Application of Statistical Thermodynamics to the Olfaction Mechanism

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Abstract

The application of the grand canonical ensemble in statistical thermodynamics to the stimulus adsorption on the olfactory receptor sites, assuming some simplifying hypotheses, leads us to an expression of the olfactory response $\mathfrak{R}$, which is a function of various physico-chemical parameters involved in the olfaction mechanism, e.g. the stimulus concentration, the saturated vapor pressure, the power law exponent and the partition coefficient. This expression of $\mathfrak{R}$ is in agreement with the olfactory response of the Hill model, but is more explicit. Stevens' law and the olfactory threshold expression are easily deduced from $\mathfrak{R}$. The expression of the threshold we established from $\mathfrak{R}$ enabled us to explain some empirical relations in the literature between the parameters quoted above. The use of the grand canonical ensemble with the chemical potential notion gave us an interpretation of Stevens' law and a better understanding of the role of some parameters involved in the olfaction mechanism, such as saturated vapor pressure and power law exponent. **Chem. Senses 22: 67–75, 1997.**

Introduction

A number of investigations in olfaction consist in looking for significant correlations between an olfactory parameter, e.g. the odor intensity, the odor quality or the olfactory threshold, and one or many physico-chemical parameters, e.g. the partition coefficient in octanol–water (Greenberg, 1979; Wolkowski *et al.*, 1977), the molecular volume (Wright, 1982), the saturated vapor pressure (Patte *et al.*, 1989) and the molecular section (Davies, 1971). These correlations are often empirical (Patte *et al.*, 1989; Laffort and Patte, 1987).

A global formulation of the dynamic olfactory response over a wide range of stimulus concentrations was proposed successively by Beidler (1954), Tateda (1967), Laffort (1977) and Patte *et al.*, (1989). Molecular kinetics was introduced in a semi-empirical model by Wright (1978), who tried to deduce directly the power law of the olfactory response. The olfactory threshold has often been independently formulated from the olfactory dynamic response problem. A mathematical model was proposed by Davies (1971), though this was based on the puncturing theory. Empirical models were also proposed by Randebrock (1971) and by Laffort and co-workers (Laffort *et al.*, 1974; Patte and Laffort, 1989; Laffort, 1994). Some statements and questions have emerged from these models and investigations, such as: (i) the lower the power law exponent, the better the olfactory power (p_{ol}) (Laffort, 1974, 1994); (ii) the models of Beidler, Tateda and Laffort have not yet been validated (Laffort, 1994); (iii) the saturated vapor pressure is very important to the olfactory dose–response curves in insects (Patte *et al.*, 1989; Laffort, 1994); (iv) what is the physical origin of the power law and the meaning of its exponent *n* (Laffort, 1977)?

The purpose of the present work is to establish an olfactory response expression that is based on a statistical thermodynamics model, using a minimum number of physico-chemical and physiological parameters. This expression will allow us to deduce some known results and to answer some of the above questions.

Theoretical model

Different stages of the stimulus

The different stages which the odorous stimulus passes through can be reduced to the two following equilibriums:

$$S_g \underset{(1)}{\overset{K_d}{\rightleftharpoons}} S_d \underset{(2)}{\overset{K_a}{\rightleftharpoons}} S_a$$

S_g, S_d, S_a represent respectively the stimulus molecule at a gaseous state in air, at a dissolved state in the mucus and at an adsorbed state on the receptor sites. The corresponding concentrations in the three states are denoted N_g, N_d and N_a. The equilibrium constant K_d is such that: $K_d = 1/K_p$, where K_p is the partition coefficient in the absence of interaction between the stimulus and the mucus, otherwise K_d contains in addition a basicity or acidity or ionization coefficient. To simplify the model we will consider only the case where the interaction is very weak. K_a is the equilibrum constant of the stimulus adsorption on the olfactory receptor sites from the dissolved state. We note $K = K_d.K_a$.

