

Field, taken in December 1995 by the Hubble Space Telescope. For two weeks, the telescope focused on a single region of sky, allowing unprecedentedly faint galaxies to be imaged. This provided astrophysicists with an extremely powerful time machine—the most distant galaxies in the Hubble Deep Field are so far away that light from them has spent more than 10 thousand million years travelling to reach us<sup>2</sup>. We observe these galaxies as they were when the Universe was only a tenth of its present age. The relationship between these very early objects and present-day galaxies remains a mystery, however.

Zepf realized that if elliptical galaxies exist at high redshift in much the same form as in the present-day Universe, they ought to be easily picked out of deep surveys like the Hubble Deep Field. The observational quantity required to do that is the ratio of optical and infrared brightness: the 'optical-infrared colour' of a galaxy is said to be red if the ratio is small; blue if it is large. Galaxies that have stopped forming stars are red, because hot, blue, massive stars quickly explode and die, leaving behind a population of cooler, less massive stars that emit most of their light at infrared, rather than optical wavelengths.

Using the Hubble Deep Field (at optical wavelengths) and data sets from infrared cameras on telescopes on the ground, Zepf finds that galaxies with colours characteristic of present-day ellipticals are almost completely absent from surveys of faint galaxies. In particular, there are far fewer very red galaxies than one would expect if the present-day population of elliptical galaxies had formed by a redshift of five.

Why are the missing ellipticals so exciting for cosmologists? The answer has to do with arguments about how these objects formed. Many cosmologists now believe that at high redshifts only low-mass galaxies existed—the building blocks of the galaxies we see today. As time went on, many of these small proto-galaxies coalesced under the influence of gravity, gradually forming the more massive galaxies that populate our corner of the Universe. This model is so popular among theorists that it is often referred to as 'the standard model of structure formation'. There is no question that galaxies do occasionally collide with one another and merge (Fig. 1).

Many famous cases are known, including an interacting pair called the Antennae, where tidal forces have ripped huge plumes of gas and stars out of the galaxies and spewed them into space. There is also strong, though more indirect, evidence from computer simulations that the remnants produced by such mergers will eventually settle down to look much like elliptical galaxies<sup>3</sup>.

Yet many other astronomers doubt

whether the majority of elliptical galaxies could have been formed by mergers. They cite the very great stellar ages, the high abundances of certain chemical elements and the uniformity of these objects (in colour, and in luminosity for a given size) as evidence that ellipticals formed very early and over a short period of time. This is called the single-burst model.

The reader should be cautioned that the fact that red galaxies appear to be missing in deep surveys does not yet spell victory for the merger model and defeat for the single-burst model. Zepf discusses two ways in which ellipticals formed in a single burst could be hidden from view, or simply avoid detection. One possibility is that ellipticals are being produced in dusty starbursts at redshifts less than five. Large amounts of dust can absorb radiation emitted by the forming galaxy, obscuring it from view. Another possibility is that ellipticals already exist at high redshifts, but continue to form stars at a low, but not vanishing, rate. The extra light produced by only a few massive stars would make a galaxy too blue to meet Zepf's criterion for selection as an elliptical.

Observations will undoubtedly settle these questions soon. Dust absorbs high-frequency radiation, but re-emits the energy at far-infrared and sub-millimetre wavelengths. Far-infrared surveys of the sky designed to detect dusty star-forming galaxies at high redshift are already under way<sup>4,5</sup>. It should also become obvious if high-redshift ellipticals are indeed out there, but unrecognized because of gentle star formation, once redshifts have been measured for large samples of distant galaxies.

It must surely be a sign of the vitality of a subject if so many answers are in the offing after so many years of debate. Readers, stay tuned for the next episode in the case of the missing ellipticals. □

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#### Erratum

In the News and Views article "Galaxies take the distance record" by Kenneth Lanzetta (*Nature* **390**, 115–116; 1997), the author's address was omitted. Kenneth Lanzetta is in the Department of Earth and Space Sciences, SUNY at Stony Brook, Stony Brook, New York 11794-2100, USA.

