the field breaks down. A more attractive medium for the next generation of particle accelerators is a plasma — a gas of atoms that has been ionized into a soup of electrons and nuclei. Plasmas can support electric fields with strengths of around a hundred gigavolts per metre, which is orders of magnitude higher than conventional accelerators.

At the centre of Blue and colleagues' apparatus[1] is a chamber 1.4 metres long containing a hot plasma created from lithium atoms. The electron density in the plasma is about 1.8×10^{14} per cubic centimetre. When a tightly packed bunch, or pulse, of positrons is fired into the plasma, it creates a rippling electric field behind it, rather like the wake of a boat (Fig. 1), and hence the name 'wake field'. Inside the chamber, the positively charged particles in the pulse 'suck in' negatively charged electrons from the plasma. To restore charge neutrality, the displaced electrons then snap back, away from the pulse, but tend to overshoot their original positions. This oscillation in plasma electron density creates an oscillating electric wake field, moving behind the pulse (Fig. 2).

Roughly the first two-thirds of the positron pulse (which overall comprises about 10^{10} particles) lose energy in setting up the intense plasma wake field. From their initial energy of 28.5 gigaelectronvolts (GeV), these positrons decelerate at a rate of 49 megaelectronvolts (MeV) per metre. But the wake field they create accelerates the trailing third of the beam, increasing these particles' energies by almost 80 MeV over the length of the chamber, which corresponds to an accelerating gradient of 56 MeV per metre. The results are in excellent agreement with a three-dimensional simulation of the process, which predicted a peak energy gain of 78 MeV.

This is the first experiment to demonstrate energy gain by positrons in a plasma, and to use and accelerate particles that are at energies of interest for high-energy physics. (An existing electron–positron collider at SLAC used beams of particles with energies up to 50 GeV; the 'next linear collider', still at the planning stage, will have beam energies ultimately of 500 GeV.) To achieve this, Blue *et al.*[1] have had to overcome some tough practical problems. For example, the transportation and focusing of the positron pulse in the long plasma chamber is a remarkable achievement. The pulse shows no evidence of instabilities, particularly of the type known as 'hosing' instabilities[2], which induce transverse oscillations in the tail of the pulse that eventually destroy it. It is also significant that the positrons can propagate in the plasma without being annihilated by their electron antiparticles.

High-gradient acceleration of electrons as well as positrons is necessary for the development of a compact electron–positron plasma collider. In fact, the positron pulse used by Blue *et al.*[1] could simply be replaced by an electron pulse. The wake field would then arise through a slightly different mechanism: the electron bunch expels all the plasma electrons within its radius (known as 'blow-out'), leaving a channel of positively charged ions or nuclei behind it; again, the oscillating charge density generates a wake field that will accelerate the tail-end of the bunch. Calculations show that the wake fields generated by positrons are weaker than for electrons, but the two would be comparable if, rather than being uniform, the plasma were shaped to form a hollow cylinder[3].

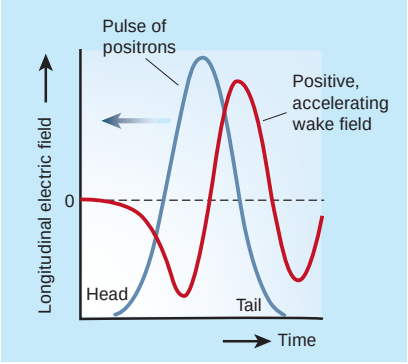

Figure 2 **Beam-driven plasma acceleration. A pulse of positrons (blue line) is fired into a plasma of lithium gas. The positively charged particle pulse attracts the negatively charged electrons in the plasma, drawing them in and creating an electric field in the wake of the pulse (red curve). Initially the longitudinal field dips negative, but then the displaced electrons snap back, overshooting their original positions and driving the longitudinal field to positive values. This strong, oscillating field is termed a 'wake field'. Although particles at the head of the pulse lose energy in setting up the wake field, particles in the tail are accelerated by it.**

Instead of particles, a laser pulse can be used to set up an accelerating wake field in a plasma. In this case, the radiation pressure of the laser pushes the plasma electrons out of its path, creating oscillations in its wake. Previous experiments[4] on plasma wake fields driven by terawatt lasers have shown that particles injected into the wake field gain about 200 MeV of energy, but the acceleration has only been sustained over millimetre distances; Blue and colleagues' beam-driven acceleration is sustained over more than a metre.

