NOBEL PRIZES IN SCIENCE : 2018

CHEMISTRY

The Nobel Prize in Chemistry for 2018 was awarded jointly to **Frances H. Arnold** of the California Institute of Technology, Pasadena, U.S.A. "*for the directed evolution of enzymes*" and **George P. Smith** of the University of Missouri, Columbia, U.S.A. and **Gregory P. Winter** of the MRC Laboratory of Molecular Biology, Cambridge, U.K. "*for the phage display of peptides and antibodies*." One-half of the nearly $ 1 million (Swedish Krona 9 million) prize money was awarded to Arnold while Smith and Winter shared the other half of the prize money equally.

Frances H. Arnold

Arnold's work has furnished a host of new enzymes which are used as catalysts to produce many important pharmaceuticals, industrial chemicals and renewable fuels in an eco-friendly manner. Smith developed the new method of 'phage display', in which a bacteriophage – a virus that infects bacteria – is used to evolve new proteins. Winter used this elegant method for the 'directed evolution' of antibodies that are used for producing new pharmaceuticals. The efforts of Smith and Gregory have led to the drug 'adalimumab', approved in 2002, for the treatment of rheumatoid arthritis, psoriasis and inflammatory bowel diseases. Phage display has till date produced many antibodies that can neutralise toxins, counteract autoimmune diseases and cure metastatic cancer.

Claes Gustafsson, Chair of the Nobel Committee, cited the trio's work as follows: "*This year's prize in Chemistry rewards a revolution based on evolution. Our laureates have applied the principles of [Charles] Darwin in the test tubes, and used this approach to develop new types of chemicals for the greatest benefit of humankind*."

Arnold was born on July 25, 1956 in Pittsburgh, USA. She received her Bachelor degree in mechanical and aerospace engineering in 1979 from the Princeton University and her Ph.D. degree in chemical engineering in 1985 from the University of California, Berkeley. She started teaching at Caltech in 1986. Following her failed attempts in the 1980s to build new enzymes *via* a randomised approach, Arnold decided to look into evolution and copy nature's design to achieve her goal.

George P. Smith

Her success story began with the enzyme. She wanted to build a variety of the enzyme subtilisin that would catalyse chemical reactions in an organic solvent (DMF). Mimicking nature, she created random mutations in the genetic code of the enzyme and introduced the mutated genes to bacteria. These bacteria, in turn, created thousands of different variants of subtilisin. She resorted to 'selection' in this 'directed evolution', i.e. she selected that variety of subtilisin which showed the best performance. She then continued to mutate it until she had the 'very best subtilisin'.

Gregory P. Winter

She then used an existing technique called 'mating in a test tube', i.e. 'DNA shuffling' or 'recombination' to produce newer enzyme varieties that speed up chemical reactions, lead to pharmaceuticals and can even exclude heavy metals in used in many classical reactions. Arnold's current

research involves the generation of renewable energy.

In 2013, Arnold became the Director of the Donna and Benjamin M. Rosen Bioengineering Center. She is currently the Linus Pauling Professor of Chemical Engineering, Bioengineering and Biochemistry in the California Institute of Technology, Pasadena, U.S.A. Of the 177 Nobel Laureates in Chemistry till date, Arnold is the fifth woman to have received this Prize – a reflection of the gender bias against women in science, technology, engineering and mathematics (STEM). But she strongly believes that more and more women winners of Nobel Prize in chemistry are sure to come.

George P. Smith, born in 1941 in Norwalk, U.S.A., received his Ph.D. degree in 1970 from the Harvard University, Cambridge, U.S.A. His work was with bacteriophages. In 1985, he developed 'phage display'. Using an antibody, he was able to get hold of the phage he had constructed out of a soup of many phages. In the 1990s, several groups utilised phage display to produce biomolecules. Smith is at present Curators' Distinguished Professor Emeritus of Biological Sciences in the University of Missouri, Columbia, U.S.A.

