

and factors intrinsic to the progenitor or stem cell. A key role of the intrinsic factors appears to be to dictate a property referred to as 'competence' — that is, which subset of neuronal types can be generated from each progenitor or stem cell in response to extracellular signals.

As the competence of progenitors changes over time in many organisms, it is thought that the intrinsic factors that control competence also change<sup>2</sup>. But there has been a lack of data to describe both the intrinsic influences and the motor that drives change. Obvious candidates for the intrinsic factors are transcription factors, proteins that could switch on and off particular programmes of gene expression to control the identities of different neurons. But the hunt for such factors was fruitless — until now. The paper by Isshiki and colleagues<sup>1</sup> has provided a welcome breakthrough in this field.

The authors<sup>1</sup> have extended previous studies<sup>3,4</sup> to find a series of four unrelated transcription factors that are expressed transiently and sequentially in dividing neural progenitors (referred to as neuroblasts in *Drosophila*), but permanently in the progeny generated at the time that each factor is expressed (Fig. 1). So, for example, the first two factors in the sequence — Hunchback and Krüppel — were found to be both necessary and sufficient to generate neural cell types that maintain the expression of those factors. If the authors removed the function of either Hunchback or Krüppel from neuroblasts, then the neurons that normally express these factors were not produced. The generation of later neurons was completely undisturbed however, indicating that the steps controlled by each of these factors could simply be skipped without affecting later development. Conversely, overexpression of Hunchback or Krüppel forced neuroblasts to make more of the cell types that express these factors, but at the expense of cell types born later; fewer of the later cells in the sequence were made.

Although these are fascinating findings in their own right, Isshiki *et al.*'s most striking observation was that these factors are expressed in the same temporal order in completely different neural lineages at different times in development. Furthermore, the same sequence of factors is used to generate different cell types in each lineage. For example, in one lineage the first cell type produced is a motor neuron, while in another the first cell is a glial cell, but in both lineages the production of these first-born cells depends on Hunchback. The authors may have uncovered elements of a fundamental mechanism used in many parts of the nervous system, and perhaps in other tissues, to regulate cell-fate choices in a temporal sequence.

As if this were not enough, Isshiki *et al.* have further findings that provide insight

into the mechanisms regulating these intrinsic changes. They show that halting the cell-division cycle prevents progenitors from changing their expression of transcription factors. Moreover, releasing the cell-cycle brake at a later time results in progenitors that express the next factor in the series, rather than playing catch-up by skipping a factor and expressing the more temporally appropriate one. This suggests that the changing behaviour of progenitors is linked to cell-cycle progression rather than absolute time.

Predictably, there are several vertebrate homologues of each of these factors. It will be interesting to see if any of them are expressed in a manner that suggests they have a similar role in the vertebrate nervous system — particularly in the retina and cerebral cortex, in which progenitors are known to pass through different competence stages<sup>5,6</sup>. Such studies will also reveal whether the changes in competence of vertebrate progenitors, and the temporal changes in *Drosophila* neuroblasts, are in fact similar cellular processes.

These findings open up several other avenues of further research. For example, how do these widely expressed transcription factors — which are also involved in another developmental process, mesoderm segmentation — confer specific cell fates on neurons? Do these factors, acting with others, control particular transcriptional networks in progenitors to regulate cell fate, and in newly generated neurons to regulate neu-

ronal identity? And what are the components of these networks in different cell types? The availability of whole-genome microarrays for *Drosophila*, which allow rapid analysis of gene-expression patterns in different circumstances, makes these questions tractable.

Another immediate problem is how cells integrate the activity of these factors with the information from extrinsic cues, brought into the cell by the signal-transduction machinery. And finally, it remains to be seen how neuroblasts use the cell cycle to control the sequential expression of transcription factors, and how these factors in turn interact with both the cell-cycle machinery and the well-described 'neurogenic' signalling pathways to regulate cell fate in *Drosophila*. ■

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## Gravitational physics

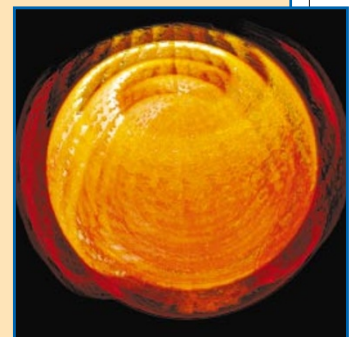
### Black hole blockbuster

What happens when one black hole hits another black hole? Does it get more black? Seriously, though, such questions are being tackled by scientists seeking to detect gravity waves. These invisible waves are ripples in the fabric of space-time, predicted by Einstein's theory of relativity, but that remain undetected. They are thought to be emitted in copious amounts by colliding black holes, and a new simulation by researchers in Germany (J. Baker *et al. Phys. Rev. Lett.* **87**, 121103; 2001) gives an advance preview.

Collisions between other astronomical giants, such as galaxies, produce light and other radiation, but black-hole collisions generate only gravity waves. Black hole binaries are

thought to emit gravity waves all the time, but only when they collide are the waves strong enough to be detected on Earth. Three detectors are expected to start collecting data soon: the US LIGO and German–British GEO600 projects in 2002, and the Italian–French VIRGO detector in 2003.

To fully simulate the merger of two black holes, the German team merged — appropriately enough — two different approaches for calculating what might happen before and after the collision. In the computer-generated image shown here, spherical shells of intense gravity waves move outwards from the centre of the collision. The authors estimate that 3% of the total mass of the black holes is released as energy by



the collision — higher than expected.

These calculations should provide experimenters with a rough estimate of what to look out for, and guide more advanced simulations that take into account, for example, the likelihood that the black holes are also spinning. Prepare for a glimpse of the darkest corners of the Universe. **Sarah Tomlin**