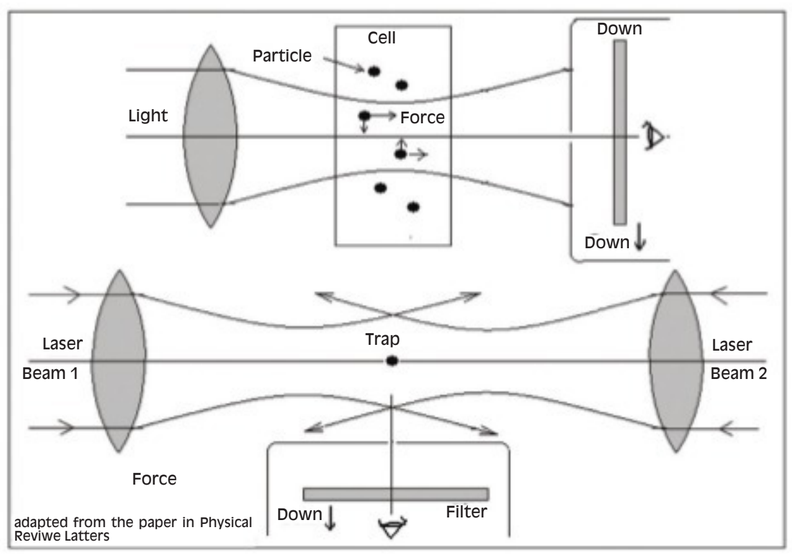
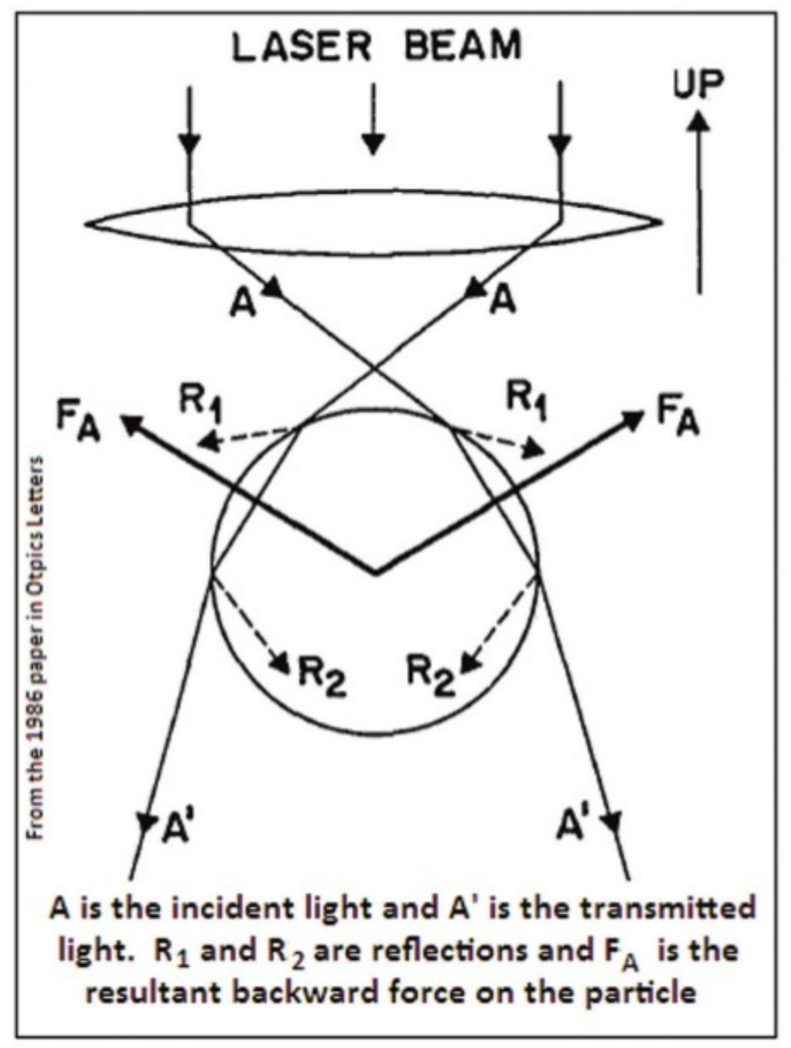
The light touch of illumination

One half of last year's Nobel Prize in physics has celebrated optical tweezers which enables detailed study of biological specimens in a way that was not possible using conventional methods

S ANANTHANARAYANAN


Arthur Ashkin





A is the incident light and A' is the transmitted light. R_1 and R_2 are reflections and F_A is the resultant backward force on the particle

No physical instrument can hope to manipulate things at the dimensions of atoms. This is equally a limitation in working with very minute objects, like biological cells and the smallest organisms. The solution, to use forceps that consist of light beams, has opened the doors to new research in many areas.

