When a budding yeast cell is unable to form a new bud, cell division pauses in G2 phase, either until a bud can grow or until the cell “adapts” to the situation by becoming dinucleate. Ciliberto et al. collected the available experimental data on this morphogenesis checkpoint, and on page 1243 they present a mathematical model that explains previous results and makes some surprising predictions.

The morphogenesis checkpoint relies on antagonism between the Swe1 kinase, which inhibits entry into mitosis, and the active form of the Cdc28–Clb2 cyclin complex, which promotes it. In the model, a set of differential equations accounts for the phenotypes of a dozen morphogenesis checkpoint mutants by incorporating a few initial assumptions. Although previous work showed that Hsl1 kinase flags Swe1 for degradation, the mathematical model demonstrates that Hsl1 must also indirectly inhibit Swe1 activity.

The model also illuminates adaptation. Numerical simulation shows that small cells keep Cdc28–Clb2 activity at a low steady-state level, but at a critical cell size, Cdc28–Clb2 activity abandons the steady-state and enters an oscillatory regime. Normally, a single oscillation ends in mitosis, producing two smaller cells that are reset to the low steady-state level. But when bud formation is impaired, the morphogenesis checkpoint enforces an intermediate steady-state level of Cdc28 kinase activity. At this level, DNA synthesis proceeds, but cells pause in G2. Once these arrested cells reach a second critical size threshold, they bypass the morphogenesis checkpoint and enter the Cdc28–Clb2 oscillatory state, dividing their nuclei.

The morphogenesis checkpoint seems to raise the size threshold for progression of the cell cycle. The model predicts that once that threshold is passed in the absence of bud formation, the mitotic cycle should continue unchecked, and the next cycle should be faster. Testing these predictions should further refine the model.

Extra mass boosts the intermediate level of Cdc2 activity to induce mitosis.

Using a biochemical approach to a longstanding problem in Drosophila genetics, Wilhelm et al. (page 1197) have identified a novel protein that links translational repression to mRNA localization and also uncovered a surprisingly specific localization pattern for a ubiquitous translation factor.

Polarized cells often rely on mRNA localization to restrict protein distribution. During fly oocyte development, for example, oskar mRNA moves from the posterior end of the oocyte to an anterior position, then back to the posterior end before being translated. As Oskar expression determines posterior patterning and germ-line establishment, the mRNA must be repressed until it reaches its final position. Something must coordinate the localization and translational repression of the message, but genetic studies have only found mutants that affected localization or repression, not both.

Wilhelm et al. now identify the product of the Cup gene as the missing link. Cup is part of a multiprotein complex that copurifies with oskar mRNA. Interfering with Cup disrupts both the localization and translational repression of oskar. Surprisingly, the ubiquitous translation factor eIF4E, which is generally assumed to be homogeneously distributed in cells, specifically binds to Cup and substantially localizes to the posterior end of fly oocytes.

The authors propose a model in which Cup binds to oskar mRNA as a repressor and also recruits the transport components of the protein complex. Once the mRNA reaches its destination, a posterior signal could then disrupt the Cup–eIF4E interaction and permit translation. Since the need to coordinate repression with mRNA localization is common to many polarized cells, recruiting transport components could be a feature of many translational repressors.

The authors are now examining Drosophila mutants with phenotypes similar to Cup in an effort to identify additional mRNA regulators.