A double-whammy

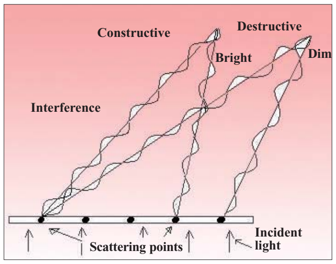
Creating lasers that emit hard X-Rays has become feasible, says s ananthanarayanan

WHILE X-Rays have been probes of high penetrating and resolving power, the laser has been useful for its properties of coherence and intensity. Creating a laser in the X-Ray region that would have a coherent and intense beam that can resolve the smallest objects has been elusive. Nina Rohringer of the Lawrence Livermore National Laboratory, California, and others report in the journal *Nature* on a technique that has worked for soft X-Rays and shows the way for more energetic X-Rays.

The value of X-Rays in science arises from their very short wavelength. At one end, this enables X-Rays to pass through soft tissue and throw shadows of bones, or lesions, to help medical diagnosis. But beyond this "bulk" application, X-Rays enable visualising very small objects, like the distribution and position of atoms in crystals. A great deal of our knowledge of materials has come from studies of how crystals, whose dimensions are similar to the wavelength of X-Rays, scatter a beam of this short wavelength radiation.

The usual method is to pass a beam of X-Rays through the crystal sample and allow the X-Rays to be reflected and scattered by the various crystal planes that the sample presents. As the beam is scattered from different points of the crystal, it is only at certain angles that the waves scattered from the different points would arrive at a screen with a path difference of a whole number of wavelengths. These points show up as bright spots, while the rest of the field is dim, with the waves having interferred destructively. The pattern of the spots created in this way can reveal the orientation of the reflecting planes and the crystal structure of the material.

In such an application, each X-Ray photon acts independently and the X-Rays produced from the usual sources are good enough. The usual sources bombard a heavy metal target with an electron beam. This creates X-Rays in two ways: one is when the path of the electrons is bent because of the atoms of the metal target. The electrons then emit radiation at all wavelengths, including X-Rays. The other way is when the atoms of the target metal get energised by absorbing part of the energy of electrons that strike them. When these atoms relax, they emit X-Rays of a characteristic wavelength. But the main thing is that each electron or atom emits at different moments and there is nothing coherent or "well timed" about the X-Rays emitted. But in the usual application of X-Rays in crystallography, each X-Ray photon is acting for itself and this does not matter.




Nina Rohringer

The laser

The laser beam is different in that the photons are emitted by the different atoms in pulses, but all together. This makes the great difference; the waves are not at different phases but are together in their stage of vibration. The difference is like a crowd rushing forward as against a platoon of soldiers marching in step. Lasers in the visible region are freely available and have made for advances in investigating materials through absorption, scattering and emission of laser light. Extending the methods to the X-Ray region has, thus, been a tempting objective.

The generation of visible light, like in the case of X-Rays, has been through the haphazard de-excitation of atoms. This is unlike the case of radiowaves, or microwaves, where these are directly, and coherently, generated by man-made devices. But these arrangements have a scale limitation and cannot create very short wavelengths. Hence the interest in devising atom-level arrangements which may be of the correct dimensions.

The effort led to the laser, which takes advantage of the fact that an atom in an excited state, that is induced to de-excite by a photon that corresponds to that state, emits a photon that is in phase with the inducing photon. The way this is done is that atoms are "pumped" into a selected excited state, one that lasts a short time before it collapses, so that momentarily there are more "excited" atoms than "ground level" ones. An event of de-excitation would then create an avalanche, or a burst of photons and all these would be in phase. In the meantime, the "pumping" continues and there is another burst, and so on.

The trouble with using this method in the X-Ray region is that for X-Rays atoms need to be energised by exciting some of the deepest, as opposed to peripheral, electrons and this takes great energy. It has been shown that the energy needed for pumping increases by the cube of the photon energy. Thus for a laser at twice the frequency, the energy need is not just twice but eight times as much. As X-Ray photons have over 1,000 times more energy than photons of visible light, the energy for "pumping" would be a billion times as much. While the "pumping" for visible light is done by an electronic oscillator or another visible light laser, in the case of hard X-Rays the energy of thermonuclear explosions is necessary.