To be in agreement with Stevens' law, Tateda has written the adsorption equilibrium (2) in the following form (Tateta, 1967; Laffort, 1994):

$$nS + \mathcal{R} \overset{K}{\rightleftharpoons} S_n\mathcal{R} \tag{3}$$

$\mathcal{R}$ is the receptor site molecule, *n* is the power law exponent of the olfactory response as a function of the stimulus concentration in air N_g.

By a classical treatment (Tateda, 1967; Laffort, 1994), the expression of the adsorption rate N_a/N_M was given by:

$$\frac{N_a}{N_M} = \frac{1}{1 + \frac{1}{KN_g^n}} \tag{4}$$

where N_M is the number of olfactory receptor sites per unit surface and N_a is the number of adsorbed stimulus molecules per unit surface.

Assumed hypotheses

To treat the adsorption problem with statistical thermodynamics we make the following assumptions:

(i) The equilibrums (1) and (2) are reached in each experimental measure of the olfactory response intensity.

(ii) K_d is constant in the used concentration range at the equilibrium temperature.

$$N_g = K_p N_d = N_d/K_d$$

(iii) The stimulus concentration is sufficiently weak (Laffort, 1994) to neglect the self and mutual interaction of stimulus molecules with mucus. This allows us to treat the stimulus molecules in solution as an ideal gas, according to the Van't Hoff law for a diluted solution (Diu *et al.*, 1989a) and to treat the mucus as an ideal solution. The problem is then reduced to an ideal gas adsorption on N_M receptor sites.

(iv) In the equilibrium (3), *n* is generally lower than 1 in psychophysics. If we take $n' = 1/n$, then $n' > 1$ and equilibrium (3) can be written as:

$$S + n'\mathcal{R} \overset{K}{\rightleftharpoons} \mathcal{R}_{n'}S \tag{3'}$$

We can see that *n'* is the number of receptor sites which are occupied by one stimulus molecule. We will consider then that *n'* is the anchorage number of one molecule of the odorous stimulus. This is in agreement with expression (4) when, written in the following form:

$$K^{n'} N_g = \left(\frac{\frac{N_a}{N_M}}{1 - \frac{N_a}{N_M}} \right)^{n'}$$

it becomes identical to the known expression (Howard and Mc Connell, 1967): $kC = [\theta/(1 - \theta)]^{\nu}$. This latter equation was experimentally established in the case of polymer adsorption and we identify *n'* with ν, which is known to be the average number of segments per polymer chain that are anchored to the surface.

(v) Although many kinds of receptor sites exist (Laffort, 1977, 1994; Wright, 1978), in a first approach we will consider only one kind of receptor, as was done in previous models (Davies, 1971; Laffort, 1977; Wright, 1978). This does not imply that n is near 1, as was mentioned by Laffort (1977). On the contrary n' ($n' = 1/n$) can be different from 1, since it is an anchorage number of the stimulus molecule on receptor sites. For a given adsorption n' is normally a whole number (Randebrock, 1971). However, the stimulus molecule can be adsorbed with many different configurations, depending on the exposed face geometry, so n' is an average and does not need to be a whole number.

(vi) An anchorage of the stimulus molecule on an adsorbing site is supposed to have only one adsorption energy level ($-\varepsilon$). The free enthalpy of gaseous stimulus adsorption ΔE_a is then:

$$\Delta E_a = N_0 n'\varepsilon \quad \text{where } N_0 \text{ is Avogadro's number}$$

This can be written as:

$$\Delta E_a = \Delta E^v + \Delta E^a$$

where ΔE^v is the free enthalpy of vaporization of pure stimulus, which approaches the free enthalpy of dissolution in the case of an ideal solution (hypothesis iii), ΔE^a is the free enthalpy of stimulus adsorption from the dissolved state.

(vii) Finally, we assume the non-impoverishment of the stimulus into the mucus at every equilibrium state. This suggests we can use the grand canonical ensemble in the study of this adsorption mechanism.

Statistical treatment

Combining the Langmuir model with that of molecular dissociation (Nagai and Hirashima 1985; Diu *et al.*, 1989b), the grand canonical partition function of one receptor site can be expressed as:

$$z = \sum_{N_i} e^{-\beta(-\varepsilon-\mu)N_i}$$

where μ is the chemical potential of one site.

