Short History of the Semiconductor Heterostructure Research

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The idea of using heterostructures in semiconductor electronics was put forward already at the very dawn of electronics. In the first patent concerned with p-n junction transistors W. Shokley proposed a wide-gap emitter in 1948. H. Kroemer considered graded heterostructures for transistors in 1957. We proposed double-heterostructure laser (DHL) in the March, 1963. Experimental realization of ideal heterostructure AlGaAs happened only in 1967 at Ioffe Institute by us and at IBM Res. Center by H. Rupprecht and J. Woodall.

After creation of room temperature DHL in our laboratory in 1968, had been started very strong international cooperation in this area which stimulated fast development of the heterostructures physics and applications. In the talk the short review of fundamental and applied researches in this area is giving and is described how international competition promoted very high speed of development of the new semiconductor physics and electronics.

Investigation of the Origins and Nature of the Highest Energy Cosmic Rays

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Cosmic rays with energy greater than 10^20 eV have been found in nature.

An energy of 10-20 eV is equal to 16 joules, a macroscopic energy in a microscopic particle as these cosmic rays are most likely protons, the nuclei of hydrogen atoms.

The origin and nature of the cosmic rays with energy above 10-19 eV is a scientific mystery whose solution will lead either to new astrophysics or new physics. The Pierre Auger Observatory has been built in Argentina in an attempt to solve the mystery. The observatory consists of an array of 1600 surface detectors and 4 fluorescence detectors covering 3000 km-2. It has been producing data since Jan 2004. A description of the detector will be presented. Our most important result has been published in the Nov 9, 2007 issue of Science magazine. The result is that the arrival directions of the very highest energy cosmic rays (energy greater than 0.6x10-20 eV) are associated with the angular positions of nearby Active Galactic Nuclei.

This is the first time that the actual sources of these cosmic rays have been identified.

Adventures in Structural Biology

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Starting with work of Max Perutz and John Kendrew in the 1950s, the exploration of the world of protein structures has been a great adventure. Even though almost 50,000 sets of atomic coordinates have been deposited in the Protein Data Bank, almost every new structure still holds some surprise.

As an example, I will discuss results of our work on the Low Density Lipoprotein Receptor (LDLR), and of its complex with the recently discovered protein proprotein convertase subtilisin/kexin type 9 (PCSK9). Cholesterol is an essential component of our cell membranes; it circulates in the bloodstream packaged inside lipoprotein particles, the most abundant form of which is LDL. The LDLR plays a crucial role in the uptake of LDL by cells in a process called receptor-mediated endocytosis. The LDLR is a membrane-anchored protein which binds LDL at the cell surface and carries it during endocytosis into vesicles, where upon acidification it releases its cargo and then returns to the surface to begin another cycle. The crystal structure of the extracellular part of the LDLR at low pH (1) sheds light on the mechanism of release, and explains the reason for inefficient transport in some of the known LDLR mutants.

Recently, a protease called PCSK9 was discovered, which appears to speed up the degradation of LDLR, and, by decreasing the number of available LDLR molecules, contributes to elevated levels of LDL in the blood (2). It binds to the LDLR in a small region next to the LDL binding region (3). The crystal structure of PCSK9 in complex with the interaction region of LDLR (4) defines an apparently attractive new drug target. A molecule that could disrupt the interaction between LDLR and PCSK9 could lead to a longer life of the LDLR and thus to lower levels of blood cholesterol.

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My Pathway into Science and Beyond

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In this lecture, I will narrate parts of my life story. The pathway into science was not exempt from ups and downs. Fascination and doubts kept themselves in balance. But looking back, my life was guided by a long sequence of lucky events that led to historical developments in Nuclear Magnetic Resonance. The overwhelming success of NMR in molecular biology and in clinical medicine came as a full surprise. Much future development of magnetic resonance can be expected, for example in exploring the detailed functioning of the brain by functional magnetic resonance imaging.