Sir Gregory P. Winter, born in 1951 in Leicester, U.K., got his Ph.D. degree in 1976 from the Cambridge University, U.K. He utilised 'phage display' to produce curative antibodies. Instead of using mice for producing therapeutic antibodies, Winter designed in 1990 an antibody that attached itself to a small molecule called phOx, a kind of molecular fishing hook, which enabled him to pull the phage with the antibody on its surface out of a soup of four million other phages. Winter thus successfully utilised 'phage display' for the 'directed evolution of antibodies'. In 1994, he developed antibodies having anticancer usefulness. His remarkable discovery of the drug adalimumab (brand name: Humira) was entirely based on human antibody. Many more potential drugs developed using human antibodies are in clinical trials. Winter is now Research Leader Emeritus at the MRC Laboratory of Molecular Biology, Cambridge, U.K.

The directed evolution of enzymes and the phage display of antibodies have enabled Arnold, Smith and Winter, the three Nobel Laureates in chemistry for 2018, to bring 'the greatest benefit to humankind and to lay the foundation for a revolution in chemistry'. ❐

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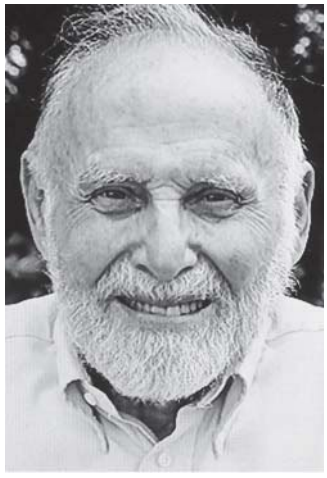
PHYSICS

The Nobel Prize in Physics 2018 was awarded for groundbreaking inventions in the field of laser physics. One half of the prize money has been given to **Dr. Arthur Ashkin** (USA) for his work on the optical tweezers and their application to biological systems, the other half jointly to **Dr. Gérard Mourou** (France) and **Dr. (Mrs) Donna Strickland** (Canada) for their unique method of generating high-intensity ultra-short optical pulses. The Nobel committee in their announcement recognized the scientists for their extraordinary contribution in translating laser light into miniature tools which are "optical tweezers" and "high-intensity ultrashort laser pulses".

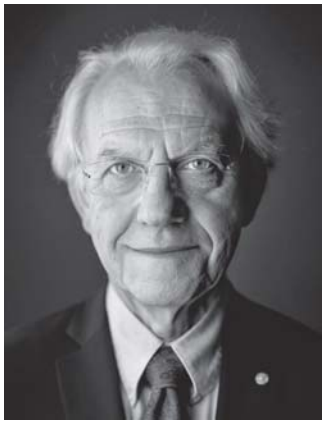
The Nobel Committee mentioned in their communication that– "Arthur Ashkin invented optical tweezers that grab particles, atoms, viruses and other living cells with their laser beam fingers. This new tool allowed Ashkin to realise an old dream of science fiction – using the radiation pressure of light to move physical objects. He succeeded in getting laser light to push small particles towards the centre of the beam and to hold them there. A major breakthrough came in 1987, when Ashkin used the tweezers to capture living bacteria without harming them. He immediately began studying biological systems and optical tweezers which are now widely used to investigate the machinery of life".



Dr. Arthur Ashkin

The intensity of a laser beam is maximum at the centre than at the edges. Light carries momentum that is proportional to its energy and in the direction of propagation. At this bright zone any change in the direction of light, by reflection or refraction, will result in a change of the momentum of the beam of light. If an object bends the light, changing its momentum, conservation of momentum requires that the object must undergo an equal and opposite momentum change. This gives rise to a force acting on the object as a result this force pulls the object into the center creating a stable trap. The play of forces within the laser beam effectively draw the ball into the center of the beam and trapped it there — a first step toward realization of optical tweezers

Dr. Ashkin was born in 1922 in New York City. After completing undergraduate degree in physics from Columbia University in 1947 he received a Ph.D. in nuclear physics from Cornell in 1952 and joined Bell Labs in Murray Hill, N.J., where he worked until 1991. Shortly after the successful demonstration of lasers in 1960, Dr.Ashkin began experimenting with coherent laser beams to understand the basics of light radiation pressure. It was earlier known that the dust tail of a comet is a trail of tiny particles ejected from its core, and the radiation pressure of light from the sun pushes it out and away from the comet's orbit. The same light pressure that sweeps from a comet's tail could be used in the lab to push a microscopic ball around.

