

Olfactory cortex as a model for telencephalic processing

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Changes to myriad synapses throughout the brain must be coordinated every time a memory is established, and these synapses must be appropriately reactivated every time it is remembered. Once stored, memories can be recognized (when re-experiencing a learned input) or recalled (e.g., via different input, such as a name evoking memory of a face, or a scene evoking memories of an experience) by many routes. We remember what tables are as well as we remember a specific table, and we recognize objects despite seeing them from quite different angles, different lighting, different settings. Computational simulations of synaptic modifications (e.g., long term potentiation; see related entries in this volume) in distinct brain circuit architectures illustrate how these minute changes can give rise to coherent properties of memory; how analyses of different brain areas yield derivations of disparate memory functions; and how interactions among connected regions give rise to still new operating principles beyond those of their constituents. The principal anatomical designs in mammalian brain are

cortical: planar arrays of neurons, arranged with their cell bodies in sheets and their apical dendrites standing in parallel. This laminar pattern contrasts with that of most reptilian brain structures, in which neurons are grouped in globular clusters (“nuclei”); an exception is the cortically organized reptilian pallium. Phylogenetic origins of the mammalian neocortex (perhaps including transformed non-pallial precursors as well as pallium) are the subject of ongoing controversy (see, e.g., Karten, 1997; Puelles, 2001). The difference is one of function, not just form. With cells arrayed in a plane, the axons providing input to the structure pass through the dendritic field making synaptic contacts randomly and sparsely. This creates a biological version of a three dimensional array or matrix in which the rows correspond to the input axons, the columns are the dendrites, and each matrix entry is a synaptic connection between an axon and dendrite (Figure 1). The neocortex undergoes vast expansion with mammalian evolution, and as the cortex comes to dominate the brain, cortical computation comes to dominate behavior.

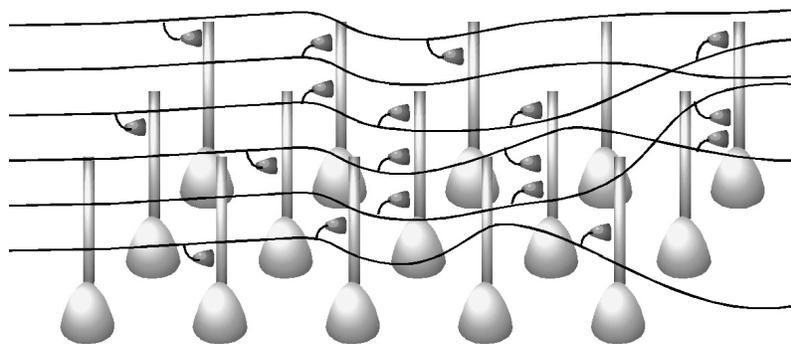


Figure 1. Characteristics of a cortical layer. Axons (horizontal lines) course through the apical dendrites of a layer of neurons making sparse, random synaptic contacts corresponding to entries in a matrix.

The Olfactory Bulb and Paleocortex.

The olfactory paleocortex, one of the oldest relics in mammals of the reptilian pallium, is an apt starting point for evaluation of cortical computation. One reason is its relative simplicity (for instance, it has three primary layers instead of the six layers of the

neocortex). Another is its relative proximity to its input environment. In other sensory systems, inputs typically proceed from a peripheral organ (e.g., cochlea) to one or more lower brain structures (e.g., cochlear nucleus; colliculus), then to a non-cortical (nuclear) structure in the

thalamus (e.g., medial geniculate nucleus), and only then on to the primary cortex for the appropriate sense (e.g., auditory cortex). By comparison, olfactory receptors (activated by chemical odorants drawn in through the nose), project to the olfactory bulb and thence straight to olfactory cortex. (The structure is variously termed olfactory paleocortex, for its phylogenetic age; piriform, pyriform, or prepyriform cortex, for its roughly pear-like shape; or primary olfactory cortex, for its placement as first cortical structure to receive olfactory input relayed from the periphery). Abstract models have been constructed based on four fundamentals of the olfactory system: i) its anatomical structure, ii) its physiological operation during behavior, iii) the characteristics of synaptic change caused by LTP, and iv) the nature of the inputs that arrive naturally at the system during olfactory-related behaviors.

