

## Modelling the Human Olfactory Stimulus–Response Function

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### Abstract

Two models, derived from the equations of Michaelis–Menten and Hill, were adapted to olfaction. Their ability to model human olfactory stimulus–response relationships was compared with that of the classical laws of Fechner and Stevens. First, these four models were systematically compared on data available in the literature concerning 20 pure odorous compounds. At the lower concentrations of the odorous compound, the model of Stevens was found to be as good as the model of Hill. However, when the concentration range was extended further and included the concentration at half the maximum intensity, the model of Hill was found to be better. Second, the four models were tested on different parts of a true stimulus–response sigmoid curve with 5% noise added. The comparison confirmed the results obtained when experimental data were used. Third, the hypothesis that the psychophysical response is the sum of sigmoidal responses generated at the more peripheral parts of the olfactory system was examined, assuming a binomial distribution of receptor affinities. Within a very large range of variation in their characteristics, the sums of several sigmoids are indeed correctly modelled by Hill equations with exponents reflecting the distribution of receptor affinities.

### Introduction

Sensory intensity characteristics of odorous compounds are of great importance both in odour and flavour research and also in perfumery and flavouring industries. The perceived odour intensity of a given substance can be expressed as a function of a physico-chemical variable, its concentration in the air arriving on the mucosa. However, for the substance to be perceived, its concentration must be higher than its olfactory threshold, and at higher concentrations the perceived intensity reaches a plateau. Laffort (1966) and Barylko-Pikielna *et al.* (1983) have argued that the theoretical curve representing the evolution of psychophysical odour intensity as a function of the logarithm of stimulus concentration should have a sigmoid shape, from the olfactory threshold to a seldom reached saturation point.

### Models used to represent stimulus–response curves

From a psychophysical point of view, several equations have been used by different authors in attempts to model the stimulus–response relationship and to ascertain the specific characteristics of odorous compounds.

Two main models, based on just noticeable differences and well-established in psychophysical studies, have been used in the field of olfaction (Cain *et al.*, 1992).

The oldest general model relating the intensity of perception to the stimulus intensity in different domains of

sensorial analysis was proposed by Fechner in 1860. In olfaction, this general equation may be written as equation (1). Although this model has been criticized for not being theoretically justified (Laffort, 1991), it is still used.

$$I = n \log C + k \quad (1)$$

where  $I$  is the calculated odour intensity,  $C$  is the concentration of odorous compound,  $n$  is the slope and  $k$  is a constant.

Stevens (1960) advocated the use of another model, generally referred to as the power law, first developed by Plateau (1872). In olfaction, the power law may be formulated as equation (2) (Berglund and Lindvall, 1982; Neuner-Jehle and Etzweiler, 1991).

$$I = k \times C^n \quad (2)$$

where  $I$  is the calculated odour intensity,  $C$  is the concentration of odorous compound and  $n$  is an exponent (generally between 0.1 and 0.9).

The power law gives better results than the model of Fechner with data based on magnitude estimations of the intensity (Köster, 1991). Parameters  $k$  and  $n$  are obtained from a linear regression of the logarithm of perceived intensity versus the logarithm of stimulus concentration.

However, the linearity is observed only until 60% of the maximum of perceived intensity (Laffort, 1966). Katz and Talbert (1930), studying the whole intensity scale, found that, for strong stimulations, the intensity tends asymptotically to a maximum value (Laffort, 1966). Moreover, King (1986) noticed that the calculated exponent of the power law suffered from stimulus-range effects and decreased as the range of stimulus concentrations increased.

The models of Stevens and Fechner have been widely used but not, until nowadays, unanimously accepted. One obvious drawback is their inability to account for both the threshold and maximum values of perceived intensity. They have been criticized in recent papers by Murray (1993) and Krueger (1989).

Other models have been proposed in other fields of psychophysics, such as light perception. Hering (1920) obtained an S-shaped curve when plotting perceived brightness as a function of the logarithm of stimulus intensity. To account for his observation, he proposed a new equation which is formally identical to the Michaelis–Menten equation (Kuby, 1991) used in enzymology. Grüsser (1979, 1993) pointed out the similarity between what he called Hering's law and the function used by Naka and Rushton (1996) to describe the horizontal cell responses of the fish retina as a function of the stimulus luminance. Murray (1993) notes that it is at the extremes of the range of intensities that Hering's law yields predicted data that are most different from those predicted by the model of Stevens or Fechner.

A similar hyperbolic model, analogous to the equation of Michaelis–Menten, was proposed in the field of chemical senses by Beidler (1954) to fit the evolution of perceived taste intensity (equation 3), since a graph of the response intensity as a function of the logarithm of the concentration of the sapid substance presents a sigmoid shape (Laffort, 1991).

$$I = \frac{I_m C}{K_m + C} \quad (3)$$

where  $I$  is the calculated odour intensity,  $C$  is the concentration of odorous compound,  $I_m$  is the maximum value of intensity obtained for high concentrations and  $K_m$  is a constant.

This model has been successfully applied to sapid substances. However, its application to odorous substances was criticized on two grounds. First, the central part of the semi-logarithmic representation of equation (3) is close to a straight line portion with a fixed slope for all compounds, which is not always correct in olfaction (Laffort, 1991). Secondly, this model does not give a good representation of psychophysical perceived intensity near the olfactory threshold (Laffort, 1966).

In an attempt to overcome these problems Laffort (1966)

proposed a new model (equation 4) to represent the results observed in sensory physiology:

$$R = \frac{R_0}{\left[ (C_0/C) + (R_0/R_M)^{1/n} \right]^n} \quad (4)$$

where  $R$  is the calculated odour intensity response,  $C$  is the odorous compound concentration,  $R_0$  is the intensity of response at a fixed point of the linear part in log–log coordinates,  $C_0$  is the concentration at a fixed point of the linear part in log–log coordinates,  $R_M$  is the maximum intensity response and  $n$  is the exponent of the power law.

This model, which does not have a firm theoretical basis, was found difficult to use, as iterative calculations could not be applied (Laffort, 1991). In a study of stimulus–response curves for honeybees, Laffort's group (Patte *et al.*, 1989) advocated the use of another model developed at the beginning of the century by Hill (1913) to model the rate of combination of haemoglobin and oxygen (Kuby, 1991). The model of Hill (equation 5) is an empirical generalization of the Michaelis–Menten equation with a variable exponent value. In the case of the combination of oxygen to haemoglobin the exponent value, different from 1, indicates a cooperative phenomenon (Monod *et al.*, 1965).

$$V = \frac{V_m C^n}{K_m^n + C^n} \quad (5)$$

where  $V$  is the enzymatic reaction rate,  $C$  is the substrate concentration,  $V_m$  is the maximum reaction rate,  $K_m$  is the dissociation constant between enzyme and substrate, and  $n$  is the exponent of Hill.

The model of Hill has never been used to model human olfactory stimulus–response functions. However, it is a hyperbolic model, more general than the model of Beidler, which can take into account the sigmoidal theoretical shape of the stimulus–response curve.

Many other models have been considered to relate the perceived intensity to physico-chemical parameters (Hahn *et al.*, 1994). Recently a new model, based on statistical thermodynamics, has been proposed (Ben Lamine and Bouazra, 1997) to relate the olfactory response to various parameters involved in the olfaction mechanism. This model is in agreement with the model of Hill and with equations used at a more peripheral level to represent the evolution of the response.

#### Stimulus–response curves at peripheral and more central levels

At the peripheral level, olfactory recognition is mediated by a large ensemble of sensory cells, each conveying a fraction of the information on the nature and concentration of the odorous compound. Considerable evidence supports the

involvement of proteins in olfactory reception (Lancet, 1986; Buck and Axel, 1991).

