A Self-organizing Model of Chemotopic Convergence for Olfactory Coding

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Abstract-**This article presents a self-organizing model of convergence for the early stages of the olfactory pathway. The model generates a chemotopic projection from olfactory receptor neurons onto glomeruli based on receptor affinity distributions. The resulting glomerular images reveal an olfactory code consistent with neurobiology, whereby odor quality is encoded by a unique spatial pattern across glomeruli, and odor concentration is related to the intensity and spread of this pattern. The model is also able to predict a broadening of the intensity tuning range of glomeruli.**

Keywords–**Olfactory coding, chemotopic convergence, receptor affinity distributions, self-organization.**

I. Introduction

The early stages of the olfactory pathway rely on the principles of redundancy and convergence in order to encode chemosensory information. Located in the olfactory epithelium, a large number of olfactory receptor neurons (ORNs) send axons to the olfactory bulb (OB), where they form spherical clusters or glomeruli (GLs) that synapse with mitral cell (MC) dendrites. MCs engage in a number of excitatory/inhibitory circuits mediated by periglomerular and granule cells. MC axons subsequently form the lateral olfactory tract, which projects OB activity primarily to the piriform cortex, but also to other cortical regions for additional processing.

The projection of ORNs onto GLs is characterized by a high degree of convergence that plays a major role in signal amplification, allowing the olfactory system to detect odors at concentrations much lower than the detection thresholds of individual ORNs. In addition, it has been shown that each GL preferentially receives projections from ORNs expressing the same receptor type, thus serving as molecular feature extractors [1]. As a result of this chemotopic projection, different odors induce unique activation patterns across the GL layer, providing the means for separating odor quality from odor intensity, which cannot be accomplished at the ORN level.

This article proposes a self-organizing model of convergence that generates a chemotopic projection from ORNs to GLs. The resulting spatial activation patterns in the GL layer bear a striking similarity to published results from neurobiology. The model decouples odor quality from odor intensity, and also broadens the intensity tuning range (ITR) of GLs as a function of the convergence ratio.

II. Olfactory Receptor Population

The concentration-response curve of individual ORNs is modeled with a sigmoidal activation function. The average instantaneous firing rate R_i^L of ORN_i when exposed to ligand L at concentration $[L]$ can be modeled as $R_i^L = \left[1+\left(K_i^L[L]\right)^{-m}\right]^{-1}$, where K_i^L is the binding affinity between ORN_i and L, and m is the molecular Hill equivalent [2]. Therefore, the affinity can be interpreted as the inverse of the effective concentration EC_{50} at which the ORN shows half-saturation, whereas m determines its ITR or $EC_{10\text{-}90}$, as shown in Fig. 1(a). For consistency with known experimental results [2], a narrow $EC_{10\text{-}90}$ of one log unit is used in this study. In addition, to simulate hypoadditivity we also assume that the response of an ORN to a mixture is equal to the highest response to any of the components.

The probabilistic distribution of affinities $\{K_1^L, K_2^L, \ldots K_N^L\}$ for ligand L across a repertoire of N receptors is modeled with the Receptor Affinity Distribution (RAD), a universal model for ligand-receptor interactions with strong implications for olfactory coding [3]. The RAD model states that the probability of a given ORN type is inversely proportional to its affinity K, following the intuition that *"most of the molecules will show a minimal absorptive affinity... while only an occasional binding site pattern will show a high affinity... for precisely similar reasons that four aces are rarely dealt in a poker hand"* (cf. [3] and refs. therein). In this work, we use the standard parameter settings $B=10$, $S=8$ and $\alpha = 1.4 Kcal \cdot mol^{-1}$, resulting in the RAD distribution shown in Fig. 1(b).

III. Chemotopic Convergence Model

To establish a chemotopic mapping we model the GL layer with a two dimensional lattice of clusters by means of

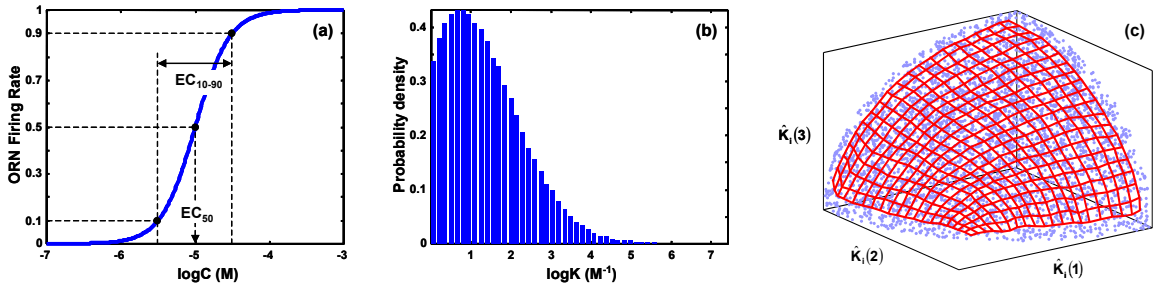

Fig. 1. Concentration-response model for ORNs (a). Receptor Affinity Distribution (b). Glomerular SOM (red) and ORN repertoire (cyan) in normalized log-affinity space for a three-ligand problem (c)