Although a stimulus molecule could have many anchorages, a given receptor site cannot have more than one anchorage. So N_i is either 0 or 1.

We obtain: $z = 1 + e^{\beta(\varepsilon+\mu)}$, where $\beta = 1/kT$, and T is the human or animal body temperature. The grand partition function of N_M sites is then: $Z_{gc} = z^{N_M}$ and the average number of occupied sites is given by (Diu *et al.*, 1989b):

$$N_a = kT\frac{\partial}{\partial\mu}\log Z_{gc} = \frac{N_M}{1+\left(e^{\beta\varepsilon}\cdot e^{\beta\mu}\right)^{-1}} \qquad (5)$$

On the other hand, from the equilibrium (3) we may express the conservation of stimulus quantity by: $N_d + N_a/n'$ = constant. At equilibrium the Helmoltz function F is such that:

$$\frac{dF}{dN_d} = 0 = \frac{\partial F}{\partial N_d} + \frac{\partial F}{\partial N_a}\frac{\partial N_a}{\partial N_d} = \mu_d + \mu(-n')$$

We then obtain: $\mu_d = n'\mu = \mu/n$, which is equivalent to the law of mass action.

In the case of non-dissociation of the stimulus molecule in equilibrium (2) we have $\mu_g = \mu_d$, where μ_g and μ_d are respectively the partial chemical potential in gaseous and dissolved states.

If we note ε_m the adsorption energy of a whole stimulus molecule, then we have:

$$\varepsilon_m = n'\varepsilon = \varepsilon/n \quad \text{and so} \quad \varepsilon = n\varepsilon_m$$

The number of occupied sites is:

$$N_a = \frac{N_M}{1+\left(e^{\beta\varepsilon_m}e^{\beta\mu_g}\right)^{-n}}$$

The partial chemical potential μ_g of the stimulus assumed to be an ideal gas is given by:

$$e^{\beta\mu_g} = \frac{N}{Z} = \frac{\frac{N}{V}}{\frac{Z}{V}} = \frac{N_g}{Z_g}$$

where Z_g is the stimulus molecule partition function per unit volume.

In general, the stimulus molecule is polyatomic and so Z_g is given by: $Z_g = Z_{gtr} \cdot Z_{gi}$. The first term Z_{gtr} corresponds to the translation partition function:

$$Z_{gtr} = \sum_{j=0}^{\infty} e^{-\beta Ej}$$

Taking the fundamental state in the gas as the origin of energy levels, we get:

$$Z_{gtr} = \left(2\pi \frac{mkT}{h^2}\right)^{3/2}$$

where m is the stimulus molecule mass.

From the Rankine formula for the saturated vapor pressure (SVP) of an ideal gas, expressed in statistical thermodynamics (Couture *et al.*, 1989), we obtain:

$$Z_{\mathrm{gtr}} = \beta\left[\left(2\pi mkT/h^2\right)^{3/2} \cdot kT\mathrm{e}^{-\Delta E^{\prime}/RT}\right]\mathrm{e}^{+\Delta E^{\prime}/RT} = \beta \cdot \mathrm{SVP} \cdot \mathrm{e}^{+\Delta E^{\prime}/RT}$$

where R is the universal ideal gas.

The second term Z_{gi} contains all the internal degrees of freedom of the stimulus molecule. Because electronic and rotational energy levels are not excited in the mucus solution, they do not contribute to Z_{gi}. As a first approach, we also assume the abscence of vibrational contribution. Thus we take $Z_{\mathrm{gi}} = 1$ and get:

$$N_a = \frac{N_{\mathrm{M}}}{1 + \left(\mathrm{e}^{\beta\varepsilon_m} \dfrac{N_{\mathrm{g}}}{\left(2\pi mkT/h^2\right)^{3/2}}\right)^{-n}} = \frac{N_{\mathrm{M}}}{1 + \left(\dfrac{\beta \cdot \mathrm{SVP} \cdot \mathrm{e}^{-\Delta E^{\bullet}/RT}}{N_{\mathrm{g}}}\right)^{n}}$$

