OLFACTORY ADAPTATION AND ODOUR LIKENESS

BY R. W. MONCRIEFF

From the Consulting Laboratory, 83 St Pancras, Chichester

The sense of smell is soon blunted; the perfume of a spray of honeysuckle can be powerful and enchanting at the first sniff, but as endeavour is made by repeated sniffs to prolong the enchantment, the smell becomes progressively weaker and less and less satisfying. As a measure of compensation, unpleasant odours also become less and less noticeable.

Adaptation is a characteristic of our sensory equipment, and if a stimulus for any one of the senses is kept constant the level of sensation wanes. Adaptation can ensue rapidly, often measurably in a fraction of a second and noticeably in a few seconds, and recovery from adaptation may be fast or slow according as the initial stimulus was weak or strong (Adrian, 1928). When adaptation is severe, olfactory 'fatigue' supervenes and it becomes impossible to smell a smell clearly and sometimes impossible to smell it at all for a time. Recovery from such fatigue is usually fairly rapid, unless exposure is habitual as it may be with some process workers. It is unlikely that olfactory fatigue is due to peripheral adaptation. Smell differs from the other senses in that it is discontinuous, there being a rest period between successive inspirations and in this rest time the nerves may recover from their refractory state. Olfactory fatigue is more likely to be due to adaptation of some more deep-seated part of the nervous system than the receptors and the fibres leading from them.

Adaptation as a basis of odour classification

That a smell rapidly reduces the sensitivity of the nose for that particular smell is incontestable, but the effect of smelling one smell on the sensitivity for other smells is less well understood. A person who is completely fatigued to hexamethylene diamine which has a putrescent ammoniacal smell so that he can no longer smell it at all will instantly smell methylamine which has a fishy ammoniacal smell, and just as easily he will be able to smell countless other smells. If sweet peas are smelt until the odour is apparently weak and then a rose is held to the nose, the rose scent is instantly perceived. But sweet pea

and rose smells are quite different and if the two successive smells are fairly
similar adaptation might be expected to ensue.

It has been accepted since the days of Zwaardemaker (1895) that the first
smell may cause some measure of adaptation so that the second smell will be less
keenly perceived. This belief was used as a basis for classifying odours by
Zwaardemaker (1895), it being one of the main justifications for his classi-
fication that any two odours from the same class would cause marked fatigue
for each other, whereas two odours from two different classes would cause no
fatigue, or only very little, for each other. Gamble (1896), reviewing the
results of his contemporaries, wrote: 'a subject whose organ is fatigued by the
continuous smelling of tincture of iodine can sense ethereal oils and ethers
almost or quite as well as ever, oils of lemon, turpentine and cloves but faintly,
and common alcohol not at all'. The same idea still persists, and Cheesman &
Mayne (1953) have described work on olfactory adaptation which had the
ultimate aim of classifying the odorants on a basis of the adaptation they
mutually induce. Just how the adaptation that a pair of smells will induce for
each other varies with the likeness of the two smells appears hitherto not to
have been defined.

Adaptation as a means of identifying fundamental odours

It has long been thought possible that all odours are built up from a small
number of fundamental odours. If this were so, and if two different smells
had one of these fundamental odours in common, it might be thought that
each would exert a high degree of adaptation for the other. So far, however,
no one has been able to point to a single one of the supposed fundamental
odours and perhaps it is more likely that there may be a small number of
types of receptors, and that similarity of patterns of stimulation of these may
give rise to similarity of smell. Each smell may well be unique, but there are
grounds for believing that many different smells may stimulate some of the
same receptors. Evidence has been presented (Moncrieff, 1955) that the
primary smell stimulus is the adsorption of odorant molecules on the olfactory
epithelium, and also (Moncrieff, 1954) that a process of *selective* adsorption
could account well for differences and similarities in odour quality. Adsorp-
tion is a process that is well known to be selective, but it is not so selective that
one adsorbent will pick up only one chemical entity; rather will it adsorb
a large number of chemicals, but some very much better than others. Two
odorants whose molecules were adsorbed in fairly similar, but not identical,
patterns would have smells that were much alike and might well produce
olfactory adaptation, each one for the other; but it is legitimate to inquire if
the degree of adaptation would ever approach closely to that which one
odorant will induce for itself. But if fundamental odours do exist then the
common possession of one of them might be expected to give rise to severe

adaptation even in a pair of unlike smells. If, however, each smell has an elementary individuality then severe adaptation would be expected only when the patterns of adsorption are similar and that is when the smells are similar; severe adaptation would never be encountered with a pair of smells not noticeably alike.

One purpose of the experiments that have been made was to find what degree of similarity of smell was necessary to induce marked adaptation, and whether for unlike substances the degree of adaptation could be comparable with that produced by one odorant for itself. It was hoped that the results would throw light on the usefulness of classifying odours by adaptation, on the existence or otherwise of fundamental odours, and perhaps on the mechanism whereby olfactory adaptation comes about.

METHODS

The odorant substances chosen for test were of two kinds:

(a) Odorants with quite dissimilar smells, namely: acetone, *iso*propanol, *n*-butanol, diacetone alcohol, cellosolve (monoethyl ether of ethylene glycol), and methanol. All the fifteen possible pairs of these were investigated.

(b) Pairs of odorants with similar smells, namely: *n*-butanol and *sec*-butanol; *n*-propanol and *iso*propanol; cellosolve and benzylamine; amyl acetate and butyl acetate; benzaldehyde and nitrobenzene; α-ionone and β-ionone.