#### Daedalus

### Shrinking or swelling?

Last week Daedalus pointed out that our body fat, like that of all organisms, is stored in liquid form. He proposed an 'oligomolecular diet' of a few well-chosen fats, whose mixture melted only just below our core body temperature. In the body it would act as thermal ballast, giving out latent heat of solidification whenever its owner was exposed to cold.

He now wonders why we store our fat as a melt in the first place. The obvious answer is that biochemistry is a liquid-phase business. A solid fat cannot be digested, mobilized or metabolized. So he now sees his high-melting oligomolecular fat as a powerful new weapon in the war against obesity.

Many dieters complain that their efforts to lose weight remove fat from exactly the wrong parts of the body. Women, for example, may shed fat from their faces (making them look lined and anxious) or from their busts; men may shrink their thighs to emaciation while retaining a corpulent paunch. But the user of DREADCO's oligomolecular fat could simply put a cold pack on those regions that he or she wished to retain. The fat beneath would solidify, and biochemistry could not touch it. Other, less becoming regions would be depleted instead. At the cost of some thermal discomfort, the dieter could lose weight in all the right places, and none of the wrong ones. Better still, solidified fat should be very firm and resilient. Many people dislike their bodies, not for their size, but for their flabbiness. Oligomolecular fat should give a lean, taut appeal even to a fairly ample figure.

This hopeful conclusion is dogged by a converse argument. If solidified fat ceases to register on the body's inventory, the body's internal weight-stat may decide that there is no fat in that deposit at all. It will hasten to lay down new fat, which of course will solidify and vanish from view in its turn. The user will gain weight endlessly in the cooled region. Daedalus recalls that immigrants to northern parts from hot areas often become grossly obese. Perhaps their fat, optimized for the tropics, simply solidifies? If so, the traditional steam-room or Turkish bath may indeed be an effective slimming treatment; and the dietary benefits of low-melting polyunsaturated fats will be confirmed. Either way, varying the melting-point of our body fat seems to offer ways into the problem of obesity. Overweight DREADCO volunteers are now putting the matter to the test.

**David Jones**

# Galaxies take the distance record

Kenneth Lanzetta

**A pair of forming galaxies are now the most distant known objects. Their knotty, irregular structure – visible with the help of an intervening gravitational lens – gives a close-up view of star formation in the early Universe.**

There was a time not long ago when the most distant objects known by far were quasars — exceptional objects powered by hot gas falling onto super-massive black holes. This is easy enough to understand: quasars are the most luminous objects that exist, outshining ordinary galaxies by large factors. Because they are so luminous, quasars appear relatively bright even when viewed across the vast stretches of the Universe.

But over the past two years or so, extremely sensitive observations with the Hubble Space Telescope and the Keck telescope have revealed a Universe of very distant galaxies — unexceptional objects which will by now have become like the ordinary elliptical, spiral and irregular aggregates of stars, gas and dust that we know nearby. These ordinary galaxies are far less luminous than quasars, so they are more difficult to see. Nevertheless, Marijn Franx and collaborators have now reported<sup>1</sup> the spectroscopic identification of a pair of galaxies at a redshift of  $z = 4.92$ . For the first time since the discovery of quasars in 1963, the most distant objects with spectroscopic identifications are ordinary galaxies rather than quasars.

Setting a new distance record might seem impressive enough, but it is not really distance that makes these galaxies of interest to cosmologists. In cosmology it is time that is paramount, and distance and time are inextricably linked. Because light travels at a finite speed, objects are seen as they were in

the past. In ordinary experience, the time delay between an event and our perception of the event is of little consequence, but in cosmology — where the distances are enormous — the delay can be many billions of years.

Cosmologists express distance, or equivalently 'look-back' time, by the redshift  $z$ , which is a measure of the fractional wavelength shift suffered by light as a result of the expansion of the Universe. At a redshift of  $z = 4.92$ , the galaxies identified by Franx and collaborators are seen as they were when the Universe was 20% of its current size, and only about 10% of its current age — or less than a couple of billion years after the Big Bang, given plausible estimates of the age of the Universe. That means that these two galaxies must be at a very early stage of development.