Perhaps the first incarnation of the plasma wake-field accelerator will be within a conventional accelerator as a 'plasma afterburner'[5]. By introducing 10-m plasma sections into a linear collider that is many kilometres long, wake-field acceleration could be used to double the energy of conventionally accelerated particles. But wake-field acceleration comes at the price of decelerating the head of the particle bunch. To counteract this, plasma lenses are included in the design, between the afterburner and the collision point. Such lenses focus the particles into a tighter bunch, far more strongly than do the conventional magnetic variety[6]. The tighter the bunches are focused, the more likely are particles in opposing bunches to collide when they meet, so the rate of collisions is not degraded by inclusion of the afterburner.

The work presented by Blue *et al.*[1] marks the most significant progress so far in the field of advanced accelerator research. It is likely to have an impact on many fields, as compact accelerators are developed for wider applications, such as in medicine. And the impact on the way particle physics is done in this century will no doubt be profound. ■

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Ageing

Microarraying mortality

David Gems and Joshua J. McElwee

Understanding how we grow old is a long-sought goal. A new large-scale study of gene expression in worms allows us to glimpse the complex biochemistry of lifespan.

The past decade has seen dramatic developments in studies of the genetics of ageing and longevity, mostly involving model organisms such as the nematode worm *Caenorhabditis elegans*, baker's yeast, fruitflies and mice[1]. This has created considerable optimism that an understanding of the biology of ageing is within reach. So far, scores of ageing-related genes have been identified, in which altered activity increases longevity or accelerates ageing. But simply identifying these 'gerontogenes' often sheds no light on the real question at stake — what are the actual

biochemical processes that determine lifespan? The findings reported by Murphy *et al.* on page 277 of this issue[2] represent an important step towards the answer. Using DNA microarray technology, these authors have identified a large set of genes whose activity is linked to lifespan, and they provide evidence that many of these genes act in concert to control longevity and ageing.

A prime example of an interesting gerontogene that had, until now, provided little insight into the mechanics of ageing is *daf-16*. This gene encodes a transcription factor, DAF-16 — a protein that modifies the activity of other genes — which is a powerful regulator of *C. elegans* lifespan[3,4]. DAF-16 is switched off by a hormonal signalling pathway akin to that activated by the mammalian insulin and insulin-like growth factor 1 (IGF-1) proteins[5]. Reduced activity of this pathway can greatly increase adult life span not only in *C. elegans*[6], but also in fruitflies[7] and mice[8]. Even ten years ago, it was clear that to understand ageing thoroughly we would need to identify the genes regulated by DAF-16 (ref. 6). Yet screening for mutants failed to identify any of these 'downstream' genes.

Fortunately, a new technology has emerged that is well suited to addressing this question: DNA microarrays. Using microarrays, researchers can take a snapshot of the activity of most of the genes in the fully sequenced *C. elegans* genome. By comparing the snapshots from normal animals to similar snapshots from animals in which a particular gene is mutated, it is possible to work out which other genes in the mutants are activated or repressed as a result of that mutation. Murphy *et al.* used this technology to identify two classes of genes that are activated or repressed by DAF-16. Class 1 genes are switched on by DAF-16 and are associated with increased lifespan, whereas class 2 genes are repressed by DAF-16, and are associated with reduced lifespan. Using these analytical approaches, the authors found 189 class 1 and 122 class 2 genes.

But do any of these genes actually have a role in determining lifespan? To test this, Murphy *et al.* analysed the genes' functions, using an elegant methodology called RNA interference. If *C. elegans* are fed bacteria that produce pieces of RNA matching a given worm gene, the activity of that gene is reduced, or silenced. The expectation was that in some cases, silencing the genes in class 1 would reduce lifespan, whereas silencing class 2 genes would increase lifespan. As it turned out, a surprisingly high proportion of genes behaved as predicted.

This is an important finding. The previous failure to identify genes that act downstream of DAF-16 had raised the gloomy prospect that this protein might regulate numerous genes that act in concert, such that inactivation of any single gene would have no perceptible effect. Instead, it appears that the increased longevity resulting from DAF-16 activation is due to the additive effects of many genes, which individually exert a small effect on lifespan. This is a satisfying discovery, because if individual downstream gerontogenes had little effect on ageing, it would be difficult to see how longevity could evolve.

