

Targeting Alzheimer's

A NEW METHOD USING AN UNUSUAL OPTICAL EFFECT TO DETECT THE DISEASE HAS BEEN REPORTED, SAYS

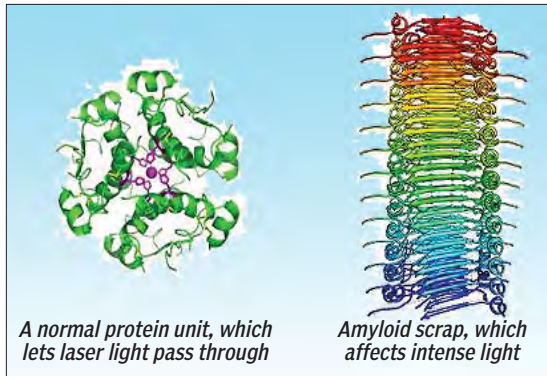
S ANANTHANARAYAN

Alzheimer's is the most common form of dementia, or loss of cognitive ability, that rapidly gets worse and, as yet, has no cure. The disease is known to arise from plaque formation in the cells of the brain but there is not even a proven preventive.

Even clear diagnosis, for what it is worth, is possible only with the examination of brain tissue and chemical agents that could be used to strike at the plaques that are toxic. Parkinson's is another disease that affects movement and can progress to dementia, where there is similar loss of nerve tissue in the brain and elsewhere. In this case also, it is the accumulation of protein matter in diseased nerve cells that is implicated, with similar difficulty of treatment.

In this context, the report of a group at Chalmers University of Technology in Sweden and the Wrocław University of Technology in Poland, in the journal *Nature*, that the kind of tissue that causes Alzheimer's, Parkinson's and some other conditions can be detected by a non-invasive method, is news indeed. And the method used is not the familiar X-ray scan or MRI or spectroscopy or scattering or any other methods usually employed, but one where a phenomenon called multiple photon absorption, of an intense laser beam in the infra-red region when it passes through a diseased tissue, is detected.

Proteins are complex molecules that have a characteristic way of packing, or folding, into a low energy shape. Sometimes, usually because of some genetic defect, the folding goes wrong and the same protein would show different properties. Amyloids are lumps of insoluble fibres arising from a group of such inappropriately folded proteins and their accumulation in neurons has been associated with a number of diseases, particularly the



A normal protein unit, which lets laser light pass through

Amyloid scrap, which affects intense light

degeneration of nerves.

There is much evidence that amyloid formation has a role in the onset and progress of Alzheimer's and Parkinson's as also some other conditions that arise from damage to nerve tissue.

The amyloid structure is the less encountered "twisted pleated sheet" structure, a stack of sheets that can be many microns long, as opposed to the more frequent coiled or helix, in three-dimensional forms of proteins. Sometimes both forms are present and the material could show great strength when extended or is resistant to shear. The amyloid structure, like some others, also affects a beam of light differently according to the planes in which the electric and magnetic vibrations in the light are oriented. But the clear identification is by actually verifying the "pleating of the sheets" by their effect on an X-Ray beam passed through a sample. But the effect now discovered by Piotr Hanczyc, Marek Samoc and Bengt Norden, the authors of the paper in *Nature*, could enable the detection and imaging of amyloid fibres by sensing the effect of absorption of laser radiation in the less harmful infra-red region selectively by these structures.

Non-linear optics

The optical effects that the group worked with belong to the field of non-linear optics, or where effects on a beam of light passing through a medium do not get uniformly stronger as the beam gets stronger but get tremendously stronger.

The reason for this response is that the effect the medium has on the beam is itself a result of the incident beam. Specifically, as light waves consist of undulating electric and magnetic effects, it is the electric part that affects the scattering or absorbing medium — and the effect is really discernable only when the electric effect is very strong, like it is at the inter-atomic level. Non-linear effects are, hence, better observed radiation created by an intense source, like the pulsed laser.

One kind of non-linear effect is when two photons that enter the medium combine to form a single photon of double the energy and, hence, twice the frequency. Another kind is when the two photons are absorbed to knock the electronic system in the medium to a state that is higher by the energy of the two photons. This is an effect that is different from absorption of the photons separately, which is linear, and is a case of non-linear absorption.

Such two-photon absorption or generation of light of twice the frequency is made use of in very high-resolution microscopy, where only the material that shows this kind of behaviour gets detected. The tissue, collagen, the structural protein in animals, is one such material and two-photon generation is used for microscopy of the cornea and nerve fibres of the optic nerve exit. Generation at twice the frequency, or the harmonic, is also used for generation of "green laser", for use in pointers, for instance. In these cases, it is necessary to filter out the intense infra-red source light to avoid damage to the users' eyes!