Arthur Ashkin, who cornered half the 2018 Nobel Prize for physics, for this work, has engaged with the effect of lasers on micro-particles, at the Bell Laboratories, New Jersey, since the 1960s. And he first demonstrated that a light beam can be used to exert a mechanical force, in a paper that was published nearly 50 years ago, in 1970. The principle was used by Steven Chu and others to coax atoms to get cooler by losing energy to particles of light. The Steven Chu group got the Nobel Prize in 1997, but Ashkin had to wait till October 2018 for the Nobel Committee to recognise his seminal work.

That rays of light exert a force was noticed by Johann Kepler as early as the 17th Century. Kepler noticed that the plume, or the vapour trail, of comets was blown in the direction facing away from the sun. In the mathematical formulation of electromagnetic waves, of which ordinary light consists, Clerk Maxwell, 19th Century, showed that the waves had momentum, or the inertia of a massive object in motion. This was later confirmed in experiment and there are ideas of using starlight to propel spacecraft on long flights where fuel cannot be carried.

Ashkin's 1970 paper, carried by the journal, Physical Review Letters, explains that with very small and lightweight objects, the acceleration produced by light pressure can be sizeable. The principle is that when a photon of light reflects off an object, its momentum is reversed and transferred to the object. As the mass of an object falls very fast when its dimensions are reduced, in the case of very small objects, the mass is drastically low and acceleration is rapid. An orange-red beam from the argon laser, with power of just 1 Watt, the paper says, can accelerate an object of the size of the wavelength of the laser, and one that reflects only a tenth of the light that falls on it, thousands of times more than the force of gravity.

The problem with getting anything out of this force, however, has been that there are other, many times more powerful forces that are in action, and the effect of the light beam is completely obscured. These forces are the effects of temperature differences in the surrounding medium and the heating effect of the laser light itself.

In the work that Ashkin reported, warming effects of the laser beam were avoided by using particles, spheres of latex, and the medium, water, in which they were suspended, which were transparent to the laser light used. The beam thus traversed the cell without any part being absorbed and the only effect on the particles was because of the light that they reflected.

A narrow argon laser beam was focused horizontally through a glass cell and manipulated to strike single particles. Particles off the axis of the beam were then drawn inwards, while simultaneously being moved along the path of the beam, as fast as microns per second, in the water medium, the paper said.

A second version of the effect is when the cell is illuminated by two, opposing beams of laser light. The particle is then constrained in all directions and is effectively 'trapped', and yet not subjected to any force other than the light pressure of the lasers.

Later, in 1986, Ashkin, with others, including Steven Chu, found a way to trap a particle with a single laser beam. As the picture shows, while the light that passes through the particle exerts no force, the light beam bends when it enters the particle and is internally reflected, leading to a backward force. The dimensions can be arranged so that, while there is a force due to backward reflection that pushes the particle forward, the backward force due to other reflections and the force towards the axis of the beam trap the particle to be motionless! The method was good with a range of particle sizes and the paper of 1986 mentions the possible use to study minute biological particles, as well as cooling atoms by constraining their thermal motion.

Steven Chu went on to develop a way to get atoms to cool down to temperatures not possible by conventional means, which employ cooling by expansion or by demagnetisation. The method was by selective transfer of energy of atoms to photons of light, at the time of reflection. In any sample of a material, the atoms are in constant motion. A photon of light, on reflection, would either gain energy and slow the atom, or lose energy and speed up the atom, depending on which way the atoms is moving. Chu used laser light of wavelength just below a characteristic wavelength at which reflection, as opposed to transmission, would take place. Now, reflection would occur only when the photon and atom were moving in opposite directions, and the atoms would lose momentum. All other atoms would be left unaffected. The result was that although only a fraction of the incident photons were reflected, the reflections led to slowing of the atoms, which amounts to cooling. Unprecedented low temperatures could be attained and Steven Chu, with Claude Cohen-Tannoudji and William D Philips, got the Nobel Prize for physics in 1997, for this work.

The basis, however, was the work of Arthur Ashkin and his work on constraining the motion of smallest particles. As suggested in his paper of 1986, the techniques developed, which have been called 'optical tweezers', have enabled detailed study of biological specimens in a way that was not possible using conventional methods of capturing and fixing samples for study. Typically, apart from trapping single atoms, the method has enabled trapping single cells, viruses and bacteria, measuring the forces exerted by components within cells and the dynamics of DNA. The properties of light and its effect on nanoparticles has become an important science and newer applications, using features like light waves where the plane of vibration of the waves is made to rotate, are enabling investigation of the most fragile states of matter.