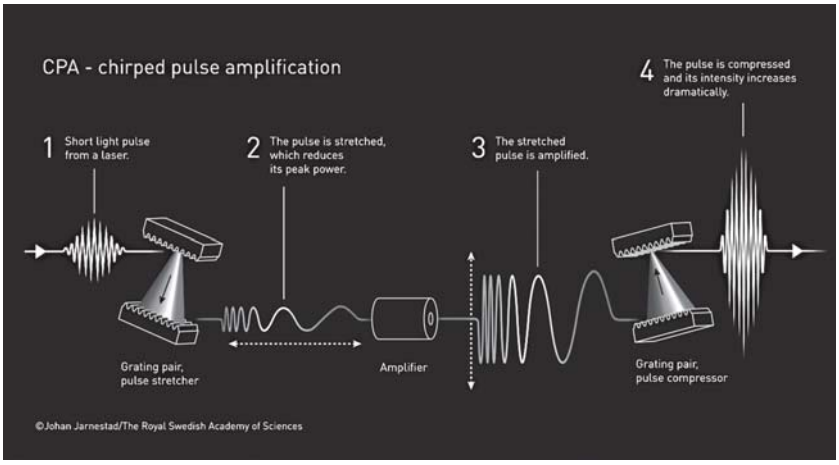


Dr. Gérard Mourou

It may be interesting to note that Prof. Steven Chu (born 1948) now at Stanford University had worked with Dr. Ashkin at Bell Laboratories and it was well understood at that time that Ashkin's work actually formed the basis for Steven Chu's work on laser cooling and trapping of atoms, which earned Dr. Chu the 1997 Nobel Prize in physics. They have couple of joint papers on this subject. Dr. Ashkin was very much disappointed with the decision of Nobel Committee that he had not been included in the award list in that year. But the justice was done in 2018.

Dr. (Mrs) Donna Strickland

As mentioned at the beginning that Dr. Donna Strickland and Dr. Gérard Mourou had shared the other half of the Nobel prize in physics in 2018. They developed a method of generating high-intensity ultrashort laser pulses, which is known as chirped pulse amplification (CPA). The work has had a wide range of real-world applications, enabling manufacturers to drill tiny, precise holes and allowing for the invention of Lasik (laser-assisted in situ keratomileusis) eye surgery which is blessings to millions of people.



CPA enabled the emission of very intense, short pulses of light using an intricate method to avoid the risk of destroying the amplifying material. Instead of amplifying the light pulse directly, it is first stretched in time domain, reducing its peak power. Then the pulse is amplified and when it is compressed more light is collected in the same place – the light pulse becomes extremely intense. As shown in the figure. Courtesy © Johan Jarnestad/The Royal Swedish Academy of Sciences.

Dr. Strickland, who was born in Guelph, Canada, in 1959, is only the third woman to win the Nobel Prize for Physics. She is now an associate professor at the University of Waterloo in Canada. Dr. Mourou was born in Albertville, France, in 1944 and earned a Ph.D. in physics from the University of Grenoble in 1973. Currently he is a professor at the École Polytechnique in France and director of the International Center for Zetta-Exawatt Science and Technology.

Ever since lasers were invented, almost 60 years ago, researchers have endeavoured to create more intense pulses. However, by the mid-1980s, the end of the road had been reached through the work of Strickland and Mourou. For short pulses it was no longer practically possible to increase the intensity of the light without destroying the amplifying material.

Dr. Strickland reported, in December 1985, in her first scientific publication about the generation of high intense laser pulse while working for her PhD work under the supervision of Dr. Mourou at Rochester University, USA. Strickland and Mourou's new technique, known as *chirped pulse amplification*, CPA, was both simple and elegant. A short laser pulse is stretched in time, amplify it and squeeze it together again. When a pulse is stretched in time, its peak power is much lower so it can be hugely amplified without damaging the amplifier. The pulse is then compressed in time, which means that more light is packed together within a tiny area of space – and the intensity of the pulse then increases dramatically as shown in the Figure. It took a few years for Strickland and Mourou to combine everything successfully.