The method used for measuring the two-photon absorption was the z-scan technique. In this method, the incident laser beam is first split into two. One beam is the source monitor, to correct the results of the scan for variations in the source. The second beam is focused through a lens and

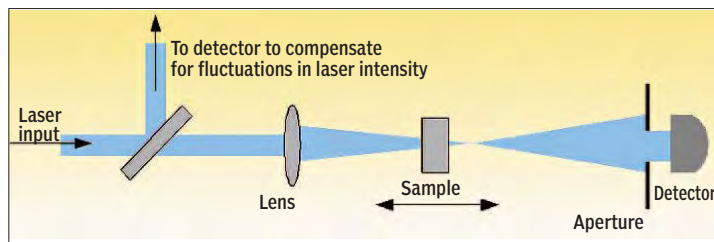
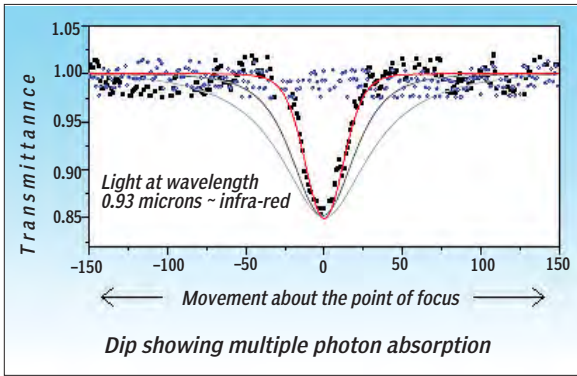
a thin sliver of the sample is placed at the point of focus. The light coming through is then detected, as shown in the picture. The sample is then moved along the axis of the beam, the "z" axis, over a short length related to the wavelength of the light used. At the correct position, there is a dip in the intensity of the transmitted beam, which yields the level of absorption.

Use with amyloids

The researchers worked with three kinds of fibre forming proteins and measured the level of multi-photon absorption both as native protein and also as amyloid fibres. It was found that the amyloid structure gave rise to marked multi-photon absorption. While there is uncertainty about the reasons, whether interactions within the molecule or between molecules are responsible, the result is one that promises a way of targeting just the amyloid protein molecules in the lumps that form on diseased nerve tissue. The ability at least opens the door to seeking curative procedures. There are problems, of course, one being that collagen tissue would also show up in multiple photon absorption scans, which pinpoints what work needs to be done.

"Nobody has talked about using only light to treat these diseases until now. This is a totally new approach and we believe that this might become a breakthrough in the research of diseases such as Alzheimer's, Parkinson's and Creutzfeldt-Jakob disease. We have found a totally new way of discovering these structures using just laser light," says Piotr Hanczyc at Chalmers University of Technology.

This research also suggests that protein-based materials may leverage multi-photon absorption for specific applications in nanotechnology, photonics and opto-electronics, say the authors of the paper.



STIMULATING GROWTH

TAPAN KUMAR MAITRA EXPLAINS THE BIOLOGICAL CONTROL OF PLANT PATHOGENS

The study of antibiotics as a means of controlling plant diseases was begun comparatively recently. The possibility, in principle, of using these to control some plant diseases was proven in the 1940s and widespread investigation and practical use of such substances followed in the '50s.

At present, the expediency of using antibiotics to control a number of diseases (burning of fruit trees caused by *Erwinia amylovora*, *pyriculariosis* and other diseases of rice, bacteriosis of beans, soya beans and certain virus diseases) — against which there are no sufficiently effective chemical fungicides — has been proven. The prospects of employing antibiotics are due to their following properties:

- Their comparatively low toxicity to humans and animals;
- Their ability to penetrate into plants and increase their resistance to diseases;
- The specific nature of their action; and
- Their high activity with respect to pathogenic organisms, which allows them to be used in very small concentrations and avoid the accumulation of their residues in products and the soil. Most antibiotics in definite concentrations stimulate the growth and development of plants and increase yield. Antibiotics may be combined with other fungicides.

Arenarin is an antibiotic of a vegetative origin. The substance is prepared from the dry flowers of sand immortelle (*Helichrysum avicularium*).

Arenarin effectively controls the development of various phytopathogenic bacteria. An especially strong inhibiting action has been noted with respect to the pathogen of bacterial cancer of tomatoes.