Figure 2 schematically illustrates the anatomical

structure of a typical mammal's olfactory system (adapted from Shepherd, 1991). The figure is oriented such that the animal's nose is on the left, with the axons from the nose comprising the first cranial nerve (Nerve I) making synaptic contact (in the regions termed glomeruli) with the primary excitatory (mitral) cells of the olfactory bulb. Mitral cells are inhibited by granule cells via specialized synapses (see Haberly and Shepherd, this volume), and mitral cell axons (comprising the lateral olfactory tract) project to cortex, where they form synaptic contacts with the apical dendrites of the primary cortical excitatory layer II and III cells. Those cells in turn project both forward, to provide the input to downstream brain structures (such as entorhinal cortex), and backward, providing feedback to the bulb directly and via the anterior olfactory cortex (often termed the anterior olfactory nucleus, despite its laminar rather than nuclear structure).

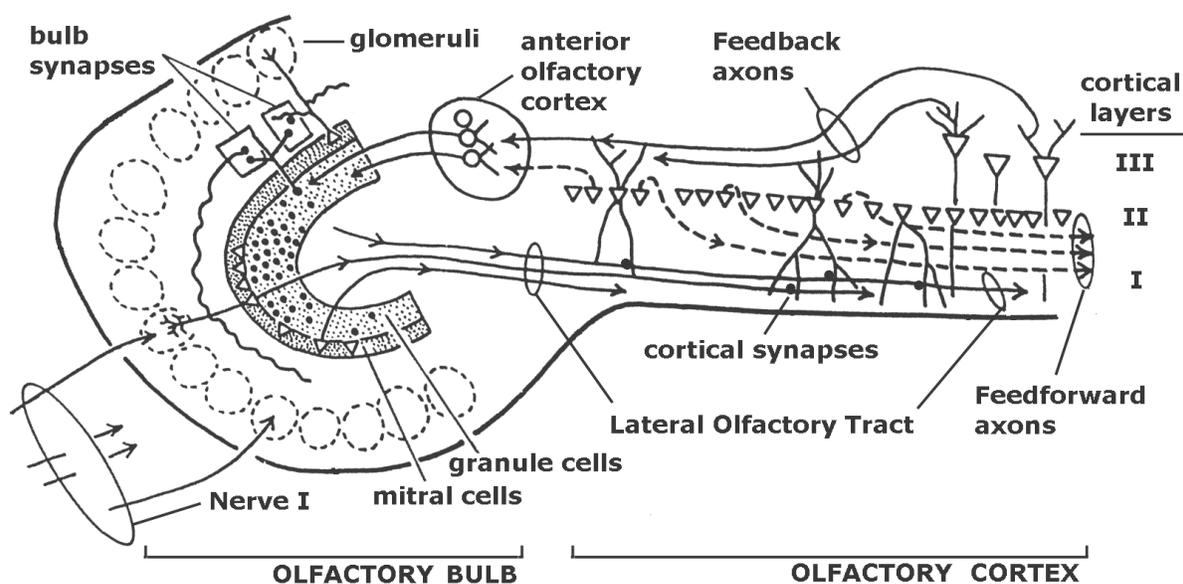


Figure 2. Schematic diagram of mammalian olfactory system anatomy. Input from receptor cells in the nose arrive via the axons comprising the first cranial nerve, making synaptic contact with the dendrites of mitral cells in the olfactory bulb. Mitral cell axons in turn make synaptic contact with the apical dendrites (projecting downward, towards the cortical surface) of primary cells in the olfactory cortex. Cortical cell axons project forward to become input to successive anatomical structures (entorhinal cortex, hippocampus) as well as projecting backwards to become feedback input to the inhibitory cells of the olfactory bulb.

