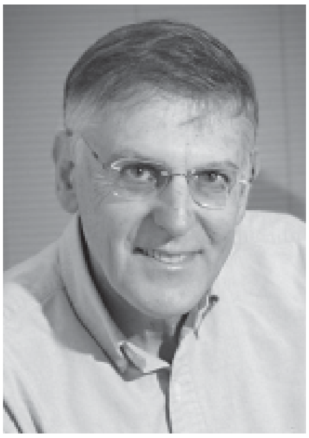
# NOBELS IN SCIENCE : 2011

## *CHEMISTRY*



Prof. Dan Shechtman

The Nobel Prize in Chemistry 2011 has been awarded to Prof. Dan Shechtman for the discovery of quasicrystals. Born in 1941 in Tel Aviv, Israel, he obtained his Ph.D degree from Technion – Israel Institute of Technology, Haifa, Israel in 1972. He holds the Philip Tobias Chair at Technion – Israel Technical Institute in Haifa.

The story began in the morning of 8 April, 1982. The material Dr. Dan Shechtman studying was a mix of aluminium and manganese which looked strange to him and he turned on the electron microscope in order to observe it at the atomic level. Surprisingly, the picture that the microscope produced was counter to all logic : he saw concentric circles, each made of ten bright dots from the same distance from each other (Figure 1)

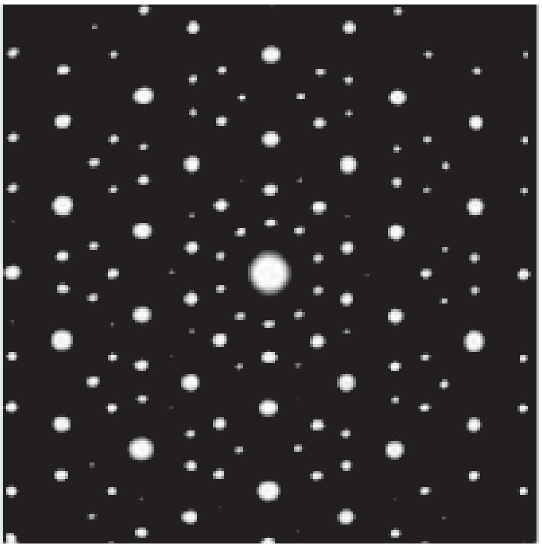


**Fig. 1.** Dan Shechman's diffraction pattern was tenfold : turning the picture a turth of a fult circle (36 degrees) results in the same pattern.

Shechtman had rapidly chilled the glowing molten metal, and the sudden change in temperature should have created complete disorder among the atoms. But the pattern he observed told a completely different story: the atoms were arranged in a manner that was contrary to the laws of nature. Shechtman counted and recounted the dots. Four or six dots in the circles would have been possible, but absolutely not ten. He made a notation in his notebook: 10 Fold???

In order to understand Shechtman's experiment and why he was so surprised, imagine the following classroom experiment. A physics teacher transmits light through a perforated metal plate, a so-called diffraction grating (figure 2). When the light waves travel through the grating, they are refracted in the same manner as an ocean wave that moves through a gap in a breakwater.

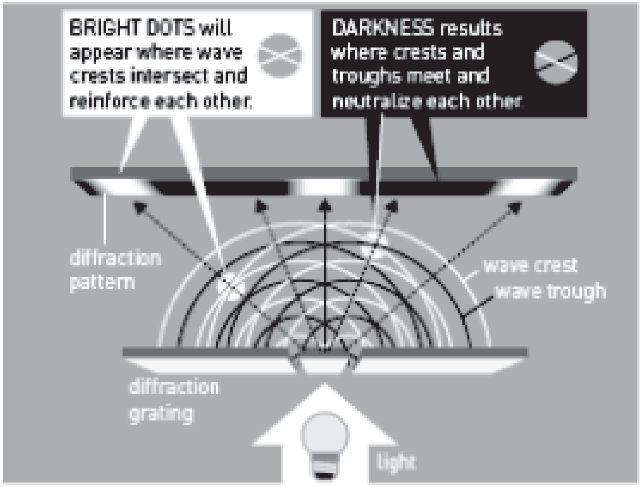


**Fig. 2.** Light passing through a diffraction grating gets scattered. The resulting waves interfere with each other, giving a diffraction pattern.

On the other side of the grating, waves spread in a semicircular manner and intersect with other waves. Crests and troughs of the waves reinforce and counteract each other. On a screen behind the diffraction grating, a pattern will appear of light and dark areas – a diffraction pattern.

It was such a diffraction pattern (Figure 1) that Dan Shechtman obtained that April morning in 1982. However, his experiment was different: he used electrons instead of light, his grating consisted of the atoms in the rapidly cooled metal, and he conducted his experiment in three dimensions.

The diffraction pattern showed that the atoms inside the metal were packed into an ordered crystal. That in itself was nothing extraordinary. Almost all solid materials, from ice to gold, consist of ordered crystals. However, the diffraction pattern with ten bright dots arranged in a circle was something he had never seen before, despite his vast experience using electron microscopes. Furthermore, such a crystal was not represented in the International Tables for Crystallography – the main crystallographic reference guide. At the time, science plainly stipulated that a pattern with ten dots in a circle was impossible, and the proof for that was as simple as it was obvious.

### *A Pattern Counter to All Logic*

Inside a crystal, atoms are ordered in repeating patterns, and depending on the chemical composition, they have different symmetries. In figure 3a, we see that each atom is surrounded by three identical atoms in a repeating pattern, yielding a threefold symmetry. Rotate the image 120 degrees and the same pattern will appear.

The same principle applies to fourfold symmetries (figure 3b) and sixfold symmetries (figure 3c). The pattern repeats itself and if you rotate the image, 90 degrees and 60 degrees, respectively, the same pattern appears.

However, with fivefold symmetry (figure 3d), this is not possible, as distances between certain atoms will be shorter than between others. The pattern does not repeat itself, which was proof enough to scientists that it was not possible to obtain fivefold symmetries in crystals. The same applies to sevenfold or higher symmetries.

Shechtman, however, could rotate his diffraction pattern by a tenth of a full circle (36 degrees) and still obtain the same pattern. Hence he was looking at a tenfold symmetry, one that was considered impossible. It is no surprise, then, that he made no less than three question marks in his notebook.

### *Wrong According to the Textbook*

Dan Shechtman peeked out from his office into the corridor at the U.S. National Institute of Standards and Technology (NIST), wanting to find someone with whom he could share his discovery. But the corridor was empty, so he went back to the microscope to carry out further experiments on the peculiar crystal. Among other things, he double-checked if he had obtained a twin crystal: two intergrown crystals whose shared boundary gives rise to strange diffraction patterns. But he could not detect any signs that he was in fact looking at a twin crystal.

In addition to this, he rotated the crystal in the electron microscope in order to see how far he could turn it before the tenfold diffraction pattern reappeared. That experiment showed that the crystal itself did not have tenfold symmetry like the diffraction pattern, but was instead based on an equally impossible fivefold symmetry. Dan Shechtman concluded that the scientific community must be mistaken in its assumptions.