This high-intensity short-pulse lasers produced by the CPA-technique opened up a new horizon of innumerable areas of use such as, to create more efficient data storage, as the storage is not only built on the surface of the material, but also in tiny holes drilled deep into the storage medium; to manufacture surgical stents, micrometre- sized cylinders of stretched metal that widen and reinforce blood vessels, the urinary tract and other passageways inside the body and many more yet to be explored.

The technique enabled us to make picoseconds (10^{-12}) to intense femtosecond (10^{-15}) laser pulses and to *attosecond* (10^{-18}) to more. Laser pulses shorter than a hundred attoseconds reveal the dramatic world of electrons. Electrons are the workhorses of chemistry; they are responsible for the optical and electrical properties of all matter and for chemical bonds. Now they are not only observable, but they can also be controlled.

There is already speculation about the next step: a tenfold increase in power, to 100 petawatts. Visions for the future of laser technology do not stop there. Why not the power of a zettawatt (one million petawatts, 1021 watt), or pulses down to zeptoseconds, which are equivalent to the almost inconceivably tiny sliver of time of 10^{-21} seconds? New horizons are opening up, from studies of quantum physics in a vacuum to the production of intense proton beams that can be used to eradicate cancer cells in the body. However, even now these celebrated inventions allow us to rummage around in the microworld in the best spirit of Alfred Nobel – for the greatest benefit to humankind. This year's discovery is significant for reasons other than its excellence in physics. Arthur Ashkin born in 1922 became the oldest Nobel Laureate and Donna Strickler became the third woman Nobel Prize winner in physics after more than half a century.

(Sources: New York Times, Nature, The Royal Swedish Academy of Sciences, and internet archive.) ❐

Shyamal Kumar Bhadra
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PHYSIOLOGY OR MEDICINE

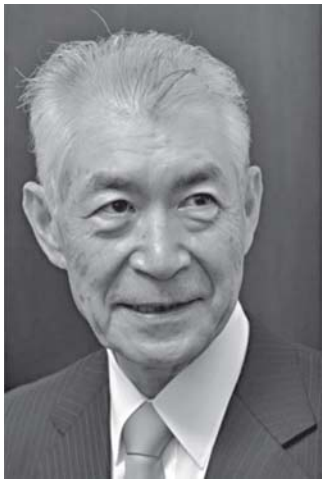
The Nobel Prize in Physiology or Medicine for 2018 was awarded jointly to **James P. Allison** and **Tasuku Honjo** "*for their discovery of cancer therapy by inhibition of negative immune regulation*," i.e, for their work on unleashing the body's immune system to attack cancer, a breakthrough that has led to an entirely new class of drugs and brought lasting remissions to many patients who had run out of options.

James Allison

James P. Allison was born 1948 in Alice, Texas, USA. He received his PhD in 1973 at the University of Texas, Austin. From 1974-1977 he was a postdoctoral fellow at the Scripps Clinic and Research Foundation, La Jolla, California. From 1977-1984 he was a faculty member at University of Texas System Cancer Center, Smithville, Texas; from 1985-2004 at University of California, Berkeley and from 2004-2012 at Memorial Sloan-Kettering Cancer Center, New York. From 1997-2012 he was an investigator at the Howard Hughes Medical Institute. Since 2012 he has been Professor at University of Texas MD Anderson Cancer Center, Houston, Texas and is affiliated with the Parker Institute for Cancer Immunotherapy. He did the work recognized by the Nobel committee while working the University of California at Berkeley and Memorial Sloan Kettering Cancer Center in New York.

Tasuku Honjo was born in 1942 in Kyoto, Japan. In 1966 he became an MD, and from 1971-1974 he was a research fellow in USA at Carnegie Institution of Washington, Baltimore and at the National Institutes of Health, Bethesda, Maryland. He received his PhD in 1975 at Kyoto University. From 1974-1979 he was a faculty member at Tokyo University and from 1979-1984 at Osaka University. Since 1984 he has been Professor at Kyoto University. He was a Faculty Dean from 1996-2000 and from 2002-2004 at Kyoto University.

