Adaptive Changes in Cell Membranes

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Models for adaptive changes in cell membranes

P. J. QUINN
Department of Biochemistry, Chelsea College, University of London, London SW3 6LX, U.K.

Cells and organisms are able to grow and divide under a wide variety of environmental conditions. Prokaryotic microorganisms are particularly versatile in this respect, and have been shown to thrive, for example, in temperatures ranging from \(-10^\circ{\text{C}}\) to nearly \(100^\circ{\text{C}}\) (Brock, 1967; Babel et al., 1972; Morita, 1975). The temperature span over which any particular organism may grow, however, is limited to between 25 and 40 centigrade degrees. Similar observations have been noted for other environmental factors, such as the availability of water, concentration of salts, light intensity etc. Apart from adaptation of different organisms to exist at environmental extremes, the success with which a particular organism is able to adapt to a change in its environment varies considerably from one organism to another. One of the major limiting factors in this process is believed to be the ability of the organism to modify its membranes so that they can function normally in the altered environment.

The consequences of a shift of environmental conditions is manifest in membranes by an alteration in activity of membrane-associated enzymes, including transport processes, or a change in permeativity and barrier properties of the membranes, or both. These effects may be exacerbated by a sudden environmental change and may be smoothened by a gradual exposure of the organism to the same change. This is particularly evident in the case of osmotic stress, and in some organisms sudden changes in temperature, such as cold shock, can prove lethal.

In general, adaptation of membranes to widely different growth conditions cannot be accomplished simply by a re-arrangement of existing components, but requires a change in chemical composition of the membrane. It is important to emphasize that it is only an assumption that the change in chemical composition is part of an adaptation process, since it is difficult to disprove the notion that membrane composition alters merely as a consequence of a direct effect on the numerous enzymic pathways involved in synthesis of membrane constituents. In other words, we like to believe that such changes operate in the best interests of the organism. The changes observed in the composition of membranes can be considerable and involve both the lipids and proteins. The types of change can be a shift in the relative amounts of individual membrane proteins or isomeric forms of particular proteins. More generally, the overall ratio of protein to lipid in the membrane may change. Usually the most conspicuous effects are seen in the lipid fraction, where there may be a change in the proportion of the different lipid classes present in the membrane, including sterols, often combined with an alteration in the molecular species associated with each lipid class. For example, differences in the fatty-acyl substituents with respect to both length and extent of unsaturation are frequently observed in the membrane lipids of prokaryotes (McElhaney & Souza, 1976; Rottem et al., 1978) and eukaryotes (Ferguson et al., 1975; Thompson & Nozawa, 1977) subjected to a change in environmental temperature.

Alteration in the chemical composition of the membrane during adaptation to environmental changes is said to be necessary to provide an appropriate physical state to match the new growth conditions. It is useful to exclude from consideration, at this point, changes associated with membrane differentiation of the type triggered, for example, by light, which stimulates synthesis of purple membrane patches on \textit{Halobacterium halobium} and differentiation of chloroplast lamellae. Two main theories have been proposed to explain the observed membrane changes. These are (1) the membrane fluidity hypothesis and (2) the lipid structure model.

The membrane fluidity hypothesis

Biophysical studies of pure analogues of lipids found in biological membranes have clearly established the influence of chemical configuration on lyotropic and thermotropic mesomorphism. The earlier studies of these effects were concentrated in particular on gel-to-liquid-crystalline phase transitions of lipids in a lamellar phase, but other phase transitions are currently receiving attention. Within individual lipid classes the nature of the hydrocarbon chains was found to dominate the phase-transition behaviour of these lipids in excess water, such that longer and more saturated chains had high transition temperatures compared with lipids with short and/or polyunsaturated fatty acids. Cholesterol and rigid hydrophobic domains of membrane proteins were shown to modify the phase-transition behaviour owing to their constraining action on motion of the lipid chains. When translated into the context of biological membranes, often with a bewilderingly complex mixture of molecular species of lipids and various proportions of sterols and intrinsic proteins, the resulting hydrocarbon domain is said to have a certain fluidity. This term is not a precise one, but is generally considered in terms of the relative motion of the membrane constituents in a particular domain in much the same way as viscosity of a bulk solution. The origins and regulation of cell membrane fluidity were reviewed by Quinn (1981).

