A technique used to visualize if and when two proteins interact.

**Fluorescent in situ hybridization (FISH)** An in situ hybridization labeling technique that uses fluorescent probes to visualize nucleic acids in a cell or tissue sample.

**Fluorodeoxyglucose (FDG)** A radioactive form of glucose used to image functional brain activity in positron emission tomography experiments.

**Fluorophore** A molecule that has the ability to absorb light at a specific wavelength and then emit light at a different, typically longer wavelength.

**FM dyes** Lipophilic dyes that fluoresce when bound to a membrane. They are particularly useful for reporting the exocytosis and endocytosis events that occur during synaptic vesicle recycling and can stain nerve terminals in an activity-dependent manner.

**fMRI** See *Functional magnetic resonance imaging*.

**Footprint pattern assay** A behavioral assay used to examine a rodent's motor coordination and balance by observing its footprint patterns.

**Forced swim test** A behavioral experiment used to assay depression by placing an animal in a narrow chamber of water and measuring how long it takes for the animal to stop trying to escape.

**Formalin assay** An assay used to examine an animal's sensitivity to noxious chemical stimuli by observing its response to a small injection of the noxious chemical formalin.

**Förster resonance energy transfer (FRET)** See *Fluorescence resonance energy transfer.*

**Forward genetics** A method used to identify genes that contribute to a phenotype. Scientists generate random mutations in eggs/larvae and then examine the phenotypes of the offspring. Contrast with *Reverse genetics.*

**Fos** An immediate early gene that serves as an indirect marker of neural activity.

**Founders** Individuals in the first generation of a genetically modified animal.

**Freezing microtome** A microtome with a cooling unit that allows a tissue sample to be frozen during sectioning.

**Functional brain imaging** Methods used to indirectly measure neural activity in the central nervous system.

**Functional magnetic resonance imaging (fMRI)** A technology that uses the principles of magnetic resonance imaging (MRI) to indirectly measure neural activity in the brain over time.

**Gain-of-function experiment** An experiment in which an investigator tests the effects of adding or stimulating some aspect of the nervous system on a phenotype.

**Gal4** A transcription factor derived from yeast that binds to a specialized promoter called an upstream activation sequence (UAS) to activate the transcription of a gene.

**Gal4/UAS system** A binary expression system that exploits a transcription system in yeast cells to control the spatial expression of a transgene. Widely used with invertebrate and zebrafish model organisms.

**Gal80** A protein derived from yeast that blocks Gal4 transcription factors from activating a UAS sequence.

**GCaMP** A genetically encoded calcium indicator used to visualize neural dynamics.

**GECI** See *Genetically encoded calcium indicator.*

**Gel electrophoresis** The process of using an electrical field to force molecules through a gel. See also *Agarose gel electrophoresis* or *Polyacrylamide gel electrophoresis*.

**Gel filtration chromatography** A chromatography technique that separates proteins on the basis of their size.

**Gel shift assay** See *Electrophoretic mobility shift assay.*

**Geller–Seifter conflict test** A behavioral paradigm that assays anxiety in rodents. A rodent is trained to press a lever to receive a food reward. In subsequent experiments, the lever is paired with an aversive foot shock. Anxious animals tend to press the lever significantly less to receive food than nonanxious animals.

**Gene** The fundamental unit of heredity.

**Gene gun** A device used in biolistic experiments to physically discharge DNA molecules into tissue specimens.

**Gene targeting** The process of incorporating a DNA construct into a specific locus in an animal's genome.

**Genetically encoded calcium indicator (GECI)** A genetically encoded transgene used to indirectly measure neural activity by visualizing intracellular calcium levels.

**Genetically encoded voltage indicator (GEVI)** A genetically encoded transgene used to indirectly measure neural activity by visualizing membrane voltage.

**Genetically modified organism** Any animal that has had its genome modified using genetic engineering techniques.

**Genome** The complete set of genes or genetic material present in a cell or organism.

**Genomic DNA library** A collection of thousands of plasmids that each contain fragments of an animal's genome.

**Genotype** The genetic constitution of an animal.

**Germ cells** Cells that pass on genetic information to an organism's offspring (sperm in males and eggs in females).

**GEVI** See *Genetically encoded voltage indicator.*

**GFP** See *Green fluorescent protein*.

**Go/No-Go task** A form of operant conditioning in which a rodent is trained to produce a response in the presence of a "go" cue yet withhold a response in the presence of a separate "no-go" cue. Used to test attention and impulsivity.

**Golgi stain** A classic histological stain used to label a small subset of neurons in their entirety.

**GRAB-5HT** A genetically encoded fluorescent biosensor that reports the presence of serotonin in a synapse.

**GRAB-ACh** A genetically encoded fluorescent biosensor that reports the presence of acetylcholine in a synapse.

**GRAB-DA** A genetically encoded fluorescent biosensor that reports the presence of dopamine in a synapse.

**GRAB-NE** A genetically encoded fluorescent biosensor that reports the presence of norepinephrine in a synapse.

**Graded potential** See *Localized potential*.

**Green fluorescent protein (GFP)** A genetically encoded protein derived from jellyfish, capable of absorbing wavelengths of blue light and emitting wavelengths of green light. Ubiquitously used in the biosciences as a reporter protein.

**GRIN lenses** Gradient refractive index lenses. Cylindrically shaped lenses with a flat bottom that vary the index of refraction of light within the lens to allow for measuring light at high resolution deep within the brain. Allows for fluorescent imaging within deep brain structures in microendoscopy experiments.

**Growth factors** Proteins produced by certain cells as cell communication molecules that stimulate the growth and differentiation of other cells.

**GtACRs** Blue light activated anion-conducting channelrhodopsins (ACRs) derived from *Guillardia theta*.

**Gyrus** A ridge on the cerebral cortex.

**Halorhodopsin (NpHR)** A genetically encoded transmembrane chloride pump that hyperpolarizes neurons upon stimulation with yellow light.

**Hanging wire assay** A behavioral assay used to measure neuromuscular deficits in rodents.

**Hargreaves assay** A behavioral assay used to measure pain in rodents by aiming a high-intensity beam of light at the hind paw and measuring the time it takes for the rodent to withdraw its paw.

**Headpost** An implant that allows an investigator to secure an animal's head in place during an experiment.

**HEK-293T cells** See *Human embryonic kidney 293T cells.*

**Hemoglobin** In vertebrate animals, the protein that transports oxygen throughout the bloodstream.

**Heterologous expression system** A dissociated cell culture system that can easily be transfected with DNA to study single proteins, especially to study ion channels in electrophysiology experiments.

**High-throughput sequencing** A high-throughput method of DNA sequencing used to read the sequences of millions of DNA fragments to sequence genomes or compare gene expression profiles between samples.

**HM3Dq** A genetically encoded DREADD transgene capable of stimulating neurons upon binding the normally inert ligand clozapine-n-oxide (CNO).

**HM4Di** A genetically encoded DREADD transgene capable of inhibiting neurons upon binding the normally inert ligand clozapine-n-oxide (CNO).