Interactions between odorous molecules and receptors located in the olfactory cell membrane may thus be compared with enzyme–substrate interactions in enzymology (Schleppnik, 1981), and these observations support the idea of using hyperbolic functions derived from enzymology in neurophysiological studies of chemical senses, as done by Naka and Rushton in 1966, to relate stimulus intensity to perceived brightness (or darkness).

For example, Tateda (1967) used Hill's model to account for his taste receptors studies in the rat. Firestein *et al.* (1993) studied the relation between stimulus and response in olfactory receptor cells of the tiger salamander. They found that the cell's response was described well by the Hill equation (equation 5), with coefficients  $n$  much greater than 1 (acetophenone: 4.3; isoamyl acetate: 4.4; cineol: 2.7) and  $K_m$  (odorous compound concentration needed to get half the maximal current) ranging from  $3 \times 10^{-6}$  to  $9 \times 10^{-5}$  M. It was concluded that the olfactory receptor cells are broadly tuned, have a low apparent affinity for odorous compounds, integrate stimulus information over time and have a narrow dynamic range.

Menini *et al.* (1995), working on current fluctuations induced by odorous compounds in olfactory receptor cells, also used the Hill equation and found, in some cases, an exponent of  $\sim 2$ . They suggested that when odorous molecules interact with spatially isolated receptors, e.g. on different cilia, the total current will be the linear superposition of the individual current events. However, when odorous molecules interact with spatially close receptors in the same cilium, the total current is not expected to be the linear superposition of the individual events because it is activated by the internal transmitter cAMP in a cooperative way, explaining the found Hill exponent.

It must be noted that if sigmoidal curves correctly represent responses of isolated cells, it does not necessarily imply that the same relation be true when higher levels are concerned.

However, Lansky and Rospars (1993) proposed a theoretical model for coding odour intensity in the first two neuronal layers of olfactory systems. They showed that occupation and activation by odorous molecules of receptor proteins of different types borne by the first-order neurons can be described using a birth and death process. This birth and death model is in fact a stochastic generalization of the deterministic Michaelis–Menten model. They concluded that the shape of the curves of response of many receptors was sigmoidal, in accordance with available experimental results of electrophysiological investigations. When a group of neurons is stimulated, the graph of response intensity of this group of neurons versus the logarithm of odorous compound concentration is a sigmoid curve, resulting from the sum of the  $m$  sigmoid curves of the  $m$  types of receptor sites involved in the response. This suggested that in the

general case of neuroreceptors bearing  $m$  types of receptor sites, the number of occupied sites, the generator potential and the firing frequency are given by a summation of  $m$  sigmoid curves. This summation is again a sigmoid, or at least an increasing monotonic curve with two horizontal asymptotes and one inflection point.

At this point, one may wonder whether this process of summation of sigmoids could continue at higher levels and lead to a similar dependence of the perceived intensity on the stimulus concentration, as reported by Hering in 1920 for the perception of brightness or by Laffort (1966) and Barylko-Pikielna *et al.* (1983), arguing that the theoretical curve representing the evolution of psychophysical odour intensity as a function of the logarithm of stimulus concentration should indeed have a sigmoid shape.

If this is correct, the statistical treatment of experimental data should enable the calculation or estimation of the most important functional parameters which characterize the function, i.e. its minimum and maximum values, the coordinate of the inflection point and the slope of the straight line portion of the curve at that point. These four parameters not only determine the shape of the curve but also define its position with respect to the axis of the independent variable (Majer, 1995); that is, the concentration of the odorous compound.

### Purpose of the work

If it is assumed that the evolution of psychophysical response intensity follows a sigmoid curve, a model derived from Hill's equation should be more general than other models used in olfaction. However, until now, no systematic comparison of models has been made on a large number of experimental data.

Our first goal in this work was to carry out a systematic comparison of the models of Fechner, Stevens, Beidler and Hill, using olfactory data available in the literature for 20 pure odorous compounds.

Assuming that the degrees of success in the use of these different models were due to limitations in the range of concentrations which were used, our second aim was to compare the models of Fechner, Stevens and Hill on a theoretical sigmoid curve of intensity versus concentration, in order to define the respective domains of application of the models.

Our third goal was to determine whether and under which conditions a sum of sigmoidal responses, normally expected from receptors and cells, remains a sigmoid. This would be a test for one of the theoretical bases of the sigmoid model.

## Materials and methods

### Materials

Experimental psychophysical data on intensity of response versus odorous compound concentration, for 20 odorous

molecules, were taken from literature. Three categories of data were used. In the first category, comprising vanillin and citral, measurements were made using the 'squeeze bottle' technique, with water as the solvent. Intensity was evaluated by a panel using the method of magnitude estimation (Voirol and Daget, 1986).

The second category concerned four compounds, acetone, ethyl acrylate (Berglund and Olsson, 1993), butanol and cyclohexanone (Laing, 1983). These stimuli were presented to the subjects with an air dilution olfactometer. For the first two compounds, intensity was measured by cross-modality matching using a finger-span method. In the case of butanol and cyclohexanone, intensity was evaluated by magnitude estimation.

For the last category (14 compounds), the odorous stimuli were presented to the subjects with an air dilution olfactometer and intensity was estimated by olfactory matching with *n*-butanol as the reference. In this last case, concentrations of *n*-butanol were converted into intensity values using the scale given by the authors (Hall and Anderson, 1983).

#### Taking into account the intensity of the 'clean air'

In several of the reported experiments, the intensity perceived by the subjects when a blank (pure air) was presented was not always zero. Accordingly, in the absence of information on thresholds, the intensity of the clean air was considered as the lower asymptote of the stimulus-response curve, and the different models were adapted to take into account this value. Graphically, this modification corresponds to a translation along the intensity axis.

##### Models of Fechner and Stevens

The model of Fechner cannot account for a parameter relative to the 'clean air' as the parameter  $k$  (equation 1) includes the additional translation needed for the 'clean air'. Therefore, equation (1) has been used in this paper without any modification.

The model of Stevens presented in equation (2) was adapted (equation 6) to take into account the intensity ( $I_o$ ) of 'clean air'.

$$I = I_o + (k \times C^n) \quad (6)$$

where  $I$  is the calculated odour intensity,  $I_o$  is the perceived intensity with pure air as stimulus,  $C$  is the concentration of odorous compound and  $n$  is the exponent (generally between 0.1 and 0.9).

##### Models of Beidler and Hill

The model of Beidler was adapted by modifying equation (3) to give equation (7). To avoid any misinterpretation of  $K_m$ , it was replaced by  $C_{ip}$ , the concentration at the inflection point

$$I = \frac{(I_m - I_o)C}{C_{ip} + C} + I_o \quad (7)$$

where  $I$  is the calculated intensity of the response,  $I_m$  is the maximum value of perceived intensity,  $I_o$  is the perceived intensity with pure air as stimulus,  $C$  is the stimulus concentration and  $C_{ip}$  is the concentration at the inflection point.

In the same way, the Hill equation was modified to give equation (8).

$$I = \frac{(I_m - I_o)C^n}{C_{ip}^n + C^n} + I_o \quad (8)$$

where  $I$  is the calculated intensity of the response,  $I_m$  is the maximum value of perceived intensity,  $I_o$  is the perceived intensity with pure air as stimulus,  $C$  is the stimulus concentration,  $C_{ip}$  is the concentration at the inflection point and  $n$  is the exponent of Hill.

For these two models, the parameter  $I_m$  (equations 3 and 4) was written as  $I_m - I_o$  (equations 7 and 8) to obtain  $I = I_m$  when the concentration tends to infinity. This modification, which has no impact on the calculation of other parameters, afforded a more coherent value for  $I_m$ .