It was necessary to make solutions of a range of concentrations, and the diluent employed was always distilled water except when the odorant was insoluble in water; for amyl acetate, butyl acetate, benzaldehyde, nitrobenzene and the ionones, the diluent used was propylene glycol (propane 1,2-diol). All dilute solutions were made up fresh twice each day from stock solutions.

The method was designed to yield for each pair of odorants a determination of: (a) the threshold concentration of each of the components of each pair after first having smelt water; (b) the threshold concentration of each component of the pair after self-adaptation; (c) the threshold concentration of each component of the pair after having first smelt the other. These determinations enable the enhancement of the threshold value of an odorant A by first smelling another odorant B to be determined and also the threshold enhancement of B by prior smelling of A. If there is considerable enhancement then one odorant causes adaptation for the other; if there is no enhancement or very little of threshold concentration, then there is correspondingly no, or very little, adaptation.

Observations were made somewhat on the lines described by Cheesman & Mayne (1953) by direct smelling of 20 ml. odorant in a wide-neck 200 ml. bottle. The subject sat on a stool near a slightly open window with eyes closed; the neck of a bottle containing water was just touched to the angle between his upper lip and his nose and the subject, as he felt the touch of the bottle, inspired once, deliberately but not especially deeply, whilst the bottle was held there. The bottle was removed and the subject breathed out; another bottle containing a dilute aqueous solution (for threshold determination) of one of the odorants was touched under his nose, and he inspired again. This time he said 'yes' or 'no' according as he could, or could not, smell the odorant; 'doubtful' responses were allowed but were not encouraged. Requests by the subject to have the test again were allowed only if the presentation of the test bottles had been faulty, for example, touched to the wrong place on the subject's nose or out of phase with his breathing; they were not allowed on the sole ground of indecision. If the odorant used was insoluble in water, then a solution in propylene glycol was used for the second sniff and pure propylene glycol, instead of water, for the first sniff. This series of tests gave the information necessary to find the threshold concentration of each odorant after first 'smelling' odourless water or nearly odourless propylene glycol.

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In the next series of tests the first bottle offered contained not the diluent (water or propylene glycol) but an undiluted odorant, and the second bottle, as before, contained a dilute solution of odorant. For purposes of homogeneous adaptation the odorant in the solution was the same as had been used pure in the first sniff; for example, the first sniff would be of pure acetone, the second of a dilute solution of acetone in water with the aim of finding the threshold concentration of acetone after prior smelling of acetone, i.e. adaptation with itself. In the third series of experiments the second bottle contained a solution of an odorant *B* different from the pure odorant *A* which had been used in the first sniff, and this method was designed to determine the threshold concentration of *B* after *A*.

Three subjects made tests; they were: R.W.M., male 52 years; S.L., female 17 years; S.T., female 17 years; and all three were known from previous work to have a reasonably uniform and normal sense of smell. Slight differences were known to exist; for example, R.W.M. was more sensitive to mercaptans and less sensitive to pyridine than the other two observers and during the trials described in this paper other slight differences emerged, but they were only slight. After every four tests the subject was rested for several minutes, usually by subject and tester exchanging their roles. In those tests involving the use of methanol it was found better to rest the subject for a few minutes after every single test. This was not necessary, as indicated by the reproducibility of results, with any of the other odorants used.

After a few pilot trials to obtain a rough idea of the threshold concentration of an odorant, a series of dilutions was prepared, some of them stronger and some weaker than the expected threshold concentration. Usually about six or eight such dilutions were prepared and they were offered to the subject to smell (*a*) after the previous inspiration had been of water, if the normal threshold concentration was being determined, or (*b*) after one of the undiluted odorants if the threshold concentration after adaptation was being determined. Each dilution was offered five times in random order and a bottle containing only water was also offered five times; this was a reliability check, and if the subject did not give at least four 'no's' out of the possible five for water his results were scrapped, he was given a period of training to distinguish the dilute solutions he was smelling from water and he was then re-tested. If the odorant was dissolved not in water but in propylene glycol, then pure propylene glycol, instead of water, was offered as the reliability check. Because interspersed in the test dilutions offered to the subject there were always tests of the diluent alone, the subject never knew whether the test solution he was smelling (with eyes closed) contained or did not contain any odorant, or whether it was likely to be a strong or a weak solution. These precautions had the effect of making the subject treat each sniff or smell on its own merits and so give an objective response. A professional pride developed among the observers of keeping a clean nil score on the diluent alone and additionally of smelling to a low threshold and this induced them to give their undivided attention to each test. About 2 months' practice was necessary before a satisfactory technique was developed. Thereafter the experiments described in this paper were spread over a period of 8 months and so time-consuming did we find this sort of work, that they took a large slice of our working day throughout this period.

RESULTS

Scoring was done on the basis of 1 point for a 'yes' response (subject could smell the test dilution offered), $\frac{1}{2}$ point for a 'doubtful', and nil for a 'no' response. The concentration, which is called PR_{50}, at which at least 50% of the possible positive responses is scored is ascertained and is taken as the threshold value.

The primary observations for acetone after adaptation with water, acetone, and *iso*propanol and for *iso*propanol adapted with water, *iso*propanol and acetone are given in full in Tables 1 and 2. These exemplify the method of

treating the results and show the spread of the results for each observer. The spread of the results was much the same when other pairs of odorants were smelt. The degree of agreement between the observers can more easily be seen from Table 3 in which the PR_{50} concentrations for each individual and for the group are shown. There is generally quite good agreement between the three observers.

