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Reframing Optogenetics through Bioinformatics: towards Multimodal Neurological Analysis

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Commentary

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ABSTRACT

Optogenetics has transformed modern neuroscience by enabling millisecond-scale control of genetically targeted neuronal populations through light. Although experimental precision has improved significantly, the field still faces important limitations, including optical scattering in deep tissue, heterogeneity in opsin expression, and the challenge of interpreting high-dimensional neural data. Artificial intelligence (AI) and bioinformatics have emerged as powerful complementary tools to address these barriers. AI methods improve light-delivery optimization, automate signal extraction from imaging and electrophysiological data, and support predictive modeling of circuit dynamics. Meanwhile, bioinformatics contributes essential frameworks for analyzing the genetic, proteomic, and transcriptomic foundations of neuronal function, offering a molecular perspective that enhances optogenetic experimental design. This review summarizes the foundational principles of optogenetics, outlines its current challenges, and presents how AI and bioinformatics can collectively accelerate neurological research. We highlight applications in epilepsy, Parkinson's disease, Alzheimer's disease, and network-level studies, emphasizing how computational tools strengthen the interpretative and translational potential of optogenetic technologies. The combined integration of optogenetics, AI, and bioinformatics represents a promising direction for understanding and manipulating neuronal systems in both health and disease.

KEYWORDS:

optogenetics, artificial intelligence, bioinformatics, neurology, neural circuits, neuroscience, machine learning

INTRODUCTION

The convergence of technology and neuroscience has driven remarkable progress in understanding brain function and developing strategies to address neurological disorders. A central example of this convergence is optogenetics, a technique capable of modulating the electrical activity of genetically defined neuronal populations using light. Its temporal precision and cell-type specificity allow researchers to establish causal

relationships between neuronal activity and behavior. However, as neural datasets grow in size and complexity, traditional analytical strategies quickly become insufficient. Artificial intelligence (AI) and bioinformatics offer the computational power needed to process and interpret large-scale data derived from optogenetic experiments. These tools are particularly valuable in neurological research, where both cellular-level

mechanisms (circuit mapping, activity decoding) and molecular-level processes (gene expression, protein interactions) must be examined in parallel. This commentary presents an integrated perspective on how optogenetics works, what challenges remain, and how AI and bioinformatics can accelerate its application in neurology. Understanding the foundations of optogenetics is essential before examining how computational tools enhance its capabilities. The following section outlines the core principles of optogenetic technology and highlights its most influential applications in neurology.

OPTOGENETICS: BASICS AND APPLICATIONS

Optogenetics relies on opsins—light-sensitive ion channels or pumps—introduced into specific neuronal populations using viral vectors or transgenic models. Once expressed, these neurons can be activated or inhibited with millisecond precision using fiber optics or implantable LEDs to deliver light deep into neural tissue. Applications in neurological research include interrupting seizure activity in epilepsy, restoring basal ganglia balance in Parkinson’s disease, activating retinal ganglion cells in retinitis pigmentosa, and identifying or manipulating engram cells in memory research. With its ability to test causal relationships in real time, optogenetics has become indispensable for neuroscience. However, these applications also reveal the need for deeper molecular insight and more advanced analytical frameworks. This growing complexity leads naturally to the emerging role of bioinformatics, which complements optogenetic tools by linking genetic, proteomic, and systems-level information.

Neurology and Neurological Research THE EMERGING ROLE OF BIOINFORMATICS IN OPTOGENETIC BASED NEUROLOGY

While AI focuses on computational modeling of neural dynamics, bioinformatics bridges the molecular and genetic domains, providing essential insights that guide optogenetic strategies. Its contributions can be understood across several molecular and computational layers, beginning with genomic and transcriptomic analysis.

Genomic and transcriptomic analysis of neuronal applications

Bioinformatics tools play a critical role in characterizing the genomic and transcriptomic landscape relevant to optogenetic interventions. They enable the identification of gene-expression profiles that inform the selection of neuronal subtypes, support the design of opsin-targeting strategies through cell-specific promoters, and facilitate the examination of genetic variants associated with neurological diseases. Together, these contributions enhance the precision and biological relevance of optogenetic manipulations. The insights derived from these analyses form the foundation upon which more refined molecular and cellular strategies can be built. Building on these genomic and transcriptomic findings, proteomic analysis provides the next layer of understanding needed to refine optogenetic tools.

Proteomic analysis and opsin engineering

Complementing genomic studies, neuroproteomic approaches offer a detailed understanding of the protein-level properties that influence optogenetic performance.

By analyzing protein stability, channel kinetics, and membrane interactions, proteomics provides essential parameters for the rational design of improved opsins. Bioinformatic modeling further supports this effort by enabling the engineering of next-generation opsins with enhanced sensitivity, greater biophysical efficiency, and reduced toxicity. These proteomic insights naturally lead into the challenge of integrating diverse biological datasets to interpret neural activity more comprehensively. Although proteomic analysis improves opsin engineering, fully understanding optogenetic experiments requires combining information from multiple molecular and systems-level sources. This need motivates the strategies described in the next section.

High dimensional data integration

Optogenetic experiments generate increasingly large and complex datasets—from imaging to electrophysiology and behavior. Bioinformatic frameworks make it possible to integrate these data sources with complementary molecular information, including single-cell RNA sequencing, connectomics, and molecular-interaction

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networks. Through this multimodal integration, researchers obtain more accurate and mechanistically grounded interpretations of neural function and dysfunction. This holistic view underscores the growing importance of bioinformatics as a unifying layer across molecular, cellular, and systems-level optogenetic research. Taken together, these genomic, proteomic, and multimodal integration approaches show how bioinformatics is shaping the future direction of optogenetic research and form the basis for the conclusions below.

CONCLUSIONS

Bioinformatics is emerging as a foundational pillar of neurologically oriented optogenetics. It enables deeper molecular understanding, enhances experimental precision, and provides interpretative power for large-scale neural datasets. As neuroscience moves toward highly integrated, multimodal research strategies, bioinformatics will be indispensable in bridging the gap between cellular identity, circuit-level function, and therapeutic innovation.



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