Involvements in other aspects of life are essential for complementing the fascinating activities in science. I will mention, as an example, my active interest in Central Asian art. The broadening of the scope of researchers beyond traditional science is relevant in the context of our responsibilities for shaping a beneficial future of our world. Universities, that educate future generations of citizens, are supposed to develop also novel concepts for mastering the expected future problems.

Fc-Receptors: Basic Science and Drug Design

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The immune response depends on the binding of opsonized antigens to cellular Fc receptors and the following initiation of cellular effector functions of the immune system. The crystal structures of a soluble Fc gamma receptor, an Fc fragment, and their complex explain a wealth of functional data of the system.

They also provide a rationale for the modulation of effector activities by changes of the domain arrangement of the Fc fragment caused by altered glycosylation.

Myelin oligodendrocyte glycoprotein (MOG) is a major autoantigen in multiple sclerosis. The crystal structures of MOG and its complex with a specific autoantibody provide a basis for new diagnostic and therapeutic strategies against the pathogenic autoantibody response to MOG.

These molecular structures offer multiple ways to interfere with the cellular immune response in autoimmune diseases:

a) by small molecules disrupting the Fc receptor-Fc contact;

b) by antibodies directed against the contact area;

c) by soluble Fc receptors as antagonists;

d) by mimetics of the MOG epitop.

Animal experiments following strategies b) and c) have been successfully completed for three model autoimmune diseases, SLE, arthritis, and EAE.

A company SUPPREMOL (www.suppremol.de) has been founded to pursue these strategies on a commercial basis and has obtained licences from the Max-Planck-Gesellschaft. Financing has been secured by a partnership with Z-cube, the Zambon Group (Milano, Italy) venture capital subsidiary. KfW and Bayern Kapital provided additional equity.

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Physics and Applications of the Nobel Prize in Physics 1985

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The Nobel Prize in Physics 1985 was awarded for the discovery of the quantized Hall effect (QHE). This quantum effect, discovered on 5.2.1980 at two o'clock in the morning during experiments on a microelectronic chip, is today a synonym for a large number of fascinating properties of electrons in strong magnetic fields with different connections to other research areas like astrophysics (edge states in gravity and black hole physics), high energy physics (quantum Hall quarks and string theory) and metrology (fundamental constants and basic units) which explains the high publicity of this effect with about one new QHE-publication per day.

The talk will mainly focus on the application of the QHE in connection with our international system of units (SI units) and will discuss the idea to introduce in 2011 fixed values of fundamental constants as base units of our international measurement system.

Science, Society and Sustainability

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The fact that our modern world is so completely and precariously balanced on Science, Engineering and Technology (SET) makes the relationship of Science with Society and issues of Sustainability vital topics for discussion. So far SET have truly revolutionised our lives and there is no doubt that the humanitarian contributions of SET have improved the quality of life of those in the developed world immeasurably. As but one of infinite examples, in the 18th century almost half of all children died by the age of 8. The improvement - in the developed world - was brought about by scientific methodology based on doubt and questioning, a philosophy completely orthogonal to the belief-based concepts that underpin mystical societal attitudes. Society has the power to use technology so that it is can benefit us or be detrimental. It is now becoming clear that our technologies have also catalysed a mindless mass-production driven plundering of the Planet's resources, which could be hurtling us towards disaster - we don't need an asteroid. For a 50:50 chance of surviving into the next century every segment of society from industrialists, engineers and scientists to politicians, farmers and fishermen must now take this matter as the most serious issue the world has ever confronted.

Our only hope for survival rests on the shoulders of those who take sustainability issues seriously and do something about it. I see a key role for Nanoscience and Nanotechnology (N&N) which is just a new name for a vast swathe of incredibly varied Chemistry in the atom/molecule scale region where this discipline overlaps Physics, Biology and Engineering.