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Identifying tumour suppressor genes

Enormous scientific progress has been made in recent years providing reasons to believe that our growing understanding of cancer will eventually allow it to be brought under control

TAPAN KUMAR MAITRA

The term cancer, which means "crab" in Latin, was coined by Hippocrates in the fifth century BC to describe diseases in which tissues grow and spread unrestrained throughout the body, eventually choking life. Cancers can originate in almost any organ; depending on the cell type involved, they are grouped into several different categories. Carcinomas, which account for about 90 per cent of all cancers, arise from the epithelial cells that cover external and internal body surfaces.

Lung, breast, and colon cancer are the most frequent cancers of this type. Sarcomas develop from the cells of supporting tissues such as bone, cartilage, fat, connective tissue, and muscle. Finally, lymphomas and leukemias arise from cells of blood and lymphatic origin, with the term leukemia being reserved for situations in which the cancer cells reside and proliferate mainly in the bloodstream rather than growing as solid masses of tissue. No matter where cancer arises, it is defined by a combination of two properties: the ability of cells to proliferate in an uncontrolled fashion and their ability to spread through the body.

Anyone familiar with the events occurring inside living cells must feel a sense of awe at the complexities involved. Given the vast number of activities that need to be coordinated in every cell, it is not surprising that malfunctions occasionally arise. Cancer is a prominent example of a disease that arises from such abnormalities in cell function. If current trends continue, almost half the population of the United States will eventually develop cancer, making it the second-leading cause of death after cardiovascular disease. The molecular and genetic defects that lead to cancer is not yet complete, enormous progress has been made in recent years and there is reason to believe that our growing understanding of this dreaded disease will eventually allow it to be brought under control.

A large body of evidence points to the role played by DNA mutations in the development of cancer. Some cancer-causing mutations are triggered by chemicals and radiation, and some are caused by infectious agents. Others simply represent spontaneous mutations, DNA replication errors, or in certain cases, inherited mutations. But in spite of these differences in origin, the final result is always the mutation of genes involved in controlling cell proliferation. The two main classes of affected genes are oncogenes and tumour suppressor genes.

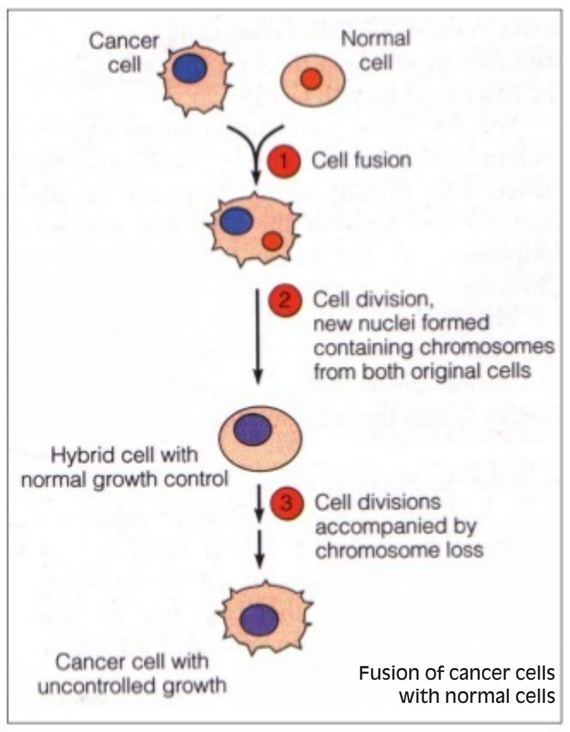
In contrast to oncogenes, whose presence can induce cancer formation, the loss or inactivation of tumour suppressor genes can also lead to cancer. As the name implies, the normal function of such genes is to restrain cell proliferation. In other words, tumour suppressor genes act as brakes on the process of cell proliferation whereas oncogenes function as accelerators of cell proliferation.

Of the roughly 30,000 genes in human cells, only a few dozen exhibit the properties of tumour suppressors. Since losing the function of just one of these genes may cause cancer, each must perform an extremely important function.

The first indication that cells contain genes whose loss can lead to cancer came from cell fusion experiments in which normal cells were fused with cancer cells. Based on our current understanding of oncogenes, you might expect that the hybrid cells created by fusing cancer cells with normal cells would have acquired oncogenes from the original cancer cell and would therefore exhibit uncontrolled growth, just like a cancer cell. In fact, this is not what happens.

The fusion of cancer cells with normal cells almost always yields hybrid cells that behave like the normal parent and do not form tumours. Such results, first reported in the late 1960s, provided the earliest evidence that normal cells contain genes that can suppress tumour growth and reestablish normal growth behaviour.