#### Determination of the parameters of the models

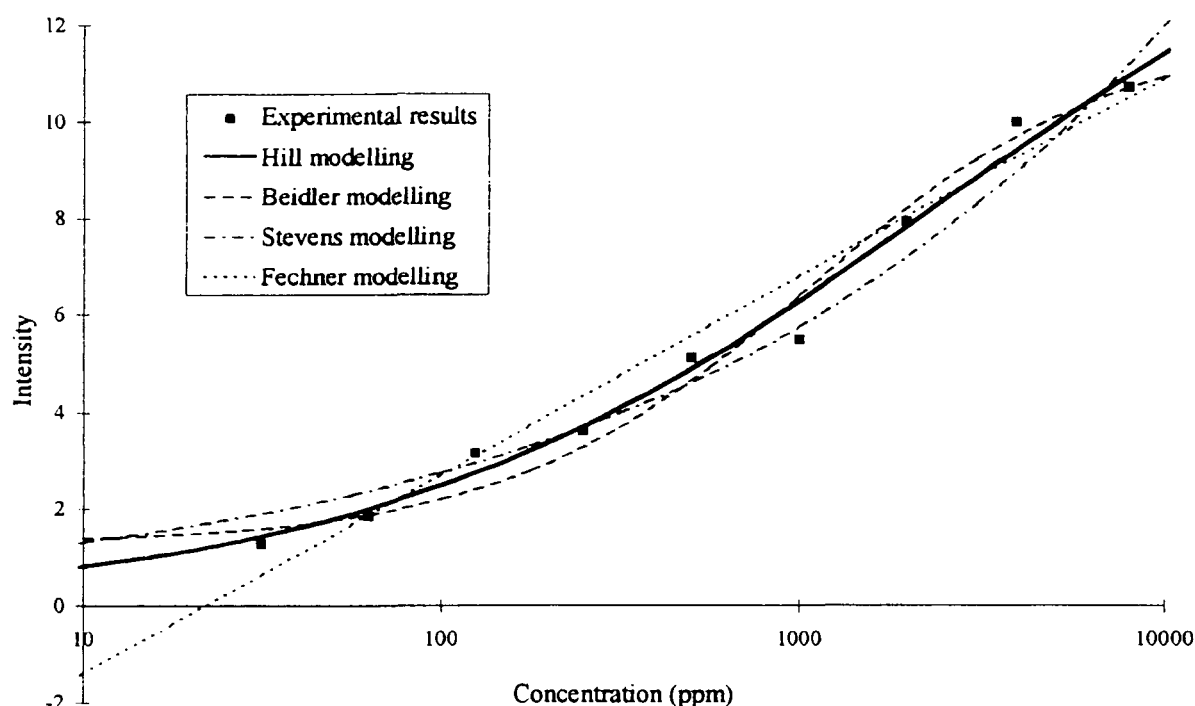
With Fechner's model (equation 1),  $n$  and  $k$  were estimated using a standard linear regression between  $I$  and  $\log C$ , using the UNISTAT® Statistical Package. For the model of Stevens, two techniques were used and compared. The parameters  $n$  and  $k$  were estimated using either a non-linear regression between  $I$  and  $C$  (according to equation 2) or a linear regression between  $\log I$  and  $\log C$ .

For the models of Hill and Beidler, the different parameters were optimized by non-linear regressions using the UNISTAT® Statistical Package, by direct fitting on experimental values to avoid any bias resulting from the linearization method (Maes, 1985). The UNISTAT® package provides a least-squares method of fitting a specified function to a data set. The regression function is written in terms of concentration, generally expressed in ppm or ppb, and any number of parameters (those of the different models). Given initial estimates of the parameter values, the program adjusted them over several iterations, to minimize the residual sum of squares between predicted and experimental values.

For the model of Beidler, initial estimates were the maximum intensity measured during experimentation for  $I_m$  and zero for  $I_o$ . An initial value of  $C_{ip}$ , the constant corresponding to the odorous compound concentration at half the maximal intensity response, was estimated from the graph  $I = f(\log C)$ .

For the model of Hill, calculations were conducted as described above, except that the exponent  $n$  was optimized





**Figure 1** Intensity–concentration curves for vanillin (data from Voirol and Daget, 1986). The stimuli were dissolved in a tasteless and odourless mineral water. Concentrations are given in ppm in solution (w/v).

as well as the three other parameters, from an initial value of 1, corresponding to Beidler approximation.

#### Statistical evaluation of the different models

To compare the different models, we used the determination coefficient  $R^2$  between the predicted intensity and the corresponding experimental perceived intensity. However, as the four models contain different numbers of parameters, with the predictable effect that the model with more parameters will seem better, the statistic  $\Psi^2$  was also used. Described by Exner (1992) and Exner *et al.* (1993),  $\Psi^2$  is comparable to  $R^2$ , but includes a correction to take into account the number  $p$  of empirical parameters used in the model (equation 9). The best model should have the smallest  $\Psi^2$  and the largest  $R^2$ .

$$\Psi^2 = \frac{(N-1) \sum_{i=1}^N (Y_i - X_i)^2}{(N-p) \sum_{i=1}^N (X_i - \bar{X})^2} = \frac{(N-1)}{(N-p)} (1 - R^2) \quad (9)$$

where  $N$  is the number of experimental points,  $p$  is the number of parameters of the model,  $Y_i$  is the calculated value,  $X_i$  is the experimental value,  $\bar{X}$  is the mean of experimental values and  $R^2$  is the determination coefficient.

#### Building a theoretical curve of intensity versus concentration

A theoretical sigmoid curve representing intensity versus concentration was built using equation (8), with the following values of its parameters:  $I_m = 110$ ,  $I_o = 10$ ,  $C_{ip} = 700$ ,  $n = 1.1$ .  $I_m$  was fixed at 110 as the graphical scale often used in sensorial analysis (magnitude estimation) is of 110 mm.  $I_o$  was arbitrarily fixed to  $\sim 10\%$  of the scale and  $C_{ip}$  was fixed to 700 in arbitrary units. The value taken for  $n$  is an average of the values obtained using experimental data.

Sixteen regularly spaced values of the concentration, ranging on five logarithmic units, were chosen to represent the whole curve. A random error of 5% on average was added to the calculated values of intensity.

The theoretical curve was divided into three parts and the adapted models of Hill, Stevens and Fechner were tested, both on the whole range of concentrations and on three different parts of this range (the lower, middle and upper parts). Beidler's model, which is a special case of Hill's, was not tested on this theoretical curve.

#### Results and discussion

##### Comparison of the models on experimental data sets

##### Intensity measured by magnitude estimation

**Vanillin.** The four models of Fechner, Stevens, Beidler and Hill were compared on experimental data obtained from Voirol and Daget (1986) (Figure 1 and Table 1), on a range of concentrations from 31 to 8000 ppm in water.

