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## Magnetic control of the nervous system (vs. Optogenetics & Chemogenetics)

### Description

Christiansen, M. G., Senko, A. W., & Anikeeva, P.. (2019). Magnetic Strategies for Nervous System Control. Annual Review of Neuroscience

Plain numerical DOI: 10.1146/annurev-neuro-070918-050241

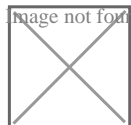
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### Show/hide publication abstract

"Magnetic fields pass through tissue undiminished and without producing harmful effects, motivating their use as a wireless, minimally invasive means to control neural activity. here, we review mechanisms and techniques coupling magnetic fields to changes in electrochemical potentials across neuronal membranes. biological magnetoreception, although incompletely understood, is discussed as a potential source of inspiration. the emergence of magnetic properties in materials is reviewed to clarify the distinction between biomolecules containing transition metals and ferrite nanoparticles that exhibit significant net moments. we describe recent developments in the use of magnetic nanomaterials as transducers converting magnetic stimuli to forms readily perceived by neurons and discuss opportunities for multiplexed and bidirectional control as well as the challenges posed by delivery to the brain. the variety of magnetic field conditions and mechanisms by which they can be coupled to neuronal signaling cascades highlights the desirability of continued interchange between magnetism physics and neurobiology."

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Wheeler, M. A., Smith, C. J., Ottolini, M., Barker, B. S., Purohit, A. M., Grippo, R. M., ... Güler, A. D.. (2016). Genetically targeted magnetic control of the nervous system. Nature Neuroscience

Plain numerical DOI: 10.1038/nn.4265

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### Show/hide publication abstract

"Optogenetic and chemogenetic actuators are critical for deconstructing the neural correlates of behavior. however, these tools have several limitations, including invasive modes of stimulation or slow on/off kinetics. we have overcome these disadvantages by synthesizing a single-component, magnetically sensitive actuator, magneto, comprising the cation channel trpv4 fused to the paramagnetic protein ferritin. we validated noninvasive magnetic control over neuronal activity by

demonstrating remote stimulation of cells using in vitro calcium imaging assays, electrophysiological recordings in brain slices, in vivo electrophysiological recordings in the brains of freely moving mice, and behavioral outputs in zebrafish and mice. as proof of concept, we used magneto to delineate a causal role of striatal dopamine receptor 1 neurons in mediating reward behavior in mice. together our results present magneto as an actuator capable of remotely controlling circuits associated with complex animal behaviors."

Adamczyk, A. K., & Zawadzki, P.. (2020). The Memory-Modifying Potential of Optogenetics and the Need for Neuroethics. NanoEthics

Plain numerical DOI: 10.1007/s11569-020-00377-1

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### Show/hide publication abstract

"Optogenetics is an invasive neuromodulation technology involving the use of light to control the activity of individual neurons. even though optogenetics is a relatively new neuromodulation tool whose various implications have not yet been scrutinized, it has already been approved for its first clinical trials in humans. as optogenetics is being intensively investigated in animal models with the aim of developing novel brain stimulation treatments for various neurological and psychiatric disorders, it appears crucial to consider both the opportunities and dangers such therapies may offer. in this review, we focus on the memory-modifying potential of optogenetics, investigating what it is capable of and how it differs from other memory modification technologies (mmts). we then outline the safety challenges that need to be addressed before optogenetics can be used in humans. finally, we re-examine crucial neuroethical concerns expressed in regard to other mmts in the light of optogenetics and address those that appear to be unique to the memory-modifying potential of optogenetic technology."

Kole, K., Zhang, Y., Jansen, E. J. R., Brouns, T., Bijlsma, A., Calcini, N., ... Celikel, T.. (2020). Assessing the utility of Magneto to control neuronal excitability in the somatosensory cortex. Nature Neuroscience

Plain numerical DOI: 10.1038/s41593-019-0474-4

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Keifer, O., Kambara, K., Lau, A., Makinson, S., & Bertrand, D.. (2020). Chemogenetics a robust approach to pharmacology and gene therapy. Biochemical Pharmacology

Plain numerical DOI: 10.1016/j.bcp.2020.113889

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### Show/hide publication abstract

