Optimal Odour Stimulus Reconstruction via Stochastic ORN Gene Selection

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1 Introduction

Olfactory perception is mediated through a population code delivered to the olfactory bulb by *ca.* 10^7 Olfactory Receptor Neurons (ORNs) that possess broadly tuned receptive fields across multiple odour stimuli. In the case of olfaction the stimulus dimensionality is considered to be very high, where most mixtures comprise of hundreds of individual chemical compounds (in our work each is considered to be a dimension). Our last paper showed that in the case of highly dimensional stimuli conducting a Poisson selection process of binary sensitivities for each dimension at each ORN, produces optimal detection performance across a population code (Sánchez-Montañés, M.A., Pearce, T.C., 2002). However, ORNs do not have the degrees of freedom necessary to independently select their tunings to each stimulus dimension in this way. Each ORN within the population selects at most one g-protein coupled receptor gene for expression from a superfamily of approx 320 (in humans), each with a unique specificity (Reed, 2000). Therefore, they must select between fixed sets of sensitivities to the complex stimulus by selecting one gene from the superfamily, which fixes the tuning to the universe of possible chemical stimuli. This process is mediated through a complex chain of gene selection mechanisms which ultimately results in monoallelic gene expression (Serizawa S. et al., 2000).

Early experimental studies using PCR methods clearly demonstrate an homogeneous distribution of ORNs expressing a given receptor gene within each of the four zones of the olfactory epithelium (Chess, A. et al., 1994). These and other more recent experiments have lead to the conclusion that the selection of ORNs is controlled locally and is stochastic within distinct subsets of the receptor superfamily (Serizawa S. et al., 2000; see Kratz et al, 2002 and Mombaerts, P., 2001 for discussion).

How can such a gene selection process be accounted for in terms of system detection performance in the case of olfaction? In other words, what are the consequences of a local stochastic selection of ORN receptor genes for the detection performance of the system? In this study we consider this issue explicitly by creating an artificial gene pool specifying tunings to highly dimensional stimuli. In a set of simulations we calculate the Fisher Information of the system, which limits the theoretical detection performance of the system to stimuli of varying dimensions. This brings us to consider the effects of receptor number, gene selection, diversity, and input dimension on population coded sensory systems.

2 Methods

We consider a sensory system consisting of a neuronal population of arbitrary size. The input to the system is a combination of many single odor components, each considered a dimension within the stimulus space. We model this input as a vector $\vec{s}$ of which component j, that is s_j, is the concentration of the single chemical compound j ($j = 1..N$). For simplicity, we approximate the response of an ORN to $\vec{s}$ as linear with Gaussian noise. This simplification is equivalent to requiring that the firing rate of the neuron is scaled with the stimulus intensity, which is a reasonable assumption for moderate concentrations. The noise assumption is reasonable since receptor neurons have no lateral connections at the level of the epithelium and the noise processes are likely to be local to the neuron and the central limit thereom over many spikes usually results in Gaussian variability in the firing rate.

The number of different receptor genes (the gene pool) that may be expressed in the population is constrained to be less or equal to M. Now if we consider the set of receptor gene tunings to the stimulus within across the gene pool, $\vec{u}_1, ..., \vec{u}_M$, we can express the Fisher information matrix of the system as

$$J = R \sum_{k=1}^{M} p(k) \frac{1}{\sigma^2} \vec{u}_k \vec{u}_k^T, \tag{1}$$

where R is the total number of ORNs in the population; $p(k)$ is the fraction of ORNs expressing receptor gene k, hence setting a receptive field, $\vec{u}_k$ for that ORN; and σ^2 is the noise variance in each receptor neuron.

In this case the optimal quadratic error in the reconstruction of the stimulus, ϵ^2, is equal to the trace of the inverse of J (Cover & Thomas, 1991). We want to know the optimal configuration under different conditions, that is, which are the configurations that minimize ϵ^2. The free parameters to be optimized are then the individual sensitivities $u_{kj}, (k = 1..M, j = 1..N)$ and the fractions $p(k)$. The individual sensitivities are constrained to be in the $-1, 1$ interval representing excitatory and inhibitory ORN responses. Note that we do not impose any particular distribution on the receptive fields.

The optimal error ϵ^2 is calculated as a function of the size of the gene pool, M. We study two different conditions: homogeneous receptive field distribution (the fractions $p(k)$ are constrained to be equal) and unconstrained receptive field distribution (the fractions $p(k)$ are free parameters). The global optimization is done using a standard genetic algorithm.

