information is transmitted via the Notch protein, which lies on the surface of the receiving cell, and that the molecule that activates Notch — Delta — is also a membrane-bound protein[5]. There is no evidence for a diffusible form of Delta that has biological activity[6,7], and sequential relay of the signal from cell to cell (Fig. 1b) has also been excluded. There is evidence that a secreted protein called Scabrous contributes to the ability of SOPs to signal at long range, but not at short range[8]. Scabrous has also been implicated in long-range signalling to control ommatidial rotation[9], whereby groups of photoreceptor cells rotate relative to other cells in the epithelial plane in the eye imaginal disc. Although Scabrous has been seen to be associated with filopodia, in these contexts it does not activate Notch, and its contribution remains to be defined.

So, how could membrane-bound Delta signal to membrane-bound Notch over several cell diameters? de Joussineau *et al.* resolve this by showing that the Delta-expressing cells use filopodia to convey the signal directly to all cells of the equivalence group (Fig. 1c). The extensions contain Delta protein, which presumably activates Notch on the responding cells by direct contact[1,8]. Interfering with the formation of these filopodia compromises the ability of the SOPs to signal, resulting in flies that have too many sense-organ bristles.

To interfere with filopodium formation, de Joussineau *et al.* blocked the activity of a protein that organizes the cellular scaffold supporting the outgrowing filopodia. This approach is not without possible caveats, but the authors were careful to show that Notch signalling between immediate neighbours was not affected. So we can be reasonably confident that the effects they report resulted from the disruption of filopodia, and not from a general perturbation of cell interactions or signalling. Interestingly, the so-called founder cells that pattern fly muscles are also selected from equivalence groups by a process involving Notch and Delta. It would not be surprising if contact-mediated signalling were involved here too.

Cells can either send signals or receive them, and the signals can either remain attached to the cells that make them or be released. It seems that epithelial cells can engage in all these modes of communication. de Joussineau *et al.*[1] have provided the first clear example of a situation in which epithelial cells use direct contact — and a surface-bound signal — to transmit instructions to distant neighbours, thereby extending the possible range of contact-mediated signalling within an epithelial layer. Other reports have suggested that cellular extensions are involved in sending secreted signals over longer distances between tissue layers, perhaps to ensure that the signal reaches its intended target and does not get lost or consumed in transit[10,11]. So it appears that epithelial cells send signals, and are not just passive recipients of information. ■

Stephen M. Cohen is in the European Molecular Biology Laboratory, Meyerhofstrasse 1, 69117 Heidelberg, Germany.
e-mail: cohen@embl.de

1. de Joussineau, C. *et al. Nature* **426,** 555–559 (2003).
2. Rorth, P. *Cell* **112,** 595–598 (2003).
3. Ramirez-Weber, F. A. & Kornberg, T. B. *Cell* **97,** 599–607 (1999).
4. Milán, M., Weihe, U., Perez, L. & Cohen, S. M. *Cell* **106,** 785–794 (2001).
5. Simpson, P. *Curr. Opin. Genet. Dev.* **7,** 537–542 (1997).
6. Parks, A. L. *et al. Development* **127,** 1373–1385 (2000).
7. Mishra-Gorur, K. *et al. J. Cell Biol.* **159,** 313–324 (2002).
8. Renaud, O. & Simpson, P. *Dev. Biol.* **240,** 361–376 (2001).
9. Chou, Y. H. & Chien, C. T. *Dev. Cell* **3,** 839–850 (2002).
10. Gibson, M. C. & Schubiger, G. *Cell* **103,** 343–350 (2000).
11. Cho, K.-O., Chern, J., Izaddoost, S. & Choi, K.-W. *Cell* **103,** 331–342 (2000).

Astrophysics

Testing time for gravity

E. P. J. van den Heuvel

The discovery of two neutron stars tightly orbiting each other suggests that the rate of neutron-star mergers in the Universe is higher than had been thought — which is good news for seekers of gravitational waves.

The emission of gravitational waves by accelerated masses — such as two compact stars orbiting each other — is predicted by Einstein's theory of general relativity. In 1993 Taylor and Hulse earned the Nobel prize for their precise measurement of the rate of orbital decay of the binary pulsar PSR B1913+16 by the emission of gravitational waves[1]. The measured orbital decay of this binary pulsar, and of two further double neutron stars with somewhat wider orbits, is exactly in accordance with the prediction of Einstein's theory and provides very strong — albeit indirect — evidence for the existence of gravitational waves.