**Holding potential** The set voltage that is held constant in a voltage clamp experiment.

**Homologous recombination** A natural phenomenon in which DNA regions with strong sequence similarity can exchange genetic material.

**Homology arms** Regions of homology that flank a genetic-targeting construct to exploit the phenomenon of homologous recombination in the production of a knockout or knockin mouse.

**Homology-directed repair (HDR)** A method of inserting DNA into the genome following nuclease-mediated double-strand break repair. A scientist introduces a DNA construct with homology arms that have the same sequence as the broken DNA strands.

**Horizontal plane** The plane in space that divides the brain and body into superior and inferior sections (top to bottom).

**Hot plate assay** A behavioral paradigm used to assay nociception in rodent models. A rodent is enclosed on a heated plate and observed for licking and paw withdrawal.

**Human embryonic kidney 293T cells** A common immortalized cell line used in cell culture experiments.

**Humanized mouse** A mouse carrying functional human genes or cells/tissues to model a human disease or condition.

**Hyperpolarization** Any change in the membrane potential of a neuron that makes the membrane potential more negative.

**i.c.v. injection** See *Intracerebroventricular injection.*

**i.p. injection** See *Intraperitoneal injection.*

**I/V curve** A plot of the voltage across a cell membrane compared with the current that flows through the ion channels of the membrane.

**IACUC** See *Institutional Animal Care and Use Committee*.

**Ibotenic acid** A pharmacological compound that causes excitotoxic effects when directly injected into the brain. Used to ablate neurons within a specific region of the brain.

**IEG** See *Immediate early gene*.

**iGABASnFR** A genetically encoded fluorescent biosensor that reports the presence of the neurotransmitter GABA in a synapse.

**iGluSnFr** A genetically encoded fluorescent biosensor that reports the presence of the neurotransmitter glutamate in a synapse.

**IHC** See *Immunohistochemistry.*

**Immediate early gene (IEG)** A gene that tends to be actively transcribed during periods of relatively high neural activity.

**Immersion** The process of fixing small brains or even entire animals by immersing them in fixative solutions.

**Immortalized cell line** A cell line manipulated so that it will continually divide and multiply indefinitely.

**Immunoblot** See *Western blot*.

**Immunocytochemistry (ICC)** A histological technique that uses antibodies to stain proteins in cells.

**Immunoelectron microscopy** A technique that combines electron microscopy with immunohistochemical processing to visualize protein expression within subcellular structures at extremely high resolution.

**Immunofluorescence (IF)** A histological technique that uses antibodies to stain proteins with fluorescent reagents.

**Immunohistochemistry (IHC)** A histological technique that uses antibodies to stain proteins in tissues.

**Immunopanning** A technique used to purify certain cell types in cell culture preparations. The bottom of a plate is coated with antibodies that recognize cell surface markers on the outside of specific cells. When heterogeneous populations of cells are added to the plate, the cells of interest can be purified by binding to the bottom of the plate, while the undesired, unbound cells are washed off.

**Immunoprecipitation (IP)** A protein purification method that uses antibodies bound to beads to purify specific proteins out of solution.

**In silico screen** A method of identifying genes or proteins of interest by searching public genome and bioinformatics databases.

**In situ hybridization** A histological method used to identify the spatial location of mRNA transcripts.

**In vitro** Any process that takes place in a controlled environment outside a living organism, such as a cell culture dish or test tube.

**In vivo** Any process that takes place in a whole, living organism.

**Independent variable** The experimental variable that is intentionally manipulated by a researcher and is hypothesized to cause a change in a dependent variable.

**Index of refraction** An important parameter of light microscopy, a measure of how much the speed of light is reduced in a specific medium, such as air, water, or oils.

**Indirect IHC** A method of performing an immunohistochemistry experiment in which a primary antibody binds to an antigen and then a secondary antibody binds to the primary antibody. The secondary antibody is conjugated to a fluorescent or chromogenic tag that allows for subsequent visualization.

**Induced pluripotent stem (iPS) cell** A somatic stem cell that has been manipulated into reverting back to a pluripotent stem cell state, capable of giving rise to multiple cell types.

**Infection** The process of delivering DNA into cells using viruses.

**Inhibitory postsynaptic potential (IPSP)** A localized potential change in a small region of a neuron that causes the membrane potential to hyperpolarize, bringing the membrane potential farther from the threshold potential.

**Inner cell mass** A group of cells within a blastocyst that give rise to all cells and tissues in an organism.

**Insertional mutagenesis** The process of causing genetic mutations by insertion of mobile genetic elements called transposons into the genomes of offspring. These transposons insert at random locations in the genome, occasionally disrupting an endogenous gene.

**Inside-out mode** A patch clamp recording method in which a tiny patch of the membrane is isolated and oriented such that the intracellular surface is exposed to the bath solution and the extracellular surface resides on the inside of the glass pipette.

**Institutional Animal Care and Use Committee (IACUC)** An academic institution's internal review committee that approves and inspects all procedures using vertebrate animals.

**Institutional Review Board (IRB)** An academic institution's internal review committee that approves and inspects all procedures that use human subjects.

**Internal ribosome entry site (IRES)** A sequence within a DNA construct (and subsequently, within a transcribed mRNA strand) that allows a ribosome to initiate translation. Thus, an IRES allows a single mRNA molecule to code for two separate functional proteins.

**Intracellular recording** An electrophysiology recording technique in which an electrode is gently inserted inside a cell.

**Intracellular signaling** The biochemical pathways that take place within a cell that affect the cell's physiology and metabolism.

**Intracerebroventricular (i.c.v.) injection** The injection of a solution directly into the ventricular system of the brain.

**Intraperitoneal (i.p.) injection** The injection of a solution into the peritoneum (body cavity) of an animal.

**Intron** A sequence of a newly synthesized RNA molecule that is spliced out of a final mRNA sequence during RNA splicing.

**Inverse agonist** A pharmacological compound that can bind to a receptor but causes the opposite effect as the endogenous ligand.

**Inverted microscope** A microscope in which the objective lens is placed beneath the sample and the light source and condenser are placed above the sample.

**Ion-exchange chromatography** A form of chromatography in which proteins are separated based on their charge.

**iPS cell** See *Induced pluripotent stem cell*.

**IPSP** See *Inhibitory postsynaptic potential*.

**IRB** See *Internal review board*.

**Irradiation mutagenesis** The use of high-intensity UV light to mutagenize hundreds or thousands of eggs/larvae for the purpose of performing a forward genetic screen.

**Isofluorane** A gaseous agent used to anesthetize mammals.

**Isotropic** The diffusion of a substance in all directions within a medium. The opposite of **anisotropic**.

**Ketamine** A chemical anesthetic agent that acts by inhibiting NMDA and HCN1 ion channels. Often used in concert with xylazine.

**Kinase assay** An assay used to determine if a protein is capable of phosphorylating a substrate protein or protein fragment.