The Internet is a major new communications technology which we must exploit to educate people on a global scale that rational attitudes are now vital to our very survival. With the Vega Science Trust, (www.vega.org.uk), which has now made some 120 TV and Internet programmes (55 shown on the BBC), we have created a platform for scientists to communicate directly and improve the public awareness and understanding of SET. Furthermore with a new Global Educational Outreach (GEO) initiative based at Florida State we are further extending the capability of the Internet to help teachers in any part of the world. A key hope is to set off a chain reaction by getting universities and schools worldwide to set up similar initiatives. The immediate focus will be to empower teachers worldwide by giving them access to the best teaching material, packaged for direct use in the classroom, together with expert examples of how the material might be presented. The protoype GEO site is to be found at www.geoset.info. The new recording technology allows us to create inexpensive, effective teaching programmes and make them available globally.

"There is a TV set in almost every village in the world we should surely be able to get the Internet into every school."

Dynamics of Chemical Reactions and Photochemical Processes

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Every macroscopic chemical transformation, whether it is atmospheric ozone depletion or the burning of a candle, consists of millions of microscopic chemical events which involve collisions between molecules. It has been the dream of scientists for a long time to observe and understand the details of molecular collisions which transform reactant molecules into product molecules with our naked eyes. During the last several decades, because of the advances in crossed molecular beams method and laser technology, especially, from the measurements of product angular and velocity distributions, it has become possible to "visualize" exact details of how chemical reactions take place through molecular collisions or through photochemical processes.

Whether two reactant molecules can transform into product molecules during collisional processes depends not only on the orientations of molecules when they approach each other, but also on the energy contents of reactant molecules. Reactants must contain sufficient energy to overcome potential energy barriers on their way to product formation. However, when a molecule is energized, there are many different modes in which the required energy could be deposited. Whether the energy is in the translational, the rotational, the vibrational, or the electronic degrees of freedom will have different effects in promoting chemical reactions. Very often reactions might also proceed with different mechanism. With the advancement of various laser techniques, it has now become possible to energize atoms and molecules quite effectively through laser excitation.

In this lecture, in addition to illustrate experimental details of crossed molecular beams method, examples will be given to demonstrate how detail information on the dynamics of chemical reactions and photochemical processes can be obtained using various experimental approaches.

Spin Charge Separation in Conjugated Polymers

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We review the occurrence of the separation of spin S and charge Q in conjugated quasi – one dimensional polymers such as $(CH)_x$, polyacetelyene. In this polymer, bonds alternate in length as one moves along n chain upon a + δ + a – δ, a ~ 2.3 Å and δ ~ 0.1 Å. This alteration of bond length leads to a doubling of the unit all and a gap in the electronic spectrum on magnitude 2.5eV.

A soliton is formed when δ changes sign from positive to negative, leading to upward sloping bonds changing into downward sloping bonds and vice versa. Using the deformation potential Hamiltonian where the hopping integral for electrons hopping from CH group n to n +1, one has

$$t_{n,\,n+1} = t_0 - (\text{alpa})\,(u_{n+1} - u_n)$$

where α ~ 4.6eV/Å. Solving for the electronic density of stated one finds that the conduction and valence bands are each missing one half a state with this weight occurring as a single state located at the gap center. A neutral soliton has one electron in the gap center state and has spin. This is observed in nuclear magnetic resonance experiments. By removing the electrons, one forms a positively charged soliton of spin zero. Such carriers are observed in the electrical conductivity g doped $(CH)_x$, doped with iodine for positively charged solutions and sodium for negatively charged solitons. These and other effects will be reviewed.

Elementary Particles and Cosmology

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The science of elementary particles has sofar resulted in the Standard Model, a wonderful model of elementary particles and the forces between them. The Standard Model has been tested to great experimental precision; yet there is an important part of this Standard Model that is not verified by experiment. First a description of the Standard Model will be presented. The Higgs forces, introduced on theoretical arguments, remain to be investigated, and will hopefully be studied in the near future at the new accelerator constructed at CERN, Geneva, Switzerland. We will have to wait a few years before the experimental results at that new machine become available. The Higgs system, within the Standard Model a mechanism to generate masses for the elementary particles, has cosmological consequences, and in fact these consequences seem to be in contradiction with astronomical observations. We therefore turn to astrophysics, asking what the situation is with respect to our understanding of the laws of gravitation, as laid down by Newton and Einstein. In Einsteins view of the Universe space-time is curved and furthermore the curvature is essentially a free parameter chosen by nature. This free parameter is called the cosmological constant. It is one of the things to be determined first by observation. Einsteins theory contains no prejudice towards the value of this constant; surprisingly observation shows a value very close to zero. There are other observed facts in astronomical observations that do not seem to have been wel understood. Two of those phenomena, dark matter and the winding problem, are discussed.

