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# Editorial overview: Computational neuroscience as a bridge between artificial intelligence, modeling and data



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Out of all that we may define (that is to say determine) what that is, which is meant by this word reason when we reckon it amongst the faculties of the mind. For reason, in this sense, is nothing but reckoning (that is, adding and subtracting) of the consequences of general names agreed upon for the marking and signifying of our thoughts.

Leviathan - Thomas Hobbes

## Introduction

Computational neuroscience continues to be a broad and dynamic discipline that transforms itself as new experimental methods make the collection of new, often multi-modal data types possible. Initially, the focus was on models of single neurons, their ion channels, the statistics of their spikes, and their processing of inputs. New multiunit recording techniques that were possible first in vitro and then gradually in vivo allowed the field to expand into the question of how populations of neurons form circuits that represent sensory stimuli or motor output. Addressing these questions revealed many mathematically and conceptually challenging directions, such as low-dimensional manifolds, their synthesis, and representational meaning. Questions about neural synchrony, phase locking, neural attractors, and their relation to learning, memory, and sleep entered the stage. In the next decades, increased automatization of connectomics studies in organisms such as flies and mice allowed the correlation of the observed activity with the probing of the underlying connectivity. Therefore, neural activity could now, for the first time, be combined with the circuit structure that generated it, enabling detailed insights into the role of cell types in generating specific aspects of neural population activity. New machine-learning methods now enable tracking and segmenting behavior into smaller units while recording neural activity. These methods are complemented by advances in cell profiling and detailed molecular characterization of neural activity and structure, such as quantitative bridges between molecules and behavior, which can be unraveled for the first time. This is an exciting time to be a computational neuroscientist for multiple reasons. First, emerging datasets that cover multiple neural and behavioral levels are emerging and demand new computational approaches. Artificial neural networks can now enable online behavioral segmentation across species and behavioral tasks, but identifying the equivalent of a "grammar" that tells how to use a specific neural activity pattern in a specific region toward the construction of a behavioral trajectory in space is still a challenge. Also, at the level of cellular and molecular mechanisms, new proteomics and connectomics data sets allow unprecedented insights into the learning mechanisms at the single synapse or dendritic branch level, but translating these insights into learning rules in artificial neural networks or revealing their functional correlates in brain circuits remains a fundamental challenge.

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In this issue, computational neuroscientists, whose diverse expertise ranges from molecular interactions to behavioral characterization, share their perspectives on our current knowledge and future challenges and highlight recent breakthroughs. These reviews can be seen as covering five broad areas: 1) machine learning for neuroscience; 2) neurosciences for machine learning; 3) neural computation; 4) computational models; and 5) data analysis methods. Below, we try to map the different contributions to these categories, although several of the reviews fit in more than one.

# Machine learning for neuroscience

The copious data and the intricate nature of neurological phenomena have prompted a profound integration of machine-learning techniques, propelling advancements in this field. Examining how various machine learning ideas have been harnessed unveils a compelling narrative of how these tools have been instrumental in deciphering the complexities of the brain and expanding the frontiers of neuroscientific knowledge. This section intricately explores the contemporary landscape of machine learning's pivotal role in shaping our current understanding of neural systems, emphasizing the incorporation of cutting-edge techniques and their contributions to expanding the frontiers of neuroscientific knowledge.

The article by Farrell, Recanatesi, and Shea-Brown [7] discusses the potential of using neural networks as models for brain function and examines the mechanisms behind neural network behavior. The authors survey the literature and focus on three questions related to how neural circuits change throughout learning. These questions include 1) when networks change their internal representations; 2) when the emerging representations isolate the task at hand; and 3) when and how compressed representations can extract hidden, latent structures of the task or environment.

In their work, Bull and Brunton [4] advocate for an approach to modeling based on modularity. Building parallels with modeling in engineering, they describe an approach relying on modules of different granularities that can be combined to build more complex models. The advantage of using modules is that they can introduce the inductive biases required for making meaningful models while being validated independently, thus reducing the overall optimization cost of the full system. They then describe the system-of-systems approach as a multi-step modeling process that consists of building and validating the modules, assembling them into a larger system, and then co-optimizing them at a system level. This can be achieved using a loss-minimization or reward-driven reinforcement learning approach.

Lindsay [13] focuses on using artificial neural network models to understand how changes in neural circuits or activity produce changes in behavior. This approach can provide causal tests for the relationship between neural and behavioral changes, and interactions with artificial intelligence can offer new insights into the underlying mechanisms.

Modern recording techniques allow studying learning-induced plasticity in large populations of neurons. In their review, Gurnani and Cayco Gajic [9] focus on three main themes: 1) learning as changes to the geometric structure; 2) learning as changes in the dynamics; 3) learning multiple tasks (avoiding catastrophic forgetting). Findings from biological and

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artificial networks are presented, shaping a new framework for task learning.