**Knockdown** The disruption of mRNA transcript expression, thus causing a decrease in functional protein products.

**Knockin** The use of gene targeting procedures to add a functional gene or gene sequence to a specific location in a genome.

**Knockout** The use of gene targeting procedures to remove a functional sequence from the genome, thus knocking out a gene of interest.

**LacZ** A bacterial gene that encodes the enzyme *B*-galactosidase. Classically used as a reporter gene in combination with the substrate X-gal to produce a dark blue byproduct.

**Lambda** Landmark on the surface of the skull, defined as the intersection between the lines of best fit through the sagittal and lambdoid sutures.

**Learned helplessness** An paradigm used to create rodent models of depression. An animal is exposed to aversive stimuli at random intervals. Theoretically, this treatment creates a condition in which the animal experiences a lack of control, causing it to show symptoms of behavioral despair.

**Lectins** Proteins that exhibit extremely high binding affinities for sugars, used in neuroscience as transsynaptic neural tracers.

**Lentivirus** A retrovirus that can be used to deliver DNA sequences to both dividing and postmitotic cells and integrate these sequences within the genome of the host cell.

**Lesion** Injury or ablation of a specific region within the nervous system.

**Light microscope** A microscope that uses visible light to illuminate a specimen.

**Light sheet fluorescence microscopy** A microscopy technique that uses thin sheets of light to optically section and image large volumes of tissue.

**Linkage analysis** A classical genetic strategy to map a gene's location in the genome by identifying the position of the novel gene in relation to the location of known genes.

**Lipofection** A chemical transfection method that uses a lipid complex to deliver DNA to cells.

**Liposomes** Tiny vesicular structures composed of a sphere of phospholipids that have the same composition as the plasma membrane. Used to transfect cells with DNA.

**Local field potential** An electrophysiological measurement of the sum of all dendritic synaptic activity within a volume of tissue.

**Localized potential** A local change in membrane potential caused by the activity of individual ion channels. These potentials include excitatory postsynaptic potentials (EPSPs) and inhibitory postsynaptic potentials (IPSPs).

**Loss-of-function experiment** An experiment in which an investigator tests the effects of diminishing or removing some aspect of the nervous system on a phenotype.

**Lox site** A 34 bp DNA sequence recognized by the Cre recombinase enzyme. Useful for gene targeting in binary expression systems.

**Luciferase** A genetically encoded bioluminescent protein cloned from various species of fireflies.

**Luciferase assay** A technique used to determine whether a protein is able to interact with a genetic regulatory sequence (i.e., a promoter sequence) and activate or suppress the transcription of a gene.

**Magnetic resonance imaging (MRI)** A structural imaging technique that uses the magnetic properties of neural tissue to noninvasively produce highly detailed structural images of the brain or body.

**Magnetoencephalography (MEG)** A functional imaging technique that measures changes in magnetic fields on the surface of the scalp produced by changes in underlying patterns of neural electrical activity.

**Magnification** A parameter in microscopy that measures how much larger a specimen appears compared to its actual size.

**Mass spectrometry** A technique used to identify proteins, peptide sequences, and post-translational modifications (PTMs) at specific amino acid residues in a given sample by determining the mass to charge ratio of proteins, peptides, and their fragments.

**Match to sample task** A memory assay that requires a test subject to identify a stimulus that was seen previously. Used as a working memory assay by adding a delay between the sample and the test stimuli.

**Matrix-assisted laser desorption ionization (MALDI)** A mass spectrometry method of vaporizing proteins into the gas phase by blasting them with a UV laser so that their mass to charge ratio can be measured.

**MEG** See *Magnetoencephalography.*

**Membrane potential** The voltage across a cell membrane generated by differential ionic charges on the intracellular versus extracellular sides of the membrane.

**Microarray** A tool used to measure the expression of thousands of genes between one or more tissue samples. It consists of a grid (array) of known nucleic acid sequences spotted on a slide so that cDNA from a biological sample can be hybridized to detect whether any of the known sequences are present in the sample.

**Microdialysis** A method of sampling neurochemicals from brain extracellular fluid by continuously collecting fluid that diffuses into an implanted semipermeable membrane.

**Microelectrode** A small (micrometer scale) metal or glass probe used to measure electrical signals from cells or tissue.

**Microendoscopy** The process of implanting a specialized lens (often a GRIN lens) into the brain for high-frequency image acquisition of fluorescent biosensors.

**Microinjection** The process of injecting small volumes of a solution (usually containing DNA) into cells with a thin needle.

**Microiontophoresis** The process of using a small electrical current to infuse substances out of a glass electrode into the brain.

**Microscope** An instrument that manipulates the trajectory of light rays so that small objects appear larger.

**Microstimulation** The process of sending electrical currents through an electrode to induce changes in membrane potential in cells close to the electrode tip.

**Microtome** A piece of equipment with a sharp knife used to cut medium thickness (25−100 μm) sections of tissue.

**Midsagittal** A view or section of the brain that perfectly divides the left and right hemispheres.

**Miniscope** A miniaturized fluorescent microscope that can be implanted on the head of a rodent. Often used in conjunction with microendoscopy to measure fluorescent signals within the brain of a freely moving animal.

**Mixed design** A type of fMRI experimental task paradigm that uses elements of both blocked and event-related designs.

**MNI template** A standardized three-dimensional coordinate map of the human brain produced by the Montreal Neurological Institute. Based on the average of hundreds of individual MRI brain scans and matched to landmarks in Talairach space.

**Modified rabies virus** A mutated form of rabies virus useful for cell type−specific retrograde tracing.

**Molecular cloning** The process of identifying, isolating, and making copies of a particular DNA fragment.

**Monoclonal antibody** An antibody that binds to a single epitope of an antigen. Contrast with *Polyclonal antibody.*

**Morpholinos** Stable, synthetic 22−25 bp antisense oligonucleotide analogues that complement an RNA sequence to block proper mRNA translation.

**Morris water maze** A spatial learning and memory task for rodents in which animals must learn to find a hidden platform submerged in opaque water using visual cues.

**MRI** See *Magnetic resonance imaging*.

**Multielectrode array (MEA)** A group of individual electrodes or tetrodes arranged into one electrical recording unit to record extracellular activity from multiple cells at the same time.

**Multiple cloning site** A region in a DNA vector with a variety of recognition sequences for different restriction enzymes that make it easier to insert a foreign DNA sequence into the vector.

**Multipotent** The ability of some cells to give rise to all types of cells found in a particular tissue—for example, the ability of a neural stem cell to give rise to neurons, astrocytes, and oligodendrocytes.

**Muscimol** A GABA receptor agonist that mimics the effects of GABA in local cells. Used as a pharmacological agent to inhibit neural activity.

**Myelin** The fatty insulating material surrounding axons produced by glial cells that provide insulation to neurons.

**Near-infrared spectroscopy (NIRS)** A noninvasive optical brain imaging method that records neural activity−induced changes in the reflectance properties of near-infrared light as it is reflected off the scalp.