**Table 1** Results of modelling on vanillin (nine experimental points and concentration range: 31–8000 ppm)

Model of Hill			Model of Beidler	Model of Stevens <sup>a</sup>		Model of Fechner
$I_o = 0.07$ (2.00) <sup>b</sup>	$I_o = 0$ (fixed)	$I_o = 0$ (fixed)	$I_o = 1.3$ (0.40)	non-linear regression	linear regression	$k = -5.5$ (0.8)
$I_m = 17.2$ (9.30)	$I_m = 17.4$ (4.5)	$I_m = 17.4$ (1.5)	$I_m = 12.0$ (0.8)	$k = 0.63$ (0.13)	$\log k = -0.38$ (0.07)	$n = 4.1$ (0.3)
$C_{ip} = 2800$ ppm (4900) NS <sup>c</sup>	$C_{ip} = 2930$ ppm (2990) NS	$C_{ip} = 2930$ ppm (878)	$C_{ip} = 1100$ ppm (297)	$n = 0.32$ (0.03)	$n = 0.38$ (0.03)	
$n = 0.54$ (0.34)	$n = 0.53$ (0.09)	$n = 0.53$ (fixed)				
	$R^2 = 0.986$ $\Psi^2 = 0.019$		$R^2 = 0.979$ $\Psi^2 = 0.028$	$R^2 = 0.973$ $\Psi^2 = 0.031$	$R^2 = 0.962$ $\Psi^2 = 0.043$	$R^2 = 0.965$ $\Psi^2 = 0.040$

<sup>a</sup>For the model of Stevens  $I_o$  was set to zero.<sup>b</sup>Values in brackets are standard errors on parameters.<sup>c</sup>NS means not statistically significant.**Table 2** Results of modelling with intensities measured by magnitude estimation and cross modality matching

Compound (reference)	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	$R^2$	$\Psi^2$
Citral (Voirol and Daget, 1986)	8	0.8–100 ppm in water	Hill	$I_m$	24	5	21	0.975	0.035
				$I_o$	0	fixed			
				$n$	0.76	0.18	24		
			Beidler	$C_{ip}$	19.7	13.5	69	WS <sup>b</sup>	0.974
				$I_m$	20	2	10		
				$I_o$	1.1	1.0	91		
			Stevens	$C_{ip}$	16	6	38	WS	0.943
				$k$	3.6	0.6	17		
				$n$	0.38	0.05	13		
			Stevens (LR) <sup>c</sup>	$\log k$	0.37	0.08	22	0.909	0.106
				$n$	0.51	0.07	14		
				$k$	1.4	0.8	57		
Butanol (Laing, 1983)	7	0–95.1 ppm	Hill	$I_m$	77	3	4	0.995	0.010
				$I_o$	11.6	1.5	13		
				$n$	2.92	0.8	27		
			Beidler	$C_{ip}$	7.07	0.7	10	WS	0.957
				$I_m$	87	9.7	11		
				$I_o$	7.4	4.5	61		
			Stevens	$C_{ip}$	8.2	3.8	46	0.843	0.188
				$k$	21.4	6.3	29		
				$n$	0.3	0.08	27		
			Stevens (LR)	$\log k$	1.2	0.06	5	0.842	0.231
				$n$	0.38	0.05	13		
				$k$	23	5.7	25		
Cyclohexanone (Laing, 1983)	7	0–67.8 ppm	Hill	$I_m$	101	3.5	3	0.999	0.003
				$I_o$	6.2	1.3	21		
				$n$	1.19	0.12	10		
			Beidler	$C_{ip}$	6.98	0.71	10	0.997	0.005
				$I_m$	107	3.5	3		
				$I_o$	4.8	1.5	31		
			Stevens	$C_{ip}$	8.01	1.04	13	0.944	0.068
				$k$	21.9	4.6	21		
				$n$	0.37	0.06	16		

Table 2 Continued

Compound (reference)	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	$R^2$	$\Psi^2$
Acetone (Berglund and Olsson, 1993)	7	96–1040 ppm	Stevens (LR)	$\log k$	1.19	0.04	3	0.92	0.179
				$n$	0.5	0.04	8		
			Fechner	$k$	21.8	4.6	21	0.946	0.066
				$n$	38	4.9	13		
			Hill	$I_m$	284	751	264	NS <sup>b</sup>	0.987
				$I_o$	0	fixed			
				$n$	0.71	0.22	31		
			Beidler	$C_{ip}$	10154	51561	508	NS	0.984
				$I_m$	108	41	38		
				$I_o$	4.0	3.0	75		
Ethyl acrylate (Berglund and Olsson, 1993)	7	0.353–1581 ppb	Stevens	$C_{ip}$	1589	1063	67	WS	0.987
				$k$	0.54	0.14	26		
				$n$	0.64	0.04	6		
			Stevens (LR)	$\log k$	−0.33	0.09	27	0.986	0.018
				$n$	0.67	0.04	6		
			Fechner	$k$	−63.2	8.5	13	0.956	0.053
				$n$	35.2	3.4	10		
			Hill	$I_m$	342	972	284	NS	0.966
				$I_o$	0	fixed			
				$n$	0.26	0.11	42		
			Beidler	$C_{ip}$	256100	3848671	1503	NS	0.928
				$I_m$	74	11	15		
				$I_o$	12.0	4.2	35		
			Stevens	$C_{ip}$	212	119	56	WS	0.967
				$k$	13.9	1.9	14		
			Stevens (LR)	$n$	0.23	0.02	9	0.967	0.040
				$\log k$	1.14	0.04	4		
			Fechner	$n$	0.22	0.02	9	0.967	0.040
				$k$	11.8	4.5	38		
				$n$	16.5	2.4	15	0.900	0.120

<sup>a</sup>Odoriferous compounds were diluted in air except for citral where the solvent was water.

<sup>b</sup>NS: not statistically significant; WS: weakly significant.

In the middle part of the graph (Figure 1) and on a range of >2 logarithmic units, the four models are quite similar.

The model of Fechner is not appropriate as it predicts negative intensities at lower concentrations, with low values for  $R^2$  and  $\Psi^2$ .

For the model of Stevens,  $I_o$  was found to be not significantly different from zero, and was set to zero. This model gives quite a good fit, but does not account for a maximum intensity at higher concentrations. Indeed, Figure 1 shows that for high concentrations, intensity tends toward a maximum. When the parameters of this power law were estimated with a linearization method instead of a non-linear regression, a less good fit was obtained and the exponent  $n$  was overestimated (0.38 instead of 0.32).

The model of Beidler does not give a better fit than these two models. However, Hill's model produces a higher  $R^2$  and a lower  $\Psi^2$ . At first, all parameters ( $I_o$ ,  $I_m$ ,  $n$  and  $C_{ip}$ ) were

allowed to vary, but as  $I_o$  was found not to be significantly different from zero, it was set to zero and another regression was made. The results (Table 1) show a decrease of the standard error on the three other parameters, especially on  $n$ , when  $I_o$  is set to zero. Considering the low standard error on  $n$ , it has been set to 0.53 and  $I_o$  to zero, in order to evaluate  $C_{ip}$  with more precision. The results show no modification of the correlation coefficients ( $R^2 = 0.986$  and  $\Psi^2 = 0.022$ ) or of  $C_{ip}$  and  $I_m$  values, but a smaller standard error on these two parameters.

**Other compounds.** The four models were used to fit data on five other compounds (Table 2). According to  $R^2$  and  $\Psi^2$ , the model of Fechner generally gives a poor modelling of the experimental data, whatever the experimental conditions and concentration ranges used.

For these compounds, the linearization method used to estimate the parameters of the power law gives generally a

poorer correlation than the non-linear method and, as has been seen with vanillin, yields an overestimated value for  $n$ . For the model of Stevens,  $I_0$  was found not to be significantly different from zero and consequently was set to zero and not included in Table 2.

For citral and cyclohexanone, the models of Hill and Beidler are equivalent and much better than the two others. As far as butanol is considered, Hill's model gives the best results and its parameters are statistically significant. For the models of Hill and Beidler,  $I_0$  was found to be different from zero, except for citral (Hill's model).

For acetone and ethyl acrylate, where intensity was also measured by magnitude estimation and stimuli were delivered using an air dilution olfactometer, the model of Stevens gave the best results. In these two cases, Hill's model seems to tend toward Stevens's model (low exponent and high values for  $C_{ip}$  and  $I_m$ ). It is noticeable that the standard deviations calculated for the parameters of Hill's model are very high, indicating that the model was not applicable. According to the low value of the exponent, this could result from the too small range of concentrations used for these products, which leads to the consideration of only the first part of the sigmoid, comparable to a power law curve. For these two compounds, the value of  $n$  obtained with the model of Hill is not far from the exponent of the power law, showing that in this range of concentrations, the power law is a limiting case of Hill's model.

