patients with receptor-containing cancers benefit from hormone therapy, but there is little chance of benefit if the tumor cells lack receptors.

Chemotherapy is a systemic therapy that, until recently, was used only as a last resort for treating the most advanced cases of breast cancer. The current trend is for chemotherapy to be used as an adjunct to the primary treatment even though the patient may be clinically free of disease. The goal is the elimination of microscopic disseminated tumors that are not yet clinically apparent. In addition, clinicians are turning to drug combinations that are more effective than the agents administered separately.

In a preliminary study, George Canellos and his colleagues at NCI found that a combination of four drugs—methotrexate, 5-fluorouracil, cyclophosphamide, and prednisone—caused regression of the tumors of 23 out of 33 patients with advanced metastatic breast cancer. Seven patients had complete remissions. The median survival time of those who responded to the drug combination was at least double that of the nonresponders. In a more extensive collaborative study conducted by the Eastern Cooperative Oncology Group, consisting of 39 medical institutions in the eastern United States, the effectiveness of a single agent, phenylalanine mustard, was compared with that of a combination of three drugs. The combination produced both a greater response rate and a longer duration of response than did the single agent.

The NSABP is now coordinating clinical trials of phenylalanine mustard as an adjuvant to surgical treatment of breast cancer. If the single drug improves the prognosis of the patients, Carbone says that combination chemotherapy, which has proved superior for treating advanced cases, can also be tested as a surgical adjuvant.

Adjuvant chemotherapy, which may have hazardous side effects, may not be necessary for all patients. Carbone noted that patients whose breast cancer has not yet spread to the lymph nodes already have a good prognosis. In fact, the extent of nodal involvement is currently the best prognostic indicator, and this must be determined by examination of nodes removed during surgery since some of the involved nodes are not clinically detectable. This is another reason for performing the more extensive surgical procedures which enable evaluation of the condition of the lymph nodes.

Other prognostic indicators, not requiring surgery, may eventually be available, however. Douglas Tormey and his associates at NCI found that more than 96 percent of patients with metastatic breast cancer have one or more of three biochemical markers—carcinoembryonic antigen, methylated guanosine, or human chorionic gonadotropin—in their blood or urine. Markers such as these may permit the identification of patients with a high risk of cancer recurrence without surgical removal of lymph nodes. Ultimately, Carbone said, clinicians hope to use a battery of diagnostic and prognostic tests to design the best treatment for each patient.—JEAN L. MARX

The Long and Short of Lasers (II): The Vacuum Ultraviolet

As in the far infrared region of the spectrum (*Science*, 7 June, p. 1062), the appearance of bright, coherent, and sometimes tunable sources in the vacuum ultraviolet (wavelengths between 100 and 2000 angstroms) is expected to open new avenues of research in spectroscopy and other studies. Photochemical studies of chemical reactions could be made because the energy of many chemical bonds falls in the short wavelength range of the vacuum ultraviolet. Holographic studies of objects that are too small to be resolved by visible wavelength lasers may find application in biological and medical science. High power vacuum ultraviolet lasers potentially have space weapons applications because the short wavelength of their light more easily penetrates (than longer wavelength light) the plasma created around a metal subjected to irradiation by a laser. This property also will be useful for studying the characteristics of the dense plasmas of controlled fusion experiments.

Interest in the vacuum ultraviolet began to accelerate in 1970 when R. W. Waynant, J. D. Shipman, Jr., R. C. Elton, and A. W. Ali at the Naval Research Laboratory, Washington, D.C., and R. T. Hodgson at the IBM Thomas J. Watson Research Center, Yorktown Heights, New York, independently obtained laser action in molecular hydrogen gases. The first laser light from hydrogen was a series of discrete lines near 1600 Å (Lyman band), due to transitions between vibrational levels of an excited electronic state and the ground state. Subsequently, other laser lines at shorter wavelengths (Werner band) were identified in hydrogen, and laser emission was also seen in deuterium and in carbon monoxide.

