Selectivity Gain in Olfactory Receptor Neuron at Optimal Odor Concentration

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***Abstract*—Recently, it has been discovered that for the selectivity gain due to fluctuations in the olfactory receptor neuron (ORN) there exists the optimal concentration of odors at which increased selectivity manifested most. We check what could be the gain value at that concentration by modeling ORN as a leaky integrate-and-fire neuron with membrane populated by receptor proteins (*R*) which bind and release odor molecules randomly. Each bound (*R*) opens a depolarizing channel, Eq. (1), below.**

***Keywords*—ORN, selectivity, receptor proteins, fluctuations**

I. Introduction

It is known from sensory biology that selectivity to stimulus of any modality grows up as the response evoked by the stimulus propagates from primary sensory receptors to more central brain areas, see e.g. [1] for vision. Better selectivity of projection neurons (stage 3 in Table I) as compared to ORNs (stage 2 in Table I) was reported in [2]. In parallel, K. Persaud and G. Dodd [3] formulated a general principle for constructing a selective electronic nose from poor selective primary units utilizing morphology similar to that of biological primary olfactory pathways, and proposed the combinatorial code for better odors discrimination.

Normally, the selectivity of receptor proteins (stage 1 in Table I) is considered as indistinguishable from that of corresponding ORN, e.g. [4]. This might not be the case if odors are applied in low concentrations, when fluctuations of receptors number bound with odor become essential. It was shown theoretically for a rudimentary model of ORN, [5], that ORN's selectivity in this case can possibly be higher than the that of R. In this note, we check this possibility for the leaky integrate-and-fire neuronal model with conductivity which fluctuates due to random binding-releasing of odor molecules by R at the optimal (Sec. III-A) odors concentration.

TABLE I. Selectivity build up steps in a biological olfactory system (modified from [5])

	constructive element	measure of response
1.	receptor proteins	fraction of bound receptors
	↓	↓
2.	receptor neurons	mean firing rate
	↓	↓
3.	projection neurons and antennal lobe	mean firing rate and combinatorial code
	↓	↓
4.	olfactory cortex	spatio-temporal activity in higher cortical circuits

II. Methods

A. Model of ORN

As model ORN we use the leaky integrate-and-fire model with fluctuating conductance input, similar to that used for another purpose in [6] (see also [7]):

$$c_M \frac{dV(t)}{dt} = -g_l(V(t) - V_{rest}) - n(t)g_R(V(t) - V_e), \quad (1)$$

where $V(t)$ — is the membrane voltage; V_{rest} — is the resting voltage; c_M — is the total capacity of ORN's membrane; g_l — is the total leakage through it; V_e — is the reversal potential for current through open R; $n(t)$ — is the fluctuating number of open channels at moment t due to odor molecules bound with receptors R; g_R — is the conductance of a single open channel. The total number of R in the ORN is denoted by N. Here we adopt the paradigm: "one bound R → one open channel", which is characteristic for insects, [8]. The model given by (1) is extended with the triggering threshold V_{th}: if the voltage $V(t)$ becomes equal to V_{th} the ORN fires an output spike and appears in its resting state with $V(t) = V_{rest}$.

In the case of $n(t)$ and $V(t)$ not depending of t (no fluctuations are taken into account and all transients are completed) the number N_0 of R bound with odor required to trigger ORN can be found from (1):

$$N_0 = (g_l(V_{th} - V_{rest}))/(g_R(V_e - V_{th})). \quad (2)$$

Our purpose is to consider concentrations at which the mean over time number $\overline{n}$ of bound R is close to N_0 and introduce fluctuations into (1). For this regime of odor perception, selectivity of ORN appears to be considerably better than that of its receptors R.