When Shechtman told scientists about his discovery, he was faced with complete opposition, and some colleagues even resorted to ridicule. Many claimed that what he had observed was in fact a twin

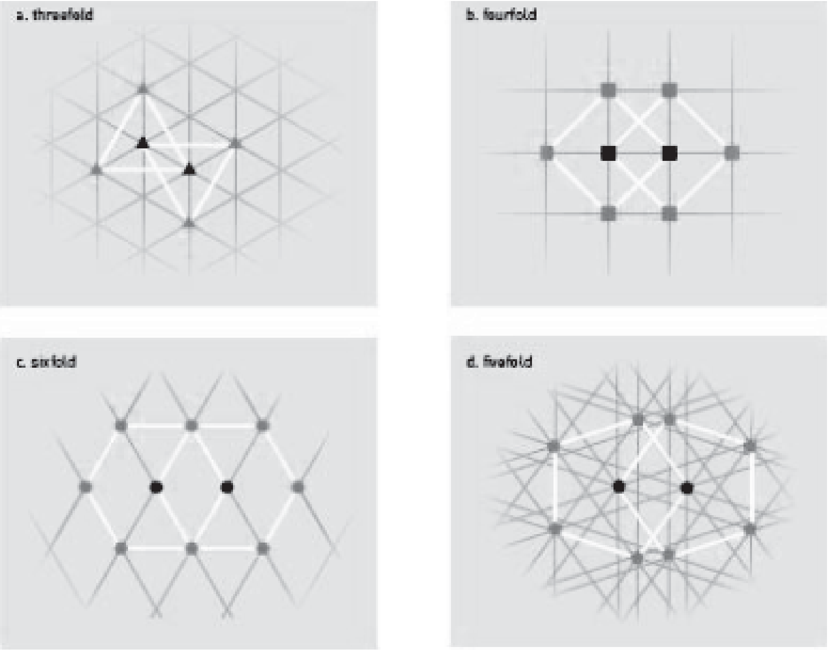
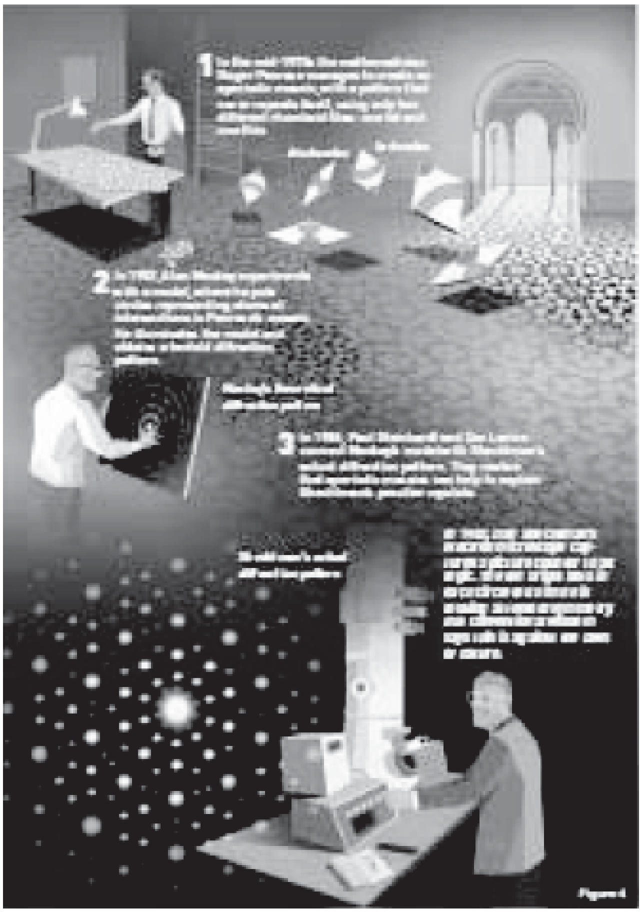


**Fig. 3.** Different kinds of symmetries in crystals. The pattern within the crystal with five fold symmetry will never repeat itself.

crystal. The head of the laboratory gave him a textbook of crystallography and suggested he should read it. Shechtman, of course, already knew what it said but trusted his experiments more than the textbook. All the commotion finally led his boss to ask him to leave the research group, as Schechtman himself recalled later. The situation had become too embarrassing.

In 1983, Dan managed to get Ilan Blech, a colleague at his alma mater, interested in his peculiar research findings. Together they attempted to interpret the diffraction pattern and translate it to the atomic pattern of a crystal. They submitted an article to the *Journal of Applied Physics* in the summer of 1984. But the article came back seemingly by return of post – the editor had refused it immediately.



Shechtman then asked John Cahn, a renowned physicist who had lured him over to NIST in the first place to take a look at his data. The otherwise busy researcher eventually did, and in turn, Cahn consulted with a French crystallographer, Denis Gratias, in order to see if Shechtman could have missed something. But according to Gratias, Shechtman's experiments were reliable. Gratias would have proceeded in the same manner had he conducted the experiments himself.

In November 1984, together with Cahn, Blech and Gratias, Shechtman finally got to publish his data in *Physical Review Letters*. The article went off like a bomb among crystallographers. It questioned the most fundamental truth of their science: that all crystals consist of repeating, periodic patterns.

The discovery now reached a wider audience, and Dan Shechtman became the target of even more criticism. At the same time, however, crystallographers around the world had a moment of déjà vu. Many of them had obtained similar diffraction patterns during analyses of other materials, but had interpreted those patterns as evidence of twin crystals. Now they started digging around in their drawers for old laboratory notes, and pretty soon other crystals began to appear with seemingly impossible patterns, such as eight- and twelvefold symmetries.

When Shechtman had published his discovery, he still had no clear grasp of what the strange crystal actually looked like on the inside. Evidently its symmetry was fivefold, but how were the atoms packed? The answer to that question would come from unexpected quarters: mathematical games with mosaics.

Previously, chemists interpreted regularity in crystals as a periodic and repeating pattern. However, the Fibonacci sequence is also regular, even though it never repeats itself, because it follows a mathematical rule. The interatomic distances in a quasicrystal correlate with the Fibonacci sequence; atoms are patterned in an orderly manner, and chemists can predict what a quasicrystal looks like on the inside. However, this regularity is not the same as when a crystal is periodic.

In 1992, this realization led the International Union of Crystallography to alter its definition of what a crystal is. Previously a crystal had been defined as "a substance in which the constituent atoms, molecules, or ions are packed in a regularly ordered, repeating three-dimensional pattern". The new definition became "any solid having an essentially discrete diffraction diagram". This definition is broader and allows for possible future discoveries of other kinds of crystals.

### *Quasicrystals in nature…*

Since their discovery in 1982, hundreds of quasicrystals have been synthesized in laboratories around the world. Not until the summer of 2009, however, did scientists first report naturally occurring quasicrystals. They discovered a new kind of mineral in samples taken in the Khatyrka River in Eastern Russia. The mineral in question consists of aluminum, copper and iron, and yields a diffraction pattern with tenfold symmetry. It is called icosahedrite, after the icosahedron, a geometrical solid with sides consisting of 20 regular three-cornered polygons and with the golden ratio integrated into its geometry.