The article by Kalidindi and Crevecoeur [11] explores closed-loop models of movement control and their relevance in understanding how the nervous system translates sensory information into motor commands. Recent research has shown that these models can adapt to changes in environmental parameters, enabling flexible adjustments in actions and decisionmaking. When the task or movement dynamics change, humans employ strategies involving adaptation and controller sensitivity modulation. The article proposes a unified framework for explaining these findings, emphasizing the importance of online estimation of model parameters with dynamic control updates.

# **Neurosciences for machine learning**

Since the inception of machine learning, the insights gleaned from neuroscience have served as a wellspring of inspiration. While contemporary machine learning architectures do not explicitly emulate the brain's intricacies, valuable neuroscience discoveries continue to play a pivotal role in advancing the state of the art. This chapter unfolds the nuanced interplay, showcasing how the cross-fertilization of ideas between neuroscience and machine learning has catalyzed innovation and progress in both domains. This section focuses on the utilization of tools derived from neuroscience to enhance the capabilities of machine learning.

In the work by Pache and Rossum [21], the energy cost of learning is addressed. This study highlights the importance of considering the metabolic energy required for acquiring and storing information in biological learning. While current computational models of neural plasticity often overlook this cost, it could be a crucial constraint. The review explores strategies to decrease energy requirements in neural networks and examines how energy efficiency may have influenced biological learning, drawing comparisons with cognitive and neurophysiological findings.

At the intersection of neuroscience and machine learning, there is a growing interest in unsupervised learning, where sensory systems learn from typical inputs without explicit training targets or rewards. Experimental advances allow the exploration of how sensory experience influences neural self-organization and synaptic mechanisms. The review by Matteucci, Piasini, and Zoccolan [16] discusses recent developments in unsupervised and self-supervised learning algorithms, emphasizing their impact on theories of the brain and their potential for breakthroughs in both understanding neural processes and real-world learning machines.

Working memory (WM) is a key function in human cognition, enabling a coherent view of the here and now. This memory system has the ability for one-shot encoding, temporary maintenance, as well as flexible updating and manipulation. WM is affected early on in several neurological and psychiatric conditions, so a better understanding of the underlying neurobiological processes would have high diagnostic and therapeutic value. The theories and mechanisms behind WM are currently being reconsidered, and one hypothesis is based on fast Hebbian synaptic plasticity, in analogy with how long-term memory depends on long-term synaptic potentiation, though on a slower time scale. The article by Lansner, Fiebig, and Herman [12] discusses the experimental and computational arguments for this view. Notably, current mainstream machine learning approaches are mostly missing WM functionality, and there

is a possibility that a better understanding of the neurobiology of WM may also contribute to the design of improved ML systems.

Dendrites are fundamental elements in the brain architecture, but their role is often overlooked in artificial neural networks. In Makarov, Pagkalos, and Poirazi [15], the authors discuss the importance of dendrites as computational units in the brain. The brain's dendrites play a crucial role in maximizing efficiency by segregating inputs and integrating them conditionally through nonlinear events, compartmentalizing activity and plasticity, and binding information through synapse clustering. This enables biological networks to process natural stimuli, infer context-specific information, and store it in overlapping populations of neurons. Dendrites contribute to the brain's overall efficiency by employing optimization strategies that balance performance and resource utilization in scenarios with limited energy and space. In Pagkalos, Makarov, and Poirazi [22], the role that dendrites could play in machine learning models is described. Brain-inspired engineering has emerged as a promising approach to overcoming these challenges and designing sustainable AI systems. Innovative solutions have been developed for crucial AI problems such as credit assignment, catastrophic forgetting, and high energy consumption by drawing inspiration from the dendritic mechanisms of biological neurons. These findings offer exciting possibilities for alternative architectures, demonstrating how dendritic research can lead to the development of more powerful and energyefficient artificial learning systems.

#### **Neural computation**

Within the realm of neural computation, the intricacies of the brain's computational prowess manifest in the execution of complex tasks marked by high accuracy and notably low energy consumption, distinguishing it from the resource-intensive demands of silicon-based computers. Despite considerable progress in recent years toward unveiling the mysteries enveloping cognitive phenomena, a substantial portion of these intricacies persists in obscurity. This section serves as a focal point for contributions that address the array of challenges confronted by the brain, engaging in discussions on the potential solutions it employs to navigate and resolve these intricate problems.

In Modirshanechi et al. [19], the authors discuss the role of "surprise" and "novelty" in neuroscience. These two terms have been used in various studies across multiple brain areas and species, but they refer to different things in different studies, raising concerns about whether they relate to the same brain functionalities and mechanisms. They address these concerns by systematically investigating how different aspects of surprise and novelty

relate to different brain functions and physiological signals. The authors propose that computational modeling and quantifiable definitions can enable new interpretations of previous findings and serve as a foundation for future studies.