**Necessity experiment** See *Loss-of-function experiment*.

**Neural progenitor** A dividing cell that has the ability to generate either a neuron, astrocyte, or oligodendrocyte, but limited ability to give rise to another dividing cell.

**Neural stem cell** A multipotent, self-renewing cell that divides and gives rise to neurons, astrocytes, or oligodendrocytes, as well as other neural stem cells.

**Neuroethology** The study of the neural basis of an animal's natural behaviors.

**Neuron doctrine** The classical theory advocated by Ramón y Cajal that discrete neurons are the basic structural and functional units of the nervous system.

**Neuropixels** See *Silicon probe*.

**Neurosphere** A ball of cells generated from a dividing neural progenitor or neural stem cell that indicates an ability to proliferate.

**Neurosphere assay** See *Primary neurosphere assay.*

**Next generation sequencing** A high-throughput method of DNA sequencing used to read the sequences of millions of DNA fragments to sequence genomes or compare gene expression profiles between samples.

**NIRS** See *Near-infrared spectroscopy.*

**Nissl stain** A basophilic stain that highlights RNA (the "Nissl substance") in cells. Cresyl violet is a commonly used Nissl stain.

**Nociception** The detection of noxious stimuli, typically perceived as pain.

**Nomarski microscopy** See *Differential interference contrast (DIC) microscopy.*

**Nonhomologous end-joining** A naturally occurring DNA break repair process that rejoins double-strand breaks, occasionally by introducing an insertion or deletion mutation.

**Nonmatch to sample task** A memory assay that requires a subject to identify a stimulus that was *not* previously observed. Used as an assay of working memory by adding a delay between the sample and the test stimuli. Contrast with *Match to sample task*.

**Nonratiometric molecule** A fluorescent biosensor whose fluorescence intensity directly varies with its ability to bind a substance such as calcium. Contrast with *Ratiometric molecules*.

**Northern blot** A nucleic acid hybridization technique used to detect the presence and relative concentration of mRNA in a sample.

**Novel object recognition** A learning and memory task in which a rodent will spend more time exploring an object that has not previously been presented, demonstrating memory for the previously presented object.

**NpHR** See *Halorhodopsin*.

**Nuclease** An enzyme that cleaves nucleic acids.

**Nucleotide** A molecule composed of a phosphate group, a nitrogenous base (adenine, thymine, cytosine, guanine, or uracil), and a sugar molecule (2-deoxyribose for DNA, ribose for RNA) that combines with other nucleotides to form a DNA or RNA polymer.

**Numerical aperture** A measure of the light-collecting ability of a microscope objective lens. The NA depends on the angle by which light enters the objective and the medium light must pass through. Higher NA objectives collect more light and consequently have better resolving power.

**Objective lens** The lens in a microscope that gathers and focuses light from the specimen in a microscope. This lens is typically placed adjacent to the specimen.

**OCT compound** See *Optimal cutting temperature compound*.

**Ocular lens** A lens located in the eyepiece of a compound microscope that typically provides 10× magnification.

**Ohm's law** The relationship between voltage (V), current (I), and resistance (R) in an electrical circuit, expressed as $V = I \times R$.

**Olfactory avoidance assay** A *Drosophila* chemosensory assay in which a scientist presents an odor on a stick in a fly chamber and measures the distance a fly maintains from the odor. Also called a *Dipstick assay.*

**Olfactory jump response** See *Chemosensory jump assay.*

**Open field test** A rodent assay used to measure exploratory behavior in a large open chamber. More anxious animals stay near the walls of the chamber and do not explore the center area.

**Operant conditioning** A method of associative learning in which the strength of a behavior is modified by reinforcement or punishment associated with that behavior.

**Optical imaging** A brain imaging technique that measures changes in light reflectance from the surface of the brain due to changes in blood flow and metabolism caused by neural activity.

**Optimal cutting temperature (OCT) compound** A clear, viscous solution applied to a brain or neural specimen before freezing and sectioning on a microtome or cryostat. When frozen, the compound embeds the specimen in a hard, protective matrix.

**Optogenetics** An approach to stimulate or inhibit neurons by expressing genetically encoded neuronal actuators capable of depolarizing or hyperpolarizing neurons in response to light.

**Optrodes** "Optical electrodes." In optical imaging techniques, sensors that record changes in light reflectance from the surface of the brain. In optogenetic/electrophysiology techniques, the integration of an optical fiber with an electrode to measure neural activity during neurostimulation/inhibition.

**Organoid** A mass of cells that is grown artificially to model an organ in cell culture conditions. Used to model organ function and neurological disease.

**Organotypic slice culture** A slice of brain tissue kept in culture conditions for multiple days to weeks.

**Oscilloscope** An instrument or computer display that presents the membrane potential over time.

**Osmotic minipump** An implantable pump capable of steadily delivering a pharmacological solution to a rodent over a period of days or weeks.

**Outside-out mode** A patch-clamp electrophysiology technique that exposes the extracellular side of an excised membrane patch to the bath solution and the intracellular side to the inside of the recording pipette.

**P element** A transposable genetic element used in *Drosophila* that is able to change locations in the genome when the P element transposase enzyme is also present.

**Packaging cells** An immortalized cell line that is transfected with the necessary recombinant DNA sequences to make viral particles. The endogenous cell machinery produces virus, which is eventually harvested in the extracellular media.

**Partial agonist** A compound that can bind to a receptor to produce agonist-like effects, but not to the maximal extent of the full agonist or endogenous ligand.

**Particle-mediated gene transfer** See *Biolistics.*

**Passaging** The process of transferring a fraction of cultured cells into a new container to provide space for the cells to continue to divide.

**Patch clamp techniques** A set of electrophysiological methods in which a glass electrode forms a tight seal with a patch of membrane, allowing for precise studies of membrane physiology and the study of single or multiple ion channels.

**Pavlovian conditioning** See *Classical conditioning.*

**PCR** See *Polymerase chain reaction.*

**Perforated patch** A category of electrophysiology patch-clamp technique in which a chemical is added to the recording pipette to cause small holes to form in the membrane. This preparation is useful for making the contents of the glass pipette continuous with the cell but without the disadvantage of cytoplasmic contents leaking into the pipette.

**Perfusion** A method used to circulate a chemical fixative through the cardiovascular system so that the brain is thoroughly preserved.

**Peri-stimulus time histogram (PSTH)** A graph of the number of action potentials recorded with respect to the time a stimulus was presented.

**PET** See *Positron emission tomography.*

**Phage** See *Bacteriophage*.

**Pharmacogenetics** See *Chemogenetics*.

**Phase-contrast microscopy** An optical method of enhancing contrast in a light microscope to amplify small differences in the index of refraction of different cellular structures.

**Phenotype** An observable trait or set of traits in an animal.

**Photoactivation** A process by which illumination causes changes in the fluorescence properties of a fluorophore, usually causing it to fluoresce at a different intensity.

**Photobleaching** The phenomenon in which fluorescence intensity emitted from a fluorophore decreases over time as it is continuously exposed to light.

