so-called PML bodies in the nucleus (S. Artavanis-Tsakonas, Mass. Gen. Hosp., Boston). These bodies are associated with 'SUMO modification'[4] — a 'tagging' process that singles proteins out for degradation.

Signal transduction often involves protein modification by phosphorylation. Visualization of this process is helping to unravel the complexity of signalling from bone morphogenetic proteins (BMPs). A gradient of BMP proteins is thought to produce different cell fates both along the dorsal–ventral embryonic axis and across the wing[5]. The phosphorylation of Mad or Smad proteins is a key step in transmitting the BMP signal to the nucleus. Monitoring of Mad/Smad activation[6] does reveal a gradient in the developing wing but, unexpectedly, there is no indication of graded activation of Mad/Smad along the embryonic axis (B. Shilo, Weizmann Inst.; T. Tabata, Univ. Tokyo; L. Raftery, Mass. Gen. Hosp., Boston). Instead, activation is detected only in a dorsal stripe of cells, whose fates require the highest levels of BMPs. This leaves unanswered the question of how signals from BMPs are propagated through the cells in which activation of Mad/Smad cannot be detected.

Signal-transduction pathways may also be influenced by the regulated targeting of their components to the nucleus. Nuclear localization of phosphorylated mitogen-activated protein kinase is the final step in an intracellular signalling pathway that begins with the activation of a 'receptor tyrosine kinase' enzyme. The Corkscrew protein appears to control this final step by affecting the recruitment of importin (L. Perkins, Mass. Gen. Hosp., Boston), which carries proteins into the nucleus. A similar intersection with the nucleus-to-cytoplasm transport machinery affects the transcription factors Dorsal and Dif (C. Samakovlis, Umeå Univ., Sweden), which are involved in *Drosophila* immunity.

It is still too soon for the full impact of the recently completed *Drosophila* genome sequence to be felt. But one post-genomic revelation is the prevalence of gene families in *Drosophila*. For example, Warniu — a new member of the Snail protein family — is, like its two siblings, present in neural progenitor cells (T. Ip, Univ. Massachusetts). There are seven relatives of Wunen (R. Lehmann, Skirball Inst., New York), an enzyme that influences germ-cell migration[7]. A protein involved in ensuring that growing neuronal axons do not recross the embryonic midline is the receptor Roundabout[8]. Two more Roundabout-like proteins have now come to light, one of which also participates in the decision of axons to cross the midline (B. Dickson, Inst. Mol. Pathol., Vienna). Intriguingly, it appears that, after crossing the midline, the axons select their lateral position according to the combination of Roundabout proteins that they express.

The importance of regulated gene expression in development is undeniable. But our understanding of fly development must also incorporate changes in the stability, activity and localization of key proteins (and mRNAs too, as illustrated by their dramatic localization within the embryo; I. Davies, Univ. Edinburgh; D. Ish-Horowicz, Imperial Cancer Research Fund, London; H. Krause, Univ. Toronto). We now need to develop more techniques to look at both spatial (subcellular) and temporal mechanisms for coordinating protein activities and cell behaviours. The result will be an increasingly four-dimensional view of *Drosophila* development.

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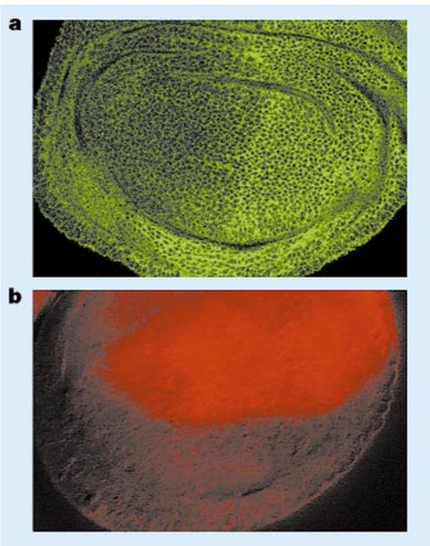

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Figure 1 **The importance of protein modification in *Drosophila* development.** a, **Levels of the Smoothened protein (green staining) vary across the wing imaginal disc. These levels are regulated by protein turnover[9].** b, ***fringe* messenger RNA (red staining) is expressed more highly in the dorsal part of the wing disc. The Fringe protein adds particular sugar groups to the Notch receptor, modifying its interactions with its ligands. So this asymmetric distribution of *fringe* mRNA results in modification of Notch only in certain parts of the wing disc.**

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Daedalus

The sound of silence

The mobile phone, that essential modern accessory, makes its user immediately unpopular with those around him. For some reason, talking into such a phone is far more annoying to external listeners than a conversation with a human companion, or even soliloquial muttering. Daedalus reckons that the phone user instinctively projects his voice to reach the distant party. He is now inventing a phone which can be spoken into silently.

Speech is formed by the mouth and tongue acting as an ever-changing resonant cavity for tones produced by the larynx. The tones themselves are very basic; someone who has lost his larynx can speak intelligibly with a simple buzzer as a replacement. Daedalus's brilliant idea is to provide an ultrasonic 'buzzer' as a larynx. His 'Ultraphone' has a narrow pipe, like a drinking straw, which projects into the user's mouth and injects a set of inaudible ultrasonic frequencies into it. The user whispers or mouths his speech silently, and a microphone detects the modulations imposed by his mouth and palate on the ultrasonic signal. A heterodyne circuit downshifts this signal into the audio range, thus reconstituting the speaker's normal voice, and transmits it to the called party. Like a normal telephone, it also injects a proportion of the speaker's reconstituted speech back into his own earpiece as a 'side-tone' for aural feedback. Thus he hears his voice quite normally, and is not tempted to speak audibly. Indeed, any attempt to do so will result in strange distortions as the audio is downshifted and aliased by the heterodyne circuit.

This simple system would produce a flat and toneless speech, rather like that of the laryngectomy patient with his buzzer. But Daedalus hopes to equip the Ultraphone with a program that recognizes the tonal clues implicit in silently mouthed speech, and varies the ultrasonic frequencies in sympathy. This should give far more realistic speaking tones, close to the user's natural voice.

The Ultraphone will sweep the market. Yuppies and poseurs will be able to make truly silent phone calls anywhere, even in concert performances and prayer meetings, without disturbing the proceedings or revealing the important, confidential matters they are discussing. And even in a boiler factory or gunnery range, ambient noise will not distract them. High above the audible clamour, their ultrasonic deliberations will travel clear and unaccompanied. **David Jones**

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