The chemical changes observed in the membrane lipids of cells adapted to growth at different temperatures tend to support the idea that membrane fluidity is adjusted to preserve this property within relatively narrow limits. Thus adaptation to growth at lower temperatures is associated with a decrease in average length of acyl chains and an increase in the number of \textit{cis}-unsaturated residues per chain, but the reverse is true for growth at higher temperatures. These changes would be expected to maintain fluidity fairly constant, and this is confirmed by a large body of evidence by using probe techniques...
as well as more direct observations of phase transitions and separations by using calorimetry, wide-angle X-ray diffraction and freeze-fracture electron microscopy. The general explanation of this change in lipid fluidity that the extent of lipid saturation is maintained by a homeoviscous adaptation process that preserves the fluidity of the membrane in a state consistent with the particular functions that the membrane performs (Sinensky, 1974). The molecular mechanisms whereby this adaptation process can take place has been suggested from observations of the efficiency of fatty acyl-CoA desaturase systems in endoplasmic reticulum and in reconstituted systems (Rogers & Strittmatter, 1975; Enoch et al., 1977). Lateral segregation of cytochrome b and cytochrome b reductase owing to increased proportions of high-melting-point membrane lipids would result in accelerated electron transfer and synthesis of unsaturated fatty acids. An incorporation of these unsaturated fatty acids into membrane lipids would redress the fluidity balance and in turn lessen the probability of collision between the components of the electron transport chain.

The main pieces of evidence usually cited to support the hypothesis are the correlation between growth rate and parameters of membrane fluidity or appearance of gel-phase lipid in the membrane, and secondly changes in energy of activation of membrane-bound enzyme processes as a consequence of changes in lipid fluidity. Both these explanations are subject to criticism. Membrane fluidity, for example, may not necessarily be the rate-limiting factor in growth regulation, and discontinuities in Arrhenius plots of enzyme activities can be due entirely to thermotropic changes in the protein and unconnected with any changes in the fluidity of the membrane.

The lipid structure model

This model emphasizes the dependence of membrane stability on an appropriate balance of lipids in the structure. It is well known that some membrane lipids, such as phosphatidylcholines, phosphatidylglycerols, phosphatidylserines and dihexosylglycerols, prefer a bilayer configuration under physiological conditions, whereas other lipids, such as phosphaditylthanolamines, monohexosylglycerols and diphasphatidylglycerols in the presence of Ca²⁺ orient into a hexagonal-II configuration. The factors that determine whether lipids dispersed in aqueous systems form a hexagonal-II or a lamellar structure are often conceptualized in terms of molecular shape; molecules possessing a cylindrical shape tend to form bilayer structures, whereas a wedge shape enables the molecules to arrange in hexagonal or micellar configurations. In thermodynamic terms, aggregation states may be said to depend on the balance and distribution of hydrophobic and hydrophilic affinities within the molecules, which in turn determines the resulting interaction free energy. These concepts have been the subject of several reviews (Israelachvili et al., 1976, 1977).

In the context of membrane adaptation, the chemical changes observed to modify the lipid components of biological membranes on changes in environmental conditions also act to preserve the balance between lipids tending to form bilayers, on the one hand, and non-bilayer structures on the other. There is evidence supporting this idea in studies of the adaptation of Acholeplasma laidlawii to growth under different conditions, in which it is found that changes in lipid composition are governed by 'molecular shape' of the molecules (Wieslander et al., 1980, 1981). In the case of this micro-organism it is thought that a balance of molecular affinities is required to form a stable bilayer, but in other membranes, such as the retinal rod outer segment disc membrane and chloroplast thylakoids, aqueous dispersions of total membrane polar lipid extracts do not form bilayers exclusively (De Grip et al., 1979; Quinn et al., 1982). It has been suggested that the non-bilayer-forming lipids may be needed to package large intrinsic membrane proteins into the structure (Williams et al., 1982), and adaptive changes are concerned with the maintenance of stable lipid–protein interactions in the membrane. It is of interest that rapid changes in the environmental conditions, such as heat stress in certain membranes, causes a disruption of lipid–protein interactions and the phase separation of non-bilayer-forming lipids (Gounaris et al., 1983).

At the present time there is not sufficient data to distinguish between the membrane fluidity hypothesis and the lipid structure model of adaptation of cell membranes to environmental change. It must also be recognized that neither model may be correct and other adaptive processes need to be considered. In all events, further experiments, especially those aimed to compare acute environmental stress with longer-term adaptive changes, are required to establish the molecular basis of membrane adaptation.


Adaptive changes in membrane-transport systems of hibernators

J. C. ELLORY* and J. S. WILLIST†
*Physiological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 3EG, U.K., and †Department of Physiology and Biophysics, University of Illinois, Urbana, IL 61801, U.S.A.

Hibernating mammals can survive for long periods with low body temperatures (0–5°C), which would be lethal for 'conventional' mammals. This adaptation differs from cold-acclimation in poikilotherms, since hibernators go through several periods of arousal during hibernation, when they rapidly warm up to the normal body temperature. This means their cells must be capable of functioning at both 5°C and 37°C without time for acclimation. Further, cold-adaptation in hibernation is of the 'resistance' rather than 'capacity' type (Precht et al., 1973), in that survival, rather than sustained activity, may be the

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