These galaxies are of particular interest, not just because of their great distances, but also because their images have been magnified by the gravitational field of an intervening cluster of galaxies (Fig. 1). This 'gravitational lens' effect — a consequence of general relativity that was first worked out by Einstein in 1936 — makes the galaxies appear both brighter and larger than they otherwise would. Plausible models of the intervening cluster suggest a magnification factor of up to around ten. Distant galaxies are difficult to study precisely because they appear faint and small, so the added boost provided by the

intervening cluster allows the galaxies to be seen in unprecedented detail.

And just what do the new observations reveal? Compared with the intricate and beautiful patterns of nearby spiral galaxies, the galaxies identified by Franx and collaborators are not much to look at. The brighter of the two (G1; Fig. 2) is resolved into one bright knot and several fainter knots, whereas the fainter (G2) is resolved into just a single knot. The knots are compact regions of intense star formation, similar to those seen in nearby 'starburst' galaxies. But the knots in galaxies G1 and G2 are even more luminous than the knots typical of nearby starburst galaxies, indicating higher star formation rates in the distant past.

This is not at all unexpected. Many models predict that a substantial fraction of the stars in today's galaxies were formed at early times, when large quantities of gas could have provided the raw material. At the rate at which galaxy G1 is forming stars, a large portion of the central bulge of our own Milky Way galaxy could be formed in just 100 million years.

But the galaxies show evidence of gas outflows, which are presumably driven by the intense star formation activity. If outflows rapidly disperse the gas from which the stars are formed, then the star formation episodes must be brief. This might explain the knotty, irregular structure of the galaxies. Galaxies of redshift  $z$  near 3 appear less irregular<sup>2</sup>, but these lower-redshift galaxies are not magnified by gravitational lenses and so are seen in much less detail.

Interpreting galaxies G1 and G2 is complicated by the same factor that complicates the interpretation of other distant galaxies: dust. Dust obscures light, especially the ultraviolet and blue light emitted by young stars. (This is the reason that the setting sun appears red. Dust in Earth's atmosphere scatters and absorbs blue light but leaves red light relatively unaffected.) If galaxies G1 and G2 are heavily obscured by dust, then their star

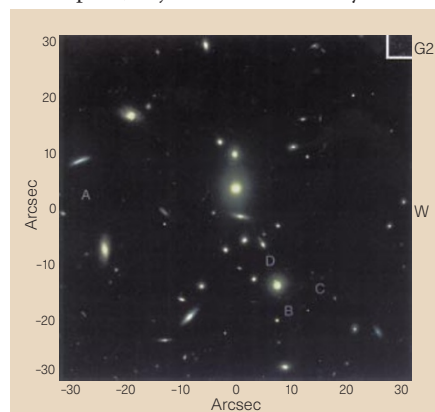


Figure 1 This cluster of galaxies acts as a gravitational lens, magnifying much more distant galaxies behind it.

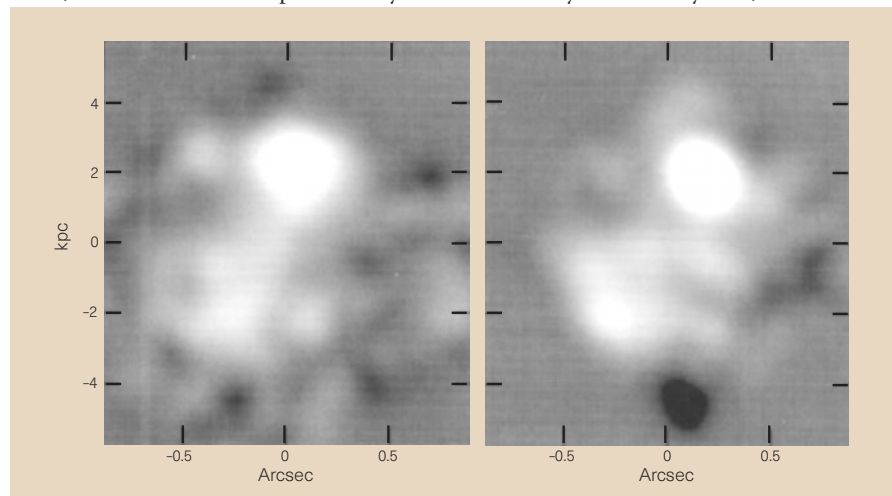


Figure 2 Two images of the galaxy G1, each reconstructed from a separate gravitationally lensed arc. At a redshift of 4.92, it and its partner G2 are the most distant known galaxies.