**Photoconversion** The process by which delivering a pulse of light to a fluorophore causes it to change emission spectra and therefore the color of light that it emits.

**Phototaxis** The tendency of an organism to move toward light and away from dark.

**Phototoxicity** The phenomenon in which illumination leads to the death of cells expressing a fluorophore, typically because illumination of the fluorophore generates free radicals.

**Physical gene delivery** A method of introducing foreign DNA into cells by physically disrupting the cell's membrane. Includes *Microinjection*, *Electroporation*, and *Particle-mediated gene transfer (Biolistics)*.

**Plasmid** An independently replicating accessory chromosome in bacteria that exists as a circle of DNA. Commonly used as a vector for molecular cloning.

**Pluripotent** The ability of a cell to generate any type of cell type, including more pluripotent cells. Contrast with *Multipotent and Unipotent*.

**Polyacrylamide gel electrophoresis** The process of using an electrical field to separate biological macromolecules, usually proteins or nucleic acids, based on their electrophoretic mobility.

**Polyclonal antibody** A collection of antibodies that recognizes multiple epitopes of the same antigen. Contrast with *Monoclonal antibody.*

**Polymerase chain reaction (PCR)** A biochemical reaction that uses controlled heating and cooling in the presence of DNA synthesizing enzymes to exponentially amplify a small DNA fragment.

**Porsolt test** See *Forced swim test*.

**Position effects** The phenomenon of transgenes having different expression patterns depending on where the transgene randomly integrates in the genome.

**Positional cloning** The process of using molecular cloning technology to map the location of a gene in the genome.

**Positron** The antimatter counterpart of an electron. When a positron contacts an electron, an annihilation event occurs that generates gamma photons. Used as a signal source in positron emission tomography.

**Positron emission tomography (PET)** A brain imaging technique in which positron-emitting isotopes generate annihilation events that can be detected by a gamma detector. Depending on the positron-emitting isotope, PET can detect neural activity or the location of specific receptors.

**Positron-emitting isotope** An unstable version of a molecule that emits positrons as it decays, allowing it to be detected in positron emission tomography (PET).

**Posttranslational modification (PTM)** A modification to a protein, usually the addition or subtraction of a functional chemical group, after it has been translated by a ribosome. For example, the addition or removal of a phosphate group.

**Potential** See *Membrane potential*.

**PPI** See *Prepulse inhibition*.

**Precess** The circular movement of the axis of a spinning body around another axis due to a torque. For example, the circular movement of a proton.

**Predictive validity** A category of animal model validity in which treatments or therapeutics useful in human patients have the same effect on the animal model.

**Prepulse inhibition (PPI)** The attenuation of a startle response caused by the presentation of a weaker sensory stimulus before the presentation of the startle-causing stimulus.

**Primary antibody** An antibody that recognizes and binds to a specific antigen in a sample. Contrast with *Secondary antibody.*

**Primary cell/tissue culture** The culture of cells extracted directly from a tissue of interest. Can be in the form of dissociated cells, explants, or brain slices.

**Primary neurosphere assay** A cell culture assay that tests for the ability to form neurospheres to examine whether they are proliferative. Compare to *Secondary neurosphere assay.*

**Primer** A short, single-stranded oligonucleotide used in PCR to hybridize to a template strand flanking the region to be amplified.

**Proboscis extension response** A reflex in *Drosophila* used to test the responses of specific gustatory receptors by applying taste ligands to gustatory receptor neurons on the leg or proboscis and examining proboscis extension.

**Progenitor** A cell that divides, but with a limited capacity for self-renewal.

**Progressive ratio reinforcement schedule** In operant conditioning, a paradigm in which a subject receives reinforcement (such as a food reward) following a progressively increasing number of actions (e.g., one lever press, then two lever presses, then four lever presses, and so on). This paradigm continues during a single experimental session until it eventually reaches a breakpoint, at which point the subject is no longer motivated. Compare to *Continuous reinforcement schedule* or *Fixed ratio reinforcement schedule*.

**Promoter** A regulatory region of DNA that controls the spatial and temporal expression of a gene under its control.

**Pronucleus** One of the nuclei present in a recently fertilized egg—either the male sperm nucleus or the female egg nucleus.

**Protein** A biological macromolecule composed of a polymer of amino acids. Proteins serve as the structural and enzymatic molecules that regulate virtually every process within cells.

**Protein kinase** A protein that catalyzes the addition of a phosphate group to another protein.

**Proteomics** The systematic large-scale study of the complete set of proteins in a system (such as a cell or tissue) at a particular time.

**Protospacer adjacent motif (PAM)** A three-nucleotide sequence of "NGG" (N can be any of the four nucleotide bases followed by two guanine bases) that must lie immediately 3′ of the genomic sequence to be targeted in CRISPR/Cas9-mediated gene editing.

**Proximity labeling** A method to identify the identity of proteins that come into close proximity with a protein of interest.

**Pseudopregnant mouse** A female mouse that has been mated with a sterile male mouse such that she produces the proper hormones to act as a foster mother before implantation of an embryo.

**PSTH** See *Peri-stimulus time histogram.*

**PTM** See *Posttranslational modification.*

**Pulse chase labeling** A process in which a labeled probe (the pulse) is briefly injected into animals or added to cultured cells, then washed away, and replaced by unlabeled molecules (the chase). By following the changes in localization of the labeled probe, different protein trafficking pathways can be observed.

**qRT-PCR** See *Quantitative real-time PCR.*

**Quantitative real-time PCR (qRT-PCR)** A method used to both amplify and quantify a specific DNA fragment (especially a cDNA fragment produced from an mRNA molecule).

**Quantum dots** Semiconductor nanocrystals that can be used as bright fluorophores.

**Rabies virus** A relatively toxic viral delivery system that can be used as a retrograde tracer.

**Radial arm maze** A behavioral test used to assay spatial learning and memory in rodents in which an animal is placed in a maze consisting of an array of arms radiating out from a central

starting point, with only some arms containing a food reward. A rodent is trained to traverse down only one arm and not others.

**Radiofrequency (RF) pulse** A pulse of electromagnetic energy used in magnetic resonance imaging to excite hydrogen protons in a human (or animal) subject. After the RF pulse is switched off, the protons relax, generating the magnetic resonance signal used to form images of the brain.

**Radioimmunoassay (RIA)** A sensitive method for measuring extremely low concentrations of proteins.

**Raster plot** A graph that visually represents individual action potentials (or membrane potentials over a threshold) as dots or tick marks over a period of time.

**Ratiometric molecule** A fluorescent molecule that is either excited at or emits light at a slightly different wavelength when bound to a substance, such as calcium. The substance concentration can be determined by the ratio of fluorescence intensity at different excitation or emission wavelengths. In contrast with *Nonratiometric molecules*.

**Real-time place avoidance/preference** A kind of place preference assay that measures the inherent reward value of a certain stimulus (such as the effects of stimulating or inhibiting a population of neurons) without conditioning.

**Recognition site** See *Restriction site*.

**Recombinant DNA technology** A set of molecular biology tools used to cut, ligate, and copy novel DNA sequences to produce useful DNA constructs of interest.