Quasicrystals have also been found in one of the most durable kinds of steel in the world. When trying out different blends of metal, a Swedish company managed to create steel with many surprisingly good characteristics. Analyses of its atomic structure showed that it consists of two different phases: hard steel quasicrystals embedded in a softer kind of steel. The quasicrystals function as a kind of armor. This steel is now used in products such as razor blades and thin needles made specifically for eye surgery.

Despite being very hard, quasicrystals can fracture easily, like glass. Due to their unique atomic structure, they are also bad conductors of heat and electricity, and have non-stick surfaces. Their poor thermal transport properties may make them useful as so-called thermoelectric materials, which convert heat into electricity. The main purpose of developing such materials is to reuse waste heat, for example, from cars and trucks. Today, scientists also experiment with quasicrystals in surface coatings for frying pans, in components for energy-saving light-emitting diodes (LED), and for heat insulation in engines, among other things.

Dan Shechtman's story is by no means unique. Over and over again in the history of science, researchers have been forced to do battle with established "truths", which in hindsight have proven to be no more than mere assumptions. One of the fiercest critics of Dan Shechtman and his quasicrystals was Linus Pauling, himself a Nobel Laureate on two occasions. This clearly shows that even our greatest scientists are not immune to getting stuck in convention. Keeping an open mind and daring to question established knowledge may in fact be a scientist's most important character traits.

## *PHYSICS*

The Universe is expanding. Some cosmologists believe that at certain point the expansion will be ceased and it will start contraction and reach the state of 'Big-bang' – a formidable fire. But if we are to believe 2011's Nobel Laureates in physics, the story may be different. They have carefully studied several dozen exploding stars, called Supernova in far away galaxies and have concluded that expansion of the universe is speeding up, may end in ice-a formidable cold. For this discovery, the Nobel award for physics has been jointly offered to three scientists: Prof. Saul Perlmutter, Prof. Brian Schmidt and Prof. Adam Riess. Prof. Perlmutter obtained his Ph.D. degree from the University of California, Barkley, USA. He is head of the Supernova Cosmology Project, and professor of Astrophysics at Lawrence Barkley National Laboratory. Prof. Schmidt is US and Australian citizen who obtained his Ph.D degree in 1993 from Harvard University, Cambridge, USA. He is the Head of the High –Z Supernova Search Team and Distinguished Professor, Australian National University, Western Creek, Australia. Prof. Riess, US citizen, obtained his Ph.D degree in 1996 from Harvard University, Cambridge, M.A. USA. He is Professor of Astronomy and Physics, Johns Hopkins University and Space Telescope Science, Baltimore, MD USA.

Saul Perlmutter

The discovery came as a complete surprise even to the Nobel Laureates themselves. What they saw would be like throwing a ball up in the air, and instead of having it come back down, watching it disappears more and more rapidly into the sky, as if gravity could not manage to reverse the ball's trajectory. Something similar seemed to be happening across the entire Universe. The growing rate of the expansion implies that the Universe is being pushed apart by an unknown form of energy embedded in the fabric of space, which is called 'dark energy.' This *dark energy* makes up a large part of the Universe, more than 70 %, and it is an enigma, perhaps the greatest in physics today.

By establishing the distance to the supernovae and the speed at which they are moving away from us, scientists hoped to reveal our cosmic fate. They expected to find

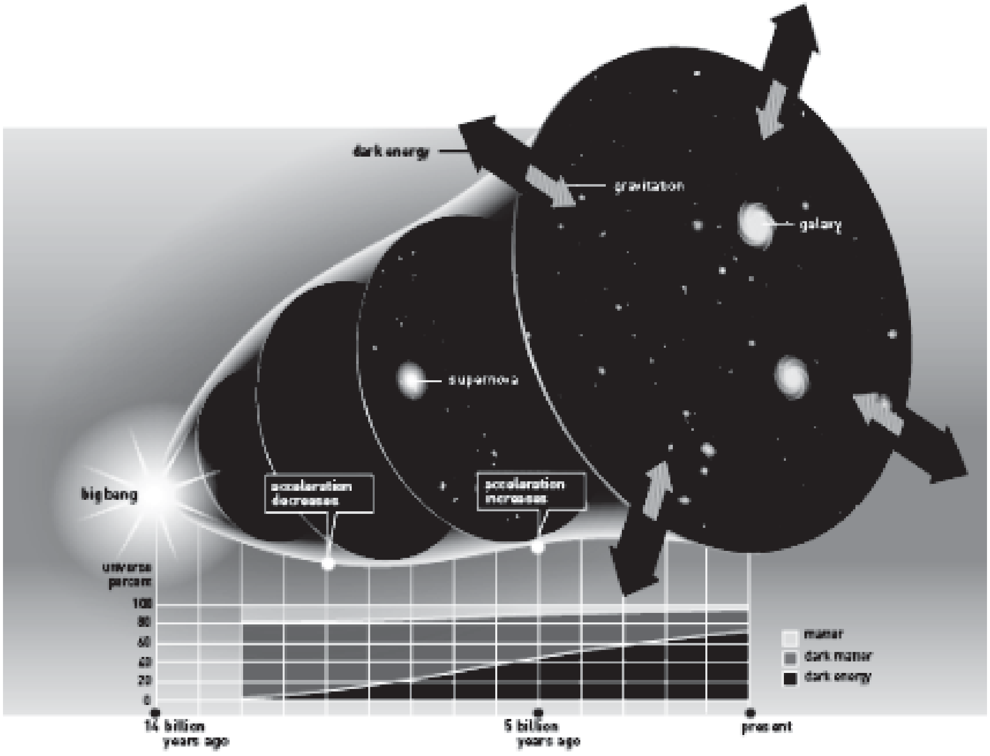


**Fig. 1.** The world is growing. The expansion of the Universe began with the Big Bang 14 billion years ago, but slowed down during the first several billion years. Eventually it started to accelerate. The acceleration is believed to be driven by darkenergy, which in the beginning constituted only asmall part of the Universe. But as matter got diluted by the expansion, the dark energy be came more dominant.

signs that the expansion of the Universe was slowing down, which would lead to equilibrium between fire and ice. What they found was the opposite – the expansion was accelerating.

At the beginning of the 20th century the American astronomer Henrietta Swan Leavitt found a way of measuring distances to far away stars. At the time, women astronomers were denied access to the large telescopes, but they were frequently employed for the cumbersome task of analyzing photographic plates. Henrietta Leavitt studied thousands of pulsating stars, called *Cepheids*, and found that the brighter ones had longer pulses. Using this information, Leavitt could calculate the intrinsic brightness of Cepheids.

Brian P Schmidt

If the distance of just one of the Cepheid stars is known, the distances to other Cepheids can be established – the dimmer its light, the farther away the star. A reliable standard candle was born, a first mark on the cosmic yardstick that is still used today. By making use of Cepheids, astronomers would soon conclude that the Milky Way is just one of many galaxies in the Universe. And in the 1920s, the astronomers got access to the world's then-largest telescope Mount Wilson in California, so they were able to show that almost all galaxies are moving away from us. They were studying the so-called *redshift* that occurs when a source of light is receding from us. The light's wavelength gets stretched, and the longer the wave, the redder its colour. The conclusion was that the galaxies are rushing away from us and each other, and the farther away they are, the faster they move – this is known as Hubble's law. The Universe is growing.