formation rates could be much higher than those directly indicated by the observations.

Just how much of the ultraviolet light of distant galaxies is obscured by dust is a question that profoundly affects our understanding of how galaxies form and evolve. Some argue for a high degree of obscuration, as in nearby dusty starburst galaxies<sup>3,4</sup>. If that is the case, galaxy formation was early and rapid. Others argue for low obscuration, reasoning that if significant early star formation were hidden from view, then there should be more old stars in today's galaxies than are actually seen<sup>5</sup>. If that is so, galaxy formation was late and slow. The difference is important because it amounts to the difference between galaxy formation by 'monolithic collapse' of protogalactic gas clouds and formation by hierarchical merging of subgalactic fragments.

Deciding between these possibilities is not going to be easy. One strategy is to observe distant galaxies at infrared wavelengths, where the effects of dust obscuration are less severe. This capability is just within reach of large ground-based telescopes today but should become commonplace as adaptive optics techniques — which compensate for the blurring effect of Earth's atmosphere — are developed and implemented. If the pace of progress continues as it has over the past few years, an answer is likely to be found soon. □

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## Apoptosis

# A Bad kinase makes good

Thomas F. Franke and Lewis C. Cantley

The regulation of cell survival is a central feature in animal development and in diseases such as cancer. Results published over the past year implicate phosphoinositide 3-kinase (PI3K) and its downstream target, the serine/threonine protein kinase Akt, in a pathway that conveys survival signals from various cell-surface receptors<sup>1</sup>. Two papers in *Science*<sup>2</sup> and *Cell*<sup>3</sup> now report a missing piece in this signalling pathway. They show that Akt phosphorylates a critical serine residue on Bad, a protein that promotes cell death (apoptosis) by binding to and blocking the activity of Bcl-x<sub>L</sub>, a cell

survival factor. Upon phosphorylation, Bad dissociates from Bcl-x<sub>L</sub>, which is then free to resume its activity as a suppressor of cell death (Fig. 1).

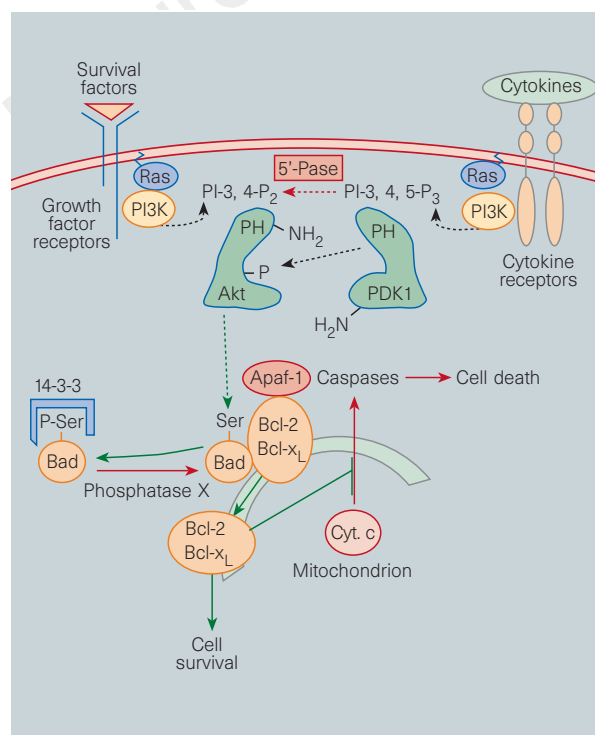
The Bcl-2 family of proteins has been implicated in cell survival decisions. Bcl-2 and Bcl-x<sub>L</sub> suppress apoptosis, in part by blocking the release of cytochrome *c* from mitochondria, a critical step in the activation of the caspase protease cascade. Other family members, such as Bad and Bax, interfere with the activity of Bcl-2 or Bcl-x<sub>L</sub> by binding to them and forming non-functional heterodimers<sup>4</sup>. In response to interleukin-3, for