which may be written in the following form:

$$N_{\mathrm{a}} = \frac{N_{\mathrm{M}}}{1 + \left(\dfrac{N_{\mathrm{g}1/2}}{N_{\mathrm{g}}}\right)^{n}}$$

where

$$N_{\mathrm{g}1/2} = \beta \cdot \mathrm{SVP} \cdot \mathrm{e}^{-\Delta E^{\bullet}/RT}$$

is the gaseous stimulus concentration in air, for which half of the receptor sites are occupied ($N_{\mathrm{a}} = N_{\mathrm{M}}/2$).

Finally we assume that the olfactory response $\mathfrak{R}$ is proportional to the number of occupied sites N_{a} and not to the number of adsorbed molecules (N_{a}/n'):

$$\mathfrak{R} = \alpha N_a = \frac{\alpha N_M}{1 + \left(\dfrac{N_{\mathrm{g}1/2}}{N_{\mathrm{g}}}\right)^{n}}$$

The proportionality coefficient α included in $\mathfrak{R}$ incorporates transduction and other effects such as an eventual porosity of the adsorbing surface. This coefficient is denoted h by Wright (1978).

Consequences and interpretations

Consequences

Olfactory response form

First we note that the expression of $\mathfrak{R}$ is in agreement with the Hill model contained in the expression (4), which was established by a classical treatment (Tateda, 1967; Laffort, 1994).

In addition we obtain the explicit expression of the equilibrium constant K of the stimulus adsorption:

$$K = \left[\left(2\pi \frac{mkT}{h^2}\right)^{+3/2} e^{-\beta\varepsilon_m}\right]^{-n} = \left[\beta \cdot \mathrm{SVP} \cdot \mathrm{e}^{-\Delta E^{\bullet}/RT}\right]^{-n}$$

This analytical expression of K cannot be derived from previous models (Beidler, 1954; Tateda, 1967; Laffort, 1978; Wright, 1978).

Different behaviours

(i) Low concentrations: When $N_{\mathrm{g}} << N_{\mathrm{g}1/2}$, the olfactory response $\mathfrak{R}$ takes the Stevens' law form:

$$\mathfrak{R} \approx \left[\frac{\alpha N_{\mathrm{M}}}{\left(N_{\mathrm{g}1/2}\right)^{n}}\right]\left(N_{\mathrm{g}}\right)^{n} \quad \text{or} \quad \frac{\mathfrak{R}}{\alpha N_{\mathrm{M}}} = \left(\frac{N_{\mathrm{g}}}{N_{\mathrm{g}1/2}}\right)^{n}$$

which is written in the literature (Laffort, 1994) as: $\mathfrak{R}/\mathfrak{R}_0 = (C/C_0)^n$.

(ii) High concentrations: When $N_{\mathrm{g}} >> N_{\mathrm{g}1/2}$, the olfactory response curve $\mathfrak{R}$ takes a hyperbolic form (Patte *et al.*, 1989; Laffort, 1994):

$$\mathfrak{R} \approx \alpha N_M \left(1 - \left(\frac{N_{\mathrm{g}1/2}}{N_g}\right)^{n}\right) \quad \text{hyperbolic law}$$

The hyperbolic asymptote, representing the case when all sites are occupied (the saturation response), is $\mathfrak{R}_{\max} = \alpha N_{\mathrm{M}}$.

General behaviour

The olfactory response curve $\mathfrak{R} = \mathfrak{R}(N_{\mathrm{g}})$ depends on the three parameters N_{M}, $N_{\mathrm{g}1/2}$ and n. The first parameter N_{M} controls the odour strength at saturation. The higher N_{M}, the more intense the saturation odour. The second parameter $N_{\mathrm{g}1/2}$ (or SVP) controls the odour strength over the whole range of stimulus concentrations. For a given concentration N_{g}, the greater $N_{\mathrm{g}1/2}$ (or SVP), the weaker the