#### *Intensity measured using a butanol scale*

Now considering the 14 data sets obtained using a  $n$ -butanol scale (Table 3), the models of Fechner and Stevens, with the linearization method, yielded generally poor results.

The models of Hill and Beidler gave the best modelling in seven cases out of 14 (the first compounds in Table 3). For these seven compounds, the deviation on the parameters of the models of Hill and Beidler was low, indicating a good modelling. The model of Beidler was the best, as far as  $\Psi^2$  is concerned, for butanal, pentanal, 2,3-pentanedione, octanal, *trans*-2-hexenal and *trans*-2-octenal. For these compounds, the exponent of Hill was close to one, according to the standard error, and the model of Beidler, with one parameter less to estimate, gave a better  $\Psi^2$ . However, for heptanal, where the exponent of Hill was very different from 1, the model of Hill was the best, with excellent correlations with experimental data.

For the seven other compounds (lower part of Table 3) the model of Stevens, Beidler and Hill gave similar results. However, in five cases, significant parameters were not obtained for the models of Hill and Beidler, due to the great dispersion of experimental points.

#### *Conclusions on the modelling of experimental data*

Modelling a large pool of experimental data with the model of Fechner shows that the fits are always poorer than those obtained with the other models. Near the threshold, negative intensities are predicted because it does not take

into account the lower asymptote of the intensity curve and does not allow an estimation of the intensity of the 'clean air'. Moreover, as its parameters depend on the intensity scale and the concentration units, it is impossible to compare the values of  $n$  obtained for different compounds. Consequently, this model should be avoided.

The model of Stevens gives a much better representation of experimental results than that of Fechner. When only the beginning of the sigmoid is available, this model gives the best fit with experimental data. Nevertheless, for high concentrations, it does not take into account the plateau of maximum intensity and this is a limitation on its validity. Consequently, for some compounds where data on the upper part of the curve are available, this model does not fit well with psychophysical data.

Two methods are available to estimate the parameters of the model of Stevens. The more common, based on a linear regression of experimental psychophysical intensity versus concentration, plotted in log-log coordinates, induces a bias because it gives greater importance to the lower concentrations and leads to the overestimation of values of  $n$ . Moreover, such transformations should be carried out with caution, because one has to ensure that the statistical properties of the variables are not changed (Einax *et al.*, 1997). Consequently, a non-linear parameter estimation should be preferred.

Hyperbolic models such as those of Hill or Beidler generally give good results and the model of Hill is preferable when the exponent of Hill is far from one. However, for some compounds where a low exponent is found, the concentration range seems to be too small to reach the maximal intensity and the parameters obtained after the regression are not statistically significant.

#### **Comparison of three models using a theoretical sigmoid curve**

Considering the results in modelling experimental data, we assumed that the reported successful uses of the different models were due to limitations in the range of concentrations used. Thus we tried to define their respective domains of application by comparing the different models on a theoretical stimulus-response curve.

The optimal values of the different parameters of the models calculated when the whole curve is considered are given in Table 4. As  $I_0$  in the model of Stevens was not statistically different from zero, it was set to zero and a new curve fitting was made. As expected in this case, the model of Hill gives the best correlation with the experimental values and low standard deviations on its parameters. However, it is important to note that the model of Fechner gives slightly better results than the model of Stevens when a whole sigmoid curve is available.

It is also worth noting that the parameters obtained with the model of Hill are very close to the values used to build the theoretical curve. For  $I_m$ ,  $C_{ip}$  and  $n$ , the deviation from



**Table 3** Results of modelling with intensities measured with an *n*-butanol scale (results from Hall and Anderson, 1983)

Compound	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	$R^2$	$\Psi^2$
Butanal	15	38–32819 ppb	Hill	$I_m$	354	109	31	0.813	0.218
				$I_o$	0	fixed			
				$n$	1.52	0.79	52		
			Beidler	$C_{ip}$	7446	3959	53	0.804	0.211
				$I_m$	448	136	30		
				$I_o$	0.0	fixed			
			Stevens <sup>c</sup>	$C_{ip}$	11779	7502	64	0.769	0.249
				$k$	1.1	1.3	118		
				$n$	0.56	0.13	23		
			Stevens (LR) <sup>d</sup>	$\log k$	-1.2	0.2	17	0.695	0.329
				$n$	0.87	0.06	7		
			Fechner	$k$	-257	73	28	0.662	0.364
Heptanal	15	14.5–6898 ppb	Hill	$I_m$	447	45	10	0.956	0.051
				$I_o$	0	fixed			
				$n$	1.82	0.36	20		
			Beidler	$C_{ip}$	1242	218	18	0.932	0.073
				$I_m$	624	92	15		
				$I_o$	0.0	fixed			
			Stevens	$C_{ip}$	2530	736	29	0.883	0.126
				$k$	3.3	2.1	64		
				$n$	0.56	0.08	14		
			Stevens (LR)	$\log k$	-0.41	0.15	37	0.801	0.214
				$n$	0.84	0.06	7		
			Fechner	$k$	-245	64	26	0.738	0.282
Pentanal	15	70–11548 ppb	Hill	$I_m$	543	239	144	0.948	0.061
				$I_o$	0	fixed			
				$n$	1.1	0.32	29		
			Beidler	$C_{ip}$	6919	5975	86	0.948	0.056
				$I_m$	627	137	22		
				$I_o$	0.0	fixed			
			Stevens	$C_{ip}$	9272	3612	39	0.941	0.063
				$k$	0.53	0.38	72		
				$n$	0.7	0.08	11		
			Stevens (LR)	$\log k$	-1.24	0.2	16	0.912	0.094
				$n$	0.96	0.07	7		
			Fechner	$k$	-324	58	18	0.813	0.202
2,3-Pentanedione	16	3.49–1808 ppb	Hill	$I_m$	264	76	29	0.933	0.077
				$I_o$	0	fixed			
				$n$	0.9	0.22	24		
			Beidler	$C_{ip}$	574	417	73	0.932	0.073
				$I_m$	240	29	12		
				$I_o$	0.0	fixed			
			Stevens	$C_{ip}$	450	124	28	0.912	0.095
				$k$	4.5	1.7	38		
				$n$	0.51	0.06	12		
			Stevens (LR)	$\log k$	0.09	0.12	133	0.856	0.155
				$n$	0.73	0.06	8		
			Fechner	$k$	-66	16	24	0.818	0.196
Octanal	15	1.54–866 ppb	Hill	$I_m$	376	168	45	0.873	0.148
				$I_o$	0	fixed			
				$n$	1.09	0.49	45		
				$C_{ip}$	317	316	100		