example, Bad is phosphorylated at two sites, dissociates from Bcl-x<sub>L</sub> and then interacts with the phosphoserine-binding protein, 14-3-3 (ref. 5). The released Bcl-x<sub>L</sub> then promotes cell survival by blocking the caspase protease cascade.

Del Peso et al.<sup>2</sup> now show that PI3K activity is necessary for the phosphorylation of Bad after interleukin-3 treatment of cells. Moreover, they have identified Akt as the kinase that phosphorylates Bad on a site that is required for its interaction with 14-3-3. Datta and colleagues<sup>3</sup> independently identified Bad as a substrate for the Akt kinase and showed that of two potential phosphorylation sites in mouse Bad, only one (Ser 136) is phosphorylated by Akt. Furthermore, they demonstrate that Akt overexpression prevents Bad-induced cell death of cerebellar granule neurons, suggesting that Akt-dependent cell survival is mediated in part by phosphorylation of Bad.

Other studies further clarify how Akt itself is regulated. Previous research has shown that Akt directly binds to phosphoinositide products of PI3K by an N-terminal pleckstrin homology (PH) domain<sup>1</sup>. Although this interaction causes partial activation of Akt, full activation requires that Akt be phosphorylated by other serine/threonine protein kinases. One such kinase, phosphoinositide-dependent kinase-1 (PDK1), which phosphorylates and activates Akt *in vitro*, has now been purified and cloned<sup>6–8</sup>. PDK1 has a carboxy-terminal PH domain that apparently is involved in its activation by phosphoinositide products of PI3K (Fig. 1). Taken together, these findings identify a sequence of signalling events that originates with the binding of survival factors to cell-surface receptors and results in the generation of second messenger molecules through the activation of PI3K. These second-messengers induce the activity of the Akt kinase by binding to the PH domains of Akt and PDK1, resulting in phosphorylation of residues on Akt, which are critical for the regulation of its activity. Activated Akt then phosphorylates the pro-apoptotic protein Bad. Phosphorylated Bad is translocated from the mitochondria to the cytosol through its interaction with 14-3-3, and the function of Bcl-x<sub>L</sub>, the gatekeeper of cytochrome *c* efflux at the mitochondrial membrane, is restored. By blocking the release of cytochrome *c* from the mitochondria, caspase activation and further execution of the cell-death cascade is prevented.

The discovery that Akt is a Bad kinase provides an intriguing explanation for the role of PI3K and Akt in cell survival. However, not all survival signals require PI3K activity and Akt-independent survival pathways exist<sup>9</sup>. Furthermore, it is likely that there are additional targets of Akt in cell survival because Bad is not ubiquitously expressed. Moreover, PI3K and Akt feature in other signalling pathways



**Figure 1 The PI3K/Akt signalling cascade and cell survival.** When various extracellular signals including growth factors and cytokines bind to their cell-surface receptors, intracellular phosphoinositide 3-kinase (PI3K) becomes activated. This results in the generation of two lipid products (PI-3,4-P<sub>2</sub> and PI-3,4,5-P<sub>3</sub>; see page 123 of this issue), which act as second-messenger molecules and activate the serine/threonine kinases Akt and PDK1 (through their PH domains). Activated Akt phosphorylates the pro-apoptotic factor Bad on a serine residue, resulting in its dissociation from Bcl-x<sub>L</sub> and its association with 14-3-3. Released Bcl-x<sub>L</sub> is then capable of suppressing cell-death pathways that involve the activity of Apaf-1, cytochrome *c* (Cyt. *c*) and the caspase protease cascade<sup>10</sup>.