developing countries (Milich). But it is EBV that has the most diverse effects. In parts of Africa and Papua New Guinea with endemic malaria, it produces neck tumours (Burkitt's lymphoma) in children, whereas in southern China the prognosis is for nasopharyngeal carcinoma in adults. Within the 'Western-style' societies of temperate climates, childhood exposure to the virus produces cold-like symptoms which are rapidly resolved. In contrast, children esconced in front of the television and protected from infection until late adolescence may contract mononucleosis — the kissing disease of the American campus — a more severe, protracted disease characterized by polyclonal B cell proliferation (Moss).

What looks like a related condition, immunoblastic lymphoma, emerges in transplant patients whose immune systems are deliberately weakened by drugs. This disease may arise either from infection of an EBV-negative recipient by an EBV-positive transplant or to reactivation of latent virus in patients exposed previously to EBV. The former is a hazard in liver transplantation in which young EBV-negative patients often receive tissue from adults (Moss).

Cytomegalovirus (CMV), another herpes virus, does not cause cancer but is the most common opportunistic infection in patients recovering from bone-marrow transplantation. About 25 per cent of such patients succumb to the virus, apparently because they cannot generate CMV-specific CD8 T cells quickly enough from their newly acquired immune system (all immune cells develop from the stem cells of the bone marrow). To plug the gap, Greenberg and co-workers have stimulated and expanded *in vitro* clones of mature CMV-specific T cells from the blood of the donor, and given them to the immunocompromised recipient along with the bone-marrow transplant. This treatment looks promising, in that none of the 12 patients receiving treatment so far has suffered from CMV disease.

Greenberg's strategy could potentially be applied against many types of cancer, particularly those induced by viruses. But for human papilloma virus this approach is stymied by the inability of investigators to generate CD8 T cells with specificity for the virus from the tissues or blood of patients with cervical cancer (Beverley). This state may arise because the epithelial tumour cells are poor at stimulating T-cell responses because they lack costimulatory molecules that are characteristic of professional antigen-presenting cells (J. Allison, University of California, Berkeley). Other findings, however, imply that the papilloma virus is invisible to the immune system (Stanley), which also seems to be the case for EBV in Burkitt's lymphoma (a tumour of the B lymphocyte, a professional antigen-presenting cell) (Moss).

To avoid destruction of virus-infected cells by CD8 T cells, viruses often evolve ways of interfering with the MHC class I pathway of antigen presentation, and this may be the case in cells infected with papilloma virus and EBV. In Burkitt's lymphoma, cellular expression of the transporter proteins that bring viral peptides into close proximity to class I molecules is highly reduced, perhaps explaining why EBNA 1 — the main EBV protein expressed by Burkitt's lymphoma cells — is not an item for immune attack. Indeed, Moss was pessimistic about the prospects of developing a vaccine against Burkitt's lymphoma but more sanguine about those for a vaccine against immunoblastic lymphomas, which express and present a greater range of EBV antigens.

In contrast to the speculative nature of vaccines against EBV and papilloma virus, a vaccine against HBV is already being used in the field and consists of subviral particles of recombinant proteins (Milich). Most HBV-infected individuals resolve the infection and maintain immunity, but a few develop a chronic infection which predisposes to hepatocellular carcinoma. Tumours develop only after 20–30 years of chronic infection, the result of an accumulation of insults arising from the cycles of lymphocyte-mediated destruction of virus-infected hepatocytes, followed by liver regeneration. More than 250 million people are estimated to be chronically infected with HBV, most of them being in developing countries. In Taiwan and Singapore, vaccination is currently targeted at neonates, who are particularly susceptible to hepatocellular carcinoma after becoming chronically infected by virus from their mothers. But although vaccination may be effective in alleviating infection, its effect on progression to cancer will only be known 50 years from now.

Vaccines against virally induced cancers could help segments of the human population for whom suffering is no stranger. This, however, is not the most attractive market for the world of commerce, which is unlikely to underwrite the inevitably expensive and long-term clinical trials. It is perhaps at that stage that the support of governments will be most urgently needed. □

Peter Parham is in the Departments of Cell Biology, and Microbiology and Immunology, Stanford University, Stanford, California 94305, USA.