Cancer comprises many different diseases, all characterized by uncontrolled proliferation of abnormal cells with capacity for spread to healthy organs and tissues. Before Dr. Allison's and Dr. Honjo's discoveries, cancer treatment consisted of surgery, radiation, chemotherapy and hormonal treatments. A number of therapeutic approaches for cancer treatment have been awarded previous Nobel Prizes which includes methods for hormone treatment for prostate cancer (Huggins, 1966), chemotherapy (Elion and Hitchings, 1988), and bone marrow transplantation for leukemia (Thomas 1990).



Tasuku Honjo

The concept emerged in the late 20th century and beginning of the 21st century that activation of the immune system might be a strategy for attacking tumor cells. Attempts were made to infect patients with bacteria to activate the defense. Earlier attempts by other researchers to recruit the immune system to fight cancer sometimes worked but more often did not. Dr. Allison and Dr. Honjo succeeded where others had failed by deciphering exactly how cells were interacting so they could fine-tune methods to control the immune system.

T-cells, a type of white blood cell, are sometimes called the soldiers of the immune system. They are deployed to fight infections and cancer, but malignant cells can elude them. The T-cells carry molecules called checkpoints, that the body uses to shut the cells down when it needs to stop them. Cancer cells can lock onto those checkpoints, crippling the T-cells and preventing them from fighting the disease.

Dr. Allison identified a checkpoint called CTLA-4. Dr. Honjo found a different one, called PD-1. Those discoveries made it possible to develop drugs that would stop the checkpoints from working, so that the T-cells would be free to fight cancer. The process is often referred to as taking the brakes off the immune system. This type of therapy is a new approach in cancer treatment. Instead of targeting the tumor cells themselves, it releases the brakes on immune cells, allowing them to attack cancer cells. The drugs that have been developed from their discoveries are known as checkpoint inhibitors.

The fundamental property of our immune system is the ability to discriminate "self" from "non-self" so that

invading bacteria, viruses and other dangers can be attacked and eliminated. T cells, a type of white blood cell, are key players in this defense. T cells were shown to have receptors that bind to structures recognized as non-self and such interactions trigger the immune system to engage in defense. But additional proteins acting as T-cell accelerators are also required to trigger a full-blown immune response. Many scientists contributed to this important basic research and identified other proteins that function as brakes on the T cells, inhibiting immune activation. This intricate balance between accelerators and brakes is essential for tight control. It ensures that the immune system is sufficiently engaged in attack against foreign microorganisms while avoiding the excessive activation that can lead to autoimmune destruction of healthy cells and tissues.

During the 1990s, in his laboratory at the University of California, Berkeley, James P. Allison an immunologist, studied the T-cell protein CTLA-4. He was one of several scientists who had made the observation that CTLA-4 functions as a brake on T cells and keep the immune system under control. He realized that by blocking that brake the immune cells could be unleashed on tumor cells, and he began developing therapies based on that principle. He developed an antibody that could bind to CTLA-4 and block its function.

Allison and co-workers performed a first experiment at the end of 1994 and found Mice with cancer had been cured by treatment with the antibodies that inhibit the brake and unlock antitumor T-cell activity. Promising results soon emerged from several groups, and in 2010 an important clinical study showed striking effects in patients with advanced melanoma, a type of skin cancer. In several patients signs of remaining cancer disappeared. Such remarkable results had never been seen before in this patient group. In 2011 a drug based on CTLA-4, ipilimumab, was approved for treating melanoma. More than 20 percent of people using the drug have complete remission from the disease.

Honjo, also an immunologist, discovered a second receptor called PD-1 that also acted as a brake, but with a different mechanism of action. This discovery has also proved to be effective in developing treatments. In 1992, a few years before Allison's discovery, Tasuku Honjo discovered PD-1, another protein expressed on the surface of T-cells. Determined to unravel its role, he meticulously explored its function in a series of elegant experiments performed over many years in his laboratory at Kyoto University. The results showed that PD-1, similar to CTLA-4, functions as a T-cell brake, but operates by a different mechanism. In animal experiments, PD-1 blockade was also shown to be a promising strategy in the fight against cancer. This paved the way for utilizing PD-1 as a target in the treatment of patients. Clinical development ensued, and in 2012 a key study demonstrated clear efficacy in the treatment of patients with different types of cancer. Results were dramatic, leading to long-term remission and possible cure in several patients with metastatic cancer, a condition that had previously been considered essentially untreatable. Two drugs based on PD-1 inhibition, nivolumab and pembrolizumab, have been approved for treating melanoma and lung cancer.

