By designing the spin labels so that the nitroxide group will be located at different regions in the membrane structure, detailed information about the localization of anaesthetics can be obtained.

Evidence from both NMR and ESR experiments suggests that molecules such as cholesterol have the effect of increasing the order or packing of the membrane. The transition from a fluidizing action to an ordering effect may be observed in ascending the *n*-alkyl alcohol series, so that both kinds of structural perturbation may be associated with anaesthetic action.

All these effects have been demonstrated directly on spin labelled nerves by Hubbell & McConnell (1968), who are responsible for this novel method of probing membrane structure and to whom I am most grateful for the opportunity of taking part in the work presented here.

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The state of quaternary ammonium ions in solution

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The rotational correlation times (the mean time taken for a molecule to rotate 1 radian in solution) of drugs can be estimated from their nuclear magnetic spin-lattice relaxation times. We have measured these for the N-methyl protons of alkyltrimethylammoniums and alkyldimethylammoniums and for some bisquaternary ammonium compounds by the method of rapid adiabatic passage (Pople, Schneider & Bernstein, 1959). Theoretical relaxation rates calculated on the assumption that the molecules behave as rigid entities in which no rotation about bond axes is permitted agree excellently with the experimental values. Rotation about C–C or C–N bond axes makes no measurable contribution to the relaxation process. This means that in these compounds the energy barrier to bond rotation is large enough to make alterations of conformation slow compared with the rotational correlation time. The population of conformations should therefore be regarded as stable in the context of discrete collisions with the receptor. By contrast in choline methyl ether and homocholine methyl ether rotation about the O bond is relatively free and this is also true of rotation of the acetyl group in acetylcholine and methacholine. These differences in ease of rotation are important in interpreting relaxation rates of drugs when they are interacting with binding sites.

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