PLASMA PHYSICS

Acceleration on a bench top

Robert Bingham

WITH the demise of the Superconducting Super Collider, the question of whether experimental high-energy physics can sustain its vitality has become an urgent one. Foreseeing the possibility of such a crisis, the high-energy physics community began investing in its own future in the form of advanced accelerator research some ten years ago. On page 527 of this issue, Joshi and colleagues report[1] a development that promises an entirely new type of technology for building high-energy accelerators. Their experiment demonstrates electron acceleration in a plasma beat-wave accelerator, which is a new breed of compact accelerators — dubbed 'bench-top' accelerators, although the bench in question would have to be a large one. The results have surpassed all expectations.

Substantial electron acceleration was observed in early experiments on inertial laser fusion and attributed to the production of electron plasma waves moving at high phase velocity. There, the energetic particles are a nuisance — they preheat the central core and prevent compression — but it was these early experiments that led Dawson and co-workers[2,3] to propose the 'laser wakefield' and 'laser beat-wave' schemes for plasma acceleration of particles. The latest work[1] uses the second of these schemes.

In both of these schemes, particles are accelerated by high-phase-velocity electron plasma waves generated in the plasma by lasers (see box for details). Electron plasma waves are longitudinal waves with their electric field parallel to the direction of propagation. Electrons moving close to the phase velocity of the plasma wave, which can approach the speed of light, are accelerated by the wave's electric field until they eventually out-run it, rather like a surfer on an ocean wave.

The essential points of the new experiments are as follows. A two-frequency carbon dioxide laser and a 2 MeV electron beam are focused to the same point in a hydrogen plasma at a density of about 10^{16} H^+ ions per cubic centimetre. The intensity of the laser is a few times 10^{14} W cm^{-2} and is roughly constant over a Rayleigh length of about 1 cm. The measured amplitude of the relativistic plasma wave is 30 per cent of its wavebreaking limit, agreeing with theoretical estimates, and giving a theoretical maximum electron energy of about 30 MeV, which is in excellent agreement with observation. The acceleration from 2 MeV to a maximum energy of 30 MeV in about 1 cm corresponds to an accelerating electric field of 2.8 GV m^{-1}, which is the largest coherent man-made accelerating field yet produced, and 30 times larger than the limit imposed by radiofrequency breakdown in conventional accelerating structures. If the beat wave could be 10 cm long rather than 1 cm as in the experiment, electrons would reach an energy of 300 MeV.

Even if such 'bench-top' machines prove unable to compete with the present high-energy colliders, they could proliferate in research laboratories just as computers have with the advent of PCs and mini-workstations. Apart from their compactness, these plasma accelerators have the interesting feature that they produce a series of very short electron bunches separated by a plasma wave period — here, 1 picosecond (10^{-12} s). These periodic electron pulses could be used to make tiny stroboscopic X-ray or light sources, opening up the prospect of making slow-motion movies of chemical reactions or dynamical biological processes that have never been observed before. In addition, the tiny bursts of X-rays might permit better imaging in biology and medicine using only a fraction of the usual radiation.

In obtaining their results, Joshi and colleagues have overcome some tough practical problems. Their plasma is uniform in density to within 1 per cent, a remarkable value achieved by tunnel ionization of a static fill of hydrogen gas. Essentially the kinetic energy of the electrons increases because of the electric field of the laser — they oscillate in the laser's field. When the laser intensity reaches a critical threshold value in the gas, electrons bound to the nucleus tunnel through the Coulomb barrier, becoming free. The ionization time is of the order of the laser period (10^{-15} s^{-1}) which is extremely small.

The tendency for strong plasma turbulence to develop, destroying the coherency of the accelerating fields, was overcome by lowering the plasma density, which effectively increased the growth time of plasma instabilities. With the laser pulse and electrons moving close to the speed of light through the plasma, turbulence effects do not have time to establish before the pulse and electrons have passed on.