Table 3 Continued

Compound	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	R <sup>2</sup>	ψ <sup>2</sup>
<i>trans</i> -2-Hexenal	15	31.6–4870 ppb	Beidler	<i>I<sub>m</sub></i>	410	90	22	0.871	0.139
				<i>I<sub>o</sub></i>	0.0	fixed			
				<i>C<sub>ip</sub></i>	387	180	47		
			Stevens	<i>k</i>	5.5	3.4	62	WS	0.856
				<i>n</i>	0.59	0.1	17		
			Stevens (LR)	<i>logk</i>	0.27	0.14	52	WS	0.832
				<i>n</i>	0.77	0.08	10		
			Fechner	<i>k</i>	–85	33	39		0.714
				<i>n</i>	103	18	17		0.310
			Hill	<i>I<sub>m</sub></i>	560	257	46		0.821
				<i>I<sub>o</sub></i>	0	fixed			0.209
				<i>n</i>	1.44	0.8	56	WS	
			Beidler	<i>C<sub>ip</sub></i>	1863	1464	79	WS	
				<i>I<sub>m</sub></i>	891	424	48		0.818
				<i>I<sub>o</sub></i>	0.0	fixed			0.196
<i>trans</i> -2-Octenal	15	1.15–392 ppb	Stevens	<i>C<sub>ip</sub></i>	4464	3497	78	WS	
				<i>k</i>	0.98	1.22	124	NS	0.809
				<i>n</i>	0.73	0.16	22		0.206
			Stevens (LR)	<i>logk</i>	–1.5	0.2	13		0.748
				<i>n</i>	1.17	0.08	7		0.272
			Fechner	<i>k</i>	–381	99	26		0.693
				<i>n</i>	199	37	19		0.330
			Hill	<i>I<sub>m</sub></i>	389	82	21		0.914
				<i>I<sub>o</sub></i>	0	fixed			0.030
				<i>n</i>	0.95	0.16	17		
			Beidler	<i>C<sub>ip</sub></i>	152	77	51	WS	
				<i>I<sub>m</sub></i>	369	33	9		0.973
				<i>I<sub>o</sub></i>	0.0	fixed			0.029
			Stevens	<i>C<sub>ip0</sub></i>	135	27	20		
				<i>k</i>	9.4	2.4	26		0.959
				<i>n</i>	0.58	0.05	9		0.044
2,3-Butanedione	16	6.81–1136 ppb	Stevens (LR)	<i>logk</i>	0.57	0.07	12		0.921
				<i>n</i>	0.78	0.06	8		0.085
			Fechner	<i>k</i>	–41.9	15.3	37		0.845
				<i>n</i>	99.5	11.8	12		0.167
			Hill	<i>I<sub>m</sub></i>	435	392	90	WS	0.843
				<i>I<sub>o</sub></i>	0	fixed			0.181
				<i>n</i>	0.7	0.3	43		
			Beidler	<i>C<sub>ip</sub></i>	1407	3509	249	NS	
				<i>I<sub>m</sub></i>	272	50	18		0.834
				<i>I<sub>o</sub></i>	0.0	fixed			0.178
			Stevens	<i>C<sub>ip</sub></i>	394	165	42		
				<i>k</i>	6.2	3	48		0.837
				<i>n</i>	0.49	0.07	14		0.176
			Stevens (LR)	<i>logk</i>	0.35	0.12	34		0.806
				<i>n</i>	0.65	0.06	9		0.208
Nonanal	15	12.3–1814 ppb	Fechner	<i>k</i>	–72	24	33		0.746
				<i>n</i>	78	12	15		0.273
			Hill	<i>I<sub>m</sub></i>	711	2657	374	NS	0.889
				<i>I<sub>o</sub></i>	0	fixed			0.129
				<i>n</i>	1.36	0.97	71	WS	
			Beidler	<i>C<sub>ip</sub></i>	3764	15934	423	NS	
				<i>I<sub>m</sub></i>	1.8E+15	1.4E+14	8		0.884
				<i>I<sub>o</sub></i>	0.0	fixed			0.125
				<i>C<sub>ip</sub></i>	1.7E+16	****			

Table 3 Continued

Compound	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	R <sup>2</sup>	Ψ <sup>2</sup>	
Hexanal	15	53.4–11498 ppb	Stevens	k	0.04	0.06	150	NS	0.888	0.120
				n	1.13	0.21	19			
			Stevens (LR)	logk	−0.68	0.12	18		0.875	0.134
				n	0.87	0.05	6			
			Fechner	k	−102	35	34		0.594	0.438
				n	69	16	23			
			Hill	I <sub>m</sub>	524	304	58	WS	0.895	0.123
				I <sub>o</sub>	0	fixed				
				n	1.53	0.63	41			
			Beidler	C <sub>ip</sub>	7287	6128	84	WS	0.885	0.124
				I <sub>m</sub>	1415	1375	97			
				I <sub>o</sub>	0.0	fixed				
1-Octen-3-ol	15	6.81–1136 ppb	Stevens	C <sub>ip</sub>	34567	41518	120	NS	0.88	0.129
				k	0.09	0.1	111			
			Stevens (LR)	n	0.89	0.14	16		0.88	0.129
				logk	−0.93	0.14	15			
			Fechner	n	0.84	0.05	6		0.607	0.423
				k	−251	76	30			
			Hill	n	115	26	23	WS	0.954	0.054
				I <sub>m</sub>	582	332	57			
				I <sub>o</sub>	0	fixed				
			Beidler	n	1.17	0.36	31	NS	0.953	0.051
				C <sub>ip</sub>	899	902	100			
				I <sub>m</sub>	821	268	33			
trans-2-Nonenal	15	0.24–64.9 ppb	Stevens	I <sub>o</sub>	0.0	fixed		WS	0.949	0.055
				C <sub>ip</sub>	1669	812	49			
			Stevens (LR)	k	1.3	0.7	54	WS	0.933	0.072
				n	0.79	0.08	10			
			Fechner	logk	−0.43	0.09	21		0.765	0.253
				n	1	0.04	4			
			Hill	k	−175	42	24	WS	0.823	0.207
				n	137	21	15			
				I <sub>m</sub>	448	334	75			
			Beidler	I <sub>o</sub>	0	fixed		WS	0.811	0.204
				n	0.71	0.38	54			
				C <sub>ip</sub>	25	57	228			
trans,trans-2,4-Heptadienal	15	1.33–115 ppb	Stevens	I <sub>o</sub>	0.0	fixed		NS	0.815	0.200
				C <sub>ip</sub>	16	7	44			
			Stevens (LR)	k	50	14	28		0.764	0.254
				n	0.44	0.08	18			
			Fechner	logk	1.3	0.1	8		0.811	0.204
				n	0.74	0.1	14			
			Hill	k	44.4	16.6	37	WS	0.782	0.254
				n	128	17	13			
				I <sub>m</sub>	1150	12387	1077			
			Beidler	I <sub>o</sub>	0	fixed		NS	0.782	0.235
				n	1.15	1.06	92			
				C <sub>ip</sub>	580	7066	1218			
trans,trans-2,4-Heptadienal	15	1.33–115 ppb	Stevens	I <sub>m</sub>	2.2E+15	2.5E+14	11	WS	0.782	0.235
				I <sub>o</sub>	0.0	fixed				
			Stevens (LR)	C <sub>ip</sub>	1.6E+15	****		NS	0.783	0.234
				k	1	1	100			
			Fechner	n	1.1	0.3	27		0.782	0.235
				logk	0.081	0.1	123			
			Hill	n	0.97	0.08	8	WS	0.569	0.464
				k	−32	21	66			
			Beidler	n	67	16	24		0.569	0.464
				k	−32	21	66			

Table 3 Continued

Compound	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	<i>R</i> <sup>2</sup>	Ψ <sup>2</sup>	
<i>trans,trans</i> -2,4- Nonadienal	15	0.81–124 ppb	Hill	<i>I</i> <sub>m</sub>	727	787	108	NS	0.924	0.082
				<i>I</i> <sub>o</sub>	0	fixed				
				<i>n</i>	0.75	0.27	36			
			Beidler	<i>C</i> <sub>ip</sub>	201	509	253	NS	0.92	0.086
				<i>I</i> <sub>m</sub>	429	73	17			
				<i>I</i> <sub>o</sub>	0.0	fixed				
			Stevens	<i>C</i> <sub>ip</sub>	58	21	36	0.922	0.084	
				<i>k</i>	18.1	5.5	30			
				<i>n</i>	0.58	0.07	12			
			Stevens (LR)	log <i>k</i>	0.9	0.07	8	0.895	0.114	
				<i>n</i>	0.81	0.06	7			
			Fechner	<i>k</i>	−23	18	78	WS	0.847	0.165
				<i>n</i>	130	15	12			

<sup>a</sup>Odorous compounds were diluted in air and delivered with an olfactometer.