Yoshida and Toyoizumi [26] explore recent theoretical models regarding the role of sleep in learning and memory. The authors discuss the potential benefits of slow waves for enhancing computation by creating distinct neuronal states and propagating traveling waves. They also examine the idea that memory transfer at varying speeds between different brain regions could improve generalization and propose that dreaming may contribute to the formation of efficient representations similar to modern machine learning techniques. The authors suggest further development of these concepts, highlighting the importance of experimental neuroscience and its connection to machine learning.

Micou and O'Leary [18] discuss the changes in neural representations, a phenomenon known as representational drift. Long-term recordings of neural activity have shown that familiar tasks and actions lead to continuous evolution in neural representations, even in the absence of obvious behavioral changes. This drift in neural activity is likely due to continual learning, which can be predicted by neural network models that use iterative learning to optimize weights. Drift can serve as a measurable signal to reveal the precision and effective learning rates of biological plasticity mechanisms at a system level.

In their work, Ashwin, Fadera, and Postlethwaite [1] discuss the modeling of brain dynamics using *network attractors*. These employ the concept of a "network" within phase space, enabling the modeling of both the discrete states of the system and the permissible transitions between them. This blurs the demarcation between conventional discrete computation and continuous dynamical systems, allowing the modeling of a wide range of phenomena.

The article by Schmidt, Rose, and Muralidharan [24] discusses the changing perspective on neural oscillations, which are now often seen as occurring in transient bursts rather than sustained patterns. This phenomenon is observed across various oscillation frequencies, cognitive tasks, and species. The article reviews recent developments in the analysis of these transient oscillations, computational modeling, and functional roles. Different methods are used to analyze their transient nature and impact on cognitive functions, and computational models are developed to account for the stonature these chastic of oscillations. functional constraints.

In their work, Basu and Ito [2] delve into the essential aspects of goal-directed navigation, focusing on how the brain identifies an animal's own location within an environment, primarily through spatially-tuned neurons in the hippocampus and parahippocampal cortices. However, understanding how the brain encodes a remote navigational goal has remained a challenge until recent developments. The study discusses the algorithmic challenges and requirements for forming a representation of such a goal when the animal is not present at the location. It also highlights evidence suggesting that neurons in the orbitofrontal cortex persistently represent a goal location as an animal navigates toward it. Finally, the authors propose a novel perspective on navigation research facilitated by this recently discovered brain's goal map.

# Computational models

The use of computational models is paramount in unraveling the intricate workings of the brain, offering a unique lens through which to understand complex neural phenomena. Modeling serves as a crucial tool for exploring diverse aspects of neuroscience, from the dynamic interactions between neurons and glial cells to the sophisticated signaling networks that underpin cellular operations. This section explores how computational models contribute to our understanding of the brain's complexities across various scales, shedding light on fundamental questions in neuroscience and providing valuable insights into synaptic plasticity, network activity regulation, and the convergence of diverse features within neuronal systems.

In the work by Linne [14], glia cells' role is discussed, focusing on their relevance for neural computation. The improvement of recording techniques has revealed an increasing number of interactions between neurons and glial cells (particularly astrocytes), including development, homeostasis, learning, and more. Even though their role is far from being understood and some of the interactions found experimentally are still controversial, computational models based on these findings have been developed to describe and predict astrocytes' complex functions in the brain.

Signaling networks play a critical role in executing cellular operations, ranging from milliseconds to a potential lifetime. Nearly every aspect of neuronal function, especially at synapses, relies on these signaling pathways. Dysfunction, whether caused by mutations, local dysregulation, or infection, can lead to various diseases, each with diverse phenotypes. The review by Viswan and Bhalla [25] emphasizes the importance of constructing computational models to grapple with the complexity of these pathways. It highlights the benefits of employing families of models at different levels of detail to gain insights into signaling in both health and disease.

Understanding the intricate world of midbrain dopaminergic neurons, a relatively small yet powerful group governing a wide spectrum of behaviors in the mammalian brain, is the focus of the article by Blaess and Krabbe [3]. Recent research has revealed the rich anatomical, molecular, and functional diversity within these neurons, leveraging sophisticated tracing, imaging, transcriptomic, and machine-learning approaches. However, the question remains: how do these diverse features converge to shape functional ensembles within the dopaminergic system? The review delves into recent studies that explore various dimensions of dopaminergic heterogeneity and consider how factors like development, behavior, and disease influence type characteristics.