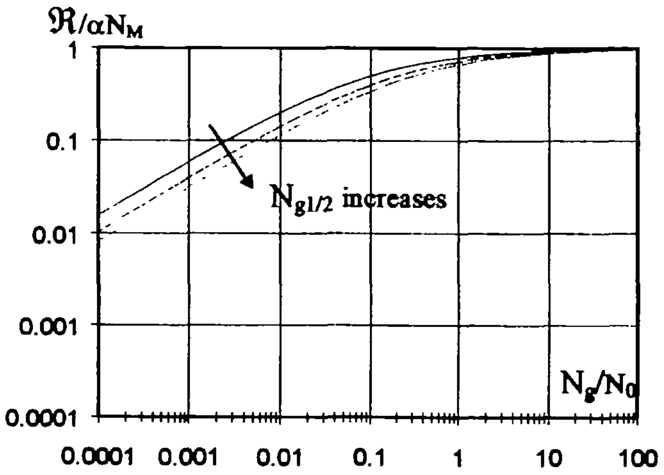

Figure 1 Olfactory response curve $\Re$ versus stimulus concentration N_g in air for different values of the parameter $N_{g1/2}$ (0.1, 0.2, 0.3) in log-log coordinates.

olfactory response $\Re$, all things (n and N_M) being equal (see Figure 1).

Finally n or n' controls the strength of the odour but not in the same way as $N_{g1/2}$. The lower n, the stronger the odour for $N_g < N_{g1/2}$ and the weaker the odour for $N_g > N_{g1/2}$ (see Figure 2).

Olfactory threshold

In this section we are going to derive the olfactory threshold from the dynamic response $\Re$. Because the olfactory signal is controlled by an action potential, the threshold is set by this action potential. We may consider that the olfactory signal becomes detectable only when the occupied sites number N_a exceeds a given number N_{at}. Therefore the concentration of gaseous stimulus must exceed the threshold N_{gt} related to N_{at} by:

$$N_{at} = \frac{N_M}{1+\left(\frac{N_{g1/2}}{N_{gt}}\right)^n}$$

Then we get:

$$N_{gt} = \frac{N_{g1/2}}{\left(\frac{N_M}{N_{at}} - 1\right)^{\frac{1}{n}}}$$

Since

$$N_{gt}/N_{g1/2} << 1, \text{ we must have } N_M/N_{at} >> 1 \qquad (6)$$

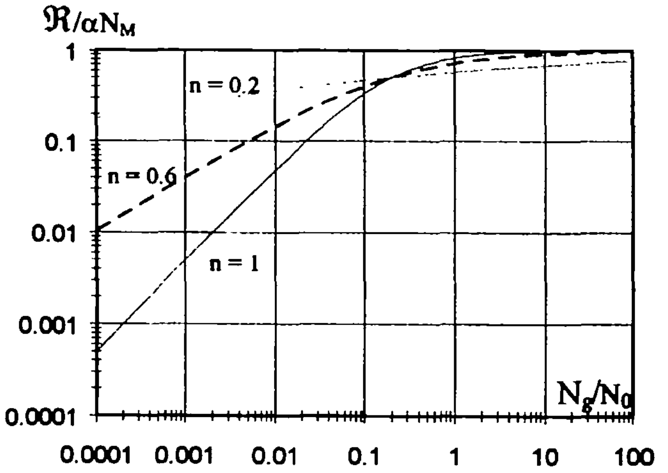

Figure 2 Olfactory response curve $\Re$ versus stimulus concentration N_g in air for different values of the exponent n (0.2, 0.6, 1) in log-log coordinates.

