The ability to predict is a more stringent test of a theory than the ability to correlate existing knowledge. The success of the vibrational hypothesis in both predicting and correlating lends confidence to a belief that the relationship between alarm pheromone activity and molecular vibration is indeed a valid general principle.

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Stereochemical and Vibrational Theories of Odour

IN a recent communication[1] and accompanying editorial comment[2], it has been asserted that Amoore's stereochemical theory of odour is validated (and the vibrational theory discredited) by a correlation coefficient of 0.90 between subjectively estimated odour similarities of a number of substances to benzaldehyde (taken as a standard), and a computer-generated scale of molecular shape resemblances. These claims can be questioned on several grounds.

The computer-generated molecular shape factor, which is derived from three orthogonal silhouettes, is used to represent the whole stereochemical aspect of the molecule by a single 3- or 4-digit number, it must surely be inappropriate to reduce anything as intricate and variable as a molecular shape to a single number. In fact, Amoore's procedure would assign exactly the same numerical parameter to very many different three-dimensional profiles[3]. The richness and variety of olfactory sensations calls for a degree of stimulus specificity that is incompatible with so simplistic a specification of the stimulus.

Several perfumers have stated that no two pure compounds have entirely similar and completely indistinguishable odours, and this assertion is based on experience with as many as 15,000 substances, not including mixtures. There must therefore be at least this number of discriminable sensations, and it seems impossible to generate such a number with only seven primary shapes. Subtle variations in the sensation demand equally subtle variations in the stimulus, and this means that olfactory specificity cannot depend on a simple molecular attribute such as the length or cross-section of the molecule.

It is also questionable whether Amoore's odour similarity numbers are as significant a parameter as the verbal descriptions given by expert perfumers[4]. Consider the examples of Table 1.

The details of the molecular parameters underlying this amount of specificity are not known, but a theory of olfaction must develop towards that end. It does not seem possible for the stereochemical theory to achieve this in any of the forms it has taken hitherto.

In his correlation between odour similarity values and the stereochemical similarities, Amoore's estimates of odour similarity are on a scale from 0 for no similarity to 8 for extreme similarity. Examination of his data shows 14 out of 26 similarity values less than 2. It is not clear how far an approximation to "no similarity" is equivalent to an approach to "complete dissimilarity" which would embrace the whole remaining gamut of odours from fried fish to sweet lavender. With more than half his points in this equivocal category, Amoore's correlation loses much of its significance.

Table 1 Comparison of Amoore's Index and Subjective Assessments of Stereochemically Similar Compounds

Compound	Amoore's odour similarity to benzaldehyde	Perfumers' verbal description
Benzaldehyde (standard)	7.14	Bitter almond
m-Ethylbenzaldehyde	1.34	Bitter almond, weak trace of sassafras
m-tert-Butylbenzaldehyde	1.40	Cumin, strong note of carrot
p-Ethylnitrobenzene	2.17	Sassafras, weak note of cumin

It is necessary to remember, too, that a correlation of "A" with "B" (for example, "people who own Rolls Royce automobiles never develop scurvy") does not necessarily signify a cause-and-effect relation. They may be co-causal or associated.

As an illustration of this, it can be shown that Amoore's odour similarity values have a correlation coefficient of 0.85 with the square root of the molecular weight, and of 0.92 with the cube root of the parachor. (The parachor, P, is a molecular volume with an allowance for self-compression by intermolecular attraction[5]. As the cube root of volume is length, $P^{1/3}$ is an approximation to the molecular diameter.) Indeed, a correlation coefficient of 0.84 can be shown with the lengths of the compounds names.

Contrary to Amoore's claim that the only "realistic" way to compare the vibrational and stereochemical theories is to compute correlation coefficients with his odour similarity numbers, it seems preferable to compare the theories on their ability to predict previously unknown or unsuspected phenomena. The vibrational theory has met this challenge in at least three different ways: the successful prediction of a "green" type of odour on the basis of infrared spectra[6], the successful prediction of insect (wasp) attractancy in some saturated and aromatic esters[7] when all previously known wasp attractants were unsaturated aliphatic esters[8]; and the prediction of an "anti-attractant" effect when certain substances, not themselves repellent, were added to known insect lures[9].

This kind of test is the most stringent and significant way to obtain "a direct measure of which theory fits the olfactory data more precisely".

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