Lipid Flow in Locomoting Cells

J. Lee et al. conclude (1) that the "retrograde lipid flow (RLF) hypothesis is no longer tenable as a general model for cell locomotion." In their experiments, they marked a line in the plasma membrane lipids of a moving polymorphonuclear leukocyte (PMN) that is parallel to the advancing edge of the cell. They then observed how this line moved with respect to the advancing edge as the cell moved forward. The membrane flow hypothesis [reference (2), itself a refinement of the lipid flow scheme (3)] predicts it would move backward. In 9 of 16 cases this is what they actually found. However, is the observed rate of rearward movement that is predicted by my hypothesis? They state that the membrane flow hypothesis demands a rearward line migration that moves two times as fast as the leading edge advances—all measured with respect to the substrate [note 21 in (1)]. This is incorrect. In a commentary (4) on an earlier paper from this group (5), I explained that the membrane flow hypothesis predicts that a particle on the dorsal surface of a cell (or in this case, a line drawn in the cell surface) will migrate rearward with respect to the leading edge. How fast it should do so depends on a variety of factors, including how fast the cell is moving and where on the cell surface the particle is. I say "potentially moving," because the advancing edge, in the process of extending, may or may not actually attach to the substrate. Whether it does or does not attach to the substrate makes no difference to the mechanism of the motor, but does affect the rate of locomotion. In other words, the cell may move forward if the front attaches, or "slippage" may occur if it does not. [An example of a cell in a purely slipping mode is one on the edge of a stationary colony of spread epithelial cells: the advancing edge can no longer advance and so slips, the slippage often seen as ruffling of the advancing edge (6).] A particle just behind the leading lamella would be expected to remain stationary with respect to the substrate if no slippage occurred, and to move backward with respect to the substrate if the cell were slipping. In assuming a rearward line migration with respect to the substrate, Lee et al. assume their PMNs are slipping badly: given the rate at which they move on glass this seems improbable.

Lee et al. (1) draw the line in the cell's plasma membrane near the middle of the cell; the predicted rearward membrane flow there would be one-half that at the front (7) (assuming these cells are flat sheets, which surely they are not). Their marker line might therefore be expected to move rearward with respect to the leading edge at half the speed that the leading edge advances over the substrate. In their terminology, this would give an R factor of 0.5, not the 3 they state. The scatter observed in their data (in their figure 4) is such that one cannot distinguish between an R of 0 or 0.5.

In figure 4 of the paper by Lee et al., it is stated that two cells (1 and 15) have R values of 0 and about −0.6. Following their method of calculation, I find these should be about −20 and −40; if these experimental measurements are actually correct, they suggest that none of the models considered by Lee et al. can be valid.

In conclusion, the report by Lee et al. sheds little light on whether the membrane flow model (2) applies to PMNs or not.

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REFERENCES
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Response

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