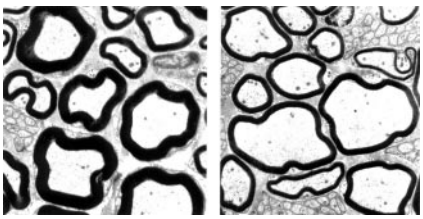
Regulation of Wrapping

Developing Schwann cells survive thanks to neuregulin, a survival and proliferation factor that is produced by neurons and detected by the ErbB2 and ErbB3 receptor tyrosine kinases. Later on, the Schwann cells rely on autocrine factors for survival, even as they start to wrap neurons (the source of the original survival signal) in myelin.

But neuregulin production continues, and on page 1035 Garratt et al. show that ErbB2 is necessary for continued myelination. Schwann cell precursors develop normally in mice with a conditional knockout of ErbB2, but myelin sheaths around neurons are thinner and wraps are less numerous than normal. This defect, and some motoneuron loss, lead to problems with gait, wasting, and even death. This is a clear example of the function of a growth factor changing as the cell achieves different stages of maturation, although the problem of how the cell normally stops the process of myelination remains a mystery.

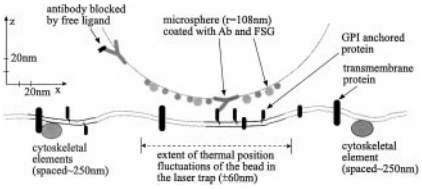


Myelination can be arrested by overexpression of P_0, as discussed by Wrabetz et al. on page 1021. P_0 is the most abundant transmembrane protein in peripheral myelin, and it helps compact successive myelin spirals. Yin et al. (page 1009) suggest one explanation for the overexpression phenotype: excess P_0 is mistargeted to mesaxonal membranes, where it mediates homophilic adhesion that presumably shuts down the wrapping process.

Tracking Movements

Small but Sturdy Rafts

Using single protein tracking, Pralle et al. estimate the size and persistence of sphingolipid–cholesterol rafts (page 997). The rafts, used in sorting and signaling, are small but stable. The researchers observe the degree to which single proteins, attached to antibody-coated beads, are restrained by increased viscous drag from unfettered Brownian motion. The mobility of raft-associated proteins is reduced to a similar level, whether or not the proteins are anchored by a transmembrane region or glycosylphosphatidylinositol (GPI) anchor. When cholesterol depletion is used to disrupt rafts, the mobility of the transmembrane proteins increases to the level seen for nonraft transmembrane proteins; for GPI-anchored proteins, the new mobility is even higher.



Protein associations with rafts seem to be extremely stable. A protein that is dragged for ~1 μm remains in the raft environment, as do proteins that are left free to wander for up to 10 min. Furthermore, the protein movement observed probably reflects movement of the entire raft, given the uniform diffusion properties of different types of raft-associated proteins. (Movement of proteins within the raft may occur, but it is predicted to be slower than raft motion.)

Pralle et al. use the assumption that they are observing movement of entire rafts to estimate that rafts have an area of ~2,100 nm^2, which is enough for a few thousand lipids and probably fewer than 50 proteins. This small size suggests, in turn, that raft clustering must be integral to many sorting and signaling events.

A Distance Switch in Dynein

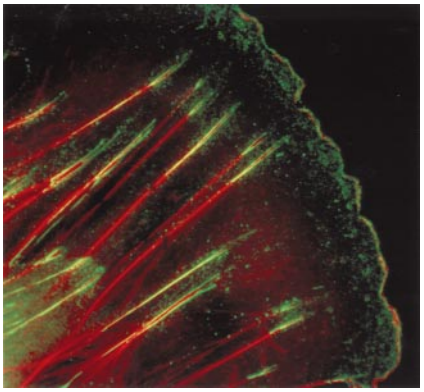
Gross et al. present a detailed analysis of the microtubule-based movements of lipid droplets in *Drosophila*, and conclude from the distribution of travel distances that a switch controls the termination of dynein-driven movement (page 945). The function of the lipid droplets is unknown, but their size and distinctive appearance allow high resolution tracking in vivo. As with many microtubule cargoes, the droplets can move towards either end of microtubules. Gross et al. confirm that the minus end–directed movement is dependent on dynein; the motor for plus end–directed movement has not been identified.