We thus obtain:

$$N_{gt} \# N_{g1/2}\left(\frac{N_{at}}{N_M}\right)^{\frac{1}{n}}$$

Finally, replacing $N_{g1/2}$ by its expression we get:

$$\log N_{gt} = \log \mathrm{SVP} + \frac{\log(N_{at}/N_M)}{n} - \frac{\Delta E^a}{RT} + \log \beta \qquad (7)$$

It is clear that expression (7) of the threshold we obtained is more general than the following relation:

$$\log C_0 = \log SVP + \frac{\log V_0}{n} - 2.33 \qquad (8)$$

This relation was empirically obtained from electro-antennographical responses in the honey bee (Patte *et al.*, 1989; Laffort, 1994), where C_0 corresponds to the threshold, noted N_{gt} in our work. In this relation (8), the authors did not take into account the adsorption energy $\varepsilon^a{}_m$ or ΔE^a which should improve the correlation between calculated and experimental values of the threshold. Note that in our derivation we used Naperian logarithms in place of decimal logarithms. This does not alter the correlation.

Physical interpretations

The adsorption treatment by statistical thermodynamics will clarify the role of some parameters in the expression of $\Re$, and will give us interpretations of some empirical relations which should help to improve our understanding of the olfactory process.

Physical origin of the power law

The two equilibriums (1) and (2) of the stimulus dissolution and adsorption in the olfactory mechanism are controlled by the partial chemical potential. Pressure and temperature are constant. The partial chemical potential of the gaseous stimulus μ_g is imposed by N_g according to: $\mu_g = kT\log(N_g/Z_g)$. In the beginning of the stimulus dissolution into the mucus, the stimulus partial chemical potential μ_g is different from μ_d. The entry of gaseous stimulus molecules into the mucus raises μ_d to the level of μ_g in the absence of a stimulating molecular dissociation. Then the change of the stimulus molecules from the dissolved to adsobed state raises μ to the level of $n\mu_d$, which depends on the anchorage number.

General behaviour. For an equilibrium concentration the occupation number of olfactory sites is given by equation (5). This equation represents the population rate of the single energy level ($-\varepsilon$), which is considered to be N_M times degenerated. This equation (5) has the same expression as the Fermi–Dirac distribution, where $\mu = n\mu_g$ corresponds to the 'Fermi level'. The olfactory response curve, which is the adsorption isotherm, behaves like the Fermi-Dirac distribution. Usually the Fermi–Dirac distribution is plotted as a function of energy level (here assumed to be fixed for a given stimulus). In olfaction, this distribution (response curve) is often plotted in semi-log coordinates (sigmoid curve) as a function of chemical potential, which is indeed proportional to log N_g since $\mu = n\mu_g = nkT\log(N_g/Z_g)$.

Local behaviour: Stevens' law. For sufficiently low concentrations ($N_g << N_{g1/2}$) μ_g or μ is very negative: $\mu << (-\varepsilon)$.

In this case, the Fermi–Dirac distribution in equation (5) tends towards the Maxwell–Boltzmann distribution:

$$N_a \# N_M e^{-\beta(-\varepsilon)} e^{\beta\mu} = N_M e^{\beta\varepsilon} e^{\beta n\mu_g}$$

Replacing μ_g with its expression we get:

$$\begin{aligned} N_a \# N_M e^{-\beta(-\varepsilon)} \left(\frac{N_g}{Z_g}\right)^n &= N_M \frac{e^{\beta\varepsilon}}{Z_g^n} \left(N_g\right)^n \\ &= \left[N_M e^{\beta\varepsilon} / (2\pi mkT)^{3n/2}\right] N_g^n \sim \left(N_g\right)^n \end{aligned}$$

which is precisely Stevens' law.

From this analysis, we can conclude that Stevens' law results from the following three facts: the partial chemical potential equilibrium of stimulus, the multiple anchorage of the stimulus molecule, and the weakness of the concentration or the greatness of the negative chemical potential (Maxwell–Boltzmann distribution).

Effect of anchorage number (or exponent n)

In the threshold expression, the term that depends on anchorage number is:

$$\frac{\log(N_{at} / N_M)}{n} = n' \log \frac{N_{at}}{N_M} = -n' \left| \log \frac{N_M}{N_{at}} \right|$$

According to (6), this term is always negative and corresponds to (log V_0)/n in equation (8). It implies that for low values of the exponent n, the threshold is low. This behaviour, which has not been explained before (Laffort, 1994), was called 'line convergence' by Laffort (1974, 1994). Before giving an interpretation to this behaviour, we define the sensitivity $\mathcal{S}$ of the olfactory organ by:

$$\mathcal{S}\left(N_g\right) = \frac{d\Re}{dN_g}$$

This sensitivity expresses the olfactory response variation per unit stimulus concentration variation, namely the response curve slope. We see that $\mathcal{S}$ is related to the discrimination threshold or the 'just noticeable difference' (j.n.d.) of concentration (Köster, 1994) by j.n.d. = $1/\mathcal{S}(N_g)$.

