X-rays and light join hands

s ananthanarayanan reports on a study of materials at the atomic scale

THE laser is a device that generates highly focused beams of light where the light comes not as barrage of photons but as photons that act "in step", as if these were parts of the same wave. The invention of the laser is a triumph of understanding the nature of processes within atoms and has enabled much new fundamental research, apart from industrial applications. While the usual methods of creating laser light do not work for the X-ray region, a workaround has recently been found and very intense and coherent X-ray bursts are possible.

TE Glover and others, a group of scientists in California, Colorado, and Rennes in France, report in the journal *Nature* that they have made use of the capacity of X-rays to resolve small dimensions in conjunction with properties of lasers to investigate details of the atom level interaction of light with matter. The researchers used the technique to investigate the known optical interaction of the structure of diamond and have verified that the technique works as theoretically predicted.

The largescale interaction of light with matter is expressed in the laws of reflection at material surfaces, the rules of bending of light when it passes through different transparent materials and also the way light is absorbed or transmitted. The actual, detailed interaction of the light wave with the atoms of which materials consist, however, has been beyond the reach of experimental methods. The advent of lasers brought about a change, in that there was now greater control of the nature of the light waves striking the atoms, which enabled analysis of interactions and also revealed new phenomena.

The basic light-atom interaction consists of the atom absorbing a photon of light, in the case of atoms, through excitation of one of its component electrons. When the electron de-excites, there is the emission of a photon that is identical to the one that was absorbed. This nature of interaction, where each photon acts independently, is generally sufficient to explain the usual laws of optics and the interactions are called *linear interactions*.

When lasers are used, however, there can be more than one photon where the waves are at the same phase of oscillation and a new, combined interaction where two photons can be re-emitted as a single photon with twice the energy has been observed.

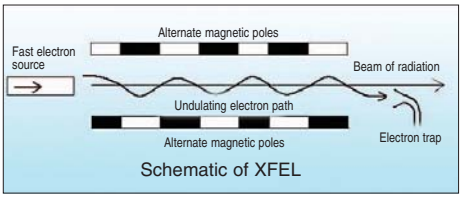
There can also be excitation by intense lasers of different frequencies and emission of a photon with the sum or difference of the frequencies. These kinds of interaction are called *non-linear interactions* and the effect has been used to generate high-frequency laser-like radiation from lower-frequency lasers.

Observing such interactions of photons with materials would reveal finer details of how photons could be separately absorbed and emitted together and increase the understanding of the structure of materials. But the difficulty has been that the wavelength of visible light or even ultra-violet light, where constructing lasers was feasible, is many times the dimension of the separation of atoms in materials. Light at the energy of X-rays has a wavelength of the order of inter-atomic distances and X-rays have been very effective in the study of crystal structure.

But these studies are through linear interactions, of individual photons being scattered by atoms in the crystal – which reveal the positions of the atoms, not of photons in phase. In the case of X-rays, however, emission of photons is not by the de-excitation of outer-shell electrons, it arises from the much more strongly bound inner-shell electrons. The energy required to create the condition of a large number of atoms excited in this way is thousands of times greater than what it takes for ordinary lasers.

X-ray lasers have, hence, been elusive and probing atomic structures by non-linear interaction of X-rays with atoms has not been possible.

In recent times, however, coherent, or laser-like light in the X-ray region has been generated through not the electrons bound within atoms but free electrons produced by a particle accelerator. High-energy electrons are made to pass through an area of alternating opposite magnetic poles. The alternating magnetic field deflects the fast moving electron beam and causes very rapid alternating acceleration. As accelerated charges emit electromagnetic waves, this rapid alternation causes the emission of very high frequency electromagnetic waves, which can be tuned to amount to a laser in the X-ray region, known as the X-ray Free Electron Laser.



Schematic of XFEL

interactions that would reveal the state of the atomic structure at the time of scattering. It is the non-linear interactions, where more than one photon generated by lasers acts in concert, which say more about the process of scattering. It was hence proposed many years ago that using laser beams in the X-ray region would be a fine way to understand detailed atomic structure and behaviour.

X-ray lasers

Lasers in the visible or ultra-violet region work by exciting the outer-shell electrons of atoms and creating a condition where there is a good number of atoms in the excited state. In this condition, it becomes possible for de-excitation of an atom, with emission of a photon, to be stimulated by photons emitted by other excited atoms and, hence, a cascade


Linear coherent light source at Stanford Linear Accelerator Centre.

Glover and his colleagues made use of the high intensity X-rays generated by the Linac Coherent Light Source XFEL at Stanford, California, to interact with the diamond crystal. Even where such intense X-rays could undergo non-linear interaction with materials, there is no material "addition" of such high frequencies. What the group did was to combine the X-ray pulses with an optical laser and were able to demonstrate an addition of frequencies. The efficiency with which the "sum-frequency" occurred revealed the effect of the optical laser on the distribution of charges in the crystal lattice, to act as an atom-scale charge distribution probe. In the case of the diamond crystal, the optical characteristics are already known and the experiment resulting in the same findings confirmed that the method works.