TABLE 1. Responses to dilute aqueous solutions of acetone after adaptation with water, acetone and *iso*propanol

1st sniff adapting substance (100%)	2nd sniff concn. of test solution of acetone (%)	Responses to second sniff of subject			Percentage positive responses of group
		R.W.M.	S.L.	S.T.	
Water	0·10	+ + + + +	+ + + + +	+ + + + +	100
	0·08	+ + + + +	+ + + + +	+ + + + +	100
	0·06	+ + + + +	+ + ? + ?	+ + + + +	93
	0·05	+ + + ? +	+ − + − +	+ − − ? +	67
	0·04	+ − − − +	+ ? + + −	+ + + − −	57
	0·03	+ + + + +	? − + + +	+ + − ? −	73
	0·02	− − − + +	+ − − + −	− − − − −	27
	0·01	− ? − ? −	− − − − −	− − − − −	7
	0 (water reliability check)	− ? − − −	− − − − −	− − − − −	3
Acetone	8·0	+ + + − ?	+ + + + +	+ + + + +	90
	7·0	+ + − − +	+ + + + +	+ + + + +	87
	6·0	+ − + − +	+ + + + +	+ + + + +	87
	5·0	− + + − −	+ + + + +	+ + + ? −	70
	4·0	− − − − +	− − − + −	− − + − +	27
	0 (water reliability check)	− − − − −	− − − − −	− − − − −	0
*iso*Propanol	0·12	+ + + + +	+ + + + −	+ − + − +	80
	0·10	+ + − + +	+ − − + +	+ − − + +	67
	0·08	− − + + +	+ ? ? + +	− + − − −	53
	0·06	+ − + + +	− + ? + −	+ − − − −	50
	0·04	? + − − −	+ − − − −	− − − − −	17
	0 (water reliability check)	− + − ? −	− − − − −	− − − − −	10

When the study was extended to include *n*-butanol, diacetone alcohol, cellosolve and methanol, the experimental results that were obtained were as shown in Table 4. Group values are shown; they differed from individual values no more than those in Table 3. For convenience of comparison absolute concentrations are not given, but instead the value of threshold concentration (adapted)/threshold concentration (unadapted). All the six odorants so far used have quite different smells; no two could be said to resemble each other in smell. It was at this stage that there were introduced into the investigation pairs of odorants that had smells as similar as possible.

TABLE 2. Responses to dilute aqueous solutions of *iso*propanol after adaptation with water, *iso*propanol and acetone

1st sniff adapting substance (100%)	2nd sniff concn. of test solution of *iso*propanol (%)	Responses to second sniff of subject			Percentage positive responses of group
		R.W.M.	S.L.	S.T.	
Water	0·20	+ + + + +	+ + + + +	+ + + + +	100
	0·10	+ + + − +	+ + ? + +	− + − + ?	73
	0·07	− + − + +	+ + + + +	− − + − −	60
	0·05	+ ? − − −	− − − + −	− − − − −	17
	0 (water reliability check)	− − − − −	− − − + −	− − − − −	7
*iso*Propanol	2·3	+ ? + + +	+ + + + +	+ + + + −	90
	2·0	+ + + − +	+ + ? + +	+ + − + −	77
	1·7	− − ? + −	+ − + + −	+ − − + −	43
	1·4	+ − − − +	? + − + +	− − − − −	37
	1·2	− − + − −	− − + − −	− − − − −	13
	0 (water reliability check)	− − − − −	− − − ? −	− − − − −	3
Acetone	0·40	+ + + + +	+ + + + +	+ + + + +	100
	0·30	+ + + + +	+ − + + −	+ + − − +	73
	0·26	+ − ? − ?	− + ? + ?	− − + − −	40
	0·23	+ − − − −	− − ? + −	− − − + −	23
	0·20	? − − − −	− − ? − −	− − − − −	7
	0 (water reliability check)	− − − − −	− + − − −	− − − − −	7

TABLE 3. Comparison of different observers' adaptation results with acetone and *iso*propanol

1st sniff adapting substance (undiluted)	2nd sniff test substance in dilution	PR_{50} concentration (%) on 2nd sniff for			
		R.W.M.	S.L.	S.T.	Group
Water	Acetone	0·03	0·03	0·03	0·03
Acetone	Acetone	6·0	5·0	5·0	5·0
*iso*Propanol	Acetone	0·06	0·06	0·10	0·06
Water	*iso*Propanol	0·07	0·07	0·10	0·07
*iso*Propanol	*iso*Propanol	2·0	1·4	2·0	2·0
Acetone	*iso*Propanol	0·30	0·26	0·30	0·30

TABLE 4. Comparison of the effect of adaptation with homogeneous and heterogeneous pairs
(Data for homogeneous pairs are shown in heavy type.)

1st sniff adapting odorant	Threshold (times normal unadapted threshold), after having previously smelt adapting odorant, for test solution of					
	Acetone	*iso*Propanol	*n*-Butanol	Diacetone alcohol	Cellosolve	Methanol
Absolute threshold concn. (%)	(0·03)	(0·07)	(0·005)	(0·01)	(0·02)	(0·2)
Acetone	**170**	4	12	10	5	3·5
*iso*Propanol	2	**29**	20	3	4	2·5
n-Butanol	7	1·5	**200**	10	3	35
Diacetone alcohol	3·5	4	8	**100**	4	1·5
Cellosolve	6·5	3	4	10	**30**	5
Methanol	6·5	3	2	6	2·5	**10**

Tests with pairs having similar smells

The six pairs of odorants with similar smells were:

(*a*) *n*-Butanol and *sec*-butanol; their structural formulae are:

$$CH_3CH_2CH_2CH_2OH \qquad \begin{array}{c} CH_3CH_2 \\ CH_3 \end{array}\Big\rangle CH.OH$$

*n*-Butanol   *sec*-Butanol

The smell of *n*-butanol is like fusel oil, bitter, burnt and very persistent; that of *sec*-butanol is similar but astringent and not so 'round' and is slightly reminiscent occasionally of diethyl ether. Water was used as the diluent.