B. Selectivity of receptor proteins

We describe interaction between receptor protein R and an analyte A by the following association-dissociation reaction:

$$A + R \underset{k_-}{\overset{k_+}{\rightleftharpoons}} AR\,. \quad (3)$$

If another analyte A' is presented to a set of R at the same concentration $[A] = c$ then similar association-dissociation

reaction takes place with different rate constants k'_+, k'_-. From the chemical point of view, the R is able to discriminate between A and A' if corresponding dissociation constants K, K' differ, where

$$K = [A][R]/[AR] \quad \text{(at equilibrium.)} \tag{4}$$

Supposing $K > K'$, chemical selectivity h of R might be expressed in terms of dissociation constants as follows:

$$h = (K - K')/K\,. \tag{5}$$

But, neither R, nor the whole neuron have knowledge of $[A]$ required to determine K. Therefore, expressing selectivity through K at this the very first stage of odor perception seems being not relevant to how a nose operates in the field. Instead of K, similar to [5] we use the probability p that a receptor R is bound with A, that at the same time is the fraction of bound R :

$$p = [AR]/([AR] + [R]). \tag{6}$$

The probability p characterizes the initial response to analyte in the set of R belonging to a single ORN. As selectivity of R we mean the selectivity of this initial response. Namely, if with analyte A' we have $p' < p$ then we define selectivity of R with respect to A, A' as

$$S_R = (p - p')/p\,. \tag{7}$$

C. Selectivity of ORN

Denote as F, F' the mean firing rate of ORN if analytes A, A' are separately applied in the same concentration. As ORN's selectivity S_{ORN} we take the following quotient:

$$S_{ORN} = (F_1 - F_2)\,/\,F_1\,. \tag{8}$$

D. Selectivity gain

We assume here that the concentration c ensures that the mean number of bound receptors pN, $p'N$ is close to the firing threshold N_0. In this case, the instantaneous number $n(t)$ will cross the firing threshold N_0 randomly due to thermal fluctuations both for A and A'. Fluctuations of this type can be observed experimentally, e.g. [9]. The rates F, F' will be heavily dependent on those fluctuations. We expect that the selectivity of ORN in this regime will be better then that of R similarly as it was shown in [5] for a simpler model.

In order to compare selectivity of ORN with that of its receptor proteins we define the selectivity gain g as follows:

$$g = S_{ORN}\,/\,S_R\,. \tag{9}$$

E. Simulation algorithm outline

We solve (1) numerically with the time step $dt = 0.1$ ms. The stochastic process $n_k \equiv n(kdt)$ is described as a Markov chain with transition matrix:

$$p(j \mid i), \quad i = 0, \ldots, N, \quad j = 0, \ldots, N. \tag{10}$$

In our case, $p(j \mid i)$ gives the probability to have $n_{k+1} = j$ bound receptors at the moment $(k+1)dt$, provided that at the moment kdt there were $n_k = i$ bound receptors (for any $k = 0, 1, \ldots$). The transition matrix is calculated in advance based on the concrete values for dt, c, k_+, k_-, N for both analytes. See Figs. 1, 2 for examples of $n(t)$ realization. The simulation of both deterministic electric transients and stochastic process n_k, $k = 1, 2, \ldots$ in (1) is running in parallel: Having n_k and $V(kdt)$ we firstly calculate the $V(kdt + dt)$ and then calculate the next random value n_{k+1} with the help of (10). It is decided that there was a spike between kdt and $(k+1)dt$ if $V(kdt + dt) \geq V_{th}$. In this case, the calculated $V(kdt + dt)$ is replaced with V_{rest}, but n_{k+1} remains untouched.

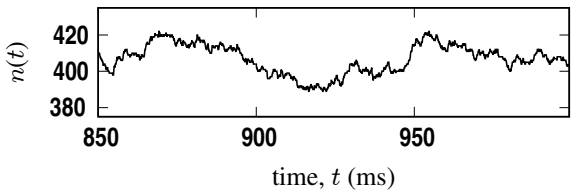

Fig. 1. Realization of stochastic process $n(t)$ near the end of long sniff.

III. Results

The R and A parameters are chosen as follows:

g_R (nS)	k_+ ($\text{ms}^{-1}\,\text{M}^{-1}$)	k_- (ms^{-1})
0.015	209	$7.90{\cdot}10^{-3}$

For the less affine odor A' we assume the same k_+ and bigger releasing rate: $k'_- > k_-$. A concrete value for k'_- is calculated based on the assumed receptor selectivity S_R with the help of (6), (7). (The program gets as input the S_R assumed value, see Tables II, III.) E.g., if assumed $S_R = 0.01$ then $k'_- = 7.98 \cdot 10^{-3}$ ms^{-1} and smaller for smaller S_R.