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a self-organizing feature map (SOM) [4]. Assuming an input space with C possible ligands, each ORN can then be uniquely described by a vector of log-affinities $\vec{K}_i = \left[\log K_i^{L_1}, \log K_i^{L_2}, ..., \log K_i^{L_C}\right]$. The selectivity of an ORN is then defined by the direction of $\vec{K}_i$, whereas its sensitivity is related to the magnitude of $\vec{K}_i$. In order to generate a chemotopic projection based on selectivity rather than on sensitivity, ORNs must then converge to GLs according to their normalized log-affinity (NLA) $\hat{\vec{K}}_i = \vec{K}_i / \left\|\vec{K}_i\right\|$, where $\left\|\vec{K}_i\right\| = \sqrt{\sum_{c=1}^{C} \left(\log K_i^{L_c}\right)^2}$. This convergence rule can be implemented by modeling the NLA distribution with an SOM.

To help visualize this mapping, we will first assume a three-ligand problem with a population of 400,000 ORNs. Separate RADs were generated for each ligand across the ORN repertoire, resulting in a matrix of 400,000×3 affinities. An SOM with 20×20 GL nodes, or an average convergence ratio of 1000:1, was trained on the NLA distribution. As shown in Fig. 1(c), the SOM arranges itself to model the ORN population in NLA space, which follows a uniform distribution on a unit-radius spherical quadrant. After training, each ORN is then assigned to the closest SOM node in NLA space, thereby forming a convergence map from which the response of each GL can be computed as $G_j^L = \sum_{i=1}^{N} W_{ij} R_i^L$, where W_{ij}=1 if ORN$_i$ converges to GL_j and zero otherwise.

IV. Encoding of Odor Quality and Odor Intensity

Having described the formation of the chemotopic convergence model, we are ready to analyze the emerging olfactory code at the glomerular level. An olfactory system with 10 ligands, 400,000 ORNs and a 20×20 SOM lattice was simulated according to the procedures outlined in the previous section. After training, the SOM was exposed to concentrations of the ligands ranging from 10^{-7}M to 10^{-3}M, resulting in the 20×20 glomerular images shown in Fig. 2 (bright colors represent high activity). The glomerular response of the different ligands at a fixed concentration of 10^{-3}M is shown in Fig. 2(a). Each ligand elicits a unique glomerular image with higher activity in those GLs that receive projections from ORNs with high affinity to that ligand. As the concentration of the ligand increases, additional ORNs with lower affinity are recruited, resulting in an increased activation level and a larger spread of the ligand-specific loci, as illustrated in Fig. 2(b) for different concentration levels. These results indicate that the glomerular SOM is capable of decoupling odor quality from odor intensity, quality being encoded by the spatial pattern across glomeruli and intensity being captured by the amplitude and spread of this pattern, in agreement with experimental results from neurobiology [5]. An additional emerging property of the proposed convergence model is a broadening of the ITR at the glomerular level, also in agreement with neurobiology [2]. Table 1 provides the average $EC_{10\text{-}90}$ across the GL layer for different convergence ratios, which indicates that the glomerular ITR increases with convergence.

Table 1. Convergence ratio vs. glomerular ITR

ORN:GL	10:1	100:1	1000:1
$EC_{10\text{-}90}$	1.790	1.869	1.870

V. Conclusions and Future Work

We have proposed a mechanism for chemotopic convergence based on biologically plausible concentration-response curves, affinity distributions and self-organization principles. The model produces a realistic odor quality-concentration code at the glomerular layer, including broader intensity tuning ranges than those of ORNs. The study of lateral inhibition for contrast enhancement at the mitral cell level constitutes the next stage of this work.

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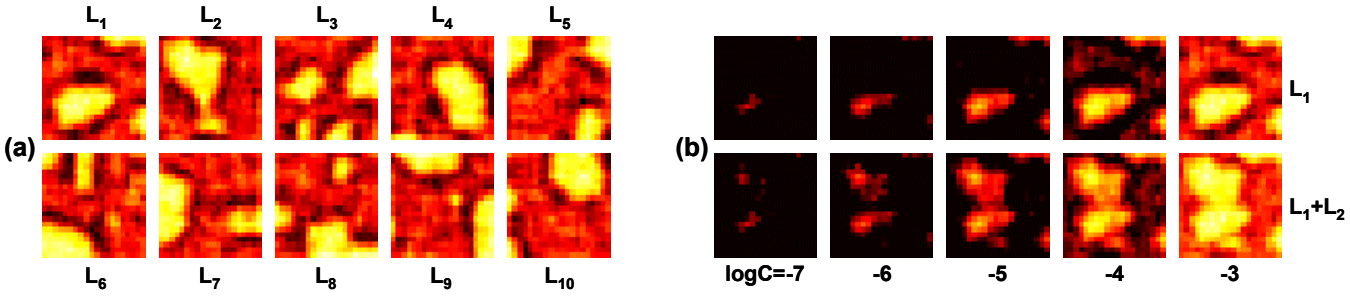

Fig. 2. Glomerular images for ten different ligands at 10^{-3}M (a). Recruitment of glomeruli with increasing concentrations for ligand L_1 and the mixture L_1+L_2 from 10^{-7}M to 10^{-3}M (b).