In 1915, Albert Einstein published his General Theory of Relativity, which has been the foundation of our understanding of the Universe ever since. The theory describes a Universe that has to either shrink or expand. This disturbing conclusion was reached about a decade before the discovery of the ever-fleeing galaxies. Not even Einstein could reconcile the fact that the Universe was not static. So in order to stop this unwanted cosmic expansion, Einstein added a constant to his equations that he called *the cosmological constant*. Later, Einstein would consider the insertion of the cosmological constant a big mistake. However, with the obser-vations made in 1997–1998 that are awarded this year's Nobel Prize, we can conclude that Einstein's cosmo-logical constant – put in for the wrong reasons – was actually brilliant.

The discovery of the expanding Universe was a groundbreaking first step towards the now standard view that the Universe was created in the Big Bang almost 14 billion years ago. Both time and space began then. Ever since, the Universe has been expanding; like raisins in a raisin cake swelling in the oven, galaxies are moving away from each other due to the cosmological expansion. But where are we heading?

Adam Riess

When Einstein got rid of the cosmological constant and surrendered to the idea of a non-static Universe, he related the geometrical shape of the Universe to its fate. Is it open or closed, or is it something in between – a flat Universe? An open Universe is one where the gravitational force of matter is not large enough to prevent the expansion of the Universe. All matter is then diluted in an ever larger, ever colder and ever more empty space. In a closed Universe, on the other hand, the gravitational force is strong enough to halt and even reverse the expansion. So the Universe eventually would stop expanding and fall back together in a hot and violent ending, a *Big Crunch*. Most cosmologists, however, would prefer to live in the most simple and mathematically elegant Universe: a flat one, where the expansion is believed to decline. The Universe would thus end neither in fire nor in ice. But there is no choice. If there is a cosmological constant, the expansion will continue to accelerate, even if the Universe is flat.

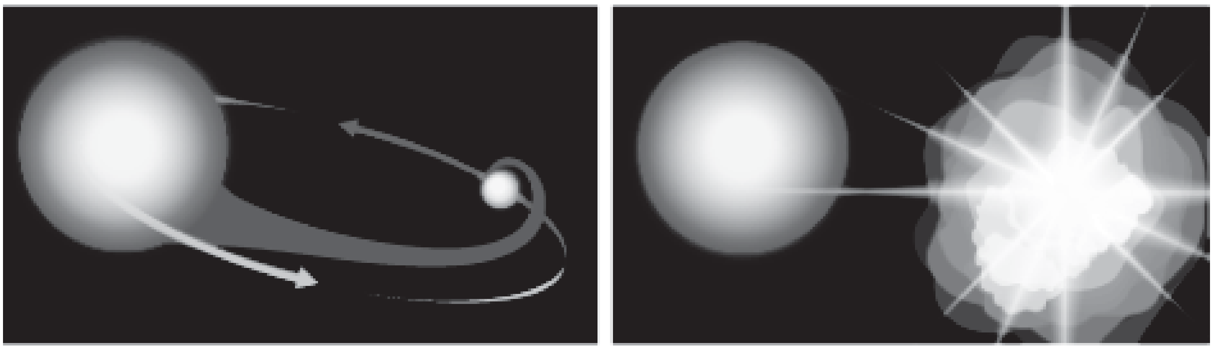


**Fig. 2.** Supernova explosion. A white dwarf steals gas from its neighbour using its gravity.

When the white dwarf has grown to 1.4 solar masses, it explodes as a type is supernova.

This year's Nobel Laureates expected to measure the cosmic deceleration, or how the expansion of the Uni-verse is slowing. Their method was in principle the same as the one used by astronomers more than six decades earlier: to locate distant stars and to measure how they move. However, that is easier said than done. Since Henrietta Leavitt's days many other Cepheids have been found that are even farther away. But at the distances that astronomers need to see, billions of light years away, Cepheids are no longer visible. The cosmic yardstick needed to be extended.Supernovae – star explosions – became the new standard candles. More sophisticated telescopes on the ground and in space, as well as more powerful computers, opened the possibility in the 1990s to add more pieces to the cosmological puzzle. Crucial were the light-sensitive digital imaging sensors – charged-coupled devices or CCD – the invention by Willard Boyle and George Smith who were awarded Nobel Prize in Physics in 2009.

The newest tool in the astronomer's toolbox is a special kind of star explosion, the *type Ia supernova*. During a few weeks, a single such supernova can emit as much light as an entire galaxy. This type of supernova is the explosion of an extremely compact old star that is as heavy as the Sun but as small as the Earth – a *white dwarf*. The explosion is the final step in the white dwarf's life cycle. Cosmologists claim that White dwarfs form when a star has no more energy at its core, as all hydrogen and helium have been burned in nuclear reactions. Only carbon and oxygen remain. In the same way, far off in the future, our Sun will fade and cool down as it reaches its end as a white dwarf. A far more exciting end awaits a white dwarf that is part of a binary star system, which is fairly common. In this case, the white dwarf's strong gravity robs the companion star of its gas. However, when the white dwarf has grown to 1.4 solar masses, it no longer manages to hold together. When this happens, the interior of the dwarf becomes sufficiently hot for runaway fusion reactions to start, and the star gets ripped apart in seconds.

The nuclear fusion products emit strong radiation that increases rapidly during the first week after the explosion, only to decrease over the following months. So there is a rush to find supernovae – their violent explosions are brief. Across the visible Universe, about ten type Ia supernovae occur every minute. But the Universe is huge. In a typical galaxy only one or two supernova explosions occur in a thousand years. In September 2011, we were lucky to

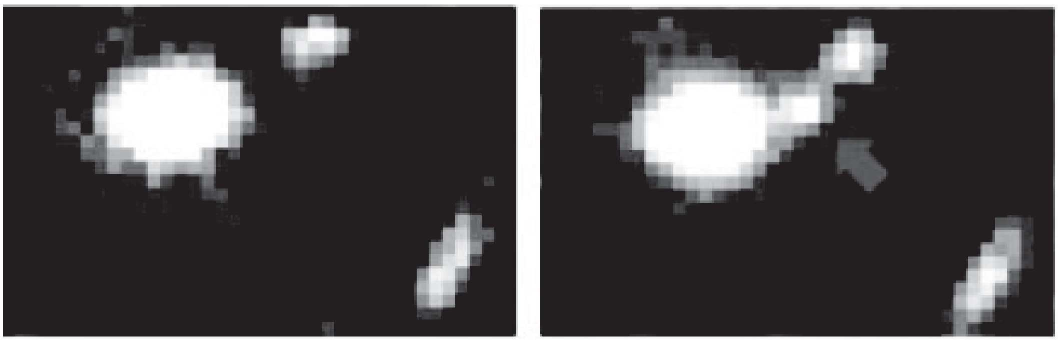
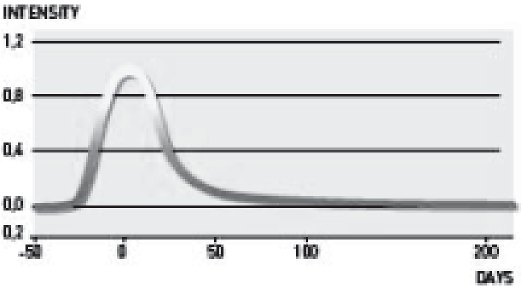