Discovering Helicobacter

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Before the 1970's, well fixed specimens of gastric mucosa were rare. Then the flexible endoscope was introduced. This enabled gastroenterologists to take numerous well-fixed small biopsies from the stomach. Gastric histology and pathology were clearly demonstrated. Whitehead accurately described it in 1972, including a feature he termed 'active' gastritis. This involved only the superficial gastric epithelium, with polymorph infiltration and epithelial cell distortion.

In June 1979, I was examining a gastric biopsy showing chronic inflammation and the active change. A thin blue line on the surface showed numerous small curved bacilli. These were clearly visible with a Warthin Starry silver stain. They appeared to grow on the surface of the foveolar epithelial cells.

Over the next two years I collected numerous similar cases. The changes were often much milder or more focal than the original biopsy, but the main features were usually similar, with chronic gastritis and usually some of the active change. These features could show considerable variation, from near normal to severe.

In 1981, I met Barry Marshal and we completed a clinico-pathological study of 100 outpatients referred for gastroscopy. There was little relation between the infection and the patients' symptoms. Peptic ulcers, particularly duodenal ulcers, were very closely related to the infection. We cultured *Helicobacter pylori*.

In 1986, with Marshall et al, I studied the effect of eradication of *H. pylori* on the recurrence of duodenal ulcer. I graded the gastritis (0 - 36) using the features seen with active gastritis. The range was 15 - 35 before treatment. After eradication of *H. pylori*, this changed to 5 - 20 within 2 weeks. This provides powerful evidence that *H. pylori* causes the active change.

Duodenal ulcer usually occurs in the duodenal cap. Gastric mucosa normally extends through the pylorus. In this study, the proximal border of all ulcers was either definite gastric mucosa, or scarred and consistent with a gastric origin. This suggests duodenal ulcer is either actually a distal pyloric ulcer or gastro-duodenal. It may well arise in the damaged, inflamed and infected mucosa in the position of maximum stress - the lip of the pyloric sphincter.

Structural Biology and Structural Genomics in Drug Discovery

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My research groups are specialized in the use of nuclear magnetic resonance (NMR) spectroscopy for studies of the molecular structure of proteins. When compared to structure determination by X-ray crystallography, the NMR method is unique by the fact that atomic resolution structures of biological macromolecules can be determined in solution. The solution conditions can also be adjusted such that they are very close to the physiological milieu in body fluids, for example, in the blood, in stomach fluid or in saliva. Today, the availability of the complete genomic DNA sequences of a wide selection of organisms presents structural biologists with new opportunities and challenges. In contrast to classical structural biology, research in structural genomics is focused on gene products with unknown structures as well as unknown functions, leading to the difficult task of predicting physiological protein functions from knowledge of the three-dimensional structure. Illustrations from our current research will be presented, with indications of practical applications in drug discovery and drug design.

My Way from Sports Instructor to Research Scientist

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I grew up on a farm in Switzerland, in close contact with nature. In addition to degrees in chemistry, physics and mathematics, I obtained a University degree in physical education and competitive sports, so that I could also experience nature through the reactions of my body to extreme stress. For five years I was a part-time high school teacher, while pursuing studies and research at the Universities of Bern and Basel. With time, my professional life turned more and more to the focus of getting ever deeper insight into the mechanisms by which nature works on the level of the interplay between the molecules of life. Today I would like to convey an impression of the joy and excitement that I had the privilege of experiencing with my interactions with nature, my activities in sports and in basic research, and with the public recognition of our work.