(*b*) *n*-Propanol and *iso*propanol; their structural formulae are:

$$CH_3CH_2CH_2OH \qquad \begin{array}{c} CH_3 \\ CH_3 \end{array}\Big\rangle CH.OH$$

n-Propanol   *iso*Propanol

The smell of *iso*propanol is the better known of the two; it is mainly spirituous, is reminiscent of thyme and slightly earthy; that of *n*-propanol lacks the suggestion of thyme and is sweeter and rather more like ethanol than is the smell of *iso*propanol. Nevertheless, the two smells are very similar. Water was used as the diluent.

(*c*) Cellosolve and benzylamine; their structural formulae are:

$$\begin{array}{c} CH_2OC_2H_5 \\ | \\ CH_2OH \end{array} \qquad \bigcirc\!\!-CH_2NH_2$$

Cellosolve   Benzylamine
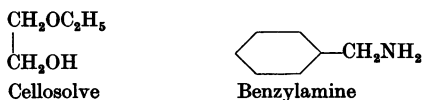
Both have smells that are fishy and bitter and they are fairly similar; that of cellosolve is the more intense and is more bloomy and sweeter, whereas that of benzylamine is sharper and a little spicy. Water was used as the diluent.

(*d*) Amyl acetate and butyl acetate; their structural formulae are:

$$CH_3CH_2CH_2CH_2CH_2OCOCH_3 \qquad CH_3CH_2CH_2CH_2OCOCH_3$$

Amyl acetate   Butyl acetate

Their smells are both of 'pear drops' and are so similar that practised smellers did not find it easy to distinguish between them. Amyl acetate has the more persistent smell, and butyl acetate has a slightly sharper higher note. Propylene glycol, which has only a negligible smell, was used as the diluent.
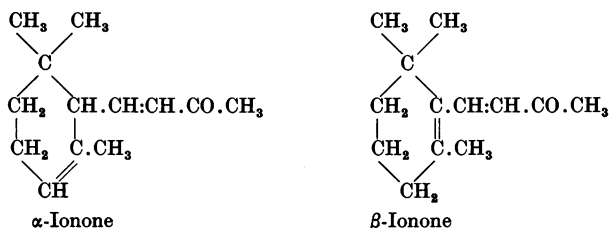
(*e*) Benzaldehyde and nitrobenzene; their structural formulae are:

$$\bigcirc\!\!-CHO \qquad \bigcirc\!\!-NO_2$$

Benzaldehyde   Nitrobenzene

Both smell of almonds. The author had no difficulty in distinguishing between them by a process of association, by keeping in mind that benzaldehyde was

nutty and that nitrobenzene was reminiscent of a students' organic chemistry laboratory. Two technicians who were hitherto unfamiliar with nitrobenzene had some difficulty at first in distinguishing between the two, and the smells are really very similar. Propylene glycol was used as the diluent.

(f) α-Ionone and β-ionone; their structural formulae are:

$$
\begin{array}{ll}
\underset{\text{α-Ionone}}{
\begin{array}{c}
CH_3 \quad CH_3 \\
\backslash \quad / \\
C \\
/ \quad \backslash \\
CH_2 \quad CH.CH{:}CH.CO.CH_3 \\
|\qquad\ | \\
CH_2 \quad C.CH_3 \\
\backslash \quad /\!/ \\
CH
\end{array}
}
&
\underset{\text{β-Ionone}}{
\begin{array}{c}
CH_3 \quad CH_3 \\
\backslash \quad / \\
C \\
/ \quad \backslash \\
CH_2 \quad C.CH{:}CH.CO.CH_3 \\
|\qquad\ \| \\
CH_2 \quad C.CH_3 \\
\backslash \quad / \\
CH_2
\end{array}
}
\end{array}
$$

Both smell of violets, and except to a trained perfumer their smells are very similar. That of the α-isomer is a little lighter and sweeter and the β-isomer is slightly woody. The odours of both are persistent. A good deal of difficulty was experienced at first in separating the faint woody odour of very dilute solutions of β-ionone from the slightly woody odour of the propylene glycol. This diluent, smelt alone, seemed to be nearly odourless and it was only whilst we were using the ionones that its own odour became troublesome. The trouble was overcome by practising to gain experience; this practice continued for about 2 hr on each of 4 successive days.

The experimental results obtained with the six pairs of similar odorants were as shown in Table 5.

DISCUSSION

Examination of the results in Tables 1 and 2 shows that there is a progressive increase in the percentage of positive responses to test odours as their concentration is increased; generally the rate of increase is fairly uniform. Occasional anomalies are to be seen as, for example, in Table 1 where 0·03 % acetone has a higher score than 0·04 %, both after water has been 'smelt' first; such discrepancies occur only between concentrations that are close together and they are relatively rare.