**Reduction** One of the guidelines for animal welfare stating that , when possible, scientists should use the minimum number of animals required to obtain statistically significant data.

**Refinement** One of the guidelines for animal welfare stating that scientists should minimize distress and pain and enhance animal well-being during experiments.

**Refractive index** See *Index of refraction*.

**Region-of-interest (ROI) analysis** Method of data analysis that measures signal intensity from a defined location within a brain, tissue, or specimen.

**Registration** In imaging experiments, the process of aligning individual images into the same coordinate system to produce animated movies that present stable structures over time.

**Relative recovery** In microdialysis, the relative concentration of a substance in the collected dialysate from the probed brain region compared to the concentration in the perfusion solution.

**Replacement** A guideline for animal welfare stating that, when possible, scientists should try to perform research without using animals, such as using computational methods or cell culture methods. Also recommends selecting a "less-sentient" animal species as a model organism, such as choosing to study invertebrates over vertebrates or mice rather than monkeys.

**Reporter gene/protein** A visible, nonendogenous gene or protein used to mark a cell type or cell structure of interest.

**Rescue experiment** A follow-up assay to a loss-of-function experiment in which whatever aspect of the nervous system that was experimentally removed is subsequently returned to determine if it rescues the normal phenotype.

**Resident-intruder assay** A social behavior assay in rodents that examines territorial behavior in males by adding an "intruder" animal into the cage of a "resident" animal and measuring specific aggressive behaviors.

**Resistance (R)** An electrical property that restricts the movement of charge, for example, across a membrane.

**Resolution** In microscopy, the minimum distance by which two points can be separated and still distinguished as two separate points.

**Resolving power** See *Resolution*.

**Resting potential** The voltage across the cell membrane of a cell at rest, generated by differential buildup of ionic charges on the intracellular vs. extracellular sides of the membrane. Neurons typically have a resting potential of about −70 mV.

**Restriction digest** The process of using restriction enzymes to cut DNA into fragments.

**Restriction endonuclease** See *Restriction enzyme*.

**Restriction enzyme** An enzyme that recognizes and cuts specific 4–8 base pair sequences of DNA.

**Restriction mapping** The process of constructing a map of the locations of various recognition sites on a piece of DNA by using restriction digests and separating the digested fragments by gel electrophoresis.

**Restriction site** An approximately 4–8 unique base pair sequence that a particular restriction enzyme recognizes and cuts.

**Retrobeads** Small fluorescently conjugated lipophilic beads that can be used as a retrograde tracer.

**Retrograde** In the direction from the synapse back toward the cell soma.

**Retrograde tracer** A probe taken up by synaptic terminals and retrogradely transported up axons back to cell bodies. Used to determine the neural populations that project to an area or cells of interest.

**Retrovirus** A type of virus that uses RNA rather than DNA as its genetic material.

**Reversal potential** The membrane voltage at which there is no overall flow of ions across the membrane.

**Reverse genetics** The directed mutagenesis of a specific gene to determine if the gene is necessary for a certain phenotype. Contrast with *Forward genetics*.

**Reverse microdialysis** The use of a microdialysis probe to introduce chemical substances into a brain region.

**Reverse transcriptase** Enzyme that produces complementary DNA (cDNA) out of template RNA strands.

**Reverse transcription** The process of creating complementary DNA (cDNA) from RNA templates using reverse transcriptase.

**Reverse transcription PCR (RT-PCR)** A PCR reaction that amplifies a cDNA fragment generated from reverse transcription of an RNA fragment.

**Ribosome** Macromolecular complexes of RNA and protein that translate mRNA into a polypeptide chain during translation.

**RISC** See *RNA-induced silencing complex*.

**RNA-induced silencing complex (RISC)** A complex of proteins that uses siRNA as a template for finding a complementary mRNA to degrade.

**RNA interference (RNAi)** The process of silencing gene expression using targeted endogenous cellular mechanisms that degrade mRNA.

**RNA polymerase** The enzyme that binds to and transcribes DNA templates to produce RNA.

**RNA-Seq** See *RNA sequencing*.

**RNA sequencing** A high-throughput sequencing technique used to identify and quantify the mRNA transcripts present in a sample.

**RNA splicing** The removal of introns and joining of exons by a spliceosome of a newly transcribed mRNA before it leaves the nucleus for translation.

**RNAi** See *RNA interference*.

**RNAscope** A commercial application of fluorescent in situ hybridization that allows for efficient labeling of one or more mRNA transcripts with fluorescent reagents.

**ROI analysis** See *Region of interest analysis*.

**Rotarod assay** An assay that investigates motor coordination, balance, and learning by placing rodents on a rotating rod and measuring the time until they fall.

**RT-PCR** See *Reverse transcription PCR*.

**Run** In a brain imaging experiment, one complete scan of the brain, during which a volume of information is collected.

**Sagittal plane** The plane dividing the brain into left and right portions such that the brain is complete top-to-bottom and rostral-to-caudal.

**Sanger dideoxy chain termination method** A technique for determining the sequences of short (~600–800 base pair) DNA molecules.

**Scanning electron microscope (SEM)** A microscope that uses electron interactions at the surface of a specimen to generate an image of the specimen's surface that appears three dimensional.

**Screen** A method that allows an investigator to identify which genes, proteins, neurons, or circuits may be involved in a particular biological process.

**SDS-PAGE** See *Sodium dodecylsulfate polyacrylamide gel electrophoresis*.

**Sealable chamber** An implant that can be installed during a stereotaxic surgery that provides long-term access to the brain via a chamber that can be sealed when not in use (to provide protection from contamination).

**Secondary antibody** In histological and biochemical techniques, an antibody that recognizes and binds to primary antibodies by recognizing epitopes indicating the species from which the primary antibody was generated.

**Secondary neurosphere assay** A cell culture assay that examines whether cells taken from a primary neurosphere are able to form new neurospheres, indicating that the cells continue to be proliferative.

**Sectioning** The process of physically or optically creating thin sections of a specimen to gain greater access and/or visibility of internal structures.

**Selection cassette** A sequence within a genetic targeting construct that encodes genes that can be used to identify cells that have properly incorporated the construct. Typically, this cassette includes a positive selection gene, such as neomycin resistance gene, that can be used to kill cells that have not incorporated the construct. It also typically includes a negative selection gene, such as thymidine kinase, that can be used to kill cells that have improperly incorporated the targeting construct.

**Self-administration** A form of operant conditioning in which animals are trained to perform a particular action, such as pressing a lever, to receive a rewarding stimulus. Used to measure the inherent motivation of an animal to work for the reward.

**SEM** See *Scanning electron microscope*.

**Session** In a brain imaging experiment, the scheduled time when an actual experiment is conducted.

**Shabire** A transgene used in *Drosophila* to reversibly silence neurons at specific temperatures.

**Short hairpin RNA (shRNA)** A strand of RNA containing complementary sequences at either end such that it can self-hybridize, producing a hairpin shape.