Free electron lasers

A halfway house was the arrangement with the linear accelerator. Free electrons, or electrons that are not bound to atoms, are accelerated to high speeds down a straight path. All along the path are placed alternating N and S magnetic poles. The electrons are thus deflected alternately one way and the other and follow a zig-zag path. As electrons that are accelerated emit radiation, the electrons emit photons that correspond to their speed and the space between the magnets. Although the emission is haphazard to start with, it can be tuned to become "self-amplifying" and emit bursts of fairly well regulated, high-energy — that is, X-Ray energy — photons in a "laser-like" manner. X-Ray laser bursts generated in this way have enabled studies of how matter behaves under high energy X-Rays and the structure of nanocrystals and viruses.

Magnets make the electron path wavy

The limitation of this radiation, however, is that the source of the electrons is still a random, thermal process and the coherence of the radiation is only approximate. As the "pulses" come from a process of self-amplification that is based on random orientation of electrons, there is a "jitter", both in the frequency of the radiation and the frequency of the pulses. As fine grain targets of X-Rays are drastically modified as soon as probed, it is necessary to have good a number of coherent X-Ray photons, which is possible only with a real X-Ray laser.

Rohringer and colleagues aimed at just this by concentrating a beam of X-Ray photons from the Linac Coherent Light Source, an X-Ray-free electron laser at the Stanford Linear Accelerator Centre, California, in bursts of a trillion photons each on to a target of neon atoms. The energy was enough to excite a good number of neon atoms to the high, partially stable state so that there were more in the higher state than in the ground state, the condition for laser action. The bulk of the neon atoms relaxed, not by emission of a photon but by an alternate process known as the Auger process, of emission of another electron. But some of them did relax by radiation, which then induced more radiation and the classic laser pulse.

The resulting radiation was found to have precise central energy, with a spread of only one part in a thousand, which is more than 10 times as coherent as the incident LCLS pulse. The radiation was of lower energy than that of the LCLS, but "the greatly improved coherence and reduced energy spread will open new areas of research that demand a well-defined X-ray energy", say Rohringer and the others. Further, the LCLS pulse and the X-Ray laser pulse are closely synchronised and could work as twin high energy X-Ray probes.

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Immunogenetics of Aids & retroviruses

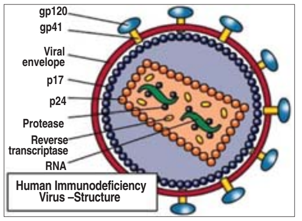
There is growing optimism that the disease may be controllable and eventually curable, says tapan kumar maitra

IN 1983, Robert C Gallo of the National Cancer Institute and Luc Montagnier of the Pasteur Institute of Paris co-discovered HIV — the human immunodeficiency virus and causative agent of Acquired Immune Deficiency Syndrome. HIV is a retrovirus that causes a disease first diagnosed in 1981 among young homosexuals in the USA.

The Aids virus attacks helper T cells; a particular protein on the surface of these T cells, called CD4, is a receptor for the HIV virus coat protein, gp120. A secondary receptor, the protein CCR5, is also needed for the virus to gain entry into the cell. (CCR5 refers to cysteine-cysteine linked cytokine receptor 5). HIV also attacks macrophages. With the destruction of the T cells, a person's immune system loses the ability to fight off common diseases. Those who develop the disease frequently fall victim to opportunistic ailments such as pneumonia caused by the protozoan *Pneumocystis carinii*, Kaposi's sarcoma, a rare cancer found in people taking immunosuppressive drugs, and several other conditions, normally rare except in those with suppressed immune systems. These conditions collectively became known as Aids.

Aids has spread throughout the world. A 1959 blood sample from Central Africa contained the first known human infection. By sequencing similar viruses in primates (Simian Immune-deficient Viruses), researchers found that the common form of Aids caused by HIV-1 jumped from chimpanzees to humans in Gabon in western Africa. HIV-2, which causes the less common form of Aids, came from sooty mangabeys. SIVs have jumped to humans at least seven times.


HIV co-discoverers Robert C Gallo (left) and Luc A Montagnier.



