Technology, and moved in 1978 to Stanford University in California, where he started his research on the vesicles of the cell. Rothman has also worked at Princeton University, Memorial Sloan-Kettering Cancer Institute and Columbia University. In 2008, he joined the faculty of Yale University in New Haven, Connecticut, USA, where he is currently Professor and Chairman in the Department of Cell Biology.

Randy W. Schekman was born 1948 in St Paul, Minnesota, USA, studied at the University of California in Los Angeles and at Stanford University, where he obtained his PhD in 1974 under the supervision of Arthur Kornberg (Nobel Prize 1959) and in the same department that Rothman joined a few years later. In 1976, Schekman joined the faculty of the University of California at Berkeley, where he is currently Professor in the Department of Molecular and Cell biology. Schekman, an investigator of the Howard Hughes Medical Institute and professor of cell and developmental biology in the Department of Molecular and Cell Biology at the University of California at Berkeley, lectured on «Membrane Transport Vesicles and Human Disease». His work laid the foundation for recombinant expression of important secretor and membrane proteins such as insulin and hepatitis surface antigen in yeast and used for treatment of diabetes and for immunization to protect against infection by hepatitis B virus.

Thomas C. Südhof was born in 1955 in Göttingen, Germany. He studied at the Georg-August-Universität in Göttingen, where he received an MD in 1982 and a Doctorate in neurochemistry the same year. In 1983, he moved to the University of Texas Southwestern Medical Center in Dallas, Texas, USA, as a postdoctoral fellow with Michael Brown and Joseph Goldstein (who shared the 1985 Nobel Prize in Physiology or Medicine). Südhof became an investigator of Howard Hughes Medical Institute in 1991 and was appointed Professor of Molecular and Cellular Physiology at Stanford University in 2008.

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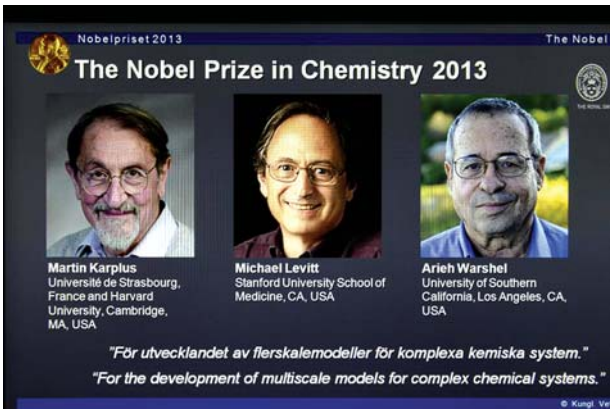
Nobel Laureates in Chemistry 2013

Chemistry was the second prize area that Nobel mentioned in his will. The Nobel Prize in Chemistry has been awarded to 166 Nobel Laureates since 1901.

The Royal Swedish Academy of Sciences has decided to award jointly to ***Martin Karplus, Michael Levitt*** and ***Arieh Warshel*** *«For the development of multiscale models for complex chemical systems»*.



Their work bridges two physical models of understanding the world. *Newtonian mechanics*, with its key concepts of force, mass, and acceleration, has long been used to describe the motion of large entities — the arc of a ball tossed in the air, for instance, or an apple falling from a tree. *Quantum mechanics*, by contrast, describes motion at the level of single atoms and molecules, a minute and bizarre world in which a particle's position is described by a probability, rather than certainty.

Quantum mechanics had always been applied in the domain of the minuscule, and classical physics in the realm of everyday objects, where the inherent randomness of any single particle would disappear once averaged among billions and trillions of other molecules. But ***Karplus*** and his colleagues were interested in large, biological molecules like proteins — too small for any microscope to see, but composed nonetheless of millions of atoms, far too many for any computer to simulate using the complex calculations of quantum mechanics. Newtonian mechanics was not sufficient either, because researchers were interested in molecules in motion — the changes in energy and molecular structure that occur, when a protein recognizes its chemical target, for instance, or an enzyme catalyzes a reaction. «Motions are very important,» said Karplus. «Evolution has made the structure of proteins... so that they have a specific function... What

the structures of the protein do is make the motions go... in a useful way».