<sup>b</sup>NS: not statistically significant; WS: weakly statistically significant.

<sup>c</sup>For the model of Stevens preliminary calculations showed that in all cases  $I_o$  was not significantly different from zero. It was set to zero and not included in this table.

<sup>d</sup>Model of Stevens using linear regression to determine the parameters.

the theoretical values is less than or equal to the maximum error added to the theoretical intensity. However, a greater deviation is observed on the parameter  $I_o$ .

When the theoretical curve was split into three parts (Table 4), only 10 points out of 16 were used, that is ~60% of the whole curve.

Considering the results of modelling on the lower part of the curve (Table 4), the model of Hill gives a good correlation coefficient, but  $I_m$  and  $C_{ip}$  are not statistically significant and  $I_o$  and  $n$  are only weakly significant. In this case, the calculated value of  $C_{ip}$  falls out of the range of concentrations used. This can, in part, explain the great deviation obtained for this parameter. The range of concentrations is too low to permit a good modelling with the model of Hill. As data near the threshold are considered here, the model of Fechner is not statistically significant (high standard deviation on the parameter  $k$ ). In this concentration range, the model of Stevens gives the best results, although its parameters are not highly significant.

When the middle part is considered, the three models are found to be significant and close to each other. All parameters have a low standard deviation, except  $I_o$  in the models of Hill and Stevens. For this last model,  $I_o$  was found not to be statistically different from zero and was therefore set to zero before another regression was made. The model of Hill is the best, as indicated by the  $\Psi^2$  value obtained when fitting with this model. In this case, the  $C_{ip}$  value is included in the concentration range and a good fit can be obtained.

In the upper part of the curve, all the parameters of the

different models are significant except  $I_o$  in the model of Stevens (later set to zero) and  $I_o$  of the model of Hill (only weakly significant). The model of Hill gives a good modelling. Lower  $R^2$  and higher  $\Psi^2$  values (Table 4) were obtained for the models of Fechner and Stevens which cannot account for the plateau at the high concentrations.

A comparison of the values of  $n$  for different parts of the curve shows low deviations from the mean for the model of Hill (21%) but larger ones for the models of Fechner (35%) and Stevens (61%). Similarly, for the model of Hill,  $C_{ip}$  values obtained using different parts of the curve or using the whole curve are close.

In agreement with observations made when modelling experimental data, the comparison among the different models, using the theoretical curve, leads to the conclusion that when a reduced range of concentrations is used, it is very difficult to fit the data correctly with any of the models. The model of Fechner can only be used in the middle of the range of stimulations but not near the threshold or saturation. When the concentrations used are near the threshold, the model of Stevens gives the best results, but its exponent is not representative of the whole range. If a larger range of concentrations is used, this exponent decreases dramatically, in agreement with published results (Poulton, 1968; Sauvageot, 1982). The model of Hill gives the best global results, but the range of concentrations used must be sufficient to include the  $C_{ip}$  value.

#### Sums of sigmoids

Assuming that the model of Hill is a general model for



**Table 4** Results of modelling on the theoretical curve of intensity versus concentration

Part of the curve	No. of exp. points	Concentration range <sup>a</sup>	Model	Parameter	Value	Standard error	Deviation (%)	R <sup>2</sup>	Ψ <sup>2</sup>
Whole	10	1–100000	Hill	$I_m$	111	4	4	0.987	0.017
				$I_o$	7.0	2.8	40		
				$n$	1.01	0.16	16		
				$C_{ip}$	752	124	16		
			Stevens	$I_o$	0		fixed	0.879	0.130
				$k$	13.2	3.6	27		
				$n$	0.20	0.03	15		
			Fechner	$k$	–14.6	6.7	46	0.908	0.099
				$n$	26.5	2.3	9		
Lower	10	1–1000	Hill	$I_m$	140	204	146	NS <sup>a</sup>	0.950
				$I_o$	6.1	4.2	69		
				$n$	0.84	0.56	67		
				$C_{ip}$	1321	4342	329		
			Stevens	$I_o$	4.7	3.8	81	WS	0.949
				$k$	1.01	0.99	98		
				$n$	0.59	0.14	24		
			Fechner	$k$	–5.1	6.8	133	NS	0.732
				$n$	17.6	3.8	22		
Middle	10	10–10000	Hill	$I_m$	124	15	12	0.988	0.015
				$I_o$	0.0		fixed		
				$n$	0.83	0.21	25		
				$C_{ip}$	965	327	34		
			Stevens	$I_o$	0		fixed	0.956	0.050
				$k$	5.7	1.6	28		
				$n$	0.33	0.03	9		
			Fechner	$k$	–45.9	8.6	19	0.946	0.061
				$n$	37.6	3.2	9		
Upper	10	100–100000	Hill	$I_m$	110	4	4	WS	0.978
				$I_o$	16.9	10.7	63		
				$n$	1.18	0.33	28		
				$C_{ip}$	925	259	28		
			Stevens	$I_o$	0		fixed	0.806	0.219
				$k$	20.7	6.4	31		
				$n$	0.16	0.03	19		
			Fechner	$k$	–34.3	14.2	41	0.895	0.118
				$n$	32.1	3.9	12		

<sup>a</sup>NS: not statistically significant; WS: weakly statistically significant.

describing stimulus–response in olfaction, we tried to find the relation between the parameters obtained with this model at a peripheral level and those at a psychophysical level. Considering that the electrical response of the olfactory receptors is well modelled by a Hill equation and that there is a summation of the signals at different levels, we assumed that the psychophysical response could result from the summation of the elementary sigmoidal responses of the receptors. Graphical representations were used to determine under which conditions, i.e. inside which range of variation of the parameters in equation (8), the sum of several sigmoids will remain a sigmoid.

Thus using equation (5), we built elementary sigmoids with a large domain of variations of  $K_m$ , a parameter related

to the affinity of the receptor toward the odorous compound (Table 5).

The determination of the domain of variation of  $K_m$  is based on the recent statements of Lancet *et al.* (1993) showing that affinities of a population of human olfactory receptors toward a ligand vary on a range of four logarithmic units and 85% of those affinities vary on a range of three logarithmic units. Moreover, they suggest that the distribution of  $K_m$  values follows a binomial law.

We considered two binomial distributions of the  $K_m$  of the elementary sigmoids, a large one with  $K_m$  from 10 000 to 1 and a smaller one with  $K_m$  from 100 to 1. Assuming that the intensity of response is one for a given elementary receptor, the  $V_m$  value of an elementary sigmoid indicates the number of receptors, with a given  $K_m$ , which have been

recruited. To simplify, the sums of the different  $V_m$  values were adjusted to 100 (Table 5). For each distribution, the same exponent value was used for each elementary response sigmoid, and calculations were made for eight cases, with  $n$  varying from 0.1 to 8. In each case, the sum of the elementary sigmoids was modelled with the model of Hill (equation 8 and Table 6).

In all cases, the sum of 3–5 sigmoids remains a sigmoid with a very good approximation (Figure 2). The resulting sigmoid is slightly asymmetric as argued by Laffort (1966). Very high determination coefficients (Table 6) were obtained when the sums were modelled using the model of Hill (equation 8).

The exponent of the model of Hill for the elementary curves had no impact on the  $C_{ip}$  of the modelled sum curves. However, it influenced dramatically the exponent of the resulting Hill curve (Table 6), which varies from a maximum of 0.7 (1.06 for a narrow binomial distribution) to a minimum of 0.1.

The parameter  $C_{ip}$  obtained when modelling psychophysical data may be seen as reflecting the sensibility of the

subject or the panel to a given substance. The parameter  $n$  would depend only on the distribution of the receptors sensitive to the considered compound.