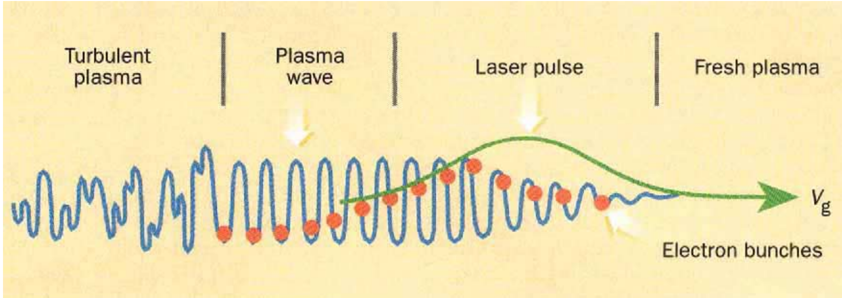
The work on plasma-based accelerators represents but one area that is being explored by researchers in the advanced accelerator field. Other schemes being investigated at present for high-gradient acceleration are the inverse Cerenkov effect and the inverse free-electron laser effect. Still other researchers, realizing that the next collider will almost certainly be a linear electron–positron collider, are proposing a novel way of building such a device known as a two-beam accelerator. And there are many groups developing an entirely new type of electron lens using focusing by a plasma to increase the luminosity of future linear colliders[4].

This plays on the fact that relativistic electron beams can be focused by a plasma if the collisionless skin depth c/ω_{pe} is larger than the beam radius. Generally, when a relativistic electron beam enters a plasma, the plasma electrons move to neutralize the charge in the beam on a $1/\omega_{pe}$ timescale. However, if the collisionless skin depth is larger than the beam radius, the axial return current flows in the plasma on the outside of the electron beam and the beam current is not fully neutralized, leading to the generation of an azimuthal magnetic field. Consequently this self-generated magnetic field pinches or focuses the beam in the radial direction. This type of lens exceeds conventional lenses by several orders of magnitude in focusing gradient.

For the beat-wave scheme, the next milestone to be achieved is the GeV energy level, and already Joshi and his team are planning this next step. It is indeed gratifying to see that some of the ideas on alternative acceleration schemes proposed more than a decade ago are coming to fruition. □

Laser acceleration of particles

In laser beat-wave experiments, as carried out by Joshi and colleagues, two laser frequencies are incident on a hydrogen plasma producing regions of constructive and destructive interference. The result is a series of light pulses velocities are close to the speed of light c in a vacuum: $v_p = v_g = c(1 - \omega_{pe}^2/\omega^2)^{1/2}$. Because ω is close to ω' and much larger than ω_{pe}, the Lorentz factor γ_p associated with the beat waves is $[1 - v_p^2/c^2]^{-1/2} = \omega/\omega_{pe} \gg 1$.



moving through the plasma at the group velocity of light.

The plasma electrons feel periodic electromagnetic pressure forces at a frequency corresponding to the difference of the two laser frequencies. If this difference frequency equals the natural oscillation frequency of the electron plasma, ω_{pe} (= $5.64 \times 10^4 n_e^{1/2}$ rad s^{-1}, where n_e is the electron plasma density in units of electrons per cubic centimetre) the plasma responds resonantly to these forces and large-amplitude plasma oscillations build up, as shown schematically above.

The laser wakefield scheme is rather different. There, a single laser pulse less than half the length of an electron plasma wave leaves a wake of relativistic electron plasma oscillations.

In both schemes, the electron plasma waves have a phase velocity, v_p, which is equal to the group velocity of light v_g in the plasma. For laser frequencies ω and ω' that are much larger than the plasma frequency, which is the case in Joshi and colleagues' experiment, these

The longitudinal electric field amplitude of these relativistic plasma waves can be extremely large, with a theoretical maximum given by $E = n_e^{1/2}$ V cm^{-1}; for plasma densities of the order of 10^{18} cm^{-3}, the field strength can be 10^9 V cm^{-1}, equivalent to fields in atoms.

In practice this maximum wave electric field value, set by wave-breaking, is never achieved because the relativistic mass increase of the oscillating electrons changes the plasma frequency and resonance is lost. So the maximum energy to which an electron can be accelerated is $W = 2\varepsilon\gamma_p^2 m_e c^2$ where ε is the ratio of the plasma wave amplitude to its theoretical maximum. As an example, if we take a plasma density of 10^{19} cm^{-3} and $\varepsilon = 0.3$, 30 per cent of the maximum value, results in an electric field of about 10^9 V cm^{-1} — capable of producing a GeV electron in a distance of 1 cm. Joshi and colleagues no doubt have their sights set on this next step, although higher-frequency lasers than CO_2 will have to be used in these denser plasmas. R. B.

Robert Bingham is at the Rutherford Appleton Laboratory, Chilton, Didcot, Oxfordshire OX11 0QX, UK.

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