Some 40 years ago, Martin Karplus, Michael Levitt and Arieh Warshel laid the foundation for the powerful programs that are used to understand and predict chemical processes. Because chemical reactions occur so incredibly fast (in a fraction of a millisecond, electrons jump from one atomic nucleus to the other) traditional chemistry has had an incredibly hard time keeping up. But the work of the trio went a long way to bridging that gap. Aided by the methods now awarded with the Nobel Prize in Chemistry, scientists let computers unveil chemical processes.

At the beginning of the 1970s in ***Martin Karplus'*** research group it was developed the computer programs that could simulate chemical reactions with the help of quantum physics and the «Karplus equation», which is used in nuclear magnetic resonance (NMR), a method well-known to chemists that builds on the quantum chemical properties of molecules. Arieh Warshel arrived at Karplus' laboratory in 1970. ***Arieh Warshel*** and ***Michael Levitt*** had developed a ground-breaking computer program based on classical theories. The program enabled modeling of all kinds of molecules, even really large biological molecules. The researchers developed a computer program that drew on quantum physics when it performed calculations on free electrons, and applied more simple classical theories for all other electrons and all atomic nuclei. In 1972, they published their results. This was the first time anyone had managed to bring about a chemically relevant collaboration between classical and quantum physics. They wanted to develop a program that could be used to study enzymes; proteins that govern and simplify chemical reactions in living organisms. The researchers found that in a large molecule like a protein, some groups of atoms could be lumped together, simplifying the number of units in the overall structure, and they developed methods for predicting how these groups could be assigned. Their work helped researchers gain insight into the «action» part of biochemical reactions — how enzymes would change shape as they did their chemical job. ***Warshel*** had become curious about how enzymes function. It is the cooperation between enzymes that makes life possible. They control virtually all chemistry in the living body. In order to be able to simulate enzymatic reactions, ***Levitt*** and ***Warshel*** were required to make classical and quantum physics collaborate more smoothly. It would take them several years to overcome all obstacles. In 1976, they reached their goal and published the first computerized model of an enzymatic reaction. Their program was revolutionary because it could be used for any kind of molecule. Size was no longer an issue when simulating chemical reactions.

Now, when scientists model molecular processes, they apply the computer power where it is needed. At the heart of the system, calculations are based on quantum physics. Further away from the action, they are based on classical physics, and at the outermost layers, atoms and molecules are even lumped together to a homogenous mass. These simplifications make it possible to perform calculations on really large chemical systems.

As already mentioned, chemical reactions occur at lightning speed. In a fraction of a millisecond, electrons jump from one atomic nucleus to the other. Classical chemistry has a hard time keeping up; it is virtually impossible to experimentally map every little step in a chemical process. Aided by the methods now awarded with the Nobel Prize in Chemistry, scientists let computers unveil chemical processes, such as a catalyst's purification of exhaust fumes or the photosynthesis in green leaves.

The work of Karplus, Levitt and Warshel is ground-breaking in that they managed to make Newton's classical physics work side-by-side with the fundamentally different quantum physics. Previously, chemists had to choose to use either or. The strength of classical physics was that calculations were simple and could be used to model really large molecules. Its weakness, it offered no way to simulate chemical reactions. For that purpose, chemists instead had to use quantum physics. But such calculations required enormous computing power and could therefore only be carried out for small molecules.

The work awarded this year's Nobel Prize in Chemistry focuses on the development of methods using both classical and quantum mechanical theory and that are used to model large complex chemical systems and reactions. In the quantum chemical model the electrons and the atomic nuclei are the particles of interest. In the classical models atoms or group of atoms are the particles that are described. The classical models contain much fewer degrees of freedom and they are consequently evaluated much faster on a computer. Furthermore, the physics that is used to describe the classical particles is much simpler and this also contributes to speeding up the modeling on a computer. This year's laureates have shown how to develop models that describe part of a system using first principle, quantum chemical models for a central part of the system and how to link this part to a surrounding, which is modeled using classical par-

ticles (atoms or group of atoms). The key accomplishment was to show how the two regions in the modeled system can be made to interact in a physically meaningful way.