**shRNA** See *Short hairpin RNA*.

**Signal transduction** The conversion of an extracellular cue, such as a ligand binding to a receptor, into an intracellular signaling cascade.

**Silicon probe** A multichannel channel probe used to record electrophysiological signals from many neurons simultaneously.

**Single cell RNA-seq** An RNA sequencing approach that determines the gene expression profile of single cells or compares gene expression profiles between single cells within a larger population.

**Single guide RNA** An RNA molecule that serves as a template for genomic targeting in the CRISPR/Cas9 system.

**Single-proton emission computerized tomography (SPECT)** A functional brain imaging technique in which radioactive probes administered into the blood generate high-energy photons that can be detected using a gamma camera placed around a subject's head.

**siRNA** See *Small interfering RNA*.

**Slice culture** A primary tissue culture technique in which sections of brain tissue are sliced using a vibratome and then placed in a culture medium. These slices can be used acutely for short-term experiments, or organotypically, for multiple days.

**Small interfering RNA (siRNA)** Short (19−23 bp) double-stranded RNA fragments used as a template in the RNAi pathway to target mRNA molecules for degradation.

**Social approach/avoidance assay** An assay used to determine the preference of animals to engage with conspecifics versus inanimate objects.

**Sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE)** The process of using an electrical field to separate proteins based on their electrophoretic mobility. Used in conjunction with a western blot.

**Somatic cell** A differentiated cell that is not part of the germline (eggs or sperm), such as skin or blood cells.

**Southern blot** A nucleic acid hybridization technique used to identify the presence of a specific sequence of DNA.

**Spatial resolution** The minimum size that can be resolved to distinguish individual components of an organ or tissue. Compare to *Temporal resolution*.

**SPECT** See *Single-proton emission computerized tomography*.

**Spheroid** Spherical structures of stem cells used in the generation of organoids.

**Spike** An informal term for an action potential.

**Spike sorting** The process of differentiating between action potentials recorded in an extracellular electrophysiology experiment and assigning them to specific neurons based on their pattern, shape of spiking activity, and signal size.

**Spliceosome** The macromolecular complex that catalyzes RNA splicing.

**Splitting** See *Passaging*.

**Startle response assay** A behavioral assay that measures the ability of an animal to exhibit a startle response, such as an eye blink or sudden muscle contraction, in response to the presentation of an unexpected sensory stimulus. Used to indicate whether sensory processing is intact.

**Stem cell** A pluripotent cell that has an unlimited ability to renew itself.

**Step function opsins** Channelrhodopsin-2 variants that have the property of staying in an open state in response to a pulse of blue light and switching to an off state in response to a pulse of yellow light for long-term optogenetic stimulation experiments.

**Stereomicroscope** A microscope that magnifies small objects and provides a three-dimensional perspective for examining the surface of brains or large neural structures. Often used for dissections, surgeries, or examining electrodes and implants.

**Stereotaxic instrument** A piece of equipment that stabilizes an animal's head and allows precise positioning for injections or implants.

**Stereotaxic surgery** A survivable surgical procedure used to place the brain in a three-dimensional coordinate scheme for the precise injection of substances or implantation of devices relative to specific neural populations or brain regions.

**Sterile** Aseptic and free from microorganisms.

**Sterile field** A dedicated aseptic surface where sterile instruments can be placed when not in use.

**Sticky end** Single-stranded DNA overhang generated by some restriction enzyme digests. Sticky ends can be matched to a complementary sticky end produced by the same restriction enzyme on a different sample of DNA. Compare to *blunt end*.

**Structural brain imaging** Techniques that are used to resolve brain anatomy in a living subject without physically penetrating the skull. Examples include *Cerebral angiography*, *Computer tomography*, and *Magnetic resonance imaging (MRI)*.

**Subcloning** The process of copying or moving a fragment of DNA from one recombinant DNA construct into a new vector to create a new recombinant DNA construct.

**Sucrose preference test** A behavioral measure of anhedonia in rodents in which an animal must choose between consuming solutions with different concentrations of sweet compounds. Normal rodents prefer sweet water, but rodent models of depression do not.

**Sufficiency experiment** See *Gain-of-function experiment*.

**Sulci** The indentations created by the folds in the brain.

**Super resolution microscopy** A collection of microscopy techniques that allows for imaging specimens at higher resolution than would otherwise be possible due to the diffraction limit

**Suture** A seam between different parts of the skull useful for identifying bregma or lambda coordinates; can also refer to a thread used after a surgery to close a wound.

**Synapto-pHlorin** A pH-sensitive fluorescent protein variant of GFP that is used to examine synaptic vesicle recycling and release. It does not fluoresce when present inside synaptic vesicles, but does fluoresce when the vesicle fuses during exocytosis.

**Systems neuroscience** The branch of neuroscience that examines how populations of neurons, in isolation or in functional neural circuits, generate behavior and cognition.

**T-maze** A behavioral apparatus with two arms oriented in opposite directions, giving it a T shape. A *Drosophila* T-maze contains an additional loading arm to move flies into the choice point between the T. Used to test sensory preferences and associational learning.

**T1** In MRI and fMRI, the time required for a certain percentage of protons that had been excited by radiofrequency pulses to realign in the longitudinal direction.

**T1-weighted image** An MRI image formed based on T1 signal intensity.

**T2** In MRI and fMRI, the time required for a certain percentage of protons that had been excited by radiofrequency pulses to relax in the transversal direction.

**T2-weighted image** An MRI image formed based on T2 signal intensity.

**Tail flick assay** A rodent assay for nociception in which painful heat or cold is applied to the tail, causing the rodent to rapidly move its tail out of the way.

**Tail suspension assay** An assay for depression in which a rodent is suspended by its tail and the amount of time the animal struggles is measured.

**Talairach space** A coordinate system based on the stereotaxic measurements of a single post-mortem brain used to normalize MRI data so that anatomical comparisons can be made among different brains.

**Tamoxifen** A molecule that binds to the estrogen receptor, causing translocation of the receptor from the cytoplasm to the nucleus. Useful to exert temporal control over the Cre/lox system when Cre recombinase is fused to the estrogen receptor.

**Task paradigm** A strategy for presenting stimuli to subjects during an experiment. In human brain imaging experiments, these paradigms are typically classified as a *Blocked design*, *Event-related design*, or *Mixed design*.

**TEM** See *Transmission electron microscopy.*

**Temporal delay** In functional brain imaging techniques, the time delay between presentation of a stimulus and measurement of neural activity due to the time it takes for blood to flow into an active region.

**Temporal resolution** The ability to distinguish discrete neural events over time.

**TeNT** See *Tetanus toxin*.

**Tesla** Units of measurement for magnetic field strength. Conventional MRI scanners create external magnetic fields at 1.5−3 T.

**Tet-off/Tet-on system** An inducible promoter system that allows transgene expression to be either turned off (Tet-off) or turned on (Tet-on) through administration of the drug doxycycline.