The article by O'Donnell [20] addresses a fundamental question in neuroscience and learning theory: how does the brain reconcile the disparity between rapid neural electrical dynamics and the slower timescales of learning behaviors? The discussion begins with experimental evidence supporting the involvement of slow-timescale factors in synaptic plasticity induction. It then explores potential cellular and synaptic mechanisms, drawing on insights from recent computational models that consider these variables. Ultimately, the article underscores the need for a comprehensive approach that combines experimental and computational studies to unravel the complex interplay between fast and slow plasticity mechanisms in brain learning across different timescales.

The complex role of calcium in regulating neuronal network activity is explored in Jedrzejewska-Szmek, Dorman, and Blackwell [10]. The authors delve into the mechanisms by which calcium directly controls or indirectly regulates critical neuronal functions, particularly synaptic plasticity and ion channel activation, which, in turn, influence neuron spiking activity. Given the technical challenges in obtaining high-resolution experimental data, they underscore the indispensability of computational models in comprehending calcium's intricate dynamics. The models presented offer insights into specific couplings between calcium sources and targets within calcium nanodomains, shedding light on the direction of synaptic plasticity. Additionally, the study considers the complexities arising from cooperativity within calcium domains, raising questions about the preferred computational unit within neurons, with dendritic branches potentially playing a pivotal role.

## Data analysis methods

Over the course of recent years, the field of neuroscience has undergone significant expansion, marked by a surge in both the volume and quality of data amassed, notably through in vivo recordings. This surge not only necessitates but also provides the opportunity to develop innovative approaches for data analysis. Concurrently, the introduction of data science tools has sparked a paradigmatic shift within the discipline. No longer confined to the role of model validation, data analysis has evolved into an active and indispensable mechanism for extracting insights from the intricate fabric of neurophysiological recordings. This section gathers diverse contributions on the compelling intersection of neural computation, offering a comprehensive exploration of the challenges and solutions within this dynamic field. This section collects contributions that explore the nuanced domain of data analysis within neuroscience, offering insights into innovative approaches and methodologies derived from the intricate fabric of neurophysiological recordings.

Esparza, Sebastián, and M. de la Prida [6] explore the growing interest in the study of the hippocampal code, which focuses on two approaches: 1) the *physiological approach* that examines individual cells' contributions based on genetic, biophysical, and circuit factors; and 2) the *population-dynamic approach* that considers how a large number of neurons represent behavioral variables. The authors suggest that projecting neuronal activity into low-dimensional manifolds can uncover the structure of population representations, but interpreting these manifolds physiologically is challenging. They propose integrating information about behavioral traits, local field potential oscillations, and cell-type specificity into neural manifolds as a strategy to make them more interpretable at the physiological level.

The work by Chiappe [5] highlights the importance of animal movement in understanding the brain's evolution and operation. Precise knowledge of body movement is crucial for functions like motor control, spatial perception, and navigation, which rely on the integration of mechanosensory and visual feedback as well as motorrelated signals. While the circuits responsible for selfmotion estimation and motor-sensory coordination in the central nervous system are still poorly understood, recent advancements have shown that studying *Drosophila melanogaster* (fruit flies) during naturalistic walking behaviors can provide valuable insights into these fundamental problems with implications for all animals.

The article by Ramaswamy [23] explores the growing importance of data-driven computational models in modern neuroscience. These models encompass neurons, synapses, microcircuits, and mesocircuits, aiming to integrate information from various brain organization levels. The article reviews recent advancements in creating data-driven models of mammalian neural networks in cortical and subcortical areas, discussing the challenges and opportunities. It emphasizes the necessity for interdisciplinary collaborations, model validation, and the potential impact on neuroscience research.

The article concludes by highlighting emerging technologies and future directions that promise more comprehensive and predictive data-driven models of brain function and dysfunction.

In their work, Gmaz et al. [8] discuss the evolution of the nervous system's role in enabling navigation and resource pursuit. While newer brain structures brought about increased complexity, they also introduced redundancy. The traditional perspective in movement neuroscience assumes a one-to-one mapping between brain regions and functions. However, recent experimental data challenges this view, suggesting functional redundancy during well-learned and constrained behaviors. This redundancy likely results from bidirectional interactions among various cortical and subcortical structures involved in motor control. The authors argue that these flexible connections allow adaptable interactions across structures depending on behavioral demands. To understand the apparent redundancies in motor control structures, it's essential to observe the system across various actions and behavioral timescales.

McNamee [17] explores the intricate neural microdynamics of cognitive processing within the entorhinal cortex and hippocampus, which are key brain regions for memory, planning, navigation, and imagination. The research reveals complex spatiotemporal patterns in these regions, shedding light on the underlying cognitive computations. The article also proposes a theoretical framework to understand these dynamics better, suggesting that aligning them with models of planning and inference may advance our comprehension of cognitive neural processes.

In summary, the articles published in this issue build bridges between different levels of computational neuroscience, from molecular, circuit, and behavioral levels, and show the wealth of open questions to be addressed in the next few decades.

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