"Modern developments in organic chemistry, molecular biology, virology, and genetics have opened new, exciting possibilities to better understand physiology and to create innovative, robust

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therapeutics. one such possibility is the burgeoning field of chemogenetics, a sub-field of chemical genetics that encompasses engineering macromolecules (particularly proteins) to modify how they interact with endogenous and exogenous ligands (particularly small molecules). early efforts in chemogenetics were focused on parsing the function of a specific enzyme within a closely-related family by creating orthogonal enzyme-ligand pairs (e.g. kinases paired with antagonists). this powerful concept quickly expanded into engineered g-protein-coupled receptors (e.g. dreadd/rassl), and more recently into engineered ligand-gated ion channels (elgic). the modifications to the receptor focused on eliminating their activation by endogenous ligands, while preserving or enhancing their interaction with pharmacological agents (e.g. small molecule agonist). creation of such an engineered receptor and delivering it selectively to specific cell types opens new possibilities of accurately and precisely controlling cellular activity. control of this activity then increases our understanding of the cells function in normal physiology, while also creating the possibility of using it as a therapeutic to address pathophysiology. the dreadd/rassl and elgic approaches have been particularly impactful in neurosciences but have applications in multiple fields. in this work we introduce the history of the chemogenetic approach, review the seminal work with dreadd/rassls and elgic, highlight the breadth of applications, and discuss the strengths and weaknesses associated with this technology, especially in the context of its development into a therapeutic."

Magnus, C. J., Lee, P. H., Bonaventura, J., Zemla, R., Gomez, J. L., Ramirez, M. H., ... Sternson, S. M. . (2019). Ultrapotent chemogenetics for research and potential clinical applications. *Science*

Plain numerical DOI: 10.1126/science.aav5282

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"Chemogenetics enables noninvasive chemical control over cell populations in behaving animals. however, existing small-molecule agonists show insufficient potency or selectivity. there is also a need for chemogenetic systems compatible with both research and human therapeutic applications. we developed a new ion channel-based platform for cell activation and silencing that is controlled by low doses of the smoking cessation drug varenicline. we then synthesized subnanomolar-potency agonists, called upsems, with high selectivity for the chemogenetic receptors. upsems and their receptors were characterized in brains of mice and a rhesus monkey by in vivo electrophysiology, calcium imaging, positron emission tomography, behavioral efficacy testing, and receptor counterscreening. this platform of receptors and selective ultrapotent agonists enables potential research and clinical applications of chemogenetics."

Poth, K. M., Texakalidis, P., & Boulis, N. M.. (2021). Chemogenetics: Beyond Lesions and Electrodes. *Neurosurgery*

Plain numerical DOI: 10.1093/neuros/nyab147

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## Show/hide publication abstract

"The field of chemogenetics has rapidly expanded over the last decade, and engineered receptors are currently utilized in the lab to better understand molecular interactions in the nervous system. we

propose that chemogenetic receptors can be used for far more than investigational purposes. the potential benefit of adding chemogenetic neuromodulation to the current neurosurgical toolkit is substantial. there are several conditions currently treated surgically, electrically, and pharmacologically in clinic, and this review highlights how chemogenetic neuromodulation could improve patient outcomes over current neurosurgical techniques. we aim to emphasize the need to take these techniques from bench to bedside."

Vlasov, K., Van Dort, C. J., & Solt, K.. (2018). Optogenetics and Chemogenetics. In Methods in Enzymology

Plain numerical DOI: 10.1016/bs.mie.2018.01.022

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"Optogenetics and chemogenetics provide the ability to modulate neurons in a type- and region-specific manner. these powerful techniques are useful to test hypotheses regarding the neural circuit mechanisms of general anesthetic end points such as hypnosis and analgesia. with both techniques, a genetic strategy is used to target expression of light-sensitive ion channels (opsins) or designer receptors exclusively activated by designer drugs in specific neurons. optogenetics provides precise temporal control of neuronal firing with light pulses, whereas chemogenetics provides the ability to modulate neuronal firing for several hours with the single administration of a designer drug. this chapter provides an overview of neuronal targeting and experimental strategies and highlights the important advantages and disadvantages of each technique."

### Category

1. General

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