Simple emergent computations from feedforward operation of the bulb-cortex system.

When an animal is actively engaged in olfactory learning behavior, the entire bulb-cortex system, its primary target output structures (entorhinal cortex and hippocampus), and even the overt behavioral sniffing activity of the animal, operate in synchrony,

at a rate of about four to eight cycles per second (Macrides, 1975; Macrides et al., 1982; Vanderwolf, 1992; Wiebe and Staubli, 2001). As the animal repeatedly samples or sniffs the olfactory environment, neurons through the entire "assembly line" of olfactory-hippocampal structures send spikes down their axons, in bursts

occurring approximately every fourth to eighth of a second. Computer simulations of the resulting feedforward neuronal activity in the cortex have shown that LTP-like synaptic change increments cause specific cortical target cells that initially responded to a particular odor, to become increasingly responsive not only to that odor but also to a range of similar odors. Figure 3 uses broad simplifying assumptions to illustrate this straightforward principle. (Models of the olfactory bulb (Anton et al., 1991; 1993), not discussed here, are assumed). In the left hand panel of the diagram, input axons b, c, and d are active (arrows), and are

assumed to be sufficient to elicit firing responses from three target cells (darkened). Synapses whose inputs and targets are co-active (highlighted) will potentiate. After potentiation, the enhanced synapses (enlarged; right panel) confer more voltage change than they did in their unpotentiated state, so fewer active inputs should suffice to elicit a target neuron response. Thus any of the depicted input patterns P, Q, and R may now suffice to activate the same three target cells, whereas none of these inputs would have activated these neurons prior to synaptic potentiation.

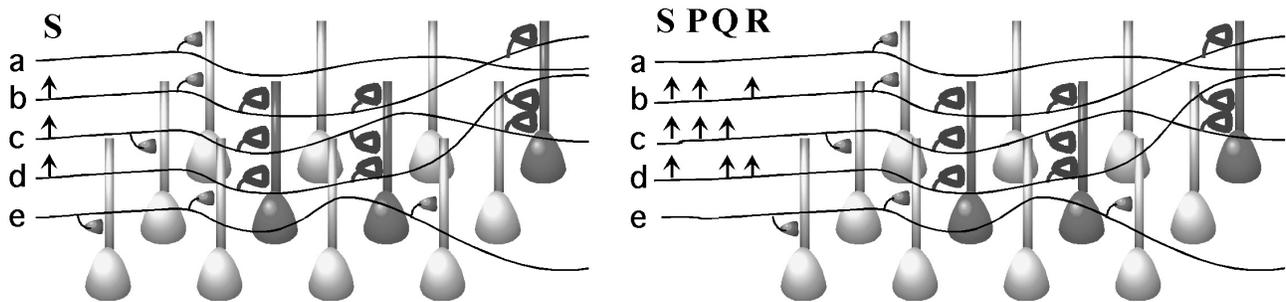


Figure 3. Simple effects of synaptic potentiation on cell response to feedforward inputs. (Left) Before potentiation, if three active synapses suffice to elicit a response from target cells, then the three darkened cells will respond to input S (the combined activation of axons b, c, and d), and their active synapses (highlighted) will potentiate. (Right) After potentiation, strengthened synapses (enlarged) contribute more voltage change to a cell whenever activated, so that the same three neurons may now fire in response to reduced inputs P, Q, and R, which would have been insufficient to elicit responses from these neurons before potentiation.