"We have demonstrated X-ray/Optical Sum Frequency Generation, a new tool for probing light-matter interactions on the atomic scale," say the authors in the paper in *Nature*.

"The ability… will potentially advance the fields of optics, energy research and materials science," says Dr Nina Rohringer of the Max Planck Institute for the Physics of Complex Systems in Dresden, and a member of the team that has pioneered work on XFELs

The writer can be contacted at simplescience@gmail.com

'Second most important killer, after malaria'

steve connor reports on toxoplasma's links to schizophrenia, bipolar disorder and increased risk-taking

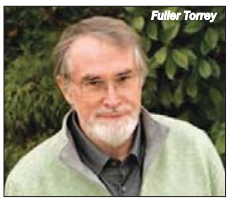
THERE is mounting evidence linking the toxoplasma parasite to changes in mood or personality even though the infectious agent is widely believed to be completely harmless in more than 80 per cent of infected people. A number of studies published in recent years has suggested that toxoplasma infection increases the chances of someone developing serious psychological disturbances, such as schizophrenia and bipolar disorder. Other scientists have shown that toxoplasma is linked with more subtle psychological changes such as increased reaction times, which could explain why infected people appear to be more likely to have traffic accidents.

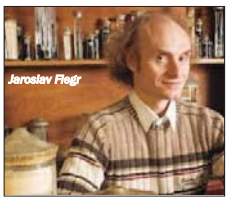
None of these studies have proven a direct cause and effect. However, they have been sufficiently robust for some experts to now call for bigger studies to investigate whether toxoplasma could trigger changes to the chemistry of the human brain, which might affect a person's behaviour.

"In terms of diseases, all we can say is that there is a correlation between antibodies to this infectious agent and serious mental illnesses, specifically schizophrenia. But correlations do not equal causation," said Fuller Torrey, a psychiatrist and director of the Stanley Medical Research Centre in Maryland.

"I would put it in the same category as the (now proven) theory of bacteria causing stomach ulcers, where only a correlation was initially shown. But until you can show that treatment of the infectious agent causes people to significantly improve, we don't have a believable cause and effect."

One of the latest studies into the subject, published in July, showed that women with

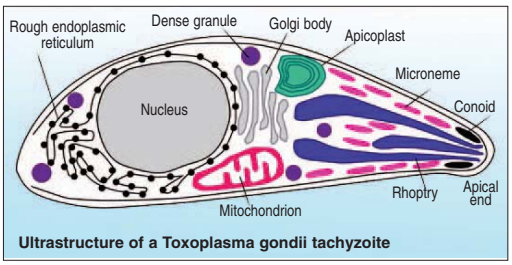




toxoplasma antibodies — which indicate past exposure to the parasite — are significantly more likely than non-infected women to show suicidal or self-harm behaviour, with the risk increasing as levels of antibodies rise. The study, based on nearly 46,000 Danish women who were tested for toxoplasma antibodies while pregnant between 1992 and 1995, also found that those who had been infected at some point in their lives were twice as likely as non-infected women to commit suicide.

Another study by American scientists, published in August, found that among 7,440 mental health patients there was a significant link between toxoplasma infection and a type of bipolar disorder where patients suffered symptoms of both manic and major depression. However, the scientists failed to find a link with other types of depression, suggesting that if there was a causal effect, it was subtle and complex.

Smaller psychological studies carried out by Jaroslav Flegr at Charles University in Prague have found gender differences between men and women infected with toxoplasma. Men were more likely than non-infected men to be expedient, suspicious, jealous and dogmatic, whereas women were more warm-hearted, outgoing, easy-going and more willing to follow rules compared with uninfected women.



Ultrastructure of a Toxoplasma gondii tachyzoite

Dr Flegr has also shown that infected people have slower reaction times compared to uninfected individuals using standard computerised tests. They are also more than twice as likely to be involved in traffic accidents, a finding that has been independently replicated by scientists in Turkey. "If it is true, then latent toxoplasmosis is the second most important protozoan killer, just after malaria," Dr Flegr said.

As regards more serious psychiatric illnesses, Dr Torrey said that two separate reviews into toxoplasma and schizophrenia had both found that people infected with the parasite were about 2.7 times more likely to develop the illness than if the person had not been infected.

Again he emphasised that this type of correlation did not show that one was causing the other. However, he believes the hypothesis is becoming increasingly plausible given that other scientists have now established a potential mechanism for how the single-celled parasite could be affecting human brain chemistry. "We know that the organism can produce dopamine, and we know that schizophrenia has the symptoms of excess dopamine, but we don't know how that comes about," Dr Torrey said.

The fact that *Toxoplasma gondii*, a single-celled protozoan microbe, had two genes for manufacturing *L-dopa*, the precursor molecule to dopamine, strongly suggested that this could be the biological mechanism that might explain how this feline parasite could be influencing the behaviour of some people who were infected, he said. "It's still a theory. We've shown conclusively that it changes the behaviour of other animals and the work from Czechoslovakia would suggest that it has an effect on human personality.

"It's probably time to follow up on children who are infected in childhood and do some long-term follow-up of outcome, to look at those infected at, say, six and see whether 15 or 20 years later there is any long-term effect on central nervous system," he said.