Martin Karplus was born in Vienna in 1930, and, along with his family, fled to the United States in 1938 to escape the Nazi occupation of Austria. He has a BA from Harvard University and a PhD from the California Institute of Technology. He is the Theodore William Richards Emeritus professor of chemistry at Harvard University. Karplus is an expert in quantum mechanics, which explains physical behavior at an extremely small scale. Karplus received the award in recognition of his lifelong efforts to understand the electronic structure, geometry, and dynamics of molecules of chemical and biological interest. Among the important contributions to nuclear magnetic resonance spectroscopy, chemical dynamics, and quantum chemistry is the Karplus Equation, which is widely used in determining the structures of small molecules and of proteins. More recently, Karplus has developed the widely used molecular dynamic simulation methodology for studying the functional dynamics and conformational changes of biomolecules. He has undertaken a detailed study of the effect of solvent on the dynamics of peptides and on the enzymatic activity of proteins and has shown how free energy simulations can be used to obtain a deeper understanding of macromolecular interactions.

Michael Levitt, PhD, professor of structural biology at the Stanford University School of Medicine, was born in 1947 in Pretoria, South Africa, and was raised there until he went to London to attend King's College to obtain a degree in physics. He holds U.S., British and Israeli citizenship. Levitt's work focuses on theoretical, computer-aided analysis of protein, DNA and RNA molecules responsible for life at its most fundamental level. Delineating the precise molecular structures of biological molecules is a necessary first step in understanding how they work and in designing drugs to alter their function. Levitt joined the Department of Structural Biology at Stanford in 1987; he has a courtesy appointment in computer science. He is also a member of Bio-X, a Stanford initiative that unites experts in biology, medicine, chemistry, physics and engineering. Levitt's early work in the late 1960s set the stage for an entirely new way to predict how proteins fold and interact. At that time, X-ray crystallography was used to ascertain the location of atoms like hydrogen, carbon and oxygen in larger molecules like proteins or DNA. Researchers then used the data to construct very large three-dimensional models out of plastic balls and metal sticks in order to better understand what the molecules looked like and how they might work. His basic research set the stage of most subsequent work in the rapidly growing field. It also led to practical methods for antibody humanization that are key for modern anticancer therapy, such as the drug Avastin. The Nobel Prize is not only fitting recognition of the significance of Levitt's work to medicine, and another extraordinary honor for Stanford, it is further proof of the success and impact of interdisciplinary collaboration.

Arieh Warshel, an Israeli-American Distinguished Professor of Chemistry and Biochemistry at the University of Southern California, was born in 1940 in Kibbutz Sde Nahum, in Israel. He earned MSc and PhD degrees in Chemical Physics (in 1967 and 1969), at the Weizmann Institute of Science. He then did postdoctoral work at Harvard University, returned to the Weizmann Institute in the early 1970s and also worked for the Laboratory of Molecular Biology, Cambridge, England. He joined the faculty of the Department of Chemistry at USC in 1976.

Warshel had long been interested in enzymes, which control almost all chemistry in the body, and continues to study their reactive properties to this day. The methods he and his collaborators developed can be used on a practical level to develop new drugs.

Scientists today use the methods developed by Warshel and his colleagues to model chemical processes both accurately and efficiently. They apply the quantum mechanical half of the method only to the free electrons and nuclei directly involved in a reaction, and use classical mechanics to study the rest of a molecule.

«So what we've done in the past 50 years is build models that allow us to put all of these atoms together on the computer and then to simulate how they do what they do and to understand what is responsible for each action», Warshel said. This field has many names, but can be classified as computer simulation of biological functions, part of computational biophysics.

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Prepeared by A. Vinogradova