After potentiation episodes, inputs with highly overlapping activation patterns tend to elude identical neuronal response patterns in the cortex. The result is the mathematical operation of “clustering,” in which sufficiently similar inputs are placed into a single category or cluster. The odor of a rose, a violet, or a lily might, after long-term potentiation, elicit only an undifferentiated response corresponding to “flower scent,” (and different odors elicit only their cluster responses, e.g., meat scent, smoke scent). This can give rise to useful “generalization” properties, informing the organism of the category of an otherwise unfamiliar odor, but somewhat counterintuitively, it prevents the system from making fine distinctions among members of a cluster. These results are almost generic, as many computational frameworks with very different characteristics, including competitive networks (e.g., von der Malsburg, 1973; Grossberg, 1976; Rumelhart and Zipser, 1985; Coultrip et al., 1992); backpropagation (Rumelhart et al., 1986); and ‘dynamical’ or excitatory feedback networks (e.g., Hopfield, 1982) can exhibit similar properties. Complex computations from combined feedforward

and feedback olfactory operation.

Absent from the foregoing analysis is the extensive inhibitory feedback projection from cortical neurons to granule cells in the bulb. This pathway selectively inhibits those bulb inputs that generate cluster responses in cortex, thereby unmasking the remainder of the bulb’s activity. That remainder becomes the subsequent input to the cortex on the next activity cycle, whereupon the same cortical operations are performed. The result is that the second cortical response (one fourth to one eighth of a second later) will consist of a quite distinct set of neurons from the initial response, since most of the input components giving rise to that first response are now inhibited by the feedback from cortex to bulb. Analysis of the second (and ensuing) responses has shown successive sub-clustering of an input: the first cycle of response identifies the odor’s membership in a particular cluster (e.g., floral), the next response (a fraction of a second later) identifies its membership in a particular sub-cluster (rose), then sub-sub-cluster (particular variety of rose), etc. Roughly five “levels” of

sub-clustering occur in the simulation before the inhibitory feedback to the bulb runs its course. That is, the system uses an unexpected type of coding across time, using specific target neurons selectively activated at a series of different time points, to discriminate among inputs.

This iterative subclustering activity turned out to be mathematically characterizable as a novel algorithm for the well-studied statistical task of hierarchical clustering. All such algorithms have differential costs or complexity in terms of time (number of mathematical steps) and space (amount of storage) required per operation performed. Surprisingly, the derived olfactory algorithm exhibited computational costs that compared favorably with those in the (extensive) literature on such methods (Ambros-Ingerson et al., 1990; Kilborn et al., 1996). These

studies represent an instance in which a novel and efficient algorithm for a well-studied computational problem emerged from simulation and analysis of a specific cortical network. The method was readily generalized to modalities other than olfaction. For instance, input patterns corresponding to speech sounds yielded naturally occurring clusters and sub-clusters on successive samples (Figure 4). Elaboration of the algorithm gave rise to families of computational signal-processing methods whose performance on complex signal classification tasks has consistently equaled or outperformed those of competing methods (interested readers are referred to: Kowtha et al., 1994; Coultrip and Granger, 1994; Granger et al., 1997; Benvenuto et al., 2002).

