Constraints on the lateral diffusion of membrane proteins in prokaryotes

Paul O'Shea indicates[1], whilst agreeing with the thrust of my original article[2], that I may perhaps have laid insufficient stress on two possibilities which might yet resolve the paradox of why protein diffusion coefficients (D) are apparently orders of magnitude below their putative hydrodynamically constrained limiting values. I certainly did consider these possibilities, which are well worth discussing[1], but I do not believe that they will substantially affect the arguments raised, so as to bring the theoretical and experimental values into line with each other. Let me indicate why I take this view.

The first possibility[1] relates to the archipelago effect[3], in which the hindering of lateral motions might be compared with the problems of moving across a crowded room. As stated in the original article[2], 'the relatively high protein content of biomembranes *per se* cannot alone account for this' (low lateral diffusibility). Jacobson and Wojcieszyn have put it thus[4]: 'Arguing against the effect of the surface density of proteins determining the low lateral diffusion rates in the cell surface is the observation that $D = 3.5 \times 10^{-9}\,\mathrm{cm}^2\,\mathrm{s}^{-1}$ for rhodopsin in the rod outer segment membrane. Yet in this membrane the protein rhodopsin is packed tightly enough to give a protein to lipid weight ratio of about 1.' Although many energy coupling membranes have protein : lipid ratios as great as 2, the *area* occupied by the proteins is only some 30–50% of the total[5], as illustrated, for instance, by the electron micrographs of Sowers and Hackenbrock[6]. Thus the archipelago effect, in which the proteins are treated as hard disks, although not entirely to be dismissed from consideration, would not

seem to help us in quantitatively accounting for the low D values.

The other possibility raised[1] is the potential role of extramembranal viscous forces. This possibility arises, of course, from the very fact that the proteins protrude from the bilayer, such that the area they take up in the membrane surface is not mirrored in the lipid : protein weight ratio. According to the equations of the most widely used model[7], the extramembranal viscous forces are relatively modest, given the viscosities of physiological aqueous solutions relative to those of the membrane phase. Even if the 'viscosity' of the bacterial cytoplasm were greater than 1P (0.1 Pa.s), protein D values would still approximate $10^{-9}\,\mathrm{cm}^2\,\mathrm{s}^{-1}$ (Ref. 8).

Whilst there is abundant room for improvement in our understanding of the cytoplasmic (micro) viscosity and organization, and the diffusion rates of molecules therein[9,10], it does not seem possible quantitatively to ascribe the lowering of membrane protein D values to a high cytoplasmic viscosity alone. Therefore, I am at one with Weaver[11]; the whole point of the article[2] was indeed that one should consider 'long range' forces in energy-coupling membrane organisation[12,13]

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A cure for baldness?

Enclosed is a clipping from the *Age* (Melbourne daily newspaper) which reminds me of the fact that one of the

● *ODD SPOT*
Two farmers, in England and Germany, say that bald men who have been licked on the head by cows are growing hair again.

richest sources of epidermal growth factor is the parotid gland! Could there be a grain of truth here, or a fortune to be made?

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Can any other readers come up with biochemical explanations for folk tales?
– The Editor