Agreement between individuals

It can be seen from Table 3 that there is good agreement between the three observers; in no case is the threshold value for one observer so much as double that for another observer. The agreement between the individuals is not so good in the data in Table 5 which relates to pairs of substances with very similar odours; the differences between observers are greater when the odorants are very similar than when they are different. The maximum differences to be found between any two of the observers is represented by a factor of 10 times, and when it is remembered that these smell tests with very similar odorants

probably represent as severe a test as could be devised, it is the over-all uniformity between the observers' results, rather than the differences between them, which seems to be remarkable. That a nearly similar smell does cause confusion in the detection, one breath later, of another smell is a clear indication that there are not exclusive receptor systems for each and every odorous chemical entity; similar smells of different chemicals clearly share at least a part of the olfactory apparatus.

TABLE 5. Responses to test odorants after adaptation with a very similar smell

1st sniff adapting odorant (undiluted)	2nd sniff test odorant	PR_{50} concentration (%) of test odorant for observer			
		R.W.M.	S.L.	S.T.	Group
Water	n-Butanol (in water)	0·005	0·01	0·005	0·005
n-Butanol	n-Butanol (in water)	1·0	1·4	0·8	1·0
sec-Butanol	n-Butanol (in water)	0·06	0·03	0·03	0·06
Water	sec-Butanol (in water)	0·005	0·003	0·005	0·005
n-Butanol	sec-Butanol (in water)	0·03	0·05	0·03	0·03
sec-Butanol	sec-Butanol (in water)	0·2	0·2	0·4	0·2
Water	n-Propanol (in water)	0·1	0·2	0·1	0·2
n-Propanol	n-Propanol (in water)	0·7	0·7	1·0	0·7
isoPropanol	n-Propanol (in water)	0·7	0·2	0·3	0·5
Water	isoPropanol (in water)	0·07	0·07	0·1	0·07
n-Propanol	isoPropanol (in water)	0·2	0·4	0·3	0·2
isoPropanol	isoPropanol (in water)	2·0	1·7	2·0	2·0
Water	Cellosolve (in water)	0·04	0·04	0·02	0·02
Cellosolve	Cellosolve (in water)	0·6	0·6	0·6	0·6
Benzylamine	Cellosolve (in water)	0·05	0·05	0·05	0·05
Water	Benzylamine (in water)	0·5	0·3	0·2	0·3
Cellosolve	Benzylamine (in water)	0·5	0·7	0·5	0·5
Benzylamine	Benzylamine (in water)	0·5	0·7	0·2	0·5
Propylene glycol	Amyl acetate (in propylene glycol)	0·002	0·002	0·002	0·002
Amyl acetate	Amyl acetate (in propylene glycol)	0·5	0·5	0·05	0·3
Butyl acetate	Amyl acetate (in propylene glycol)	0·3	0·3	0·1	0·3
Propylene glycol	Butyl acetate (in propylene glycol)	0·03	0·03	0·03	0·03
Amyl acetate	Butyl acetate (in propylene glycol)	0·3	0·5	0·5	0·4
Butyl acetate	Butyl acetate (in propylene glycol)	0·5	0·5	0·7	0·5
Propylene glycol	Benzaldehyde (in propylene glycol)	0·03	0·05	0·05	0·05
Benzaldehyde	Benzaldehyde (in propylene glycol)	0·5	0·7	0·5	0·5
Nitrobenzene	Benzaldehyde (in propylene glycol)	0·05	0·1	0·2	0·1
Propylene glycol	Nitrobenzene (in propylene glycol)	0·05	0·05	0·1	0·05
Benzaldehyde	Nitrobenzene (in propylene glycol)	0·4	1·0	0·3	0·4
Nitrobenzene	Nitrobenzene (in propylene glycol)	0·4	0·4	1·0	0·5
Propylene glycol	α-Ionone (in propylene glycol)	0·05	0·05	0·01	0·05
α-Ionone	α-Ionone (in propylene glycol)	1·0	2·0	1·5	1·5
β-Ionone	α-Ionone (in propylene glycol)	0·3	0·7	0·3	0·3
Propylene glycol	β-Ionone (in propylene glycol)	0·3	0·3	0·1	0·3
α-Ionone	β-Ionone (in propylene glycol)	0·7	1·0	1·5	1·0
β-Ionone	β-Ionone (in propylene glycol)	0·5	1·0	1·5	1·0

Homogeneous and heterogeneous adaptation

The data in Table 3 indicate that homogeneous adaptation is much more powerful than heterogeneous. Whereas the threshold concentration for acetone is only doubled by a previous sniff of pure *iso*propanol, it is raised some 170 times by a previous sniff of acetone; although the threshold concentration of

*iso*propanol is raised some 4 times by previously smelling acetone, it is raised nearly 30 times by adaptation with *iso*propanol itself. The figures are of the same kind for each of the three observers. More light on this tendency for self-adaptation to be much more powerful than heterogeneous adaptation is shed by Table 4. For five of the six odorants the threshold concentration is enhanced much more by *self*-adaptation than by adaptation with any of the other odorants. The sixth odorant, methanol, is exceptional; whereas the threshold concentration after self-adaptation is 10 times the normal threshold, it is 35 times the normal threshold after adaptation with *n*-butanol.

