cent per deg. C, whereas the oxygen reduction current shows no temperature dependence.

These electrodes have been successfully used in tissues over the past year.

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[1] Clark, jun., L. C., *Trans. Amer. Soc. for Art. Int. Organs*, **2**, 41 (1956).
[2] Evans, N. T. S., and Naylor, P. F. D., *J. Polarog. Soc.*, No. 2, 26 (1960).
[3] Bartels, H., Reinhardt, W., and Bürger, H., *Naturwiss.*, **46**, 672 (1959).
[4] Bartels, H., and Reinhardt, W., *Pflüg. Arch. ges. Physiol.*, **271**, 105 (1960).
[5] Naylor, P. F. D., and Evans, N. T. S., *J. Polarog. Soc.*, No. 2, 46 (1960).
[6] Cowell, T. K., and Styles, P. R., *J. Polarog. Soc.*, No. 2, 49 (1960).

Stereochemical Theory of Olfaction

IN his recent article on this subject J. E. Amoore[1] ascribes the odours of substances to the size and shape of their molecules: the olfactory epithelium, he suggests, contains receptor sites of definite shapes and dimensions, and a substance with a molecule of configuration appropriate to fit into one of these sites will have one of the primary odours.

It is well known that some people are unable to detect the odours of certain substances: hydrogen cyanide is a case in point, many being unable to detect it. In fact, a few years ago, R. L. Kirk and N. S. Stenhouse[2] showed that ability to detect it was inherited, a sex-linked recessive gene being possibly involved. There are also other odours (such as vanilla, violets, etc.) which cannot be detected by everybody. In the case of hydrogen cyanide there is a further complication. Those who can detect it describe it as having an almond odour. The same kind of odour, though different in degree, is reported for benzaldehyde and nitrobenzene: however, people who are unable to detect hydrocyanic acid can, I believe, detect both the latter substances.

It would be of interest to hear how these phenomena can be fitted into Amoore's theory. In his article, he refers to the almond odour but not in the present connexion.

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[1] Amoore, J. E., *Nature*, **198**, 271 (1963).
[2] Kirk, R. L., and Stenhouse, N. S., *Nature*, **171**, 698 (1953).

FULLMAN (preceding communication) has raised the important question of how cases of partial anosmia can be fitted into my stereochemical theory of olfaction[1]. Unfortunately, the question cannot be answered as succinctly as it can be posed, because I have no single comprehensive answer. Each chemical example of partial anosmia will probably need special consideration.

I would anticipate that, by analogy with colour-blindness, certain individuals might be deficient in one type of receptor (or more), and hence lack the ability to perceive a whole class of primary odours. This kind of anosmia has been reported to appear artificially during recovery from vitamin A deficiency[2], and during recovery from accidental damage to the olfactory area by an alcoholic solution of gymnemic acid[3]. The majority of reported anosmias, however, involve not large classes of odours but circumscribed families of chemicals, or even single compounds, as pointed out by Fullman.

Where a family of chemicals cannot be perceived by a subject, it could be suggested that his receptor sites for the corresponding primary odour have an abnormal shape. For example, Guillot[4] found a number of individuals who normally could not perceive the macrocyclic musks, one subject who could not detect the steroid musks, and one who could perceive neither, but this last case was able to smell the nitro musks. Guillot explained this by postulating at least three fundamental odours for the musk sensation. However, Johnston and Sandoval[5] have shown that muskiness is a valid primary category, organoleptically and semantically. I would attempt to explain Guillot's observations by suggesting that his deficient subjects have musk receptor sites which are abnormally short (say 10·5 Å long instead of the normal 11·5 Å), while retaining the usual width of 9 Å. Such a site would exclude the longer steroid and macrocyclic musk molecules while still accepting the shorter, wider nitro musks. More detailed consideration of Guillot's observations will have to await refinement of my postulated dimensions for the normal musk site.

Most of the known subjects with partial anosmia have been tested on far too few compounds for it to be possible to map out the true extent of their anosmia. In the absence of evidence to the contrary, I suggest that such anosmias are to be explained as indicated here, by an abnormal configuration of the receptor site in the deficient individuals.

However, Fullman cites the example of hydrogen cyanide, which some persons are unable to smell, but those who can do so sometimes consider it to have an odour reminiscent of bitter almonds. It should be noted at the outset that Meyer, who made a special study of the odour of liquid HCN and its aqueous solution, reported that the smell of HCN is quite different from that of bitter almonds, with which he considered it was frequently incorrectly associated. He described its odour merely as penetrating and pungent[6]. Actually (assuming that the almond odour is not simply due to an impurity) hydrocyanic acid represents a yet more fundamental difficulty than those mentioned by Fullman, for I am rather at a loss to explain why it has an almond odour at all. Its molecule is very small, far too small to satisfy any of the three receptor sites (camphor, floral and pepperminty) which I postulated[7] go to make up the complex almond odour. In fact I conceded that hydrocyanic acid represents the only odorant example I encountered which really defied all reasonable explanation[8].

I am inclined to treat hydrocyanic acid as a special case for the time being, rather than distort the whole stereochemical theory to include one recalcitrant exception. It must be remembered that hydrocyanic acid possesses a number of special properties, very rarely found in a single compound. It is an exceptionally strongly associated liquid, very chemically reactive, and exceptionally poisonous. Any or all of these three unusual properties might conceivably account for its odour, as follows.

Hydrogen cyanide molecules, even in the vapour state at room temperature, have a remarkable tendency to associate by hydrogen bond polymerization into chains of indefinite length[9]. Lateral association of such chains by dipole attraction might also be anticipated. Perhaps in this way assemblages of hydrocyanic acid molecules build up to sufficient size to satisfy the three receptor sites to produce an almond odour. Alternatively, the chemical reactivity of hydrocyanic acid suggests the possibility that it might combine with some compound present in the nasal mucus or the olfactory epithelium, thereby converting it into a molecule which has an almond odour. Wright[10] noted that hydrocyanic acid does not fit into his (vibrational) odour theory either, and suggested that its odour is produced indirectly, on account of its chemical reactivity. Meyer[6] observed that hydrocyanic acid anæsthetizes the olfactory nerves in a few seconds, so that the odour soon cannot be perceived. Possibly the various primary odour receptors are anæsthetized at different rates. If the other four receptor types were extinguished before the camphor, floral and pepperminty types, then the residual resting discharge in these three would remain