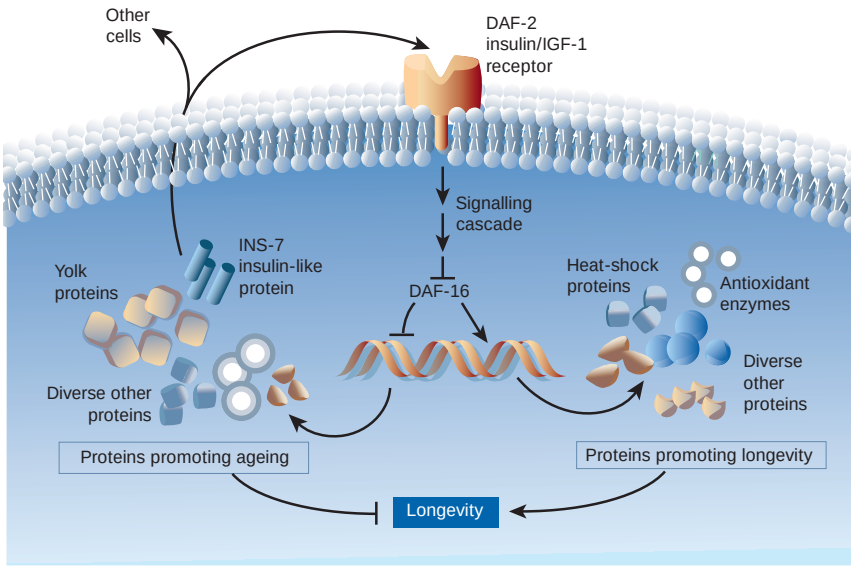

Figure 1 **Ageing versus long life: the molecules involved. Murphy *et al.*[2] have found that the transcription factor DAF-16 controls the expression of a battery of genes, many of which have small effects on lifespan — promoting either ageing or longevity — in *Caenorhabditis elegans*. Consistent with earlier studies, the pro-longevity genes include some that encode antioxidant enzymes and others encoding heat-shock proteins, which can restore misfolded proteins to their active conformations. Genes that promote ageing include some that encode yolk proteins, consistent with a link between ageing and reproduction. Another pro-ageing protein is the insulin-like INS-7, which, by binding to the insulin/IGF-1 receptor (DAF-2), may repress DAF-16 on the same and other cells. This suggests the presence of a positive feedback loop that regulates DAF-2 activity. There are also many other proteins whose mechanistic links to ageing are as unclear as they are intriguing. Arrows indicate activation; T-bars indicate inhibition.**

So does the identity of DAF-16-regulated genes explain the biochemistry of ageing, or is it just another big list of gerontogenes? The list certainly gives a few inklings. One influential theory of the biochemistry of ageing is the oxidative-damage theory: over time, oxidative by-products of metabolism cause molecular damage, which accumulates and eventually causes ageing and death[9]. Consistent with another recent microarray study involving *daf-16* (ref. 10), Murphy *et al.*[2] found that some of the genes that are upregulated by DAF-16 do encode enzymes that protect against or repair oxidative damage (Fig. 1).

But numerous other biochemical processes are implicated; DAF-16 also regulates genes involved in antimicrobial responses, genes for several protein-digesting enzymes, metabolic genes, and many genes of unknown function. Finally, several signalling molecules seem to influence longevity, including an insulin-like protein encoded by *ins-7* — one of the bewildering multiplicity of 39 such genes in the *C. elegans* genome. Potentially, the most important proteins identified are among the many whose mechanistic link to ageing is mysterious. It is tantalizing to think that among these proteins could be some that determine the differences in longevity between animal species, and control human ageing.

Seeking insight into the biochemistry of ageing, Murphy *et al.* panned their mine of microarray data for genes that fit existing expectations — an approach sometimes referred to as 'fishing'. But the drawback with fishing is that it is all too tempting to fit your data to the hypothesis, rather than the other way around. What is needed now is an unbiased and statistically rigorous analysis of which functional classes of genes are controlling lifespan. Such an approach would be better able to identify processes not previously known to be involved in ageing. The raw microarray data generated by Murphy *et al.* are publicly available, so other researchers should be able to analyse the data further and fully realize the value of this information.

Understanding the function of the impressive list of genes identified here[2], and their role in ageing, must be the next major task — one likely to take years of painstaking analysis. This will mean much hard work at the molecular-biology coalface, after the heady interlude of microarray analysis. ■

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Global change

The past and future of El Niño

Sandy Tudhope and Mat Collins

A new study of past variations in El Niño behaviour provides a much improved record from pre-instrumental times. It will be a valuable resource for testing the models used in climate prediction.

Droughts, floods, forest fires and changed patterns of storms and ocean conditions — these are some of the hallmarks of the El Niño Southern Oscillation (ENSO) climate cycle. On page 271 of this issue, Cobb *et al.*[1] describe how their analysis of fossil corals provides new evidence of how the ENSO cycle can strengthen and weaken without an obvious external driving force. Not least, these data provide helpful indications as to how ENSO might change in the future.