In the threshold vicinity, the concentration is low: $N_g << N_{g1/2}$. Stevens' law ($\Re \sim N_g^n$) indicates that the sensitivity $\mathcal{S} \sim nN_g^{n-1}$ increases with decreasing n for any n and for a given concentration in linear or semi-log coordinates (see Figure 2). This tendency of sensitivity is inverted for a concentration in the vicinity of $N_{g1/2}$. We can see then that the exponent n controls the sensitivity $\mathcal{S}$ or the chemical potential μ, which controls the threshold N_{gt}.

In concrete terms, we can say that this 'line convergence' phenomenon may be explained by the fact that for a given concentration N_g, the smaller n (e.g. a large size molecule), the larger the anchorage number n' of a stimulus molecule. Therefore, for the Stevens' law region, the sensitivity and the excited number of receptor sites are increased with the three facts quoted above, from which Stevens' law originates.

Importance of the saturated vapor pressure

The SVP of the stimulus is reported to play an important role in the olfaction mechanism (Randebrock, 1971; Patte *et al.*, 1989; Laffort, 1994). According to our statistical model, we can see that the constant of equilibrium K depends explicitly on SVP, since the two equilibria (1) and (2) represent an adsorption in two stages of the gaseous stimulus and this adsorption is indeed a particular condensation. From equation (7) we deduce the expression of the exponent n:

$$n = \frac{\log(N_M / N_{at})}{p_{ol} + \log \mathrm{SVP} - \Delta E^a / RT + \log\beta} \qquad (9)$$

where $p_{ol} = -\log N_{gt}$

We are now able to give an interpretation of the correlations established by Patte *et al.* (1989) and Laffort and Patte (1987). In order to predict exponent values from experimental olfactory thresholds, Laffort and Patte (1987) have used, both in psychophysics and electrophysiology, the following empirical expressions to calculate n:

$$n_1 = \frac{1}{p_{ol}}$$

$$n_2 = \frac{1}{p_{ol} - F} = \frac{1}{p_{ol} + \log K_p + H}$$

$$n_3 = \frac{1}{p_{ol} - \mathrm{ICE}} = \frac{1}{p_{ol} + \log \mathrm{SVP}} \quad \text{or} \quad \frac{1}{p_{ol} - \Delta E^v}$$

where $F = \log K^{air}{}_{mucus} + H = \log K_p + H$ (Laffort *et al.*, 1974), ICE = –log SVP, (Laffort and Patte, 1987) or ICE = ΔE^v, where ΔE^v is the free enthalpy of vaporization (Laffort and Patte, 1976).

Electrophysiology

By recording honey bee electrophysiological responses, Laffort and co-workers have established that the correlation between calculated and experimental values of n is better for n_3 than n_1, which is better than n_2. (See figure 2 in Laffort and Patte, 1987.) The Spearman ρ coefficient is 0.87, 0.33 and 0.22 respectively for n_3, n_1 and n_2.

This expression (9) can perfectly explain the established correlations in electrophysiology. From (9) we can see indeed that n_3 approaches n better than n_1 or n_2. For n_2 the correlation is not as good because of K_p intervention which is different from SVP in the case of a polar solution. We can confirm the previous interpretations (Keil, 1982; Laffort and Patte, 1987; Patte *et al.*, 1989): this behaviour is explainable by considering the mucus to be an ideal solution, or more probably by a dry route of the stimulus, the gaseous stimulus is adsorbed by receptor sites directly from air. The derivation of the expression of $\mathfrak{R}$ in these two cases leads to the same formula in the absence of interaction.