Gravitational waves represent one of the great challenges of present-day fundamental physics. No one has ever detected them directly, but the chances of doing so have just improved. On page 531 of this issue, Burgay and colleagues[2] describe their discovery of a remarkable system of two neutron stars that are orbiting each other, elliptically, in only 2.4 hours. This orbital period is three times shorter than that of the Hulse–Taylor binary pulsar, hitherto the closest double neutron star known. Peculiar as it may seem, double neutron star systems are of crucial importance for

100 YEARS AGO

Doubts about Darwinism. **By a Semi-Darwinian. Pp. vi+115. (London: Longmans, Green and Co., 1903.) Price 3*s*. 6*d*.**

The preface of this work informs us that its author has endeavoured to conform strictly to the principle laid down by Lord Kelvin, as follows:— "If a probable solution, consistent with the ordinary course of nature, can be found, we must not invoke an abnormal act of Creative Power." Unfortunately the "Semi-Darwinian's" practice is not in accord with his profession. Whenever he meets with a problem in evolution which appears to him inexplicable on the lines of natural selection, so far from seeking a "probable solution, consistent with the ordinary course of nature," he resorts at once to the intervention, by a direct creative act, of "a Being possessing intelligence, intention and power." This is bad science, and we much doubt whether it is good theology.

ALSO

Dr. Alcock, in his recent paper at the Royal Society, finds the rate of transmission of nerve impulses in man to be 66 metres per second. Sir Michael Foster, in his "Physiology" (1888, part i. p. 76), gives it as 33 metres per second. The difference is considerable, and places us in a dilemma :— (1) either Sir Michael Foster or Dr. Alcock is widely wrong; or (2) the rate of transmission has become greatly accelerated during the last fifteen years. Of the two, the latter seems to me the simpler explanation.

From *Nature* 3 December 1903.

50 YEARS AGO

One of the most fundamental problems, both for genetics and embryology, is that of whether the genes in the nuclei of differentiated tissues retain their full range of capacities, or whether some irreversible alteration affects them. The most direct method of investigating this is to develop techniques which permit the transplantation of nuclei from differentiated cells of one kind into enucleated cells of different developmental potentialities. Briggs and King have reported some attempts in this direction… We have carried out somewhat similar experiments with the eggs of the newt *Triturus palmatus*… A reasonably high proportion of injected eggs cleaved, but none of them succeeded in completing gastrulation, even when the injected nucleus came from a blastula.

From *Nature* 5 December 1953.

Box 1 LIGO

CALTECH

LIGO, the Laser Interferometer Gravitational Wave Observatory[6], is one of several detectors around the world aiming to prove, by direct measurement, that gravitational waves exist. Through the observation of such waves, LIGO should also be able to study cosmic cataclysms such as supernovae and coalescing double neutron stars.

The difficulty is that gravitational waves are extremely weak. For example, if two neutron stars, each with a mass equal to that of the Sun, coalesce 100 million light years away, the gravitational waves reaching Earth would displace the oceans by a distance that is only ten times the diameter of an atomic nucleus[9].

LIGO is, in fact, two observatories, at 'seismically quiet' sites in Hanford, Washington state (see picture), and in Livingston, Louisiana (so that a detection at one site can be validated by a similar detection at the other). The two arms of each interferometer are 4 km long, containing vacuum tubes that are 1.2 m in diameter. The central building, where the arms meet, houses lasers and control equipment.

Heavy weights are suspended at the ends of the vacuum tubes. The distance between the weights, which are free to move horizontally, is measured accurately using laser beams that bounce back and forth between the weights' mirrored surfaces. A passing gravitational wave will change, very slightly, the distance between the weights in each of the arms, creating a characteristic interference pattern between the laser beams. Measuring this interference signals the detection of a gravitational wave.

LIGO is ultimately expected to be able to detect the coalescence of double neutron stars 60 million light years away. A funding application has already been submitted to upgrade the existing detector, from 2007, to 'Advanced LIGO', which could probe the Universe out to 10 times that distance. **E.v.d.H.**

the detection of gravitational waves: at the end of their inward-spiralling motion, the two neutron stars collide and merge; during the last minute of their lives, there is an enormous release of gravitational radiation that is likely to be detectable on Earth. Several instruments capable of picking up such gravitational waves have been built, including VIRGO in Italy[3], GEO600 in Germany[4], TAMA in Japan[5] and LIGO, the Laser Interferometer Gravitational Wave Observatory[6], based on sites in Washington and Louisiana, USA (see Box 1).