The Navy scientists applied a method of pumping the laser medium known as traveling wave excitation. In the case of hydrogen, the gas is contained in a long tube, and a high power electrical pulse is applied transversely across one end of the tube to pump the hydrogen into excited states. A sequence of these excitation pulses is applied along the tube in such a way that the excitation proceeds down the tube at the speed of light (traveling wave). Thus, as the light pulse emitted travels from one end of the tube to the other, excited gas molecules are waiting to be stimulated to emit more light by the traveling light pulse (amplification). This method of excitation is necessitated by the very short time before the excited molecules decay, since excited molecules at the far end of the tube could decay before the light pulse from the other end arrived if the entire tube of gas was excited simultaneously. In this arrangement, no mirrors are used, hence there is no optical cavity and no true laser oscillator. This "one pass laser" mode of operation is variously described as superradiance, superfluorescence, and amplified spontaneous emission.

A vacuum ultraviolet laser with a noble gas as the laser medium offers a substantially higher power than can now be obtained from the hydrogen laser (up to 100 megawatts compared to 2 megawatts), and also a limited degree of tunability. A noble gas under high pressure, such as xenon under as much as 20 atmospheres, is excited by bombarding it with a pulse of high energy (relativistic) electrons. Some of the xenon atoms are ionized, but eventually most of this xenon is left in an excited atomic state. Subsequently, an excited xenon atom and one still in the ground state react to form an excited xenon dimer (Xe_2^*), which is only stable in the excited state (excimer). Lasing

X-Ray Lasers: Here in the Not Too Distant Future?

In recent years, x-ray lasers have been the subject of much speculation but of somewhat less actual research. Now, it seems, the tide is turning. Experimental efforts are under way in a few laboratories, and more may be beginning soon in what could be a race to achieve the next big breakthrough in laser physics.

An x-ray laser ("soft" x-rays have wavelengths shorter than 300 angstroms; "hard" x-rays are shorter than 10 angstroms), would represent the shortest wavelength coherent source yet achieved, although gamma ray lasers of even shorter wavelengths are also beginning to be taken seriously. And contrary to the Buck Rogers death-ray image conjured up by the idea of an x-ray laser, the most likely application of such a device would be in basic studies of the structure of materials and in biology, such as holograms of proteins in cells.

The reason that x-ray lasers present such a challenge to scientists is related to their short wavelength, or conversely, their high frequency. In order to maintain the population inversion (more atoms or ions in upper excited states than in lower lying states) required for lasing, the energy pumping the laser medium must be imparted in a time shorter than that in which the excited states spontaneously decay. The decay time rapidly becomes shorter as the frequency of the light given off becomes higher. Moreover, because the quantum energy of an x-ray photon is much higher than that of a visible photon, more energy must be pumped into the laser medium than is the case with longer wavelength lasers in order to initiate lasing.

At the University of Rochester, a group lead by J. Forsyth (and including M. Lubin and T. Bristow) is experimenting with high power, ultrashort pulse (10^{-11} second) neodymium-doped glass lasers to produce a plasma. For example, if the laser beam were focused onto an oxygen target in the shape of a thread, oxygen near the surface would be rapidly stripped of five or six outer electrons, and the electrons would be excited to very high energies (hundreds of electron volts). Subsequently, collisions between the oxygen ions and the hot electrons would raise the ions to excited ionic states. Relaxation of the excited ions would result in the emission of light with wavelengths in the range 120 to 128 Å. Because there are no mirrors for x-rays, amplification must take place during one pass of the light pulse down the length of the target. A traveling wave type of excitation would be used (see accompanying article). So far, the excitation intensities used by the Rochester researchers have been too low to result in such laser action. Other targets, such as iron (66 Å) and copper (44 Å), could give rise to shorter wavelength lasing.

Scientists at the Lawrence Livermore Laboratory, Livermore, California, who have been simulating the operation of x-ray lasers on computers, believe that an aluminum target (1 micrometer in diameter and 3 centimeters long) imbedded in an iron or gold heat sink could be completely stripped of all electrons by a high power laser pulse 10^{-10} second long, in a traveling wave mode of excitation. When electrons that had subsequently populated higher excited states of the ions (collisional recombination) then decayed into lower-lying states, x-ray radiation (39 Å) would be given off. Such experiments are planned for next year, according to Lowell Wood of the Livermore group.