It is recommended for the pre-planting treatment of tomato seeds against bacterial cancer. This treatment of seeds also facilitates the reduction of infection of the plants with black bacterial spot, soft blossom-end rot and other rots, and also with virus diseases. The seeds are soaked in an aqueous solution of arenarin with a concentration of 1:1,000 and kept in it for two and a half hours. To treat one kilogram of seeds, 100 ml of the liquid formulation of arenarin is needed. The working solution for soaking the seeds is taken with a

surplus in a dose of five litre/kg of seeds. After being soaked, the seeds are spread out in a thin layer and dried. The formulation has a low toxicity to humans and warm-blooded animals (LD₅₀ for mice is 3,000-4,000 mg/kg).

The antibiotic phytoantibacteriomycin is the product of vital activity of an actinomyce from the group *Actinomyces lavendula*. The formulation is available with an activity of 20,000 unit/g. It is a cream-coloured or light-brown powder well soluble in water.

Phytoantibacteriomycin is moderately toxic to humans and warm-blooded animals (LD₅₀ for rats when ingested orally is 550 mg/kg, for mice it is 320 mg/kg and for guinea pigs 158 mg/kg). The formulation has a moderate ability of cumulation, with a coefficient of 1.9. It has an irritating action on the skin and mucous membrane of the eyes.

Phytoantibacteriomycin is recommended for the pre-planting treatment of seeds against the bacterial burning of beans and soya beans. Soya bean seeds are treated with phytoantibacteriomycin by powdering with the dust on the day of planting at a rate of three gm/kg of seeds. The maximum tolerated concentration in the air of the working zone is 0.002 mg/m³. Treated soya bean seeds must never be used in food.

Trichothecin is an antibiotic produced by the vital activity of the fungus *Trichothecium roseum*. It has fungistatic and fungicidal activity. It is marketed in the form of the pure substance — a yellow crystalline solid insoluble in water with an activity of 750 unit/mg. It is well soluble in organic solvents and is also available as a 10 per cent sol-

uble powder. Trichothecin is moderately toxic (LD₅₀ for laboratory animals is 263-400 mg/kg). Its cumulation coefficient is seven. The tolerance level in cucumbers is one mg/kg. The maximum tolerated concentration in the air of the working zone is approximately 0.2 mg/m³.

It is used to control true powdery mildew and root rots and is also highly effective in controlling powdery mildew of cucumbers in sheltered soil. The plants are sprayed with a 0.02 per cent solution of the pure substance or a 0.4 per cent suspension of the dust. The dose per hectare is 200 gm of the 10 per cent dust. The latter is dissolved in acetone to a creamy paste and then water is added, up to 500 litres. The soaking agent OP-7 must be added to the working liquid in an amount of not over five ml per 10 litres.

The cucumbers are sprayed two to four days before the appearance of the powdery mildew or when its first symptoms are observed. If the disease does not develop after the first treatment, the second one may be performed not earlier than in 15 days. If powdery mildew appears again after the first treatment, the second one must be performed in three to five days and repeated subsequently two or three times.

Trichothecin has no negative effect on the *Phytoseiulus persimilis* widely used to control spider mites in sheltered soil. Harvest time is three days and washing the products with water is obligatory.

THE WRITER IS ASSOCIATE PROFESSOR AND HEAD, DEPARTMENT OF BOTANY, ANANDA MOHAN COLLEGE, KOLKATA, AND CAN BE CONTACTED AT tapanmaitra59@yahoo.co.in



A mystery solved

CRASH INJURIES SUGGEST KING TUTANKHAMUN WAS THE FIRST OF THE BOY RACERS, WRITES JONATHAN OWEN

It has taken thousands of years but a combination of 21st-century forensic science and luck has finally revealed what happened to

Working with forensic archaeologist Matthew Ponting, Connolly used a scanning electron microscope to determine that the flesh had been burnt. Subsequent chemical tests confirmed that Tutankhamun's body was burnt while sealed inside his coffin. Researchers discovered that embalming oils combined with oxygen and linen caused a chemical reaction that "cooked" the king's body at



Dr Chris Naunton believes the Pharaoh's body was burnt.

Tutankhamun — the world's most famous Pharaoh.

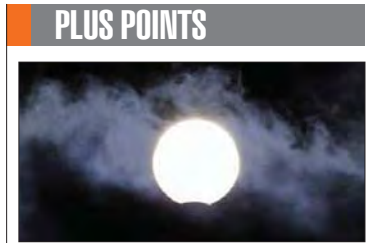
Mystery has surrounded the boy king ever since his death in 1323 BC, aged 19. The mystery intensified when archaeologist Lord Carnarvon died in Cairo shortly after he and Howard Carter discovered Tutankhamun's tomb in 1922. Now British experts think they have solved the riddle of the king's death. They believe injuries on his body are akin to those sustained in a chariot accident and that his mummification was botched.