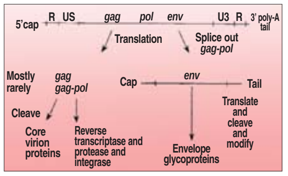
Human Immunodeficiency Virus –Structure

The term gp stands for glycoprotein of molecular weight. The gp120 connected to the gp41 stem is collectively called gp160 and it is this protein, together with other coreceptors, that must connect to the CD4 receptor of T cells. There are about 75 gp160 spikes on each virion. p24 is found both on and within the capsid.

There seem to be two worldwide patterns in the spread of Aids, which is not transmitted by casual contact. In the New World, Australia and Western Europe, homosexuals and intravenous drug users primarily spread the disease and constitute the groups at highest risk. In Africa and the Caribbean, the disease is spread primarily through heterosexual sex. Parts of Southern Africa have infection rates between 16-32 per cent while Eastern Europe, Asia and North Africa have relatively low infection rates. In the USA, over 750,000 people have the Aids virus, with 350,000 deaths reported. Worldwide, more than 33 million people are affected and most who got the disease before 1990 have died.

As mentioned, a retrovirus minimally contains only the *gag* (group antigen gene), *pol* (polymerase) and *env* (envelope) genes. The viral messenger RNA is translated, starting with gag. There is a translation termination signal at the end of the gag gene that is occasionally read through, resulting in a gag-pol protein. The env gene is translated only after the viral RNA is spliced to remove the gag-pol region.

The protein products of all three genes are further modified by cleavage and other changes (*phos-phorylation* and *glycosylation*), resulting in core *virion* proteins from gag, reverse transcriptase, protease, and integrase frompol and glyco-proteins from env. The HIV retrovirus is especially complicated. Not only does it have the gag, pol and env genes, it also has six other genes, including two main regulatory genes, *tat* and *rev*. Tat (for trans-activating transcription factor), has a protein product that binds at a sequence in the long terminal repeat named Trans-Activating Response element. Tat enhances the processivity of transcription of the proviral DNA and also recruits chromatin-remodelling proteins to the promoter. The product of the other regulatory gene, rev (regulation of expression of virion proteins), binds at a region in the env gene called Rev Response Dement and enhances the transport of viral messenger RNAs into the cytoplasm.



Expression of a retroviral mRNA. Translation begins with the gag gene and occasionally, due to read-through, proceeds through the gag-pol genes.

Together, tat and rev are responsible for the major expression of viral structural genes (gag, pol, and env). The four remaining genes — *vif*, *vpr*, *nef* and *vpu* — are called accessory genes because it first seemed that their action was not necessary for viral functioning. We now know that each gene produces a protein that has a role in viral replication and infectivity.

The vpr protein is involved in transporting the viral RNA to the nucleus. Vpr can also induce cell cycle arrest at G2, which may have a role in protecting infected cells from cytotoxic T-cell activities. Vpu degrades CD4; this action frees viral surface protein precursors from the endoplasmic reticulum. In addition, degradation of CD4 helps prevent super-infection of cells, keeping them alive longer. The main function of vif is to stabilise the virion. Nef was originally thought to be a negative regulator of viral activity, hence its name. However, it is now known that nef can reduce production of cellular CD4 protein and enhance infection by viruses free in the blood.

Aids testing is done by various techniques, such as western blots, looking for antibodies to the Aids proteins, usually gp120, gp4l, and reverse transcriptase. Initially, dideoxy nucleotides, such as the drug *3'-azido-2', 3'-dideoxythymidine* (AZT) and *dideoxyinosine* were used to treat Aids. AZT is a thymidine analogue without a 3'-OH group, meaning that it causes chain termination during DNA replication. It seems that during the reverse transcription process, reverse transcriptase preferentially chooses AZT over normal thymidine-containing nucleotides, whereas mammalian DNA polymerases prefer the opposite. Thus, AZT preferentially prevents the reverse transcription of the HTV RNA, keeping it at levels that are not toxic to the cell.

Dideoxyinosine has the same effect and has also been licensed as an Aids treatment. In 1996, treatment success improved remarkably when new therapies involving a combination of drugs, including protease inhibitors, were developed. (Dr David Ho of the Aaron Diamond Aids Research Center in New York City was named *Time* magazine's "Man of the Year" for his role in this therapy.) At the moment, optimism is rising that Aids may be controllable and eventually curable.

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Ohm's law survives at the nanoscale

And Moore's law may get a reprieve, writes saswato r das


Michelle Simmons.