**Figure 4. Supernova 1995ar.** Two images of the same small piece of the sky taken three weeks apart were compared. Then, on the second image, a small dot of light was discovered! Its status as a type Ia supernova was established after further observations of its light curve. A type Ia supernova can emit as much light as an entire galaxy. The light curve is the same for all type Ia supernovae. Most light is emitted during the first few weeks (see diagram to the right).



observe one such supernova in a galaxy close to the Big Dipper, visible just through a pair of regular binoculars. But most supernovae are much farther away and thus dimmer. So where and when would you look in the canopy of the sky?

An astounding conclusion The two competing teams knew they had to comb the heavens for distant supernovae. The trick was to compare two images of the same small piece of the sky, corresponding to a thumbnail at arm's length. The first image has to be taken just after the new moon and the second three weeks later, before the moonlight swamps out starlight. Then the two images can be compared in the hope of discovering a small dot of light – a pixel among others in the CCD image – that could be a sign of a supernova in a galaxy far away. Only supernovae farther than a third of the way across the visible Universe were used, in order to eliminate local distortions. The researchers had many other problems to deal with. Type Ia supernovae are not quite as reliable as they ini-tially appeared – the brightest explosions fade more slowly. Furthermore, the light of the supernovae needed to be extracted from the background light of their host galaxies. Another important task was to obtain the correct brightness. The intergalactic dust between us and the stars changes starlight. This affects the results when calculating the maximum brightness of supernovae.

Chasing supernovae challenged not only the limits of science and technology but also those of logistics. First, the right kind of supernova had to be found. Second, its redshift and brightness had to be measured. The light curve had to be analyzed over time in order to be able to compare it to other supernovae of the same type at known distances. This required a network of scientists that could decide quickly whether a particular star was a worthy candidate for observation. They needed to be able to switch between telescopes and have observation time at a telescope granted without delay, a procedure that usually takes months. They needed to act fast because a supernova fades quickly. At times, the two competing research teams discreetly crossed each other's paths.

The potential pitfalls had been numerous, and the scientists actually were reassured by the fact that they had reached the same amazing results: all in all, they found some 50 distant supernovae whose light seemed weaker than expected. This was contrary to what they had envisioned. If cosmic expansion had been losing speed, the supernovae should appear brighter. However, the supernovae were fading as they were carried faster and faster away, embedded in their galaxies. The surprising conclusion was that the expansion of the Universe is not slowing down – quite to the contrary, it is accelerating.

### *To Eternity*

So what is it that is speeding up the Universe? It is called *dark energy* and is a challenge for physics, a riddle that no one has managed to solve yet. Several ideas have been proposed. The simplest is to reintroduce Ein-stein's cosmological constant, which he once rejected. At that time, he inserted the cosmological constant as an anti-gravitational force to counter the gravitational force of matter and thus create a static Universe. Today, the cosmological constant instead appears to make the expansion of the Universe to accelerate. The cosmological constant is, of course, constant, and as such does not change over time. So dark energy becomes dominant when matter, and thus its gravity, gets diluted due to expansion of the Universe over billions of years. According to scientists,

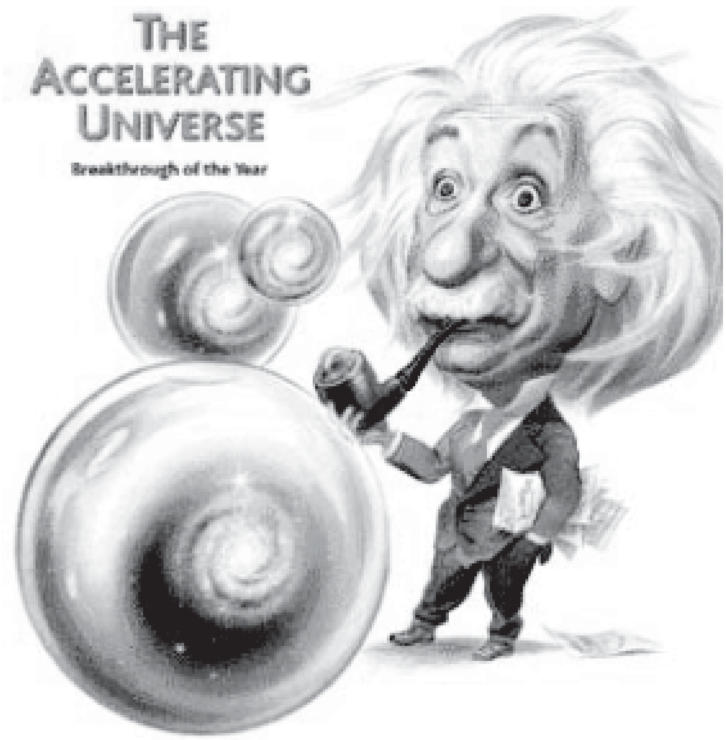


**Fig. 5.** The discovery. The accelerating expansion of the Universe was proclaimed "Breakthrough of the Year" in the December 1998 issue of *Science*. On the cover, Albert Einstein gazed upon his cosmological con-stant, which has returned to the forefront of cosmology.

that would account for why the cosmological constant entered the scene so late in the history of the Universe, only five to six billion years ago. At about that time, the gravitational force of matter had weakened enough in relation to the cosmological constant. Until then, the expansion of the Universe had been decelerating.

The cosmological constant could have its source in the vacuum, empty space that, according to quantum physics, is never completely empty. Instead, the vacuum is a bubbling quantum soup where vir-tual particles of matter and antimatter pop in and out of existence and give rise to energy. However, the simplest estimation for the amount of dark energy does not correspond at all to the amount that has been measured in space, which is about 10120 times larger (1 followed by 120 zeros). This constitutes a gigantic and still unex-plained gap between theory and observation – on all the beaches of the world there are no more than 1020 (1 followed by 20 zeros) grains of sand. It may be that the dark energy is not constant after all. Perhaps it changes over time. Perhaps an unknown force field only occasionally generates dark energy. In physics there are many such force fields that collectively go by the name *quintessence*, after the Greek name for the fifth element. Quintessence could speed up the Universe, but only sometimes. That would make it impossible to foresee the fate of the Universe.

According to current consensus, about three quarters of the Uni-verse consist of dark energy. The rest is matter. But the regular matter, the stuff that galaxies, stars, humans and flowers are made of, is only five percent of the Universe. The remaining matter is called *dark matter* and is so far hidden from us. Whatever dark energy is, it seems to be here to stay. It fits very well in the cosmological puzzle that physicists and astronomers have been working on for a long time.