Conclusion

The older psychophysical model proposed by Fechner gave, in all cases, poorer fits to experimental data than the three other models tested in this paper and should be avoided.

The model of Stevens gave a much better representation of experimental results than that of Fechner and was found to be better than hyperbolic ones when the data were taken near the threshold and covered only a small range of concentrations. However, the concentration range used to determine the parameters has a great influence on the parameter  $n$ . The study of a theoretical stimulus–response curve showed that the larger the concentration range, the lower will be the exponent. The power law may thus be reserved for data near thresholds or to odorous compounds whose physico-chemical properties do not allow to reach the inflection point of the stimulus response curve. Moreover, considering the great influence of the range of concentrations used to determine its parameters, this model should not be used in extrapolations.

The model of Beidler is more convenient as it takes into account both the threshold and the maximum intensity. Furthermore, correlations given by this model are often better than those obtained with the models of Fechner or Stevens. However, it assumes that  $n$  equals one, and it has been shown that it is not the case for all the compounds we tested. The model of Beidler can give more accurate values of  $I_m$ ,  $I_o$  and  $C_{ip}$  for compounds with  $n$  close to 1, as there is one parameter less to determine. However, it fails when exponents of the Hill equation are very different from one, such as for vanillin ( $n = 0.53$ ).

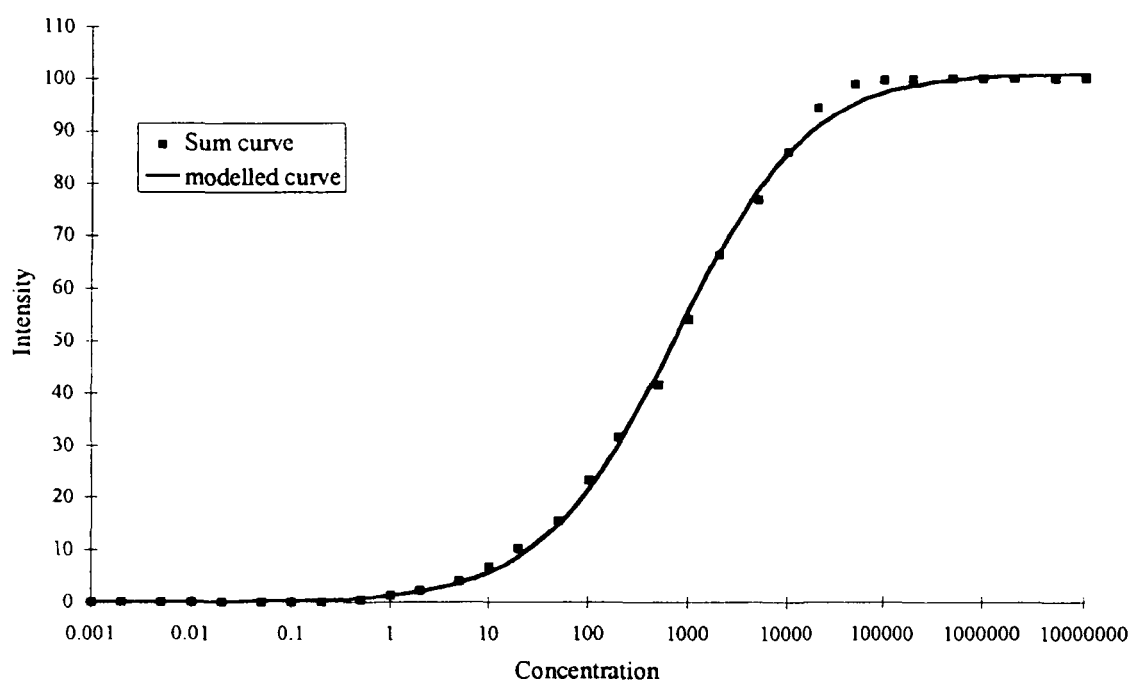
The model of Hill (equation 8) takes into account the theoretical sigmoidal shape of the stimulus–response

Table 5 Parameters of the elementary sigmoids

Large binomial distribution			
$V_{m1}$	27	$K_{m1}$	10000
$V_{m2}$	38	$K_{m2}$	1000
$V_{m3}$	24	$K_{m3}$	100
$V_{m4}$	8.7	$K_{m4}$	10
$V_{m5}$	2.3	$K_{m5}$	1
Narrow binomial distribution			
$V_{m1}$	59	$K_{m1}$	100
$V_{m2}$	33	$K_{m2}$	10
$V_{m3}$	8	$K_{m3}$	1

Table 6 Parameters of the different sum curves

	<i>n</i> of elementary sigmoids							
	8	3	2	1	0.6	0.3	0.2	0.1
Large binomial distribution of $K_m$								
$I_m$ of sum curve	101	101	101	101	101	101	100	100
$C_{ip}$ of sum curve	738	733	727	719	700	670	643	613
<i>n</i> of sum curve	0.70	0.68	0.66	0.56	0.44	0.27	0.19	0.10
$R^2$ regression	0.997	0.999	0.999	1.000	1.000	1.000	1.000	1.000
$R^2$ between data and modelling	0.993	0.997	0.999	1.000	1.000	1.000	1.000	1.000
Narrow binomial distribution of $K_m$								
$I_m$ of sum curve	101	101	101	100	100	100	100	100
$C_{ip}$ of sum curve	39	38	37	35	34	33	33	33
<i>n</i> of sum curve	1.06	1.02	0.96	0.74	0.52	0.29	0.20	0.10
$R^2$ regression	0.994	0.997	0.999	1.000	1.000	1.000	1.000	1.000
$R^2$ between data and modelling	0.988	0.995	0.998	1.000	1.000	1.000	1.000	1.000



**Figure 2** Modelling of the sum of elementary sigmoids with  $n = 2$  and  $K_m$  distributed on a large binomial variation range.

relation. The predicted intensity accounts for  $I_o$  (intensity of 'clean air') when the true odorous compound concentration is zero and tends toward  $I_m$  when the concentration increases.

Comparisons using a theoretical curve show that this model gives coherent values of the parameters over a variety of concentration ranges. However, when the range of concentrations is too small to include the  $C_{ip}$  value, the modelling is not statistically significant. Thus, to use this model, the concentration range must be as large as possible and include the inflection point of the stimulus–response curve.

Our study of the sums of elementary sigmoidal signals, using a statistical distribution of the affinities of receptors, pleads in favour of the sigmoidal shape of the human olfactory stimulus–response curve. Moreover, this study has shown that while  $I_o$  and  $I_m$  depend on the experimental conditions,  $C_{ip}$  and  $n$  seem to be more characteristic of the compound. In fact,  $C_{ip}$  and  $n$  do not depend on the concentration range or on the scale used to evaluate intensity.  $C_{ip}$ , expressed in concentration units, seems to reflect the sensitivity of the subject to the odorous compound, or an average sensitivity if a panel is considered. The parameter  $n$  might represent the distribution of the receptors sensitive to the considered compound and may reflect the processes of recruitment of receptors.

In conclusion, the data found in the literature are generally taken in the middle of the range of concentrations, that is, in the linear part of the sigmoid, and, in this part, all models are close to each other. However, if one wishes to

predict the intensity outside of this range, the model of Hill should be preferred, as more stable parameters and more realistic intensity values are obtained. The model of Hill, once adapted to olfaction problems, fits the data as well as or better than the other models. This is really a simple model, compatible with the recent models proposed in this field (Ben Lamine *et al.*, 1997), that can be easily applied to experimental data using computerized methods. Moreover, it enables the acquisition of a limited number of parameters which are characteristic both of odorous compounds and of sensorial analysis conditions. We suggest that it should be used more widely in quantitative studies of olfaction.

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