Electric parameters used in (1) are as follows:

c_M (pF)	g_l (nS)	V_{rest} (mV)	V_{th} (mV)	V_e (mV)
4.26	0.213	-80	-54	-53

Now, (2) gives $N_0 = 369$. For the total number of receptors we choose $N = 2556000$. These parameters are chosen based mainly on the paper [10]. As regards V_e, experimental data was not available. The only thing which is certain is that $V_e > V_{th}$, otherwise spiking due to odor would be impossible.

A. Optimal concentration

For a more rudimentary model considered in [5] it was found in [11] that the selectivity gain due to fluctuations is

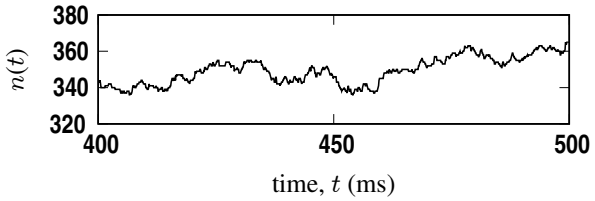

Fig. 2. Realization of stochastic process $n(t)$ near the end of short sniff.

TABLE II. SELECTIVITY GAIN FOR LONG SNIFFS

input:	S_R	0.1	0.01	0.001	10^{-4}	10^{-5}
output:	S_{ORN}	0.96	0.18	0.024	0.007	0.005
output:	g	9.6	18	23.5	72	538

better pronounced if concentration of any odor is taken in the vicinity of c_0, where

$$c_0 = K(N_0 - 1)/(N - N_0). \tag{11}$$

In the model of [5], achieving the value N_0 by $n(t)$ results in immediate firing. This is not the case for the model (1), (2), above, due to the relaxation processes in the membrane. But not having another estimate for c_0, we take the one given by (11) with N_0 given by (2), which for above given parameters and $K = k_-/k_+$ is $c_0 = 5.44 \cdot 10^{-09}$ M. We choose $c = c_0$ for all numeric simulations.

B. Long sniff paradigm

The ORN starts at its resting state with no bound R. The number $n(t)$ relaxes from zero to its mean number with relaxation time $\tau = 127$ ms, Fig. 1. The sniff / run duration is 1 sec and 1000 runs have been performed without resetting the random numbers generator (the `knuthran2002` generator from GNU Scientific Library, [12]; three different seeds were used). This is equivalent to have a single sniff with 1000 ORNs converging onto a single glomerulus. The obtained mean firing rate per neuron in a single sniff is 55 Hz for A and 45 Hz for A' if $S_R = 0.01$ was chosen. The selectivity gain depends on the chosen S_R as shown in the Table II.

C. Short sniff paradigm

Here, sniff duration is 500 ms, and 5000 sniffs was performed. This is equivalent to 5000 identical ORNs converging onto a single glomerulus and performing a single sniff 500 ms long. One example of $n(t)$ relaxing to its mean value is given in the Fig. 2. The results obtained are shown in the Table III.

IV. CONCLUSIONS AND DISCUSSION

In this note, we used numerical simulation in order to compare selectivity of ORN with that of its receptor proteins (R). As the neuronal model we use the leaky integrate-and-fire one with fluctuating conductivity due to random nature of odor binding-releasing by receptors. The possible selectivity gain, see Tables II, III, appears to be large provided that odors are applied in the optimal concentration (11) and R has a poor selectivity. The limitation to have the fixed concentration can be alleviated in ORN by known biophysical mechanisms able to change effective concentration, [13], and the threshold N_0, [14]. In artificial bio-inspired sensors, [15], there should be wider technical possibilities to ensure that odors are sensed by ORNs in the optimal for selectivity gain concentration.

TABLE III. SELECTIVITY GAIN FOR SHORT SNIFFS

input:	S_R	0.1	0.01	0.001	10^{-4}	10^{-5}
output:	S_{ORN}	0.97	0.23	0.042	0.021	0.019
output:	g	9.7	23	41.7	208	1867

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