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Review

Neuronal circuits and computations: Pattern decorrelation in the olfactory bulb

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ABSTRACT

Neuronal circuits in the olfactory bulb transform odor-evoked activity patterns across the input channels, the olfactory glomeruli, into distributed activity patterns across the output neurons, the mitral cells. One computation associated with this transformation is a decorrelation of activity patterns representing similar odors. Such a decorrelation has various benefits for the classification and storage of information by associative networks in higher brain areas. Experimental results from adult zebrafish show that pattern decorrelation involves a redistribution of activity across the population of mitral cells. These observations imply that pattern decorrelation cannot be explained by a global scaling mechanism but that it depends on interactions between distinct subsets of neurons in the network. This article reviews insights into the network mechanism underlying pattern decorrelation and discusses recent results that link pattern decorrelation in the olfactory bulb to odor discrimination behavior.

1. Computational functions of neuronal circuits and the olfactory system

Higher brain functions are not directly determined by the biophysical properties of individual neurons but emerge from interactions between many neurons in synaptically connected networks. Deciphering such networks is central to understanding the principles of biological computation, the relationship between brains and computers, brain dysfunction in mental disorders, and the very nature of humans and other animals. Neurons are organized in structured networks, or circuits, that are typically defined as circumscribed populations of interconnected neurons. Small circuits such as repetitive columnar elements of the optic lobes in Drosophila may be comprised of <100 neurons [1] while large circuits such as mammalian piriform cortex or cerebellar lobules can contain 10^6 neurons or more [2]. Most neuronal circuits consist of functionally diverse types of neurons and contain prominent feedback loops. The computational potential of such systems is enormous [3] but we are only beginning to understand how this potential is realized in biological circuits. A systematic and somewhat reductionist approach to understand brain functions may thus ask *what* different circuits compute, and *how* these computations are achieved mechanistically as neurons exchange and integrate biophysical signals.

The challenge to understand a neuronal computation obviously depends on the complexity of the computation and the underlying circuit. Some computations can be described based on first-order statistical properties of neuronal connectivity (average connection strength) and based on univariate properties of neuronal activity or simply mean firing rate. These quantities can often be measured using well-established methods and the computations can often be described by tractable mathematical models. One example of such a computation is "normalization", an important elementary operation that scales responses of individual neurons as a function of the mean population activity [4,5]. Other computations, however, depend on higher-order properties of connectivity and on multivariate properties of activity patterns. These diverse and potentially complex computations have not yet been explored exhaustively. Some of these computations are likely to depend on the activity of specific subsets of neurons and on specific connectivity. For example, receptive field properties of neurons in primary visual cortex are thought to be shaped by specific

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connectivity among neurons with similar feature selectivity [6], and storage of arbitrary information in memory networks such as the hippocampus is thought to depend on experience-dependent modifications of synaptic connections between specific subsets of neurons [7]. Analyzing the mechanisms underlying such computations, and even defining the computations themselves, is often hampered by experimental constraints. It is, for example, possible to record activity only from subsets of neurons within a large population. The sample size of population activity measurements may thus be sufficient to determine simple statistical properties of neuronal activity patterns but fail to resolve higher-order features. Detailed descriptions of the connectivity among individual neurons are lacking for most circuits, with few exceptions [1,8–10]. Furthermore, mathematical analyses of networks with higher-order structure can become extremely complex. Understanding neuronal computations depending on higher-order circuit features is therefore a major challenge in neuroscience.

This review focuses on the decorrelation of odor-evoked activity patterns in the OB, a computation that reduces the overlap (Pearson product-moment correlation coefficient) between activity patterns representing different, yet structurally similar, odors. A neuronal activity pattern at time t may be represented by a vector where each element represents the firing rate of one neuron, measured during a small time window around t. Highly overlapping activity patterns are thus represented by vectors that have a high Pearson correlation coefficient, i.e., they project in similar directions within the high-dimensional coding space. Pattern decorrelation reorganizes activity patterns so that the Pearson correlation coefficient of the corresponding activity vectors decreases and their angular separation increases. As a consequence, it becomes easier to find a procedure – a classifier – to distinguish between the activity vectors. Pattern decorrelation is thus useful for pattern classification, a key operation in many higher brain functions such as object recognition, decision making and associative memory. Models of pattern classification in the brain assume that activity patterns are at least partially decorrelated. This assumption is often necessary to achieve good performance, to avoid destructive phenomena such as catastrophic interference, and to enable various other operations [11–17]. However, few studies have directly analyzed pattern decorrelation in the brain, possibly because it has been difficult to measure neuronal activity patterns across large numbers of neurons.