A different approach is being taken at the Battelle Columbus Laboratories, Columbus, Ohio, according to P. J. Mallozzi. In one Battelle scenario, if, simultaneously with the capture of an electron into an excited state by one of the metal ions in a laser generated plasma, a second electron already in the ion is excited to a higher state (dielectronic recombination), then it would be possible to maintain a population inversion for a longer time than many have thought possible. This would reduce the requirement for very short pulse length laser for generating the plasma. The lasing transition would then occur when one of the excited electrons relaxes to a lower state. Very rapidly thereafter, the other electron would also relax, thus depopulating the low energy state at which the lasing transition terminates and maintaining the population inversion. The Battelle group uses four neodymium-doped glass lasers (125 joules, 3.5-nanosecond pulse) to create plasmas in a slab shaped target. Four such plasmas lined up in a row provide a path of plasma in which amplification can take place. So far, no proof of lasing has been obtained.

A group of theorists (M. O. Scully of the University of Arizona, Tucson, W. H. Louisell of the University of Southern California, Los Angeles, and W. B. McKnight of the Army Missile Command, Redstone Arsenal, Alabama) is collaborating with a group of experimentalists (led by K. Boyer) at Los Alamos Scientific Laboratory, Los Alamos, New Mexico, on a plan to produce a 304-Å laser. In this scheme, a high energy beam of alpha particles (He^{2+} ions) is to be deflected into a supersonic stream of hydrogen gas by an electric field. Collisions between the alpha particles and the hydrogen will cause an electron to be transferred to the hydrogen, leaving the helium ion in an excited state. When the ion relaxes, radiation is given off. A traveling wave type of excitation is to be employed. No experiments have been tried yet, although beams of alpha particles are being produced at Los Alamos and the higher currents needed for lasing seem likely to be obtained. Other ions, such as triply ionized lithium (Li^{3+}) could result in wavelengths as short as 50 Å.

A group at the Naval Research Laboratory, Washington, D.C., is trying to create coherent x-ray sources by amplifying the intensity of coherent x-rays to be obtained (through the use of nonlinear frequency conversion processes) from visible or ultraviolet lasers, according to R. C. Elton of the Navy laboratory. A laser generated plasma of highly stripped metal ions would be the amplifying medium. At present, experiments aimed at producing such amplification are under way.

Applications of x-ray lasers are still several years off, because the first x-ray lasers probably will not have sufficient coherence. Hard x-rays are also regarded as a distant prospect. In the meantime, the effort just to produce an x-ray laser has created an atmosphere of intense interest among laser scientists.—A.L.R.

occurs when the excimer decays into two xenon atoms and 1720-Å radiation is emitted. Unlike the hydrogen laser, mirrors are used, and therefore a true laser oscillator is obtained.

In principle, a limited tunability could be achieved (about 120 Å in xenon) because the natural (spontaneous) decay of the excimer emits light over a broad wavelength range. A grating at one end of the laser optical cavity could thus select a narrow part of this emission for lasing. Since lasing also has been observed with krypton (1457 Å) and argon (1265 Å) between the three gases, a large part of the vacuum ultraviolet between 1200 and 1800 Å is available. Such tunability has not yet been demonstrated, however.

After early work by N. Basov and his colleagues at the P. N. Lebedev Physical Institute, Moscow, and H. A. Koehler, L. J. Ferderber, D. L. Redhead, and P. J. Ebert at the Lawrence Livermore Laboratory, Livermore, California, three groups working independently have successfully made high power xenon lasers: a second research team at Livermore (P. Hoff, J. Swingle, and C. Rhodes), a group at Sandia Laboratories, Albuquerque, New Mexico (J. B. Gerardo and A. W. Johnson), and a cooperative effort by scientists at the Northrop Research and Technology Center, Hawthorne, California (E. Ault and M. L. Bhaumik), the Maxwell Laboratories, San Diego, California (A. Kolb and J. Shannon), and the Los Alamos Scientific Laboratory, Los Alamos, New Mexico (W. Hughes, R. Jensen, and P. Robinson). The first two groups have emphasized characterizing, both experimentally and theoretically, the properties of excimer lasers, while the latter group has been working on obtaining the highest possible power output.