Dr Chris Naunton, director of the Egypt Exploration Society, was intrigued when he came across references in Carter's records of the body having been burnt. A clue came from Dr Robert Connolly, an anthropologist at Liverpool University, who was part of the team that X-rayed Tutankhamun's remains in 1968. Among the bones in his office he recently found a piece of the pharaoh's flesh — the only known sample outside Egypt.

temperatures of more than 200 Celsius. Dr Naunton said, "The charring and possibility that a botched mummification led to the body spontaneously combusting shortly after burial was entirely unexpected, something of a revelation." Working with scientists from the Cranfield Forensic Institute, researchers performed a "virtual autopsy" that revealed a pattern of injuries down one side of the body. Their investigation also explains why King Tut's mummy was the only pharaoh to be missing its heart: it had been damaged beyond repair.

The pharaoh's injuries have been matched to a specific scenario — with car-crash investigators creating computer simulations of chariot accidents. The results suggest a chariot smashed into him while he was on his knees — shattering his ribs and pelvis and crushing his heart.

THE INDEPENDENT



'Hybrid' solar eclipse

The total solar eclipse that took place on 3 November was the year's most interesting because it was a rare "hybrid", meaning that some sections of the path were annular (where the moon does not completely block out the sun) while other parts were total. The Science Popularisation Association of Communicators and Educators, a pioneer organisation working towards the development of science and astronomy in India, has provided an opportunity to view the entire event while sitting at home. Simply click on to the Eclipse Chasers Athenaeum website (<http://www.eclipsechasers.in/>) and refer to the details and link provided.

This eclipse was even more unique because the central path began annular and ended total. Because hybrid eclipses occur near the vertex of the moon's umbral/antumbra shadows, the central path was quite narrow. The hybrid eclipse was visible from within a thin corridor, which traversed the North Atlantic and equatorial Africa. A partial eclipse was seen within the much broader path of the moon's penumbral shadow, which included eastern North America, northern South America, southern Europe, West Asia and Africa. When the shadow left earth, it was Somalia where a one-second total eclipse occurred at sunset.

Earth-like planets

The Milky Way galaxy is teeming with Earth-like planets that are not too hot and not too cold for liquid water to exist at their surface — and therefore capable of supporting life, according to a study. Astronomers have calculated that about one in every five of the billions of sun-like stars in our galaxy has at least one rocky planet orbiting them at a distance where water is neither frozen solid nor boiled dry.

Knowing how many rocky planets existed in the so-called Goldilocks zone — neither too hot, nor too cold — was one of the central goals of the Kepler satellite mission to estimate the total



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number of "exoplanets" existing beyond the Solar System.

The latest estimate, based on Kepler data, is the most accurate assessment so far of the number of potentially habitable planets in our own galaxy of between 100-400 billion stars.

"What this means is that when you look up at the thousands of stars in the night sky, the nearest sun-like star with an earth-size planet in its habitable zone is probably only 12 light years away and can be seen with the naked eye. That is amazing," said Erik Petigura of the University of California, Berkeley, who led the research.

The now-defunct Kepler space telescope, launched in 2009, was designed to detect the tiniest changes in a star's brightness as an orbiting planet crosses in front of it. The signal had to be highly repeatable to confirm the existence of an orbiting planet. The Kepler scientists reported about 3,000 planetary "candidates", estimated by taking photographs every 30 minutes of about 150,000 stars. Many of these planets are much larger than earth and unsuitable for water and life, such as gaseous giants like Jupiter or those with thick atmospheres like Neptune, or hot planets that orbit much too close to their star.

"This number — that every fifth star has a planet somewhat like earth — is really important, because successor missions to Kepler will try to take an actual picture of a planet, and the size of the telescope they have to build depends on how close the nearest earth-size planets are," said Andrew Howard of the University of Hawaii.

The scientists focussed on 42,000 stars that are similar in size and temperature to our own sun. They found 603 planets orbiting these stars, but only 10 of them were in the same size-range as earth and with an orbit suitable for liquid water. They scaled up their analysis to provide a total estimate for the entire galaxy and tested their computer algorithms with fake planets, which were designed to see how many planets were being missed in their analysis.

"What we're doing is taking a census of extrasolar planets, but we can't knock on every door. Only after injecting these fake planets and measuring how many we actually found could we really pin down the number of real planets that we missed," Petigura said.

STEVE CONNOR/THE INDEPENDENT