One brain area where pattern decorrelation was observed is the dentate gyrus of the hippocampus [18,19], which is assumed to pre-process activity patterns representing complex, multisensory information for storage and classification in other hippocampal subfields such as CA3 [20,21]. However, the underlying mechanisms are not understood in detail. Another brain area where pattern decorrelation has been studied is the OB, particularly in zebrafish [22–26]. Among the multiple targets of the OB is the piriform cortex, a large paleocortical area with an architecture similar to that of hippocampal area CA3. Like CA3, piriform cortex has been proposed to function as an associative memory system for the storage of information encoded by distributed activity patterns [27–29]. Pattern decorrelation may therefore subserve similar general functions in the OB and in the dentate gyrus although differences in the neuronal architecture of these circuits suggest that the underlying mechanisms are not identical.

The OB is the only olfactory processing center between sensory neurons in the nose and multiple higher telencephalic areas. Olfactory input reaches the OB through an array of discrete input channels, the olfactory glomeruli (Fig. 1), each of which receives convergent input from sensory neurons expressing the same odorant receptor [30]. Individual odorant receptors and glomeruli respond to multiple odorants, and each odorant activates a specific combination of glomeruli [30,31] (Fig. 2A). Odors are therefore

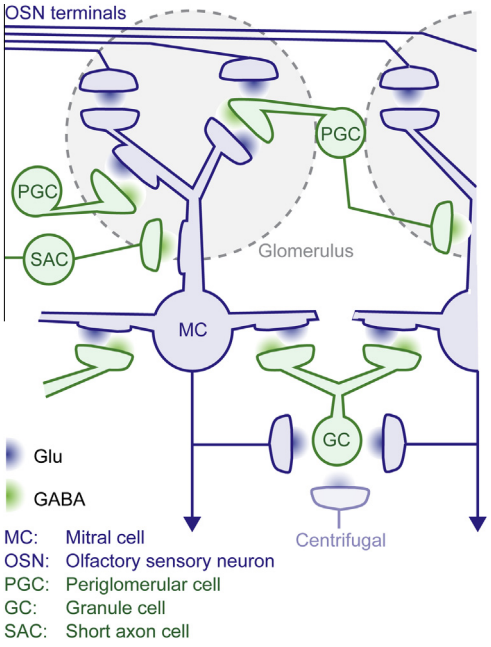

Fig. 1. Schematic illustration of selected cell types and synaptic connections in the OB. Modified from [91].

encoded in a combinatorial fashion and presented to the OB as discrete, usually distributed, glomerular activation patterns. Odorants with similar molecular features activate overlapping combinations of glomeruli, probably as a direct consequence of the molecular mechanisms governing receptor-ligand interactions. Glomerular representations of chemically similar odorants are therefore highly correlated. In order to facilitate stimulus classification, autoassociative memory and other tasks it appears useful to reduce these correlations at an early stage of sensory processing.

Sensory input from the array of glomeruli is processed in the OB by a network of principal neurons, the mitral/tufted cells (MCs), and multiple classes of interneurons including periglomerular cells, short-axon cells and granule cells [32] (Fig. 1). MCs are glutamatergic, receive glutamatergic input from sensory neurons and inhibitory input from interneurons, and convey the output of the OB to multiple higher brain areas including piriform cortex. Individual MCs receive sensory input only from one or a few glomeruli and are not directly coupled to MCs associated with other glomeruli. Periglomerular cells are located in the input (glomerular) layer of the OB and comprise multiple subtypes [33]. They are small neurons that receive input from various sources and provide GABAergic output to MCs. Short-axon cells are also located mainly in superficial layers but often have long processes [34]. They can have inhibitory or depolarizing effects on MCs that are mediated by GABAergic synapses and gap junctions, respectively [35]. Granule cells are located in deep layers and are by far the most numerous cell type in the OB. They are axonless, receive glutamatergic input from dendrites and axon collaterals of MCs, and make GABAergic synapses back onto MCs. Many of the dendro-dendritic connections between MCs and granule cells are reciprocal. The synaptic connectivity among neurons in the OB therefore provides multiple paths for interactions between MCs, even though MCs are not directly connected across glomeruli. These synaptic pathways extend over multiple spatial scales and often have inhibitory effects on MCs. In addition, multiple types of interneurons, but not MCs, receive input from higher brain areas.

MCs respond to odor stimulation with slow modulations of their firing rates (Fig. 2B) and with oscillatory synchronizations

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