Other investigators have devised coherent vacuum ultraviolet sources using nonlinear frequency conversion techniques related to those used by far infrared researchers. In the ultraviolet case, however, frequencies are added, rather than subtracted, in order to generate short wavelength radiation. (Frequency multiplication, or harmonic generation, is the special case where the frequencies to be added are the same.) Another characteristic of frequency conversion into the ultraviolet is that, because of the lack of transparent nonlinear crystals for wavelengths shorter than 2000 Å, gases are used as the nonlinear medium. Finally, when experiments are planned so that the frequencies involved are close to those of atomic transitions in the gases, orders of magnitude improvement in the conversion efficiency (the fraction of the low frequency light that is transformed into high frequency light) over what would be achieved if arbitrary frequencies were used are obtainable. This effect is called resonant enhancement.

At Stanford University, Stanford, California, S. E. Harris and J. F. Young have pioneered many of these nonlinear techniques in the ultraviolet. In one experiment at Stanford, A. H. Kung, Young, and Harris generated 3547-Å coherent radiation by tripling the frequency of the light at 1.06-micrometers from a pulsed laser made of yttrium aluminum garnet containing neodymium ions (neodymium-doped YAG). Ten percent conversion of the neodymium laser light to this third harmonic was achieved in a 50-centimeter long cell containing a mixture of rubidium metal vapor and xenon gas. In this mixture, rubidium serves as the nonlinear medium, while an adjustable concentration of xenon is used for phase matching (adjusting the index of refraction of the gas so that the incident and the generated light waves maintain the correct phase relationship as they travel through the gas).

887 Å Is Shortest Wavelength

In a second experiment, the 3547-Å radiation generated in this way is passed through a xenon-argon mixture (where xenon is now the nonlinear material and argon is for phase matching) for a second round of third harmonic generation. The overall efficiency of converting the initial neodymium laser light to 1182 Å is 0.3 percent.

By using different gases, several different ultraviolet wavelengths can be produced. The shortest one generated so far has been 887 Å. Tunability could be obtained in the future. For example, the light from a neodymium laser can be used to drive a tunable coherent visible source (such as a dye laser or a parametric amplifier), and the frequency of the light from the tunable source is then converted to the desired wavelength. The Stanford researchers have demonstrated this principle in the long wavelength ultraviolet.

G. C. Bjorklund, Young, and Harris have already used the 1182-Å coherent light to do elementary experiments in holography. Using this light and photolithographic techniques, they have also fabricated elementary integrated optical components. Plans for even shorter wavelengths (450 Å, which borders on the soft x-ray region of the spectrum) are also being tried out.

Hodgson, P. P. Sorokin, and J. J. Wynne of the IBM research center are working on a tunable coherent source for the ultraviolet. In their present experiments, the IBM scientists use two tunable dye lasers pumped by a pulsed nitrogen laser (3371 Å). The visible dye laser light beams are mixed in strontium vapor. The resulting ultraviolet light has a frequency equal to $2\nu_1 + \nu_2$, where ν_1 and ν_2 are the dye laser frequencies. Resonant enhancement of the nonlinear process is crucial to its success. In fact, at IBM a kind of atomic spectroscopy study is under way that makes use of the appearance and disappearance of resonant enhancement as the dye laser frequencies are varied. So far, tuning in the range 1750 to 2000 Å has been possible with a number of different dyes. According to Wynne, tuning to 1500 Å ought to be possible with strontium, and, ultimately, wavelengths as short as 800 Å may be achievable with other gases.

At the Oregon Graduate Center, Beaverton, G. A. Massey has used one of the most venerable of nonlinear materials, ammonium dihydrogen phosphate, to produce tunable coherent light between 2500 to 2000 Å. This system, whose development was motivated by a desire to make a source for use in photoelectron spectroscopy studies of cell surfaces, begins by doubling the frequency of the visible light from a rhodamine 6G dye laser to obtain long wavelength ultraviolet radiation. This ultraviolet is then converted to the wavelength of vacuum ultraviolet light by mixing the longer wavelength light with infrared laser light from a neodymium laser in the nonlinear crystal. Tuning is achieved by changing the dye laser frequency, and two or three dyes are needed to cover the range 2350 to 2000 Å. Phase matching is determined by the temperature of the ammonium dihydrogen phosphate crystal.

Once characterized as "a solution looking for a problem," the laser has long since proved to be a widely used tool of scientist and engineer alike. The emergence of lasers and coherent sources in the far infrared and vacuum ultraviolet regions of the spectrum promises to continue this tradition by reawakening interest in what were previously somewhat neglected parts of the optical spectrum.

—ARTHUR L. ROBINSON