**Tetrode** A bundle of microelectrodes used to perform extracellular electrophysiological recordings, often in vivo recordings in awake, behaving animals.

**Tetrodotoxin (TTX)** A toxin produced by specific species of fish, such as pufferfish, that binds pores of voltage-gated sodium channels to block action potentials.

**Thermocycler** A machine that controls the heating and cooling of samples, most often used for PCR.

**Time of flight (TOF) detector** In mass spectrometry, an instrument that measures the mass to charge ratio of molecules in the gas phase.

**TIRF Microscopy** *See Total internal reflection fluorescence microscopy.*

**Tissue clearing** A technique for making intact tissue transparent, allowing for three-dimensional visualization of the nervous system without slicing the tissue.

**Total internal reflection fluorescence (TIRF) microscopy** A form of microscopy used to image molecules and/or events that occur at the cell surface. A TIRF microscope uses a rapidly decaying evanescent wave of fluorescence excitation to restrict imaging to a thin ($\sim$100 nm) region of contact between a specimen and a glass coverslip.

**Tracer** A chemical that can be injected and transported along neural processes to highlight axonal paths and connections.

**Transcranial magnetic stimulation (TMS)** A noninvasive method used to manipulate neural activity in the brain. A coil is positioned adjacent to a subject's head. This coil generates magnetic field pulses that induce electrical activity in superficial brain structures. Depending on the specific sequence and strength of pulses, TMS can reversibly activate or inactivate brain regions.

**Transcription** The process of synthesizing RNA from a DNA template, performed by the enzyme RNA polymerase.

**Transcription factor** A DNA-binding protein that recognizes a specific genetic regulatory element and regulates transcription by recruiting or blocking RNA polymerase.

**Transcriptional start site** The location within a gene where RNA polymerase begins transcription.

**Transduction** The process of using a nonreplicating viral vector to deliver foreign DNA into a cell.

**Transfection** The process of delivering DNA to cells using nonviral methods.

**Transformation** The process of delivering and expressing DNA in competent bacteria.

**Transgene** A foreign gene expressed in an organism that does not normally express the gene.

**Transgenic organism** An organism that carries foreign DNA that it does not normally express.

**Translation** The process by which a ribosome synthesizes a chain of amino acids based on an mRNA template.

**Transmission electron microscopy (TEM)** A form of microscopy in which an electron beam is transmitted through a thin specimen to generate an image based on differences in electron density of the material. Produces extremely high-resolution images of cellular ultrastructure.

**Transposable element** See *Transposon*.

**Transposase** An enzyme that acts on specific DNA sequences at the end of a transposon to disconnect the sequence from flanking DNA and insert it into a new target DNA site.

**Transposition** The natural process of a transposon moving to different positions within the genome.

**Transposon** A genetic sequence capable of translocating to different positions within the genome.

**Transsynaptic tracer** A tracer capable of transmitting through two or more synapses to label multisynaptic connections.

**TRAP system** Targeted Recombination in Active Populations, a binary transgenic system used to genetically tag cells of interest based on their activity patterns.

**TRAP-Seq** A high-throughput sequencing technique used to identify which RNA species in a sample are actively translated by a ribosome at a specific moment in time.

**TrpV1** See *Capsaicin receptor*.

**TTX** See *Tetrodotoxin*.

**Two-photon microscopy** A specialized form of fluorescence microscopy that illuminates fluorophores with two lower energy pulses of laser light that can summate in a restricted region of a specimen to excite fluorophores. Regions beyond the restricted region do not receive enough energy for excitation, reducing out-of-focus background fluorescence.

**UAS** See *Upstream activation sequence*.

**Ultrasonic neuromodulation** A noninvasive neuromodulation technique in which focused sound waves slightly heat an area of the brain, causing transient neuromodulatory effects.

**Unconditioned stimulus (US)** In classical conditioning, the salient stimulus that eventually becomes associated with a previously neutral stimulus.

**Unipotent** Describes a cell that is capable of dividing but only capable of giving rise to a single cell type.

**Upright microscope** A standard light microscope in which the objective lens is located above the specimen and the light source and condenser are located beneath the specimen.

**Upstream activation sequence (UAS)** A strong promoter derived from yeast that is activated by the Gal4 transcription factor.

**Validity** A subjective measure of the suitability of an animal model for studying a human behavior, physiological condition, or disease. Categories include *Construct validity*, *Face validity*, and *Predictive validity.*

**Vector** A carrying vehicle composed of DNA that can hold an isolated DNA sequence of interest for cloning and recombinant DNA experiments.

**Vertical pole test** A behavioral paradigm used to assay motor coordination and balance in rodents.

**Vibratome** A device that uses a vibrating blade to section a fresh, unfrozen specimen into tissue slices that can be kept alive.

**Viral gene delivery** The delivery of DNA constructs into cells in vivo or in vitro using one of many available viral vectors.

**Visual cliff assay** An assay used to examine normal visual function in rodents.

**Voltage (V)** A measure of the electromotive force or potential difference that exists across a membrane.

**Voltage clamp** An electrophysiology technique that allows a scientist to hold the membrane potential at a constant voltage to measure currents generated by ions moving across the membrane.

**Voltage sensitive dye imaging** A cell or tissue visualization technique that uses dyes that shift their absorption or emission fluorescence based on the membrane potential, thus allowing scientists to visualize changes in membrane potential over time.

**Voltammetry** An electrochemical method used to measure the presence and relative amounts of neurochemicals in living tissue.

**Volume** In brain imaging experiments, a complete scan of the brain consisting of several individual slices.

**Von Frey assay** A behavioral test used to assay noxious mechanical and pinch stimuli in rodents.

**Voxel** In noninvasive brain imaging experiments, a three-dimensional unit of brain space.

**Voxelwise analysis** A strategy for analyzing data in a functional imaging experiment in which each voxel of data is examined for significant changes in signal intensity.

**Western blot** A method used to detect the expression of a protein in a biological sample.

**Whole-cell mode** An electrophysiological patch clamp recording technique in which a glass pipette is placed adjacent to a cell membrane and a small membrane patch is removed, allowing the interior of the pipette to become continuous with the cytoplasm of the cell.

**Whole-mount preparation** A histological preparation in which a chunk of tissue or an entire small animal brain is mounted onto a slide for analysis.

**Wide-field fluorescent microscopy** See *Epifluorescent microscopy.*

**Within-subjects study** A study that compares data from the same subject pool in two or more conditions. Compare with *Between-subjects study.*

**Worm tracker** Computer software that automatically tracks locomotor behavior in *C. elegans*.

**X-ray** A structural visualization technique used to image parts of the body with natural contrast, such as a bone in tissue.

**Xylazine** A chemical sedative and analgesic, often used in combination with ketamine to anesthetize small rodents.

**Yeast artificial chromosome (YAC)** A large (100−2000 kb) DNA vector capable of replicating in yeast. Useful for manipulating large sequences of DNA.

**Yeast two-hybrid assay** A method that takes advantage of yeast transcriptional machinery to determine whether two proteins directly interact with each other.