Consideration of the data in Table 4 shows that self-adaptation has more influence than heterogeneous adaptation on the threshold concentration in thirty-five pairs out of thirty-six considered and has less influence once. Methanol, which is concerned in the exceptional instance, had a weaker smell than the other odorants, and it was for this reason that it was introduced into the investigation. Early results with several different odorants all showed that self-adaptation caused a much greater rise in the threshold concentration than did heterogeneous adaptation, but it seemed unlikely that such a relationship would hold for pairs consisting of one weak and one strong odorant. Evidently it does not. But wherever the two components of a pair are of somewhat similar strength, then self-adaptation raises the threshold concentration several times more, and sometimes 50 times more, than does adaptation with a different odorant. These findings made it all the more interesting to see what would happen when the two components of a pair had very similar odours. In such a case would heterogeneous adaptation have as great or nearly as great an effect as self-adaptation? The first pair (Table 5), *n*-butanol and *sec*-butanol, behave as if their likeness is of little account; whereas self-adaptation of *n*-butanol raises the threshold concentration some 200 times, adaptation with *sec*-butanol raises the threshold concentration of *n*-butanol by only 12 times; similarly, self-adaptation of *sec*-butanol raises its threshold by 40 times, whereas adaptation with *n*-butanol raises it only 6 times. But the results are very different for the next pair, *n*-propanol and *iso*propanol. Self-adaptation of *n*-propanol raises its threshold concentration by 3·5 times but adaptation with *iso*propanol raises it nearly as much, 2·5 times; whereas self-adaptation of *iso*propanol raises its threshold concentration nearly 30 times, adaptation with *n*-propanol raises it only 3 times.

It may seem odd that of a pair A and B, adaptation with A may have a much greater effect on the threshold concentration of B, than adaptation with B has on that of A. This oddness is not confined to the propanols; for example, adaptation with benzaldehyde raises the threshold of nitrobenzene 4 times as much as adaptation with nitrobenzene raises the threshold of benzaldehyde. It can be interpreted readily on the basis that the primary stimulus consists of adsorption of the odorant molecules on the olfactory membrane. The

spatial patterns of adsorption will be much the same, but not exactly the same, for A and for B. If A, for example, is adsorbed on 90% of the receptor sites that B is, and is additionally adsorbed on a number of sites that B is not adsorbed on at all, and this number is equal to 50% of the total number of sites on which B is adsorbed, then A will exert much more adaptation for B, than B for A. Adaptation with A excites (say) 140 receptors, and then when B takes its place only 10 of the 100 receptors it is adsorbed on have not just been activated; but when adaptation is made with B first and then A takes its place, some 50 new receptors come into play, so that the adaptation is less severe.

Table 5 includes adaptation data for twelve pairs of similar odorants (counting AB as different from BA) and of these twelve pairs, nine show heterogeneous adaptation to be lower than self-adaptation, and the other three show it to be about the same.

These results show that it is quite possible to secure a high degree of adaptation for one substance with another which is a separate chemical entity, but they also show that the degree of similarity of smell has to be high, and that in fact it is only when two substances have smells so similar that it is possible to confuse them, that a very high degree of heterogeneous adaptation can take place.

Coefficient of odour likeness

The results of adaptation tests, similar to those described, enable a numerical assessment to be made of the likeness of two smells. The basis of this assessment is that two perfectly like odours would cause equal adaptation for each other, they would enhance the threshold concentration each for the other by the same number of times. In assessing the likeness of A and B account must be taken both of the adaptation caused by A on the threshold concentration of B and of that caused by B on the threshold concentration of A. If for two substances A and B

c_{OA} is the threshold concentration of A without previous adaptation (or with only water or another inodorous liquid),
c_{OB} is the similar threshold concentration of B,
c_{AA} is the threshold concentration of A after adaptation with itself,
c_{BB} is the similar self-adaptation threshold concentration of B,
c_{BA} is the threshold concentration of A after adaptation with B,
c_{AB} is the threshold concentration of B after adaptation with A,

then the threshold enhancement of A caused by self-adaptation is c_{AA}/c_{OA} and that for B is c_{BB}/c_{OB}. The threshold enhancement of A caused by B is c_{BA}/c_{OA} and that for B caused by A is c_{AB}/c_{OB}. The more closely these last two adaptation factors approach to the first two self-adaptation factors

the greater will be the likeness of the odours of A and B. We can, therefore, take the product of these two ratios, and then to regain the correct dimensions take the square root and so express the likeness, L, as

$$\left(\frac{{}^{C}BA/{}^{C}OA \cdot {}^{C}AB/{}^{C}OB}{{}^{C}AA/{}^{C}OA \cdot {}^{C}BB/{}^{C}OB}\right)^{\frac{1}{2}},$$

so that

$$L=\left(\frac{{}^{C}BA \cdot {}^{C}AB}{{}^{C}AA \cdot {}^{C}BB}\right)^{\frac{1}{2}}.$$

For n-propanol and *iso*propanol we can substitute in this expression

$$L=\left(\frac{0\cdot5 \cdot 0\cdot2}{0\cdot7 \cdot 2\cdot0}\right)^{\frac{1}{2}}=0\cdot27.$$

The pair of substances that were found to be closest in smell, viz. amyl and butyl acetates, have an 'L' value of 0·89. The corresponding coefficients of likeness for the other pairs of substances used in this investigation have been similarly derived and are shown in Table 6.