Psychophysics

In the absence of interaction (hypothesis iii), the parameter SVP can be replaced by the partition coefficient K_p (Henry's law). The expression (9) is then completely equivalent to the following expression:

$$n = \frac{\log(N_M N_{at})}{p_{ol} + \log K_p - \Delta E^a / RT + \log\beta} \qquad (10)$$

In the case of stimulus–mucus interaction, expression (9) is no longer valid. On the other hand, expression (10) can implicitly incorporate the interaction effect through the partition coefficient K_p, which is affected by this interaction.

Therefore, expression (10) can perfectly explain the established correlations in psychophysics.

In this case the authors have used many different sets of experimental data, which are noted K, D, B, S (Laffort and Patte, 1987). The correlation coefficient ρ and its variations are not the same for each set of data.

However, an average trend can be drawn: from four sets of data, three of them, B, K, S, show a better correlation of experimental n with n_2 than n_1. This is easily explainable with the analytical expression (10) of exponent n, which is better approached by the n_2 than the n_1 expression. The decreasing of the correlation in the case of n_3 is due to the fact that Henry's law is no longer valid where there is a strong interaction. The parameter ICE (–log SVP or ΔE^v) does not incorporate the interaction effect. To improve this correlation, ICE should be replaced by the free enthalpy of dissolution in a polar solution.

Adsorption energy

The term ΔE^a or ΔE_a can affect the olfactory threshold: the higher the adsorption energy, the better the adsorption, the lower the threshold. To our best knowledge, there have not yet been any investigations about this subject in olfaction.

Conclusion

The statistical thermodynamic model, which we have applied to stimulus adsorption in the olfactory mechanism, turns out to be quite powerful. The established expression of the olfactory response by this model clearly brings the relation between the dynamic response and the threshold.

The use of stimulus chemical potential in this model resulted in a physical interpretation of Stevens' law and of 'line convergence' behaviour. Furthermore, using this model, we derived the empirical relation of the threshold, which was established by Laffort and co-workers, and also interpreted the correlations between empirical expressions of the law exponent and the experimental values, which were also obtained by Laffort and co-workers. Thus this model confirms the role of the adsorption phenomenon in the olfaction mechanism.

However, we notice that this model can be further improved by changing the starting hypotheses in order to take into account some experimental effects such as the dependence of the saturation olfactory response on each stimulus, or the fact that the olfactory response corresponding to the inflexion point in the semi-log coordinates is higher than the half-saturation response.

Appendix: glossary of symbols

K_d	equilibrium constant of stimulus dissolution from air into mucus.
K_a	equilibrium constant of stimulus adsorption from mucus to receptor sites.
K	equilibrium constant of stimulus adsorption from air to receptor sites.
K_p	stimulus partition coefficient, i.e. equilibrium constant of stimulus vaporization from mucus to air.
n'	stimulus molecule anchorage number on receptor sites.
N_g	stimulus molecule number per unit volume in gaseous state.
$N_{g1/2}$	gaseous stimulus concentration of half saturation olfactory response.
N_{gt}	threshold stimulus concentration at gaseous state.
N_M	receptor site number per unit surface.
N_a	adsorbed stimulus molecule number per unit surface.
N_{at}	adsorbed stimulus molecule number per unit surface at olfactory threshold.
N_i	stimulus molecule number which are anchored on a receptor site.
N	total number of stimulus molecules.
ΔE_a	free enthalpy of stimulus adsorption from gaseous state.
ΔE^a	free enthalpy of stimulus adsorption from dissolved state.
ΔE^v	free enthalpy of vaporization of pure stimulus.
z	grand canonical partition function of the energy level $(-\epsilon)$ of one site.
Z_{gc}	grand canonical partition function of N_M sites.
Z	canonical partition function of N stimulus molecules at gaseous state.
Z_g	canonical partition function of N_g stimulus molecules.
Z_{gtr}	translation canonical partition function.
Z_{gi}	canonical partition function of internal degrees of N_g stimulus molecules.
μ_g, μ_d, μ	chemical potential of gaseous, dissolved and adsorbed stimulus.

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