The dark matter is yet another mystery in our largely unknown cosmos. Like dark energy, dark matter is invisible. So we know both only by their effects – one is pushing, the other one is pulling. They only have the adjective "dark" in common. Therefore the findings of the 2011 Nobel Laureates in Phys-ics have helped to unveil a Universe that is to 95% unknown to science. And everything is possible again.

## *PHYSIOLOGY OR MEDICINE*

Scientists have long been searching for the gatekeepers of the immune system by which man and other animals defend themselves against attack by bacteria and other microorganisms. Bruce A. Beutler and Jules A. Hoffmann discovered receptor proteins that can recognize such microorganisms and activate innate immunity, the first step in the body's immune response. On the other hand, Ralph M Steinman discovered the dendrite cells of the immune system and their unique capacity to activate and regulate adaptive immunity, the later stage of immune response during which microorganisms are cleaned from the body. For these discoveries the trio have been given this year's Nobel Prize in Physiology or Medicine. The prize has been divided with one half jointly to Bruce and Jules and the other half to Ralph.

The Nobel Assembly ar Karolinske Institute which gives this prize, declated "This year's Nobel Laureates have revolutionized our understanding of the immune system by discovering key principles for its activation providing novel insights into disease mechanism. Their work has opened up new avenues for the development of prevention and therapy against infections, cancer and inflammatory diseases."

The fact is that there are two lines of defence in immune system. We live in a world of pathogenic organisms – bacteria, virus, fungi and parasites. They threat us continuously. Thanks to nature our body is equipped with powerful defence mechanism.

The first line of defense, innate immunity, can destroy invading microorganisms and trigger inflammation that contributes to blocking their assault. If microorganisms break through this defense line, adaptive immunity is called into action. With its T and B cells, it produces antibodies and killer cells that destroy infected cells. After successfully combating the infectious assault, our adaptive immune system maintains an immunologic memory that allows a more rapid and powerful mobilization of defense forces next time the same microorganism attacks. These two defense lines of the immune system provide good protection against infections but they also pose a risk. If the activation threshold is too low, or if endogenous molecules can activate the system, inflammatory disease may follow.

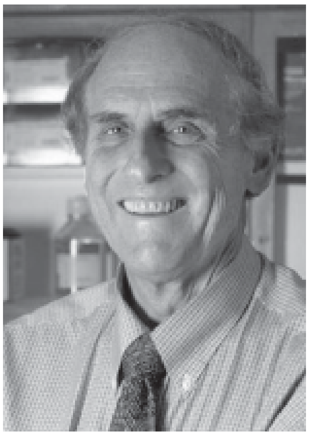
The components of the immune system have been identified step by step during the 20th century. We know, for instance, how antibodies are constructed and how T cells recognize foreign substances. However, until the work of Beutler, Hoffmann and Steinman, the mechanisms triggering the activation of innate immunity and mediating the communication between innate and adaptive immunity remained enigmatic.

Jules Hoffmann

Jules Hoffmann made his pioneering discovery of Sensors' in 1996, when he and his co-workers investigated how fruit flies combat infections. They had access to flies with mutations in several different genes including Toll, a gene previously found to be involved in embryonal development by Christiane Nüsslein-Volhard (Nobel Prize 1995). When Hoffmann infected his fruit flies with bacteria or fungi, he discovered that Toll mutants died because they could not mount an effective defense. He was also able to conclude that the product of the Toll gene was involved in sensing pathogenic microorganisms, and Toll activation was needed for successful defense against them.

Bruce Beutler

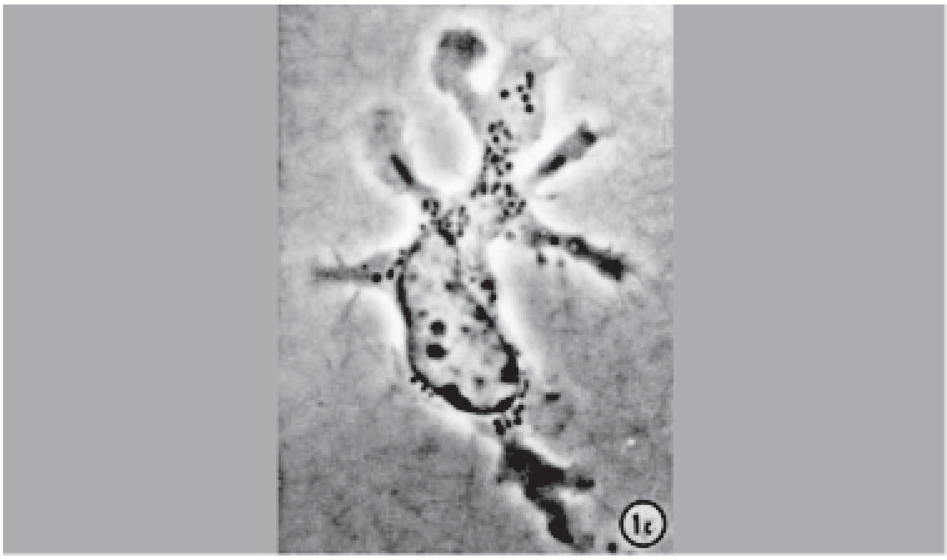
Bruce Beutler was searching for a receptor that could bind the bacterial product, lipopolysaccharide (LPS), which can cause septic shock, a life threatening condition that involves overstimulation of the immune system. In 1998, Beutler and his colleagues discovered that mice resistant to LPS had a mutation in a gene that was quite similar to the Toll gene of the fruit fly. This Toll-like receptor (TLR) turned out to be the elusive LPS receptor. When it binds LPS, signals are activated that cause inflammation and, when LPS doses are excessive, septic shock. These findings showed that mammals and fruit flies use similar molecules to activate innate immunity when encountering pathogenic microorganisms. The sensors of innate immunity had finally been discovered.



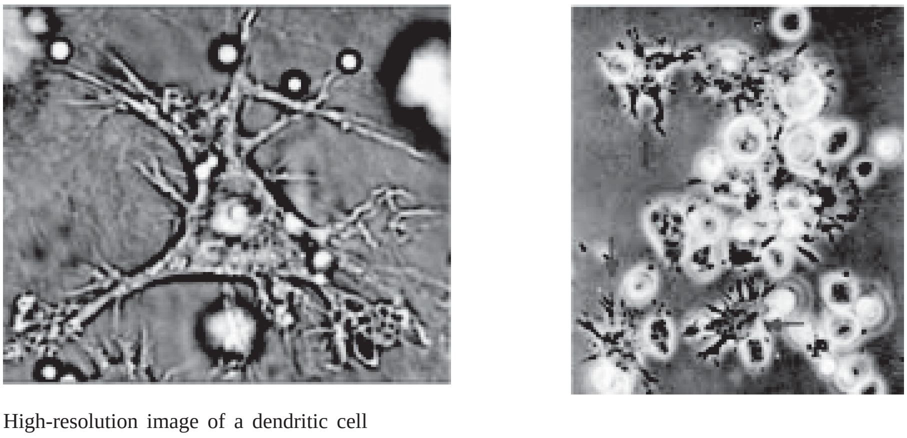
Ralph M. Steinman

The discoveries of Hoffmann and Beutler triggered an explosion of research in innate immunity. Around a dozen different TLRs have now been identified in humans and mice. Each one of them recognizes certain types of molecules common in microorganisms. Individuals with certain mutations in these receptors carry an increased risk of infections while other genetic variants of TLR are associated with an increased risk for chronic inflammatory diseases.

