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## Editorial overview: Systems neuroscience

### Michael Long and Rosa Cossart

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For a complete overview see the [Issue](#)

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Michael Long is an associate professor in the Neuroscience Institute at the NYU School of Medicine. He completed his graduate studies with Barry Connors (Brown University) and his postdoctoral work with Michale Fee (MIT). His laboratory studies the neural circuits that underlie skilled movements, often in the service of vocal interactions. To accomplish this, he has taken a comparative approach, examining relevant cellular and network mechanisms in the songbird, the rodent, and the human.

#### Rosa Cossart



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Systems neuroscience classically studies how neuronal circuits dynamically interact at varying spatial and temporal scales to process sensory information, represent the external environment to guide decision making, and execute movements. A recent explosion of techniques for studying neural dynamics has revolutionized this discipline and therefore our understanding of brain function. Indeed, these tools have provided unprecedented observations of neural activity and elegant means of manipulating specific components of these circuits, albeit in a more consolidated number of animal models. Such approaches have enabled systems neuroscientists to go beyond the description of reflexive behaviors or of the first stages of sensory processing, opening the way for the understanding of how cognitive processes such as memory are implemented at the level of large scale interacting circuits to support adaptive behavior.

This volume of *Current Opinion in Neurobiology* provides a snapshot of the state of this field with an emphasis on the contextual modulation of multisensory processing, on memory circuits, or on the development of long-range interacting networks. It also offers an overview of recent methodological advances and new animal models with an emphasis on a meso-circuit level of description.

Perhaps the most rapidly maturing aspect of neuroscience is our ability to measure the activity of large neural ensembles in action. For instance, in the olfactory bulb, [Chong and Rinberg](#) use imaging methods capable of monitoring complex spatiotemporal patterns of activity during the performance of odor-guided behaviors and examine ways in which such activity can be experimentally manipulated or even recapitulated in order to test the importance of such codes. In their review, [Pakan et al.](#) discuss how the recent development of genetic tools and imaging techniques has led to the urgent need to standardize experimental conditions and analysis methods.

Sensory processing represents the most commonly studied aspect of systems neuroscience. Although other sensory modalities, such as vision, may receive more experimental attention, tremendous progress is being made in other sensory systems as well. In his contribution, [Gu](#) explores the primate vestibular network, focusing on a substantial cortical representation that enables the perception of self-motion and spatial orientation. Additionally, [Bokinić et al.](#) examine the circuitry underlying the perception of innocuous thermal stimuli and highlight recent advances that address the functional organization of networks underlying the processing of skin surface temperature.

How “non-sensory” signals (arousal, experience, prediction, attention, social context, etc.) affect the processing of sensory inputs is an important and

Aix-Marseille University, a pioneering Institute in the field of Systems Developmental Neuroscience. After graduating in Mathematics and Physics from the Ecole Centrale Paris, she studied the functional rewiring of GABAergic circuits in epilepsy during her PhD with Drs. Bernard and Ben-Ari. As a postdoctoral fellow with Pr. Yuste at Columbia University, she pioneered the use of calcium imaging to study cortical circuit function. Her lab made seminal contributions to the understanding of how development scaffolds hippocampal circuits. They discovered “hub cells” and more recently “assemblies” forming the functional building blocks of hippocampal function.

timely topic and a recent matter of debate. The issue of “contextual modulation”, when a primary feedforward input interacts with modulatory influences arising from top-down networks is therefore becoming a central focus in systems neuroscience. Pakan *et al.* discuss the impact of these ‘non-sensory’ variables, such as state-dependent and experience-dependent modulation of visual processing, implicating both corticocortical and thalamocortical pathways as well as neuromodulation. Khan and Hofer explore how such information enables bottom-up and top-down influences to be integrated in order to form predictions about the visual world. Batista-Brito *et al.* examine the microcircuitry that enables these contextual influences to be implemented in neocortex and focus on the role of inhibitory interneurons and neuromodulation in both normal and pathological brain processing. Kuchibhotla and Bathellier demonstrate the importance of such contextual use for adding perceptual richness to the auditory cortex and shaping behavioral responses.