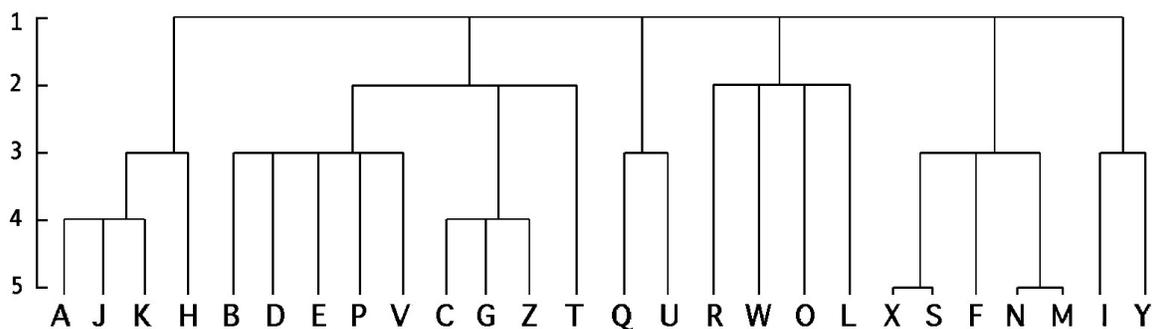


Figure 4. Hierarchy created by computer simulation of successive feedforward and feedback activity in an olfactory bulb-cortex-like structure, operating on spoken sounds rather than on olfactory input. Each sound is a letter of the alphabet. After simulated long-term potentiation, the initial simulated cortical response (1) does not differentiate among any letters, all of which are similar enough to each other (and different enough from other auditory inputs, from traffic noises to bird whistles) to belong to a single cluster. The next cortical response (2) differentiates “A, J, K” sounds from “B, C, T” sounds, and others. Successive responses (3-5) make iteratively finer distinctions. Eventually each letter belongs to its own sub-cluster.

Biological findings and psychological implications.

If the olfactory system operates in this way, it should show striking results behaviorally and electrophysiologically. Behavioral experiments showed that rats recognized novel similar odors as members of a category, yet nonetheless also distinguished and recognized individual category members, providing evidence that animals build unsupervised similarity-based perceptual clusters (Granger et al., 1991). Individual olfactory cortical neurons, measured chronically in behaving animals, were found to respond selectively when tested on very different odors. Moreover, responses were transient, corresponding to the time course of a specific sniff cycle, but not to multiple cycles, again consistent with the computer simulations

(McCollum et al., 1991). Findings arrived at under different experimental conditions have yielded various hypotheses of olfactory function (e.g., Schoenbaum and Eichenbaum, 1995; Haberly, 2001). Studies of unit neuron recordings in behaving animals have only rarely been carried out, and further studies will be needed to discriminate among competing interpretations of the observed data.

The computational and neurobiological findings enable the formulation of hypotheses about psychological function. Operations emerging from cortical circuits presumably constitute elemental psychological acts, and contribute via combination to more complex mental processes,

in ways not yet understood. The evocation of successively finer-grained information about a stimulus via sequential cortical responses suggests a fundamental operation of repetitive perceptual sampling. Visual, auditory and somatosensory cortices have anatomical architectures analogous to the olfactory bulb-cortex template, including excitatory feedforward and inhibitory feedback interactions with thalamic nuclei (see Herkenham, 1986; Jones 1998, for reviews). Perhaps the second glance of a scene educes qualitatively different information from the first glance (even when such “glances” are covert cycles operating within these cortical structures, rather than behavioral eye movements). Humans exhibit synchronized rhythmic firing during learning and during complex sensory processing (Caplan et al., 2001; Sobotka and Ringo, 1997). And human subjects in perceptual and conceptual studies robustly recognize objects first at categorical levels and subsequently at successively subordinate levels (Mervis and Rosch, 1981; Schlaghecken, 1998; Kuhl et al., 2001), suggesting the presence of structured memories that are hierarchically configured and sequentially

traversed during recognition.

Modeling and analysis of other brain areas, including constituents of the hippocampal formation, auditory neocortex, the striatal complex, and thalamo-cortical loops, has yielded a range of additional, starkly different emergent fundamental computations for each structure, as well as novel complex operations from combinations of these (see, e.g., Lynch and Granger, 1992; Gluck and Granger, 1993; Granger et al., 1994; 1997; Myers et al., 1995; Kilborn et al., 1996; Aleksandrovsky et al., 1996; 1997). As in the case of the hierarchical clustering algorithm identified in the olfactory system, new functions derived from other brain regions exhibited computational characteristics comparable to algorithms of known power, often equaling or surpassing the best extant algorithms in terms of cost and efficacy. Moreover, as in the case of the olfactory system, the results suggested new interpretations of both simple and complex psychological operations, intimating the development of more advanced hypotheses of human brain function.

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