The distance traveled by the droplets in any given minus end–directed run is shorter than expected based on in vitro measurements of dynein processivity. Termination because of a failure in processivity, should be characterized by a disengagement from the microtubule and, therefore, a pause, but most runs are ended by rapid direction reversals not pauses. Therefore, Gross et al. suggest that a switch imposes a constant probability of stopping and that, once the dyneins have been stopped, the switch immediately turns the plus end–directed motors on.

A partial failure in this switching process, perhaps leaving oppositely directed motors in competition with each other, may explain a second class of minus end–directed runs. These latter runs are more abundant but cover less distance and are slower.

Pulling Fibronectin into Shape

Pankov et al. report on page 1075 that the centripetal motion of integrins may pull extracellular protein assemblies into their final fibrillar shape. The pulling may both align fibronectin proteins and expose cryptic self-association sites to allow fibrillogenesis.

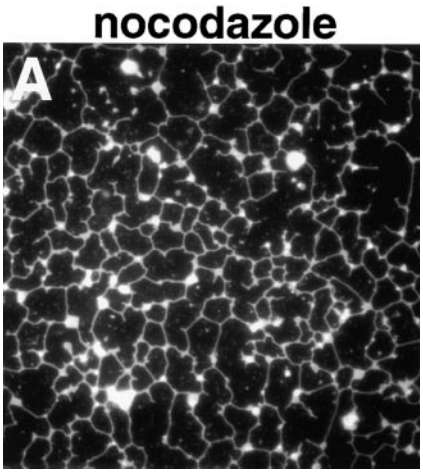


The integrin in question, $\alpha_5\beta_1$, starts off at focal contacts before ligation with fibronectin prompts its movement into extracellular matrix (ECM) contacts. The integrin and the ECM contacts slowly sweep inwards towards the center of the cell. Bound extracellular fibronectin (the primary ligand of $\alpha_5\beta_1$) follows the same pattern, and Zamir et al. (Zamir, E., M. Katz, Y. Posan, N. Erez, K.M. Yamada, B.-Z. Katz, S. Lin, D.C. Lin, A. Bershadsky, Z. Kam, and B. Geiger. *Nat. Cell Biol.* 2000. 2:191–196) show that tensin does too. Pankov et al. find that tensin, which may link integrins and actin in ECM contacts, and actin contractility are required for integrin movement and fibronectin fibrillogenesis.

Another integrin, $\alpha_v\beta_3$, and its ligation with vitronectin are also required for $\alpha_5\beta_1$ movement and fibronectin fibrillogenesis. The $\alpha_v\beta_3$ integrin may function by signaling or by fulfilling an essential role in focal contacts, thus, allowing $\alpha_5\beta_1$ and the attached fibronectin to be dragged off.

Making the ER without Microtubules

Contrary to previous work, Dreier and Rapoport show on page 883 that microtubules are not required for the in vitro remodeling of membranes into ER-like tubules. Dreier and Rapoport began by attempting to dissect an in vitro nuclear envelope formation reaction in frog egg extracts. But the reaction was complicated by associated chromatin decondensation and remodeling reactions and, in the meantime, the researchers observed that the reaction conditions yielded ER-like membrane structures. (In any case, success with the simpler ER formation assay may be applicable to nuclear envelope formation, as the two reactions seem to share many characteristics.) The reaction requires only a light membrane fraction and cytosol. By itself, a washed membrane fraction fuses to form larger vesicles but does not form tubules.



In previous in vitro assays, ER tubules were observed only after they adhered to glass; Dreier and Rapoport suggest that microtubules are required for the adherence, but not the formation, of tubules. In vivo, microtubules may help form ER tubules, and almost certainly distribute those tubules to the cell periphery. In the absence of microtubules, the possible culprits for tubule formation include large and rigid protein complexes, which are enzymes that remodel lipids in one face of a bilayer, and internal fusion reactions that can turn a large flat vesicle into a doughnut shape.

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