Checkpoint inhibitors have proved to be stunningly successful treatments for many different kinds of cancer, in particular, melanoma. They also show promise for lung cancer, kidney cancer and lymphoma of the two treatment strategies, checkpoint therapy against PD-1 has proven more effective and positive results are being observed in several types of cancer, including lung cancer, renal cancer, lymphoma and melanoma. New clinical studies indicate that combination therapy, targeting both CTLA-4 and PD-1, can be even more effective, as demonstrated in patients with melanoma A large number of checkpoint therapy trials are currently underway against most types of cancer, and new checkpoint proteins are being tested as targets. Checkpoint therapy has now revolutionized cancer treatment and has fundamentally changed the way of cancer management. ❐

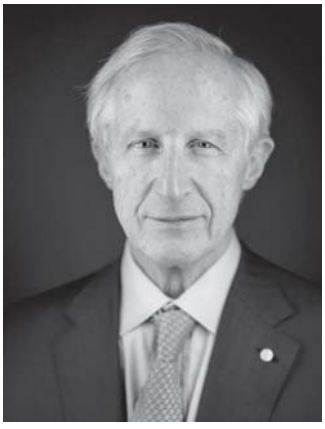
Dr Amit Krishna De

Compiled from

1. https://www.nobelprize.org/prizes/medicine/2018/press-release/
2. https://www.insidescience.org/news/2018-nobel-prize-medicine-story
3. https://www.nobelprize.org/prizes/medicine/2018/press-release/

ECONOMICS

The Royal Swedish Academy of Sciences has decided to award the Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 2018 to **William D. Nordhaus** of Yale University, New Haven, USA*"for integrating climate change into long-run macroeconomic analysis"* and **Paul M. Romer** of New York University Stern School of Business, New York, USA*"for integrating technological innovations into long-run macroeconomic analysis"*



William D. Nordhaus

William D. Nordhaus and Paul M. Romer have designed methods for addressing some of our time's most basic and pressing questions about how we create long-term sustained and sustainable economic growth.This year's Laureates William Nordhaus and Paul Romer have significantly broadened the scope of economic analysis by constructing models that explain how the market economy interacts with nature and knowledge.

Romer demonstrates how knowledge can function as a driver of long-term economic growth. When annual economic growth of a few per cent accumulates over decades, it transforms people's lives. Previous macroeconomic research had emphasised technological innovation as the primary driver of economic growth, but had not modelled how economic decisions and market conditions determine the creation of new technologies. Paul Romer solved this problem by demonstrating how economic forces govern the willingness of firms to produce new ideas and innovations.

Romer's solution, which was published in 1990, laid the foundation of what is now called *endogenous growth theory*. The theory is both conceptual and practical, as it explains how ideas are different to other goods and require specific conditions to thrive in a market. Romer's theory has generated vast amounts of new research into the regulations and policies that encourage new ideas and long-term prosperity.

Paul M. Romer

Nordhaus' findings deal with interactions between society and nature. Nordhaus decided to work on this topic in the 1970s, as scientists had become increasingly worried about the combustion of fossil fuel resulting in a warmer climate. In the mid-1990s, he became the first person to create an *integrated assessment model*, i.e. a quantitative model that describes the global interplay between the economy and the climate. His model integrates theories and empirical results from physics, chemistry and economics. Nordhaus' model is now widely spread and is used to simulate how the economy and the climate co-evolve. It is used to examine the consequences of climate policy interventions, for example carbon taxes.

In spite of his winning Nobel Prize and sustained effort of about four decades trying to persuade governments to address climate change, preferably by imposing a tax on carbon emissions, he sadly noted that he has not been able to convince the government of his own country.

The contributions of Paul Romer and William Nordhaus are methodological, providing us with fundamental insights into the causes and consequences of technological innovation and climate change. This year's Laureates do not deliver conclusive answers, but their findings have brought us considerably closer to answering the question of how we can achieve sustained and sustainable global ❐

S. C. Roy
email : editor.scienceandculture@gmail.com
Sources: 1. https://www.nobelprize.org/prizes/economic.../2018/
2. New York Times