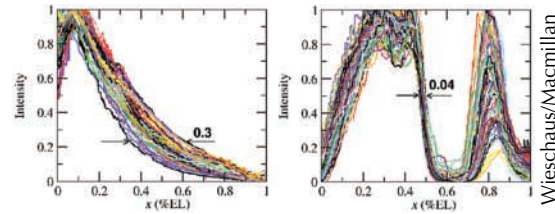


Put that hunchback over here

Fly embryo development is the classic example of refinement. From initial gradients of proteins like Bicoid (Bcd) come first the broad domains of gap gene expression and, finally, the narrower segmentation patterns. Now, Bahram Houchmandzadeh, Eric Wieschaus, and Stanislas Leibler (Princeton University) have looked at just when this cascade establishes precision. They find that precision is initiated not gradually but suddenly and early, with the onset of expression of the gap gene *hunchback* (*hb*). Perhaps not surprisingly, the Bcd gradient itself shows significant variation. A particular threshold level of Bcd occurs across a range of 30% of the embryonic length in different embryos. Hb, however, is turned on so precisely that in two-thirds of the embryos the Hb boundaries are



Bcd gradients vary wildly between embryos (left), but Hb (right) is tightly controlled.

defined over a region corresponding to less than the size of one nucleus.

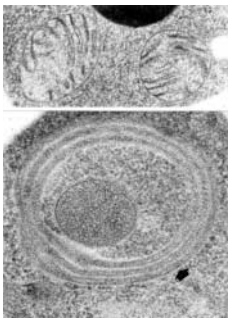
Cooperative activation of Hb could sharpen a Bcd-directed Hb gradient to a tightly defined area in a particular embryo. But this does not solve the problem of activating Hb at precisely the same relative position in every embryo. To accomplish this feat, there must be information in addition to the Bcd gradient that can vary with factors such as temperature, exact gene dosage, and the age of the eggs.

That extra information does not appear to come from a variety of other gap genes tested by Wieschaus, or from *nanos*, a candidate posterior gradient molecule. Mutation of the gene *staufer* does, however, have a marked effect. Staufer helps carry mRNAs for gradient proteins (such as Bcd) to both the anterior and posterior of the fly embryo. The interplay of several such proteins, either known or unknown, may refine the Hb expression pattern. In any simple model involving Bcd, says Wieschaus, the additional gradient molecule “has to be something that varies in the same way as Bcd.” In this way, effects on the two gradients by factors such as temperature would oppose each other and be cancelled out in the Hb readout. ■

Reference: Houchmandzadeh, B., et al. 2002. *Nature*. 415:798–802.

Cristae in crisis

Cristae, the complex involutions of the mitochondrial inner membrane, vastly increase the surface area across which ATP synthase can generate a proton gradient. Now, new findings from Jean Velours (Université Victor Ségalen, Bordeaux, France) and colleagues suggest that ATP synthase may be important in forming cristae in the first place.



Mitochondrial cristae (top) turn onion shaped in the absence of an ATP synthase subunit (bottom).

Velours/EMBO

Velours’ theory is that oligomerization of ATP synthase in the mitochondrial inner membrane helps tubulate the membrane. This idea was first suggested based on the zippered rows of ATP synthase molecules visible on the cristae of *Paramecium* mitochondria. Velours does not yet know if yeast has the same arrangement. But in the new work he detects the formation of yeast ATP synthase oligomers biochemically. Loss of the nonessential *e* or *g* subunits of ATP synthase both disrupts oligomerization and results in mitochondria that lack conventional cristae. The mutant mitochondria have an inner membrane that is wound around itself in an onion shape.

The new evidence provides only a correlation between oligomerization and cristae formation, but Velours is now planning more direct electron microscopy experiments to see if oligomerization is indeed responsible for curving the membrane into cristae. ■

Reference: Paumard, P., et al. 2002. *EMBO J*. 21:221–230.

Systemic destruction

A transmembrane protein identified by Craig Hunter and colleagues (Harvard University) may act as a channel that allows an RNAi signal to spread throughout a worm’s body and, perhaps, even a mouse or human body.

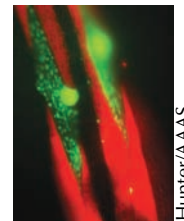
RNAi may target the double-stranded RNA (dsRNA) forms of invading viruses or mobile transposons, but in the laboratory dsRNA is used to trigger the destruction of mRNAs with the same sequence. In worms and, in a similar process, in plants, the destruction spreads systemically.

“This systemic effect greatly simplifies the use of RNAi as a genetic tool,” says Hunter, as worms can even be treated by soaking them in a solution of dsRNA. “But nobody has addressed it experimentally to discover how it works.” Hunter set out to find mutants that could still do localized RNAi, in cells expressing both a dsRNA and a corresponding target gene, but could no longer spread that RNAi signal to other cells expressing only the target gene.

One of the three genes that he found, called *sid-1*, encodes a protein with 11 predicted transmembrane domains. There are homologues in mice and humans and “the strongest homology is in the transmembrane regions, so we’d like to think it’s acting as a channel.” The alternative explanation—that SID-1 is a receptor mediating endocytosis of an RNAi signal—would be more likely if the homology was concentrated in the extracellular domain.

Hunter hopes to test the channel theory in worm primary tissue culture cells. And with SID-1 in hand, he can test whether systemic RNAi operates in mice and other mammals, and what it might be doing there. ■

Reference: Winston, W., et al. 2002. *Science*. 10.1126/science.1068836.



RNAi can eliminate GFP expression (green) only in cells making SID-1 (red).

Hunter/AAAS