MOORE'S law, the cornerstone of the semiconductor industry, may get a reprieve, according to research by a group in Australia that shows that classical behaviour extends significantly into the microscopic realm and well-understood laws of classical physics hold at the nanometre scale.

Michelle Simmons and colleagues at the University of New South Wales in Sydney, Australia, together with collaborators at the University of Melbourne and Purdue University, have built low-resistance silicon wires that show that Ohm's law works at the atomic level. This empirical law discovered by German physicist Georg Ohm in 1827 says that the current through a conductor is directly proportional to the potential difference across the conductor. Introducing the concept of resistance, it is a mainstay of circuit theory and is taught to high school and college students in physics and engineering.

Writing an accompanying commentary in *Science*, where the research was reported recently, David Ferry of Arizona State University called the finding "surprising", saying it was expected that classical behaviour would break down at the microscopic level. "The point-like electron motion of the classical world would be replaced by the spread out quantum waves. These quantum waves would lead to very different behaviour," he wrote.

In the 1960s, Gordon Moore of Intel predicted that the processing power of a semiconductor chip would double every 18 months while the price would fall by half. This prediction, now called Moore's law in his honour, has held true for more than four decades and has become a mantra of the semiconductor industry. But now the size of components on a silicon chip has gotten so small that researchers fear esoteric quantum effects like tunnelling would stop the march of Moore's law. It is for this reason that chips today have gone into multi-core architecture so that more processing power can be got without scaling down the dominant Complementary Metal Oxide Semiconductor technology.

Dick Slusher, head of the Georgia Tech Quantum Institute, explained, "The limit to scaling CMOS to smaller dimensions and higher densities and speeds is the power dissipation from parasitic resistances that cannot be eliminated from current designs and materials."

Simmons and her collaborators built fine nanowires out of silicon that were one atom tall, four atoms wide (about 1.5 nanometres) and 106 nanometres in length. Previous experiments had shown that at widths below 10 nanometres, the resistivity of silicon nanowires increased exponentially (Ohm's law is linear). The researchers were able to get around this and keep to Ohm's law-like behaviour by heavily doping the silicon nanowires with phosphorus so that their resistivity was independent of either their length or width. They used scanning tunnel microscopy to pattern the wires on a silicon surface and then silicon crystal growth to bury the wires in crystalline silicon to protect them from surfaces and interfaces that could suck up any free electrons and interfere with Ohm-like behaviour, Simmons said. "The phosphorus atoms therefore have one more electron than silicon and these extra electrons allow the nanowires to conduct," she explained. "Within the wires we place the phosphorous atoms less than one nanometre apart so that the wave-functions of the electron overlap to form a metallic-like state and that gives us this low resistivity."

Computer modelling helped them understand the low resistances measured and showed that the resistance scaled according to Ohm's law. Independent experts were impressed. Electrical engineer John Kymissis of Columbia University said, "Top-down strategies have been pursued for decades using etching, embedding, break junctions, etc, without approaching the theoretical conductivity limit. This system is probably as close as anyone can get to a metallic wire using a top-down technique; it avoids all of the interfaces, surface scattering, and grain boundaries seen in other approaches."

Simmons also said the work could be useful in developing a scalable quantum computer in silicon using the electron spins of single phosphorus atoms in silicon as the quantum bit or qubit. She said, "In Sydney we have recently demonstrated that single phosphorus atom electron spin qubits have very long lifetimes —of several seconds. We are on the edge of being able to make truly single atom devices with precision control electrodes to manipulate and couple the spin state of these qubits."

Steven Simon of Oxford University called it "an impressive piece of technology" but said that one worry would be "the fact that each sample is inherently different due to the different precise locations of the dopant impurities. For macroscopic samples this does not matter, for microscopic samples it certainly does matter…unless one can control exactly where the impurities are, there may always be samples which don't conduct at all."

Of course, the experiments by Simmons and colleagues do not conform to CMOS technology currently in use in the semiconductor industry, and further research would be needed to extend CMOS. "Fundamentally, we have shown that we can maintain low resistivities in doped silicon wires down to the atomic scale," Simmons said. "When the first integrated circuit was developed by Jack Kilby in 1958 the current production line technology wasn't developed. I can see our new technology akin to this; it may not be in production now but who knows 20 years from now."

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