The Hulse–Taylor binary pulsar is expected to merge 320 million years from now; for the new system found by Burgay *et al.*[2], the merger is 'only' 85 million years away. But there must also be systems, born long ago, that are merging today. Near the end of the spiral-in process, one minute before the stars merge, their orbit has shrunk to a size of only a few hundred kilometres, and the two neutron stars move around each other some 30 times each second, producing strong gravitational waves with that same frequency (30 hertz). In the last minute before the merger, the orbital frequency increases rapidly, from 30 to 1,000 times per second; the strength of the gravitational wave emission increases simultaneously. Converted into an audio signal, this is the characteristic 'death chirp' of a double neutron star. The chirp signal, as well as the final, giant pulse of gravitational waves as the stars merge, is so strong that it should be detectable by gravitational wave antennas such as LIGO, out to a distance of about 60 million light years.

What makes the discovery of the new star system so exciting is that it indicates that these detectable 'death chirps' of double neutron stars occur much more frequently than the previous disappointing estimate of one event in 10–20 years (see, for example, ref. 7). How is this rate calculated? Multiplying the estimated merger rate of double neutron stars in our Galaxy by the number of galaxies within LIGO's detection range gives the expected event rate for LIGO. The expected merger rate in our Galaxy is simply the number of double neutron stars in our Galaxy divided by the average time it takes them to merge. Going through all the statistics, the merger rate thus calculated for our Galaxy depends heavily on the shortest-lived system known — which so far has been the Hulse–Taylor binary pulsar.

Burgay and colleagues' new system[2] appears to be much nearer to us than the Hulse–Taylor binary pulsar — around a tenth of the distance. Its radio emission is also very much weaker, suggesting that, as most detections of this kind rely on radio observations, many similar sources are as yet undetected. These facts together imply that there must be many more such systems in the Galaxy. Given also the short merging timescale of the new system, Burgay *et al.* calculate that the merger rate of double neutron stars in our Galaxy (and also in other galaxies) must be at least 10 times — possibly even 30 times — the rate previously estimated. Of course, the statistics are small, so the error margins on these estimates are still sizeable. But even taking that into account, the most favourable new estimate for the rate of death chirps detectable with existing detectors on Earth is around one in every one to two years.

Apart from its relevance to the search for gravitational waves, this new binary pulsar is also in itself an outstanding laboratory for testing general relativity. In addition to the orbital shrinking by gravitational-wave emission, double neutron stars show four other relativistic effects, which in principle can be accurately measured. Three of these are 'classical' relativistic effects — tiny corrections to newtonian theory that were first measured in the Solar System. The clearest observable of the three is the rotation, or precession, of the major axis of the elliptic orbit in the orbital plane. The measured Solar System equivalent of this is the precession of the orbital axis of the planet Mercury; but the Hulse–Taylor binary pulsar held the record, with a precession 36,000 times faster than Mercury's. That record has now fallen: the orbital axis of Burgay and colleagues' system rotates four times faster still — more than 16 degrees in a year. The other two, smaller, classical effects will also soon be measured for this system, but it will take time.

The fourth relativistic effect is called 'geodetic precession', so far only detected with relatively low precision, after 25 years of observations, in the Hulse–Taylor binary pulsar[8] (where it has a period of 300 years). In the newly discovered system, the period of geodetic precession is only 75 years, and the effect is expected to be clearly measured in a relatively short time. Also, because of the great distance from Earth of the Hulse–Taylor binary system, the accuracy of measurements of relativistic effects there is always limited by the influence of galactic rotation. In the new, much closer, system[2], this problem disappears. In principle, much higher accuracy can be reached in the measurement of all relativistic effects, and the accurate confirmation of geodetic precession will be an important new test of general relativity. In addition, there are other, tiny relativistic effects that have never yet been detected in binary neutron stars, but may be measurable for the first time here.

There is, no doubt, much more to be learned from this double neutron star system. If gravitational waves can be expected more frequently than previously thought, that is exciting news indeed. ■

E. P. J. van den Heuvel is at the Astronomical Institute Anton Pannekoek and the Centre for High Energy Astrophysics, University of Amsterdam, 1098SJ Amsterdam, The Netherlands.

e-mail: edvdh@science.uva.nl

---

1. Taylor, J. H. *Rev. Mod. Phys.* **66,** 711–719 (1994).
2. Burgay, M. *et al. Nature* **426,** 531–533 (2003).
3. www.virgo.infn.it
4. www.geo600.uni-hannover.de
5. http://tamago.mtk.nao.ac.jp
6. www.ligo.caltech.edu
7. Kim, C. *et al. Astrophys. J.* **584,** 985–995 (2003).
8. Weisberg, J. M. & Taylor, J. H. *Astrophys. J.* **576,** 942–949 (2002).
9. http://archive.ncsa.uiuc.edu/Cyberia/NumRel/LIGO.html