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NEWS AND VIEWS

Gravitational radiation and the binary pulsar

from Virginia Trimble

GRAVITATIONAL radiation not only exists, but it is apparently also doing exactly what general relativity says it ought to, at least in the binary pulsar PSR1913 + 16. This is the conclusion drawn by J.H. Taylor and J.M. Weisberg writing recently in the *Astrophysical Journal* (253, 908; 1982). It comes after more than six years of observing gradual changes in the eight-hour orbit of the pulsar and its invisible companion, probably also a neutron star.

The pulsar period itself (0.059 s) acts as the known emitted frequency from whose Doppler shifts the orbit is determined as part of a total solution including up to 20 variables. These represent intrinsic properties of the pulsar, classical orbital elements, and relativistic corrections for the advance of the perihelion (about 4° per yr compared with $43''$ per century for Mercury) and variable parts of the gravitational redshift and the transverse Doppler effect. The relativistic parameters together define a small set of allowed values for the masses of the two stars. These, plus the orbit period, can be plugged into a standard formula for gravitational radiation from orbiting point masses to yield a unique prediction of the rate at which the orbit should be decaying, $\dot{P} = -2.4 \times 10^{-12}$. The measured value, from the multi-variable fit, is $-2.30 \pm 0.22 \times 10^{-12}$, in exact agreement to within the experimental errors.

The high precision and self-consistency of these results mean that they have interesting implications for three problems of current interest in astrophysics.

First, if no important effects have been left out, the binary pulsar orbit provides as accurate a mass for a neutron star as has ever been determined, and the first one for an honest-to-goodness radi pulsar. The other measured masses all come from X-ray binaries, for which the energy source is not the rotation of the neutron star (as in 'true' pulsars) but accretion of gas from a companion, an inherently messy process. The answer is $1.4 \pm 0.1 M_\odot$ for each component. Existing data¹ are² consistent with all known neutron stars having about this mass. It is just above the maximum stable mass (Chandrasekhar limit) for a star or stellar

core supported by degenerate electron pressure and may reflect a fairly universal truth — you get a neutron star when an inert core builds up to the Chandrasekhar limit and so collapses.

Second, we are encouraged to ask more seriously than before how gravitational radiation will affect the evolution of other short-period binary systems, whose orbits are less clean than that of PSR1913 + 16, but which are astronomically at least as interesting. The classic case is that of the cataclysmic variables (CVs)²⁻⁶ — novae and related systems consisting of a normal star transferring material to a white dwarf companion. Many kinds of binaries show such mass transfer. In some, the flow is driven from a more massive to a less massive star by newtonian effects; in others, a star spills over because it is trying to expand and become a red giant⁷. But in some low-mass CVs, neither of these explanations works. The shedding star is the less massive and has not yet begun to expand. What drives the transfer? Gravitational radiation must gradually bring the two stars closer together. The surprise is that it does so at precisely the rate needed to produce the otherwise inexplicable mass transfer in these short-period, low-mass CVs⁸⁻¹⁰. In addition, beyond a certain point, gravitational radiation-driven mass transfer begins to move the stars apart again, and so may also explain some puzzling gaps in the distribution of orbit periods of CVs.

Third, the binary pulsar provides a test of the standard formula, first derived by Einstein¹¹, for the gravitational radiation expected from a binary system. Over the years, many theorists have tackled the problem within the framework of general relativity. Some have confirmed the so-called quadrupole formula¹²⁻¹⁴, whilst others have found different results, or, more often, concluded that a proper derivation has not yet been carried out and is currently beyond them, too¹⁴⁻¹⁶. The agreement to within 10 per cent between

prediction and observation for the binary pulsar strongly suggests that the quadrupole formula is very nearly right, at least for relatively weak-field cases (again, unless some important effect has been left out of the multi-variable analysis). This should help theoretical relativity both with this particular problem (it is always easier to do a calculation if you know the answer in advance) and with others by suggesting appropriate approximation methods. General relativity is not the only theory of gravitation currently under investigation. But most of the others (except some cases of the Brans-Dicke theory) predict orbit changes due to gravitational radiation that disagree with the binary pulsar result¹⁷. We cannot, however, quite rule them out yet, if only because the calculations leading to that conclusion have been done with methods analogous to those that lead to the quadrupole formula for general relativity, which may, just possibly, not be appropriate.

What can we expect from PSR1913 + 16 and gravitational radiation in the future? Observations are continuing. And the nature of the problem is such that precision increases roughly with the square of the observing time. Thus another five years could narrow the error bars on the relativity parameters from about 10 per cent to about 1 per cent, providing neutron star masses with that precision and testing agreement (or disagreement) to 1 per cent between the quadrupole formula prediction and the observed value for the orbit decay due to gravitational radiation. Beyond this we probably cannot go. Fluctuations in the newtonian gravitational potential of the Galaxy (due to stars, clusters, gas clouds, spiral arms and all the rest) cause random, undecipherable accelerations of a test particle and so will put noise into the pulsar timing measurements at a level near 2×10^{-14} on time scales comparable with the effects being sought.