Although brain state can influence sensory perception, individual sensory streams (e.g., olfaction) often have a significant impact on ongoing brain function. Choi *et al.* review the processes underlying the integration of sensory information from multiple modalities, focusing on the dynamic modulation of these factors and the importance of this process on perception. Robbe examines the integration of sensory signals with motor information within the striatum and argues that the somatotopic organization may facilitate motor learning. Ben-Tov *et al.* use the archerfish, which can integrate sophisticated visual information to localize and target prey, to examine dynamic sensorimotor processes underlying an ethologically relevant behavior. Knafo and Wyart use advanced optical methods to identify the cell types involved in mechanosensory feedback in the larval zebrafish that are engaged in active locomotion.

Although thalamocortical inputs to sensory structures have been traditionally thought to simply relay afferent information to the neocortex, several lines of evidence suggest that the thalamus may be carrying out a diverse set of functions. For example, Gent and Adamantidis discusses recent findings that implicate the thalamus in the regulation of sleep-wake states, expanding the view that such arousal states are primarily determined by brainstem structures. Antón-Bolaños *et al.* explore the role of extrinsic versus intrinsic factors in the establishment of functional networks during development, with a focus on the early dialogue between thalamic nuclei and sensory cortices, and Colonnese and Phillips examine the changes in inhibitory cell types that may enable the developmental switch from “pre-sensory” early thalamocortical coordinated activity to high resolution sensory processing.

Systems developmental neuroscience, an emerging subdiscipline at the interface between development and systems neuroscience is particularly well-represented by several reviews in this special issue including the two cited above. In that respect, the review by Valero and Menendez de la Prida exemplifies how much development may shape the functional structure of adult memory circuits. Indeed, it reviews recent evidence indicating a segregation between temporal and contextual information flows along the radial axis of the CA1 hippocampal region, an emergent outcome structure of development. This issue includes several additional reviews related to the systems neuroscience of cognition. Piskorowski and Chevalleyre highlight the critical role of CA2 in memory circuits, not only for social behavior but also regarding spatial information. They argue that CA2 may act as a conflict detector, comparing contextual information with internal representation. Mably and Colgin discusses how gamma oscillatory activity is involved in

memory processes, providing a window into the brains interworkings in health and disease and potentially a means for novel therapeutic interventions. The hippocampus and related structures have long been known to play a role in spatial navigation, and [Maimon and Green](#) use the drosophila as a model system to study the computational similarities that exist between insect and mammalian head direction systems to enrich existing models for the circuitry that provides directional information for such behaviors.

Another advantage of modern techniques is the ability to examine the impact of long-range connectivity. A pair of reviews explore the importance of a specific interconnection, linking the prefrontal cortex to the amygdala, for two distinct brain processes. [Yizhar and Klavir](#) examine these interactions in the context of establishing and modifying associations between a cue and an outcome in the service of adaptive and maladaptive learning, while [Rozeske and Herry](#) link the connections between these structures to the rapid and flexible expression of fear behavior.

Movement is the final outcome of nervous system function. [Muscatelli and Bouret](#) review recent literature regarding a highly important innate behavior, namely the suckling reflex that must be initiated immediately after birth and is influenced by hypothalamic circuits that regulate feeding. [Aranha and Vasconcelos](#) examine female innate behaviors in the drosophila, specifically courtship responses and egg-laying decisions. For skilled behaviors, [Yoshida and Isa](#) present comparative results from rodents and primates focusing on the role of the corticomotorneuronal pathway in enabling dexterous hand movements.

Despite the impressive progress in systems neuroscience in recent years, many aspects of brain function remain poorly understood. For instance, although an enormous amount of effort within the field is presently being directed towards simple model organisms, [Bansal et al.](#) tackle the complexity of the human brain by developing personalized models constrained by anatomical and functional data, providing a means for querying the human brain function through ‘virtual experiments’ as well as a potentially powerful new tool for neurosurgical applications. Another potential gap in our knowledge is rooted in the paucity of circuit-oriented studies that focus on social neuroscience. [Brecht et al.](#) address existing literature, highlighting differences in sensory processing based on social context and address sexually dimorphic aspects of nervous system function as early steps towards establishing a mechanistic understanding of the social brain.

Collectively, these reviews reveal how much systems neuroscience is experiencing an exciting period supported by unprecedented technological breakthroughs. It is by essence an interdisciplinary field which is in turn currently giving rise to the emergence of new subfields, such as ‘systems developmental neuroscience’ or ‘systems social neuroscience’. In the close future, systems neuroscientists throughout these various subfields will certainly need to work hand in hand with data and computational neuroscientists to standardize their experiments and analysis and bridge the gap between data and understanding.

### **Conflict of interest statement**

Nothing declared.