TABLE 6. Coefficients of likeness of certain pairs of smells

		Threshold concentration (%) for				Coefficient of likeness $\left(\frac{{}^{C}BA \cdot {}^{C}AB}{{}^{C}AA \cdot {}^{C}BB}\right)^{\frac{1}{2}}$	Characteristics (adsorption)	
		A, after adaptation with		B, after adaptation with				
Smell A	Smell B	A $({}^{C}AA)$	B $({}^{C}BA)$	A $({}^{C}AB)$	B $({}^{C}BB)$		A	B
n-Butanol	*sec*-Butanol	1·0	0·06	0·03	0·2	0·09	0 1 4 0 9	1 2 3 2 9
n-Propanol	*iso*Propanol	0·7	0·5	0·2	2·0	0·27	0 0 0 1 6	0 0 1 1 5
Cellosolve	Benzylamine	0·6	0·05	0·5	0·5	0·29	1 0 1 2 3	2 1 1 2 2
Amyl acetate	Butyl acetate	0·3	0·3	0·4	0·5	0·89	6 5 5 7 8	7 6 6 7 8
Benzaldehyde	Nitrobenzene	0·5	0·1	0·4	0·5	0·40	0 2 7 1 6	0 2 7 2 4
α-Ionone	β-Ionone	1·5	0·3	1·0	1·0	0·45	1 1 2 2 7	1 1 2 2 4
Acetone	*iso*Propanol	5·0	0·06	0·3	2·0	0·04	4 3 7 8 9	0 0 1 1 5
Acetone	n-Butanol	5·0	0·2	0·06	1·0	0·05	4 3 7 8 9	0 1 4 0 9
Acetone	Diacetone alcohol	5·0	0·1	0·1	1·0	0·04	4 3 7 8 9	0 0 2 1 7
Acetone	Cellosolve	5·0	0·2	0·1	0·6	0·08	4 3 7 8 9	1 0 1 2 3
Acetone	Methanol	5·0	0·2	0·7	2·0	0·12	4 3 7 8 9	1 2 4 3 4
*iso*Propanol	n-Butanol	2·0	0·1	0·1	1·0	0·07	0 0 1 1 5	0 1 4 0 9
*iso*Propanol	Diacetone alcohol	2·0	0·3	0·03	1·0	0·07	0 0 1 1 5	0 0 2 1 7
*iso*Propanol	Cellosolve	2·0	0·2	0·08	0·6	0·12	0 0 1 1 5	1 0 1 2 3
*iso*Propanol	Methanol	2·0	0·2	0·5	2·0	0·16	0 0 1 1 5	1 2 4 3 4
n-Butanol	Diacetone alcohol	1·0	0·04	0·1	1·0	0·06	0 1 4 0 9	0 0 2 1 7
n-Butanol	Cellosolve	1·0	0·02	0·06	0·6	0·04	0 1 4 0 9	1 0 1 2 3
n-Butanol	Methanol	1·0	0·01	7·0	2·0	0·19	0 1 4 0 9	1 2 4 3 4
Diacetone alcohol	Cellosolve	1·0	0·1	0·08	0·6	0·12	0 0 2 1 7	1 0 1 2 3
Diacetone alcohol	Methanol	1·0	0·06	0·3	2·0	0·09	0 0 2 1 7	1 2 4 3 4
Cellosolve	Methanol	0·6	0·05	1·0	2·0	0·20	1 0 1 2 3	1 2 4 3 4

Four threshold concentrations must be determined in order to estimate the coefficient of likeness of a pair of substances; it is not necessary to measure their individual threshold concentrations without adaptation.

Examination of Table 6 shows that the coefficients of likeness for five of the first six pairs, which were originally chosen because they had very similar smells, are a great deal higher than those for any of the other fifteen pairs. The one pair, amyl and butyl acetates, that are almost indistinguishable have an outstandingly high likeness coefficient of 0·89, the two ionones which are very close olfactorily have a coefficient of likeness of 0·45, and nitrobenzene and benzaldehyde, well known to have similar smells, have a coefficient of 0·40. Next come the two propanols and cellosolve and benzylamine, both pairs having coefficients approaching 0·3 and not really sufficiently alike to be confused. The low likeness coefficient of *n*- and *sec*-butanols was unexpected; their smells are not so dissimilar, one would think, as to warrant a coefficient as low as 0·09. All the other twenty pairs have yielded coefficients of likeness which are fairly in line with organoleptic appraisal.

Comparison of odour likeness values derived by two methods

The coefficients of likeness of pairs of odours determined by their cross- and self-adaptation can be compared with the odour characteristics of the same odorants determined by their behaviour towards adsorbents as described in an earlier paper (Moncrieff, 1954). This method enabled a number, or rather a group of digits, to be assigned to an odorant to represent its adsorption behaviour; for example, the number 0 1 4 0 9 for *n*-butanol indicated that it was adsorbed very rapidly (0) by active carbon, nearly as rapidly (1) by silica gel, relatively slowly (4) by activated alumina, very rapidly (0) by fuller's earth and hardly at all (9) by vegetable fat. The lower the number, the faster the rate of adsorption. The adsorption characteristics of some of the odorants that had been used in the adaptation experiments were known; the others had to be determined. For example, α-ionone was known from earlier work to have the characteristics 1 1 2 2 7 and those of β-ionone were found to be 1 1 2 2 4. The only significant difference is in the behaviour of the two isomers towards fat; towards carbon, silica gel, alumina and fuller's earth they behave one like the other. (When this paper was submitted for publication it was pointed out to me that the data in it show a fairly strong correlation between the threshold enhancement due to self-adaptation and the index for the degree of adsorption by fat.) Two substances with unlike odours have quite different characteristics, e.g. acetone 4 3 7 8 9 and benzaldehyde 0 2 7 1 6, but benzaldehyde is not very different from nitrobenzene, 0 2 7 2 4, to which it has a close olfactory resemblance. How do such resemblances compare with the coefficients of likeness already found for twenty-one pairs of odorants? The comparison is to be seen in Table 6, which discloses some examples of interesting

degrees of correspondence. Thus of the six pairs which were picked as having similar odours (top six in the table) four pairs have very similar adsorption characteristics, namely, (1) the propanols, (2) amyl and butyl acetates, (3) benzaldehyde and nitrobenzene, and (4) the ionones. Furthermore, these four have high coefficients of likeness. The fifth pair, cellosolve and benzylamine, have similar although not quite so similar adsorption characteristics and have a high coefficient of likeness. From the twenty-one pairs of odorants in Table 6 those five pairs that have the highest coefficients of likeness have also the most similar odour characteristics as measured by adsorption.