Finally, once a phenomenon has shown up indirectly in an astronomical context, it is natural to ask whether it can be seen directly in the laboratory. Detectors designed to search for gravitational radiation pulses have been in fairly continuous operation one place or another for

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about 15 years. Ferrari *et al.*¹⁸ have reported a recent data set in which widely separated detectors were simultaneously excited by some sort of background and reference earlier results. Helium-cooled detectors of higher sensitivity are being developed or are in operation at Rome, Stanford, Maryland, Tokyo and other places. The expected gravitational

radiation flux at the Earth from the binary pulsar is, however, only about 10^{-8} ergs $\text{cm}^{-2} \text{s}^{-1}$, less than 10 per cent that expected from the Crab Nebula pulsar, and some 10 orders below the sensitivity of foreseeable ground-based equipment at the relevant frequencies. Indirect methods will, therefore, clearly continue to be important for a long while, at least for PSR1913 + 16!

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Antibodies and cancer therapy

from P.C.L. Beverley

A RECENT report describes the dramatically successful use of a monoclonal antibody in the treatment of a human B-cell tumour¹. The patient has now been clinically free from disease for eleven months without further treatment. This striking success was largely due to the exquisite specificity of the antibody for the tumour cells, but is something of a special case. The monoclonal antibody was anti-idiotypic: that is, it was raised against specific determinants on the antibody expressed on the surface of the tumour cells. The method would thus seem limited because a different antibody has to be produced for each individual tumour and because only B-cell tumours, which are uncommon, are known to carry sufficiently specific determinants. Whether it will be possible to find markers that will allow a similar specificity to be gained against other tumours is not yet clear.

Several other patients have, however, already been treated with monoclonal antibodies and it is possible to assess something of the general potential of antibodies for therapy.

The questions to be faced are: are the monoclonal antibodies safe, and are they effective? So far, there is a clear answer to only the first question. Administration of mouse monoclonal antibodies produces remarkably few side effects even when free antigen is present in the serum and it must be presumed that the infusion of antibody leads to the formation of circulating immune complexes¹. At first sight the apparent safety of monoclonal antibodies might be assumed to stem from their monospecificity — they do not contain the contaminating specificities that give problems when conventional antibodies, for example anti-lymphocyte globulin, are

administered. This may, however, be an over-simplification since it has been predicted that many monoclonal antibodies will give unexpected cross-reactivities². Indeed, cross-reactivity has been demonstrated for some of the antibodies which have been used *in vivo*: for example, the J5 antibody used in treatment of acute leukaemias³ was found also to react with renal tubules. The moral to be drawn is that before an antibody is used *in vivo* it is wise to screen widely for unexpected reactions with different tissues.

If the antibodies are safe the major problem of antibody specificity remains. Antibodies to differentiation antigens can be used when the loss of normal cells with the same antigens would not matter or when tumour cells have completely replaced the normal population. Thus, antibodies against T-lymphocyte antigens have been used to treat advanced stages of mature T-cell tumours. In the first patient, a significant response of skin lesions was seen and treatment was continued for 17 weeks until the tumour progressed in lymphoid organs⁴. This patient showed no immune response to the mouse immunoglobulin but in subsequent trials and in patients given anti-T cell antibody as immunosuppression for renal allograft rejection episodes, antibody to the mouse protein was produced and limited the duration of treatment⁵.

While antibodies to differentiation antigens can be used for tumour therapy, their potential would be much greater if tumour-specific antibodies were available. Several claims for the existence of such

antibodies have been made, notably of those to a common acute lymphoblastic leukaemia antigen (CALLA)⁶. However, further examination in another laboratory showed the antigen to be present on some normal bone marrow cells⁷, suggesting it might be best to treat all claims with some scepticism, at least until candidate antibodies have been examined in several laboratories. Nevertheless, an anti-CALLA antibody (J5) was used to treat leukaemic patients and revealed another problem of antibody therapy, that the tumour cells rapidly lost the target antigen when antibody was administered. Similar antigenic modulation could be demonstrated *in vitro*.

While treatment *in vivo* has not yet produced spectacular results, with the exception of the anti-idiotypic antibody, treatment *in vitro* holds more immediate promise. Bone marrow grafting has become a recognized treatment for leukaemia but has considerable problems, including graft-versus-host disease (GVH) caused by T lymphocytes in the donor marrow. Removal of T lymphocytes from bone marrow before grafting had been attempted with conventional antisera and it was a logical step to see if better results could be obtained with more specific monoclonal antibodies. So far the published data are limited to a single study in which the marrow cells were merely incubated with monoclonal anti-T cell antibody before infusion⁸. The procedure relies for effect on the removal of antibody-coated cells from the circulation by the reticuloendothelial system — hardly likely to be very effective in transplant recipients who have been irradiated and treated with cytotoxic drugs to condition them to accept the graft. Nevertheless, the early results are not discouraging and the use of antibodies with complement or coupled to drugs or toxins should improve its effectiveness. Leukaemia can also be treated by an autologous transplant. Remission bone marrow is collected and stored until the patient relapses. Aggressive chemo- and radiotherapy can then be administered and the patient rescued with the stored marrow. This approach suffers from the problem that the re-infused marrow may contain leukaemic cells but these might be removed if sufficiently specific antibodies can be produced⁹. *In vitro* treatment has the advantage that surplus antibody, or antibody-drug or antibody-toxin conjugate, can readily be washed away before the marrow is infused.

It is notable that the research discussed so far all deals with tumours of the haematopoietic system and common tumours (all carcinomas) have not been mentioned at all. This is in part because many of the earliest and best characterized monoclonal antibodies have been directed to leukocyte antigens, and also because the therapy of solid tumours poses additional problems, particularly the penetration of antibody into tumour masses. Nevertheless

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