3 Results

In figure 1 left we can see the optimal error as a function of the pool size, for an arbitrary input dimension (N) equal to 20. The behavior of the homogeneous receptive field solution (solid line) is very similar to the unconstrained solution (circles), being practically equal for a pool size greater than 200. This is shown in detail in figure 2 right, where we plot the relative error of the homogenous receptive field distribution with respect to the unconstrained distribution $\frac{\epsilon^2_{hom} - \epsilon^2_{unc}}{\epsilon^2_{unc}}$. We see that indeed the optimal error of the homogeneous case converges to that of the optimal unconstrained solution.

4 Discussion and Conclusions

We have constrained a homogenous solution, where the proportions of expression of each gene $p(k)$ are identical, since this is compatible with the experimental observations of receptor gene

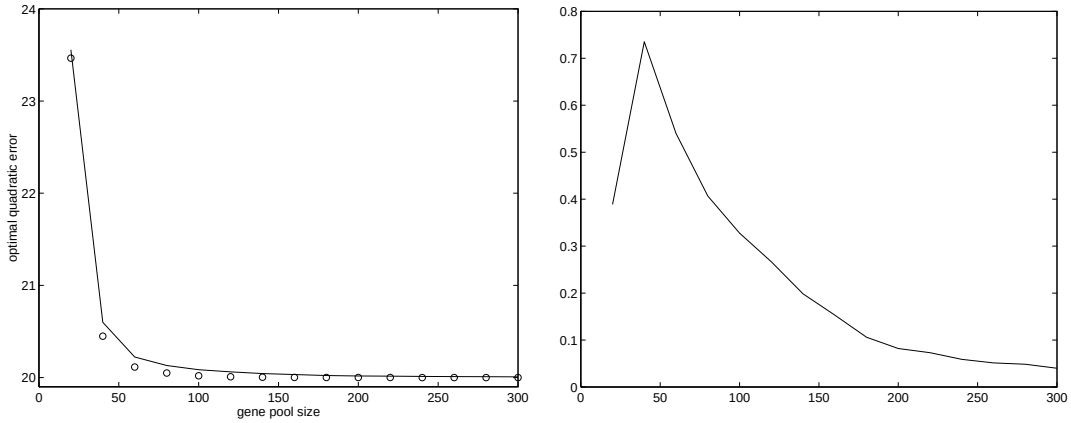

Figure 1: Left – optimal global error in units of receptors noise variance as a function of receptor pool size, M. Solid: homogeneous receptive field distribution. Circles: unconstrained receptive field distribution. Right – relative error between the homogeneous and the unconstrained distributions.

expression within a zone of the olfactory epithelium (Serizawa S. et al., 2000). By constraining the proportions in this way for the homogeneous case solution we are able to quantify the performance of the biological case with respect to the unconstrained optimal solution. It is seen to be very close and converges for biological relevant numbers of gene pool size (*ca.* 320 in humans). The simulations demonstrate that a local stochastic gene selection process (giving rise to homogeneous gene expression across the receptor population) can potentially lead to near optimal detection performance within a population coded sensory system responding to high stimulus dimensions.

Critically a homogeneous constraint allows the gene selection process to be a completely random local process. A key point here, since no overall control is required across the population. This arrangement is seemingly adequate to obtain near optimal detection performance – a surprising result considering the inherent randomness of the process. A local selection process also becomes fundamental when we consider that there is a continual turnover of ORNs over the lifetime of the animal and so gene selection is an ongoing process. Under these circumstances a locally defined selection process would also make sense for maintaining stable detection performance over time. We could test this explicitly by adding fluctuations to the $p(k)$ parameters.

The framework outlined here further permits the quantitative assessment of receptor pool size, receptor noise, stimulus dimension and population size in terms of determining detection performance in these systems which is ongoing.

5 References

Chess, A., Simon, I., Cedar, H., Axel, R., 1994, Allelic activation regulates olfactory receptor gene expression, Cell 78, 823-834.

Cover, T.M., Thomas, J.A., 1991. Elements of Information theory. Wiley, New York.

Kratz E., Dugas J.C., Ngai J., 2002, Odorant receptor gene regulation: Implications from genomic organization, Trends in Genetics 18(1), 29-34.

Mombaerts, P., 2001, How smell develops, Nature Neuroscience. 4, 1192-1198.

Reed, R.R., 2000 Regulating olfactory receptor expression: controlling globally, acting locally, Nature Neuroscience, 3(7), 638-639.

Sánchez-Montañés, M.A., Pearce, T.C., 2002. Why do olfactory neurons have unspecific receptive fields ?. BioSystems, 67 (1-3), 229-238.

Serizawa S., et al., 2000, Mutually exlusive expression of odorant receptor transgenes, Nature Neuroscience 3(7), 687-693.