El Niño events occur every three to seven years, and arise naturally through the strong inter-action between the ocean and atmosphere in the tropical Pacific[2]. The effects are felt worldwide because the tropical Pacific is a powerful source of heat for driving atmospheric circulation. Even small changes in the sea-surface temperature in this region have major repercussions for global climate. Dry conditions in the western Pacific, warmer-than-average conditions in the northern United States and wetter-than-average conditions to the south, and suppressed hurricane development in the Atlantic, are all indicators of an El Niño event. Consequently, when the ENSO cycle is particularly strong, as occurred in 1982–83 and again in 1997–98, the changed weather patterns have profound social, economic and ecological consequences[3].

Although much of the basic physics of the ENSO cycle is now reasonably well known, some aspects remain poorly understood. What, for instance, causes one El Niño event to be different from another? One obstacle to progress is the paucity of instrumental data before the mid-twentieth century. From the data that do exist, it is clear that ENSO varies considerably in strength and frequency, but the instrumental records are too short to tell with confidence if this variability is internal or driven by changes in background climate[4].

Cobb *et al.*[1] use the skeletons of annually banded reef-building corals as natural 'proxy' archives of tropical climate, and thereby extend the record of ENSO further into the past. Their approach involves analysing the oxygen isotopic composition of the coral skeletons as a measure of the combined effects of changes in sea-surface temperature (through a temperature-dependent fractionation between water and calcium carbonate), and seawater isotopic composition (which is strongly influenced by rainfall and evaporation). At their study site, Palmyra Island in the central tropical Pacific, warm temperatures and increased rainfall during the El Niño phase of the Southern Oscillation combine to drive the oxygen isotopic composition of the coral skeletons towards lighter (more negative) values. The excellent match between an isotope record from a living coral and the instrumental records of recent ENSO activity provides proof of concept.

However, living corals yield only about 100 years of record, so Cobb *et al.* also analysed cores collected from ancient corals, washed onto the top of the reef by storms. Using an approach borrowed from tree-ring reconstructions of climate, they combine high-precision dating with 'wiggle matching' of the monthly-resolution isotope records to create continuous coral chronologies. The final record is not complete: they have reconstructed several periods, representing a total of some 430 years since about AD 930, but the method has yielded much more robust, and extended, ENSO proxy records than have been produced before for this period.

The key finding is that ENSO appears to have varied considerably in strength over the past millennium, with changes occurring rapidly, on timescales of decades or so. Compared with earlier periods, the events in the twentieth century appear to have been relatively strong, but not exceptionally so. The inferred changes in ENSO strength do not appear to be correlated with documented changes in Northern Hemisphere regional climate — for instance, the Little Ice Age

100 YEARS AGO

Rutherford and Soddy pointed out that the almost invariable presence of helium in minerals containing uranium indicated that that gas might be one of the ultimate products of the disintegration of the radio-elements. Rutherford, moreover, determined the mass of the projected particle which constitutes the "α-ray" of radium to be approximately twice as great as that of the hydrogen atom, an observation that points in the same direction… We have been engaged for some months in examining the spectrum of the "radio-active emanation" from radium… We have found that after removing hydrogen and oxygen from the gases evolved from 20 mgrs. of radium bromide, the spectrum showed the presence of carbon dioxide. On freezing out the carbon dioxide, and with it, a large proportion of the radium "emanation," the residue gave unmistakably the D_3 line of helium.

ALSO…

It has been stated that the radium rays have been successfully applied in the treatment of a case of cancer by Prof. Gussenbauer, of Vienna. The tumour completely disappeared as a result of the application, radium bromide being made use of as a source of the rays. The early publication of these details in the public Press before there has been time to test the method effectually is much to be deprecated.

From *Nature* 16 July 1903.

50 YEARS AGO

Personality Development. By J. S. Slotkin. **The author, who is a social anthropologist, begins by saying that he has tried to work out a systematic theory of personality development, from the hypotheses and evidence of various relevant sciences. The material is, however, systematic only in so far as it has been distributed under four major headings: inheritance, socialization, culturization and individualization. Within each of the fields the approach is mainly descriptive and anecdotal, and is adorned by a wealth of quotations from ancient and modern writers. It may well be that in the meantime this kind of approach is repaying. Certainly it does not suffer from the aridity of some recent statistical work in the same field. But perhaps we can only be scientific about people if we are content to be dull.**

From *Nature* 18 July 1953.