Thus two methods of assessing odour likeness depending on (1) olfactory adaptation, and (2) times of adsorption on different adsorbents, both pick out the same five pairs from twenty-one pairs. The nose, i.e. direct smelling, did almost exactly the same thing in picking out six pairs which included these five; the nose also picked out n-butanol and sec-butanol. The otherwise good correspondence of the three methods, (1) direct smelling, (2) adaptation, (3) adsorption, in picking out the pairs of smells that are alike not only suggests that methods (2) and (3) of determining likeness are both sound, but also supplies confirmatory evidence for the view that adsorption is the primary olfactory stimulus and that *selectivity* of adsorption is the basis of quality discrimination of smells.

Mechanism of olfactory adaptation

There is considerable evidence from earlier work that olfactory fatigue is not entirely peripheral, but is mainly or perhaps wholly central in origin. Thus, Zwaardemaker knew that unilateral stimulation could cause bilateral fatigue, and came to the conclusion that 'olfactory fatigue has to be considered as a synaptic phenomenon' (Noyons, 1931). Elsberg (1935), who pointed out that there was anatomical evidence from Luciani & Seppilli (1886) and from Cajal (1909) that cells on either side of the nose were connected to both sides of the olfactory lobe of the brain, concluded from his own experiments that 'the structures concerned in fatigue of the sense of smell are in the brain itself, and in the parts of the brain that have to do with the perception and the memory of olfactory impressions'.

Adrian (1950) has suggested from observations on lightly anaesthetized rabbits that the olfactory bulb is in a constant state of electrical activity, that olfactory perception is due to the electrical signals from the receptors disorganizing the intrinsic electrical activity of the bulb; 'ultimately, however, the intrinsic activity builds up again...swamping the transmission of the olfactory signals'. Significantly 'there is no sign of failure of the receptors under repeated stimulation at each breath', and furthermore under deep anaesthesia the intrinsic activity of the bulb is entirely suppressed and the olfactory stimuli give persistent electrical discharges in the bulb at each

breath, without adaptation for as long as an hour. Adrian (1953) has found that there is specificity of sensitivity in the mitral cells to which groups of olfactory receptors are connected; one will be much more sensitive than its neighbours to acetone, another to amyl acetate and so on.

If the view is accepted that normally there is constant electrical activity in the olfactory nervous system, and that perception of odour depends on disturbance of the normal activity by the reception of impulses from the receptors and that adaptation is due to the normal activity adjusting itself to the new conditions and regaining control, then it follows that self-adaptation should be severe. So, in our experiments we found it to be. The other finding that different chemical entities with extremely similar smells could cause a degree of adaptation approaching self-adaptation shows that parts of the olfactory apparatus that they use have much that is common, and makes it unlikely that there are parts of it that are so specific in their sensitivity that they react to only one chemical entity. The finding that there is a not inconsiderable degree of adaptation exerted by one substance such as *iso*propanol for another such as cellosolve with a quite dissimilar smell suggests that there is a proportion, if only a small proportion, of the olfactory apparatus which is used by all smells; although the smells that we used were very diverse we found no pair that did not exert some adaptation one for the other.

SUMMARY

1. Experiments on olfactory adaptation have been made, to investigate the effect of likeness of pairs of smells on their mutual adaptation effects.

2. Self-adaptation, i.e. using the same odorant for adaptation and for test smells, is as a rule very much greater than heterogeneous adaptation, i.e. using one odorant for adaptation and another for test smells.

3. The relative slightness of the degree of adaptation found in most pairs of unlike odorants makes the classification of smells into a small number of groups appear impossible, although adaptation might provide a means of classifying them into a very large number (probably of thousands) of classes. The same finding makes it very unlikely that there is a small number of fundamental smells, although it does not exclude the possibility that there may be a small number of types of olfactory receptors.

4. Only when two odorants have very similar smells do they mutually cause a high degree of adaptation.

5. The adaptation caused by A (of a pair of odorants A and B) for B may be different from that caused by B for A.

6. If two different chemical entities, e.g. amyl and butyl acetates, do have smells which are so similar that they are easy to confuse, then the degree of adaptation one for the other will approach that of self-adaptation of either.

7. From a knowledge of the cross-adaptation and self-adaptation of a pair of odorants, a property defined as 'coefficient of likeness' can be derived. For two smells exactly the same, the coefficient of likeness would be unity; for amyl and butyl acetates it is 0·89, for α- and β-ionones it is 0·45 and for benzaldehyde and nitrobenzene it is 0·40. For those pairs of smells investigated that were not noticeably alike the coefficient of likeness varies from 0·04 to 0·20.

8. The likeness of a pair of smells determined by this adaptation method agrees well with the likeness determined by comparison of adsorption characteristics.

9. This agreement supplies further evidence that the primary olfactory stimulus is a process of adsorption and that quality discrimination of smells depends on selectivity of adsorption of odorants on the olfactory receptors.

10. The finding that different chemical entities with almost indistinguishable smells exert a high degree of mutual adaptation has a bearing on contemporary ideas of olfactory stimulation.

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