Ralph Steinman discovered, in 1973, a new cell type that he called the dendritic cell. He speculated that it could be important in the immune system and went on to test whether dendritic cells could activate T cells, a cell type that has a key role in adaptive immunity and develops an immunologic memory against many different substances. In cell culture experiments, he showed that the presence of dendritic cells resulted in vivid responses of T cells to such substances. These findings were initially met with skepticism but subsequent work by Steinman demonstrated that dendritic cells have a unique capacity to activate T cells.



High-resolution image of a dendritic cell made by Ralph M. Steinman in 1973.



High-resolution image of a dendritic cell

Further studies by Steinman and other scientists went on to address the question of how the adaptive immune system decides whether or not it should be activated when encountering various substances. Signals arising from the innate immune response and sensed by dendritic cells were shown to control T cell activation. This makes it possible for the immune system to react towards pathogenic microorganisms while avoiding an attack on the body's own endogenous molecules.

The discoveries that are awarded the 2011 Nobel Prize have provided novel insights into the activation and regulation of our immune system. They have made possible the development of new methods for preventing and treating disease, for instance with improved vaccines against infections and in attempts to stimulate the immune system to attack tumors. These discoveries also help us understand why the immune system can attack our own tissues, thus providing clues for novel treatment of inflammatory diseases.

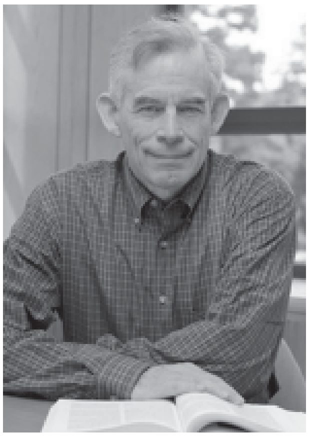
Bruce A. Beutler received his MD from the University of Chicago in 1981 and has worked as a scientist at Rockefeller University in New York, at UT Southwestern Medical Center in Dallas, where he discovered the LPS receptor, and the Scripps Research Institute in La Jolla, CA. Very recently, he rejoined the Southwestern Medical Center in Dallas as professor in its Center for the Genetics of Host Defense. Jules A. Hoffmann. He studied at the University of Strasbourg in France, where he obtained his PhD in 1969. After postdoctoral training at the University of Marburg, Germany, he returned to Strasbourg, where he headed a research laboratory from 1974 to 2009. He has also served as director of the Institute for Molecular Cell Biology in Strasbourg and during 2007-2008 as President of the French National Academy of Sciences. Ralph M. Steinman studied biology and chemistry at McGill University Canada. After studying medicine at Harvard Medical School in Boston, MA, USA, he received his MD in 1968. He was affiliated with Rockefeller University in New York since 1970, where he was professor of immunology from 1988. Sadly, Ralph Steinman passed away just four hours before the announcement of the Nobel Prize.

Steinman died of cancer of pancreas. Pradoxically, he had applied his own research dentritic cell on himself and prolonged his life, but could not wait to hear the announcement.

## *ECONOMIC SCIENCES*

How are GDP and inflation affected by a temporary increase in the interest rate or a tax cut ? What happens if a central bank makes a permanent change in its inflation target or a government modifies its objective for budgetary balance? They developed methods for answering these and many other questions –Thomas J. Sargent and Christopher A. Sims. Their contribution was splendid and timely. As a recognition of this, the Sueringes Riskbank Prize in Economic Sciences in Memory of Alfred Nobel 2011 has been awarded jointly to Thomas J. Sargent and Christopher A. Sims “for their empirical research cause and effect in the microeconomy.” Both Thomas J. Sargent and Christopher A. Sims are U.S. citizens. Prof. Sargent obtained his Ph.D. degree from Harvard University, Cambridge USA. He is William R. Barkely Professor of Economics and Business at New York university, N.Y. Prof. Sims did his Ph.D. from Harvard in 1968. At present he is Harold H. Helm’20 Professor of Economics and Banking Management at Princeton University, Princeton., USA.

Thomas J. Sargent



Christopher A. Sims

True, in many cases unexpected events affect the economy constantly, under the circumstances the central bank sets an interest rate – unforeseen by borrowers and lenders, and household consumption suddenly declines. Such unexpected occurrences are usually called “Shocks.” On the other hand the economy is also affected by more long run changes, such as a shift in monetary policy towards structure disinflationary measures or fiscal policy with more stringent budget rules. One of the main tasks of microeconomic research is to comprehend how both shocks and the systematic policy shifts affect microeconomic variables in the short and long run. To this work, Sargent and Sim’s contributions pose an indispensable role. Sargent has primarily helped us understand the effects of Systematic policy shifts. While Sims has focused on how shocks spread throughout the economy.

Sargent's awarded research concerns methods that utilize historical data to understand how systematic changes in economic policy affect the economy over time. Sims's awarded research instead focuses on distinguishing between unexpected changes in variables, such as the price of oil or the interest rate, and expected changes, in order to trace their effects on important macroeconomic variables. The questions which the laureates have dealt with are obviously interrelated. Although Sargent and Sims have carried out their research independently, their contributions are complementary in many ways.

### *Two-way Relationships and Prevailing Expectations*

The question is to understand whether it is policy that influences economic development or is there a reverse causal relationship? One reason for this ambiguity is that both private and public agents actively look ahead. The expectations of the private sector regarding future policy affect today's decisions about wages, prices and investments, while economic-policy decisions are guided by expectations about developments in the private sector.

Is it possible to determine whether changes in the economy depend on shifts in economic policy? Could such changes instead depend on fluctuations in the overall economy that prompt decision-makers to adopt a different policy? Sargent has examined these issues using a three-step method.

Sargent's first step involves developing a structural macroeconomic model, i.e., an accurate mathematical description of the economy. A number of parameters, which determine the relationships among different variables, are introduced into the model. For instance, if we know that consumers' aggregate demand for goods and services is affected by the expected real interest rate, this relationship should be incorporated in the model. The parameters governing such basic relations should not be affected by the changes in economic policy. This includes preference parameters, which describe how individuals choose between saving and consumption depending on interest rates and income.

The second step consists of solving the mathematical model. Sargent's method focuses on expectations as to how macroeconomic variables will change. For example, are expectations about inflation in the future affected by changes in economic policy? A reasonable prerequisite for solving the model is that individuals' inflation expectations in the model correspond to the forecasted inflation generated by the model itself. Imposing such a requirement is easier said than done, however, and the second step in Sargent's analysis demonstrates how a solution may be found.

The third and last step is entirely statistical. Historical data are used to *estimate* the fundamental parameters that do not change after a policy shift. To simplify, this implies that parameter values are chosen so that the model will describe historical events as well as possible. In this way, numerical values are obtained for the parameters which describe the economic structure. The complete model can than be used as a "laboratory" to study the effects of different hypothetical experiments, such as a shift in monetary policy.