Although fusing cancer cells with normal cells generally yields hybrid cells that lack the ability to form tumours, this does not mean that these cells are normal. When they are allowed to grow for extended periods in culture, the hybrid cells often revert to the malignant, uncontrolled behaviour of the original cancer cells. Reversion to malignant behaviour is associated with the loss of certain chromosomes, suggesting that these particular chromosomes contain genes that had been suppressing the ability to form tumours. Such observations eventually led to the naming of the lost genes as "tumour suppressor genes."As long as hybrid cells retain both sets of original chromosomes-that is, chromosomes derived from both the cancer cells and the normal cells-the ability to form tumours is suppressed. Tumour suppression is even observed when the original cancer cells possess an oncogene, such as a mutant RAS gene, that is actively expressed in the hybrid cells. This means that tumour suppressor genes located in the chromosomes of normal cells can overcome the effects of a RAS oncogene present in a cancer cell chromosome. The ability to form tumours only reappears after the hybrid cell loses a chromosome containing a critical tumour suppressor gene.



Although cell fusion experiments provided the initial evidence for the existence of tumour suppressor genes, identifying these genes is not a simple task. By definition, the existence of a tumour suppressor gene only becomes evident after its function has been lost. How do scientists go about finding something whose very existence is unknown until it disappears?

One approach involves families that are at high risk for developing cancer. While most cancers are known to be environmentally triggered, about 10-20 per cent of cancer cases can be traced to inherited gene defects. When it is said that such cancers are hereditary, this does not mean that people actually inherit cancer from their parents.

What can be inherited, however, is an increased susceptibility to developing cancer. The reason for the increased risk is usually an inherited defect in a tumour suppressor gene. Since tumour suppressor genes are entities whose loss of function is associated with cancer, two successive mutations are typically required-one in each copy of the gene carried on two homologous chromosomes.

The chances of two such mutations occurring: randomly in the two copies of the same gene is very small. However, if people inherit a mutant (or missing) version of a particular tumour suppressor gene from one parent, they are at much higher risk of developing cancer because only one mutation (in the second copy of that tumour suppressor gene) in a single cell is now needed to cause cancer.

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PLUS POINTS

Boosting crop growth

Scientists have genetically engineered plants so they grow up to 40 per cent larger by tweaking the process they use to turn sunlight into food.

Photosynthesis allows plants to harvest the sun's energy and produces vital oxygen fuelling the rich array of life on Earth. However, this mechanism is hampered by an energy intensive process called photorespiration. "Photorespiration is anti-photosynthesis," said Paul South, a molecular biologist at the US Department of Agriculture who led the international team responsible for study, published in the journal Science.

One of the key components in photosynthesis is Rubisco, a substance that helps to convert carbon dioxide and water into sugars. Around 20 per cent of the time Rubisco mistakenly grabs oxygen instead of CO2 resulting in the production of a toxic substance that must be removed by photorespiration.

Photorespiration uses a large amount of energy. To cut down on energetic costs, South and his colleagues created plants with much shorter pathways, a feat of plant engineering they compared to the Panama Canal in the way it boosted efficiency.

By fixing this "glitch" a huge amount of energy wasted in photosynthesis can be saved, boosting productivity thereby helping to feed the expanding human population. Using tobacco plants to test their ideas, the scientists conducted field studies over the course of two years and found engineered plants were around 40 per cent larger.

They are now attempting the same thing with edible crops including soybeans, rice and potatoes.

As higher temperatures are known to increase photorespiration rates, this research could have particular relevance in warmer climates.

The work, which is part of Realising Increased Photosynthetic Efficiency project, will probably not be applied to food crops for over a decade.

However, the scientists and funders behind the endeavour have committed to providing royalty-free access to the fruits of their labour to farmers in areas like Sub-Saharan Africa and Southeast Asia. Besides plants with improved photosynthesis, others that have been developed include crops with higher nutrient content, or strains that are resistant to common diseases.

The independent

Depression in girls

Teenage girls are twice as likely as boys to show depressive symptoms linked to social media use-- mainly due to online harassment and disturbed sleep, as well as poor body image and lower self-esteem, researchers said.

In a study analysing data from nearly 11,000 young people in Britain, researchers found that 14-year-old girls were heavier users of social media, with two-fifths of them using it for more than three hours a day, compared with a fifth of boys.

The study also found that 12 per cent of light social media users and 38 per cent of heavy social media users showed signs of having more severe depression.

When the researchers looked at underlying processes that might be linked with social media use and depression, they found that 40 per cent of girls and 25 per cent of boys had experienced online harassment or cyber bullying. Disrupted sleep was reported by 40 per cent of girls compared with 28 per cent of boys. Yvonne Kelly, a professor at University College London's Institute of Epidemiology and Health Care who co-led the study, urged parents and policymakers to note its results.

"These findings are highly relevant to current policy development on guidelines for the safe use of social media and calls on industry to more tightly regulate hours of social media use for young people," she said in a statement. She added that families may "want to reflect on when and where it's okay to be on social media" and consider placing restrictions on teens having mobile devices in their bedrooms.

The study, funded by the UK Economic and Social Research Council, was published online in the journal EClinicalMedicine recently.

The straits times/ann