The Independent, London

Malignant growths

tapan kumar maitra dwells at length on oncogenic DNA-containing viruses

ALTHOUGH the infectious nature of malignant new growths of human ingenuity has not been proven as yet, the scientific data recently obtained give sufficient grounds to presume that some viruses are linked with human neoplastic diseases.

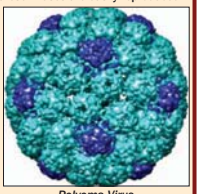
At the turn of this century, V Ellerman, O Bang and P Rous proved by experiments that viruses were capable of inducing leucaemia and sarcoma in chickens. These first studies gave impetus to intensive research into the virus aetiology of tumours in different live organisms. The viral origin of human skin papilloma, rabbit fibroma and papilloma, mammary cancer and leucaemia in mice has been proven in the past 80 years. The oncogenic nature of polyoma viruses, Simian vacuolating virus (SV40) and numerous adenoviruses of humans and animals was established in the '50s and '60s, while the aetiological role of herpes viruses in neoplastic processes in humans and animals was established in the '60s and '70s.

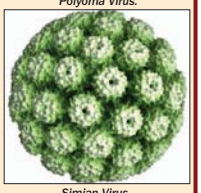
Papillomaviruses: This subgroup includes viruses of skin and mucosal papillomas of rabbits (Shope fibroma virus), hamsters, susliks, cats, dogs, sheep, goats, deer, cattle, horses and monkeys and human wart viruses.

The papilloma virus is about 55 nm in size, the virion has a cubic symmetry (icosahedron) and contains 72 capsomeres.

Polyomaviruses: This subgroup includes the mouse polyoma virus, SV40, and SV40-like human viruses. These are small (40 nm) viruses with cubic symmetry of the nucleocapsid and contain 72 capsomeres. The polyomavirus induces multiple tumours when inoculated into mice (natural hosts) and into other species of mammals (hamsters, rats, guinea pigs, rabbits, polecats). SV40 causes tumours only in hamsters and rats and is not oncogenic for its natural hosts, monkeys. SV40-like viruses of humans resemble SV40 in oncogenic and transforming properties.

The polyomavirus and SV40 are one of the best models for studying virus carcinogenesis, because separate stages of tumour formation occurring *in vivo* under the effect of these viruses are easily reproduced *in vitro* in tissue cultures.


Polyoma Virus.


Simian Virus.

Adenoviruses: Among 31 adenovirus serovars, 13 human serovars, six monkey serovars, one cattle serovar, one dog serovar and two avian serovars are oncogenic. These viruses induce tumours in rats, mice and hamsters. All attempts to prove the aetiological role of adenoviruses in the origin of malignant new growths in humans were unsuccessful.

Herpesviruses: This is a group of DNA-containing viruses which induce lymphoid and epithelioid tumours in different animal species. The Lucke virus causes adenocarcinoma of frog kidney, Marek's disease virus causes avian lymphomatosis, Epstein-Barr herpes virus is a causative agent of human infectious mononucleosis and possibly lymphoma of African children (Burkitt's lymphoma) and carcinoma of the cervix uteri in women.

The Epstein-Barr herpes virus is of considerable interest in this group. It was discovered in lymphoblastoid cell cultures of Burkitt's lymphoma, which is endemic for some regions of Africa. Patients with Burkitt's lymphoma have a high titre of antibodies to this virus. The Epstein-Barr virus is always found in the epithelial cells of nasopharyngeal carcinoma of the Chinese in Southeast Asia; the sera of the patients contain antibodies to this virus in a high titre.

Oncogenic properties of the Epstein-Barr virus were confirmed in experiments involving infection of monkeys (marmosets) with this virus. They developed malignant lymphomas.

Partly inactivated herpes simplex virus of the first and second serovars as well as cytomegalovirus are capable of inducing transformation of normal animal and human cells *in vitro*. Patients with carcinoma of the cervix uteri have a high titre of antibodies to herpesvirus of the second serovar in blood, while specific virus antigens are found in the tumour cells. Experimental and serological and epidemiological studies suggest that herpesviruses may probably play a certain role in the aetiology of malignant tumours in humans.

In the group of herpesviruses, the Marek's disease virus, which induces malignant avian lymphomatosis, has been studied most thoroughly. It is widespread at poultry farms, affecting up to 80 per cent of the chickens and causing much loss. It has a typical morphology of herpesviruses and induces transformation of lymphoid tissue T-cells. A live vaccine against this disease has been developed. Thus, in distinction from polyoma — and adenoviruses — herpesviruses are evidently the aetiological agents of neoplastic diseases among humans and animals.

Poxviruses induce malignant spontaneously regressing connective-tissue tumours in various animals (rabbits, hares, squirrels). The molluscum contagiosum virus included in this group causes the formation of hard spherical tumours in humans, from which a gruel-like mass containing oval "molluscous bodies" is pressed out. These tumours form on the genitals, pubis, abdomen, eyelids, face, neck, etc, grow to a fair size and then regress.

The writer is associate professor and head, Department of Botany, Ananda Mohan College, Kolkata