In the 1970s, Sargent showed how structural macroeconomic models could be constructed, solved and estimated. His approach has turned out to be particularly useful in the analysis of economic policy, but is also used in other areas of macroeconometric and economic research.

Some of Sargent's contributions were solely methodological, although he has also applied the new methods in highly influential empirical research. For instance, he has analyzed historical episodes of

Investors base their decisions on expectations about future economic policy

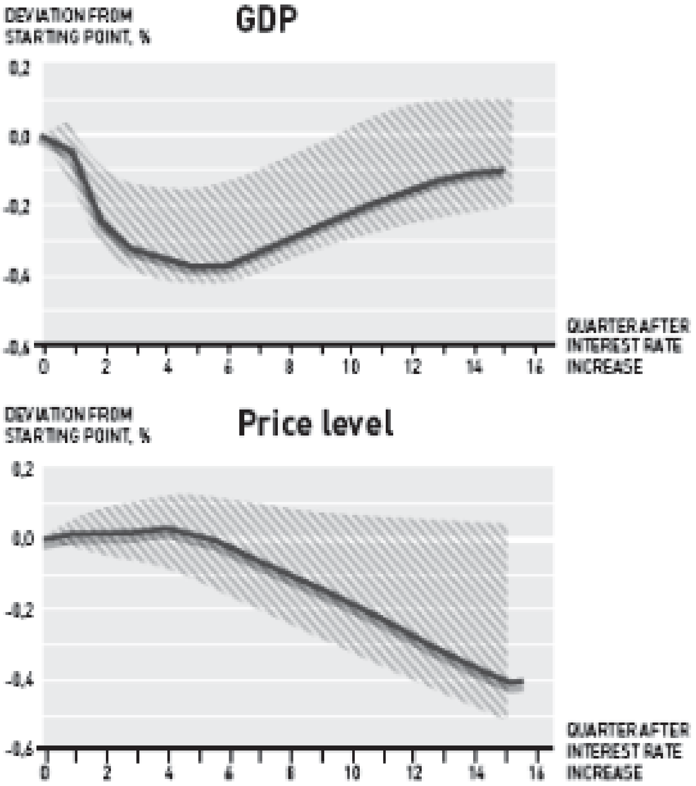
Central banks set the interest rate based on expectations about private sector developments.

hyperinflation in different European countries. He has also examined the above-mentioned course of events in the 1970s when many economies initially adopted a high-inflation policy and then reverted to a lower rate of inflation. Sargent showed that the way expectations are formed by the general public as well as central banks' understanding of the inflation process were based on gradual learning. This could explain why the decline in inflation took such a long time.

Sims shared Sargent's criticism of the large macroeconometric models which were earlier used by research-ers, central banks and ministries of finance. In his article "Macroeconomics and Reality". Sims introduced a new way of analyzing macroeconomic data. He also concurred with Sargent in emphasizing the importance of expectations. Sims proposed a new method of identifying and interpreting economic shocks in historical data and of analyzing how such shocks are gradually transmitted to different macroeco-nomic variables. His approach has had an enormous impact on research. It has also been used extensively as a basis for decision-making in economic policy. Sims's methodology may also be described in three steps.

In the first step, the analyst makes a forecast for macroeconomic variables using a vector-autoregression model (VAR model). This is a relatively simple model for statistical time series, where previously observed values of the variables of interest are used to achieve the best possible forecast. The difference between forecast and outcome – the forecasting error – for a specific variable may be regarded as a type of shock, but Sims showed that such forecasting errors do not have an unambiguous economic interpretation. For instance, either an unexpected change in the interest rate could be a reaction to other simultaneous shocks to, say, unemploy-ment or inflation, or the interest-rate change might have taken place independently of other shocks. This kind of independent change is called a fundamental shock.

The second step involves extracting the *fundamental shocks* to which the economy has been exposed. This is a prerequisite for studying the effects of, for example, an independent interest-rate change on the economy. Indeed, one of Sims's major contributions was to clarify how identification of fundamental shocks can be carried out on the basis of a comprehensive understanding of how the economy works. Sims and subse-quent researchers have developed different methods of identifying fundamental shocks in VAR models.



The figures on the left shows how an impulse in the form of an increase in the interest rate set by the central bank leads to responses in macroeconomic variables with different time profiles. The graphs are based on a VAR analy-sis of U.S. postwar data where the shocks have been indentified using a method proposed by Sims.

The example shows the responses of two variables in the VAR model, GDP and the price level. GDP falls continu-ously for several quarters following the interest rate increase and does not turn upwards until after six quarters. The price level, on the other hand, is hardly affected at all until after six quarters, when prices start to fall – the rate of inflation goes down.

Effects of an increase in the interest rate on GDP and the prize level. The shaded areas show other statistically possible outcomes.

Once the fundamental shocks are identified based on historical data, the third step in Sims's method is an *impulse-response analysis*. This illustrates the impact over time of the fundamental shocks to the macroeco-nomic variables.

Impulse-response analysis has impro-ved our understanding of the dynamic properties of the macroeconomy and has thereby affected the conduct of monetary policy. It is now common for central banks with an inflation target to adjust the interest rate in order to reach its goal over a horizon of one to two years, i.e., the time lag indicated by the figure. The graphs also illustrate that a contractionary monetary policy faces a trade-off between lower inflation after one to two years and an immediate reduction in GDP. Analogous VAR analyses of fiscal policy have shown how increased public spending may counteract a temporary dip in the business cycle. Today, VAR models are indispensable tools for central banks and finance ministries in their analyses of the impact of various shocks on the economy and of how the economy is affected by different policy measures.

### *Empirical Macroeconomic Research Today*

Sargent's analysis of macroeconomic time series based on historical data opened up a rich field for macroeconomic research and has led to new insights about the workings of economic policy. Sims research, start-ing somewhat later, has also had an extraordinary influence, both in macroeconomics and other fields of research. Today, the directions of research that were inspired by Sargent's and Sims's contributions have much in common. In modern research, the solution to models developed using Sargent's methods are often expressed in the form of a VAR system and evaluated by impulse-response analysis.

The empirical strategies proposed by Sargent and Sims are intercomparable. In order to study the impact of systematic policy changes on the economy, Sargent's method requires specific assumptions about the structure of the economy – assumptions that may be questionable. The assumptions underlying a VAR model, on the other hand, are more general and hold across a wide class of economic models. Researchers have a choice of method depending on the application. With detailed knowledge about the structure of the economy, Sargent's method may be preferable, in particular since it allows a counterfactual analysis of sys-tematic changes in economic policy. When knowledge of the field is less exact, Sims's method may be safer.

Owing to the scientific contributions of Sargent and Sims, research in macroeconomics and analysis of eco-nomic policy have advanced substantially. Their combined work constitutes a solid foundation for modern macroeconomic analysis. It is hard to envisage today's research without this foundation.

**Samarjit Kar**
*Source : Nobel Foundation*
*www.nobelprize.org*