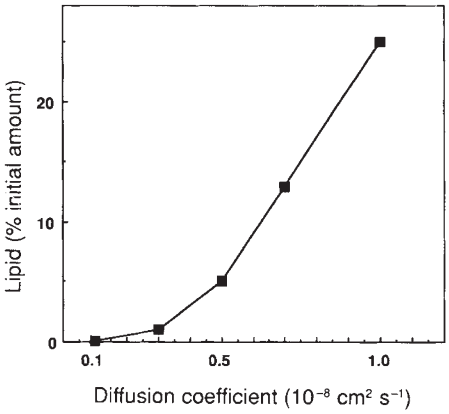
Lipid diffusion in neurons

SIR — Kobayashi *et al.*[1] suggest that the compositional differences between the axonal and somatodendritic domains of neuronal membranes are maintained by a diffusion barrier at the axon hillock. This novel suggestion is based on observations of the movement of fluorescently labelled lipids inserted exclusively into the axons of neurons infected by viruses. Although the fluorescent lipid is mobile in the axonal membrane, labelling is abruptly interrupted at the point where the axon emerges from the cell body; the cell body and dendrites do not appear to become labelled even after an hour of observation.

Using analysis similar to that developed for quantifying diffusion from a spherical cell surface to a tubular projection[2], we have calculated the amount of lipid that would diffuse from the axon to cell body after 1 h in the absence of a barrier, for lateral diffusion coefficients ranging from 10^{-9} to 10^{-8} cm^2 s^{-1} (see figure). For a lipid diffusion coefficient of 6×10^{-9} cm^2 s^{-1}, as measured in spinal cord neurons[3], only 9% of the lipid initially present in an axon of 100-μm length would diffuse into the cell body after 1 h. Under these conditions, labelling in the axonal initial segment would not disappear, as was observed[1]. Direct measurement of the diffusion coefficient of the fluorescent lipids in the virus-infected neurons would permit evaluation of the contribution of a diffusion barrier in restricting movement of axonal lipids into the cell body.



Amount of lipid in the cell body after 1 h (as a percentage of the initial amount in the axon) against diffusion coefficient. The diameters of the cell body and axon were taken as 10 and 1 μm, respectively, and the axon length as 100 μm. The amount of lipid in the cell body after 1 h does not vary significantly for longer axon lengths or larger cell body diameters (not shown). Note also that for low diffusion coefficients (10^{-9} cm^2 s^{-1}), lipid that diffuses from the axon to cell body is restricted to the area of the cell body proximal to the axon, but for higher diffusion coefficients (10^{-8} cm^2 s^{-1}), lipid is almost uniformly distributed over the whole cell body surface.

We propose that a physical barrier may not be necessary to maintain the polarized distribution of cell surface molecules in axons. Mature axons in the central nervous system are often several millimetres long and can be as long as a metre in the peripheral nervous system. Assuming typical diffusion coefficients of approximately 10^{-8} cm^2 s^{-1} for lipids and 10^{-9} cm^2 s^{-1} for proteins (although many proteins move more slowly), and using the equation $t = L^2/2D$ (where D is the lateral diffusion coefficient, L is length and t the time taken for the molecule to move L), a lipid would take approximately 6 days to move 1 mm from the distal to proximal end of an axon, and a protein 60 days. Even for a shorter axon of 100 μm, a lipid would take 80 min and a protein 14 h to diffuse this distance. It is generally assumed, at least in growing axons, that membranous material is added at the distal end of an axon. As approximately 50% of the membrane surface is internalized every hour (as measured in baby hamster kidney cells[4], although a direct measurement of the rate of membrane internalization has not been performed in neurons), the time a molecule spends in the axonal membrane before internalization will be much shorter than the time taken to diffuse long distances. Thus, the polarized distribution of a cell surface molecule could be obtained by targeting and inserting intracellular vesicles containing axonal molecules to a location in the axon that would prevent diffusion back to the cell body within a reasonable time. The significance of a physical barrier to lipid diffusion should be considered in the light of these geometrical considerations.

Anthony H. Futerman
Department of Membrane Research and Biophysics
Raya Khanin
Lee A. Segel
Department of Applied Mathematics and Computer Science,
Weizmann Institute of Science,
Rehovot 76100, Israel

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Odour detection in bees

SIR — Breed and Julian[1] argue that data they obtained from controlled agonistic interactions of worker honey-bees ". . . suggest a system of ordering of priority of cues by the bees. . ." in the context of nestmate discrimination. This interpretation builds on the "hierarchy of importance of cues" hypothesis proposed by Carlin and Hölldobler[2] to explain nestmate discrimination behaviour in carpenter ants. But Carlin and Hölldobler's data are also consistent with a concentration or, more correctly, proportion hypothesis in which the recognition signature of the queen has diminishing influence as the size of the colony increases[3,4].

Similarly, Breed and Julian's data are also consistent with a proportion hypothesis which predicts that as the proportion of a salient odorant component increases in a blend, the blend is perceived as being increasingly similar to this component (as has been demonstrated for the case of blends of two fatty acids and blends of two *n*-alkanes[5] and provided that the total concentration of the blend does not reach the point where the perception of quality is lost through saturation of the olfactory system[6]). Because the molecular mass, volatility, and receptor affinity varies among odorants, without the right sort of controls we cannot be sure that an odorant at one concentration dominates another at the same or a different concentration. Our understanding of salience of odorants as cues is complicated because salience may vary with the genotype and experience of individuals. Further, we could misinterpret our results if we do not identify the threshold concentrations below which the odorants are not detected[7]. This point is not considered by Breed and Julian who hypothesize that ". . . the presence or absence of each cue, rather than the relative concentrations of cues, seems to have the greatest importance [in mediating kin discrimination]."

To exclude the effect of relative concentration, Breed and Julian would have needed to vary the relative concentration of their odorants in binary mixtures of the two, ranging from the hexadecane component increasing from its detectability threshold concentration to methyl docosanoate decreasing to its detectability threshold concentration. A proportion hypothesis — assuming concentrations c_1 and c_2 provide equally salient stimuli of odorants 1 and 2, respectively — predicts that worker bees would increasingly favour introduced bees exposed to odorant 2 over those exposed to odorant 1, if for some increasing value of α ($0<\alpha<1$) the receiving bees themselves had been exposed to a