Biological Physics

Bringing Life to Physics

Chalmers University of Technology
and
Göteborg University

BIOLOGICAL PHYSICS

Objective

To make the School of Physics and Engineering Physics at Chalmers University of Technology and Göteborg University internationally recognized in Biological Physics both in teaching and research within 5 years.

Motivation

Without comparison molecular biology and biotechnology are the two scientific fields with the fastest development today. This will revolutionize the conditions for and the content of physics itself. To establish a strong research and educational activity with biological aspects has not only great potential but is necessary for our survival as an internationally competitive physics department.

Approach

The attached plan was developed by a working group which studied material at all levels and from all possible sources.

Main suggestion

From 1999 the school of physics and engineering physics offers a physics program in *Biological Physics*, an engineering program in *Bioengineering Physics*, a masters and a graduate program in *Biological Physics*. Including research the total investment needed over a five year period is 82 millions, with major part coming from Chalmers Foundation capital. During this period a redisposition of physics faculty research funding has to be made to make the project of lasting value. Maximum synergetic effects have to be found within Chalmers and Göteborg University, in the region, nationwide and through international collaborations.

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Peter Apell

SUMMARY OF PROPOSAL

Biological Physics is the study of physics using biological systems. *Biological Physics* is at the meeting place between natural and life sciences and we also witness an increased coupling of those to engineering sciences To increase the emphasis on the human being and medical engineering we also include a discussion about *Medical Physics.*

Biological Physics is entirely a physics education. It takes physical processes and model building as its core, rather than empirical relationships or chemistry. It is also different from Biophysics. To cite Hans Frauenfelder, University of Illinois: *The biophysicist is using tools of physics to study biosystems but the biological physicists are using biosystems to study physics, complexity, physics of functions, and hopefully new concepts.*

The area is incredibily rich and has many facetts. It can be the study of model systems such as the structure of water at biological surfaces, protein dynamics studied with femtosecond spectroscopy, electronic properties and transport properties of DNA, neural networks (real and virtual), structure and phase transitions in biomembranes, biolelectronics, sensors, (artificial) life, microlithography and micromanipulations, etc. *Biological Physics* is not unlike astrophysics where many different disciplines meet. Physical concepts, methods and theories will to a large extent contribute to the development of these different areas and physics will see new challenges to develop experimental and theoretical methods. In other words, with biological physics, physics itself will get new inspiration and become more attractive to the students of today and tomorrow. In short the biological world offers physics unique possibilities to learn new physics on complex and often elegant systems.

The present study has been made on behalf of the board of the School of Physics and Engineering Physics (see Appendix A; Mission and project group, and Appendix B; Contacted). The task is identified as important at central Chalmers level and resources have already been allocated for this study and for one research assistant in Biological Physics. The present project plan is the basis for discussions of the board and in the physics department. Based on these discussions the board will decide if *Biological Physics* shall be a strategic component of the school and if additional support shall be solicited at central levels of Chalmers and Göteborg University as well as in "Stockholm".

The project plan contains the following major proposals:

1. The area of *Biological Physics* will be an identifiable branch of research and teaching within the School. This requires dedicated, long-time, support.

2. The School of Physics and Engineering Physics will *quickly* offer an under-graduate branch in *Biological Physics* for students from both Engineering Physics and Physics. The students will have the option of doing this within the international master's program: Physics and Engineering Physics - Nanophysics or as separate courses. The official start is scheduled for fall of 1999.

3. Our students must have the possibility of meeting *Biological Physics* within our regular educations already during their first year. We therefore have to plan a start already 1999 for our physics students (Biological Physics) and our engineering physics students (Bioengineering physics).

4. The proposed undergraduate program incorporates new pedagogical techniques which differ from traditional engineering pedagogy as well as the teacher intensive physics education. Extra emphasis will be put on group work and interpersonal skills. Courses are developed in conjunction with teachers from medicine/chemistry/biology and fragmentation should be avoided. Furthermore it is not a multi-disciplinary education. We want students fully trained in mathematics and physics to be able to meet as qualified students in medicine and biology, in their disciplines.

5. Teaching material must be accessible to other courses in the way of examples and problems of biological and/or medical origin. Each course or semester can be seen as a project with specific goals to increase the flow of information between different disciplines.

6. Every student is assigned to a research group which will be hers/his *home* during the studies at Chalmers and Göteborg University.

7. It is absolutely necessary to coordinate the resources between undergraduate engineering physics and physics, graduate courses, mastersprogram and the graduate studies in (bio)materials science. The development of strong ties and collaboration with bio- and medical departments at Göteborg University are also important for success.

8. A bottom-up approach for the implementation of the program instead of the traditional way of recruiting a new professor in Biological Physics. We thus suggest an extensive program for recruiting young post-docs and researchers to join groups already present including encouraging members of the present departments to switch groups.

9. A strong and frequent program for guest scientists and lecturers is created to stimulate the creation of the new program.

10. There is probably no need for a new Phd or Licentiat in *Biological Physics.* Existing graduate programs will, however, offer new courses in *Biological*

Physics to all PhD students and research projects are performed in already existing groups. The time for obtaining a PhD should not be longer than eight years.

11. An extensive already existing collaboration should be developed further and be complemented by some well-known international players. Contacts have already been established with Imperial College (London), ETH (Zürich), University of Pennsylvania (Philadelphia), Tokyo University of Agriculture and Technology and Indian Institute of Technology (Mumbai).

12. Any coordination of the present resources and interest in *Biological Physics and Medical Physics* will develop best if left alone without unnecessary umbrella organizations or the creation of new departments at this stage. The start-up of the program is best made in the form of a project with continuous follow-up and evaluation.

13. Based on this work plan we will need resources of the order of 82 (48) millions during a five year period.

14. We suggest that the school of physics and engineering physics approach the Chalmers Foundation for a large scale support of *Biological Physics*.

15. Strong areas within our section in the area of *Biological Physics* are biomaterials, surface biophysics, complex systems, polymer- and nanophysics.

16. At the same time as we offer our own physics students a deeper insight into Biology and Medicine we should offer a course in Physics for biological and medical students at Göteborg University.

I. INTRODUCTION

Historically, Life and Physics have been studied in parallel, with little or no overlap. But recent discoveries in cell biology and genetic engineering have changed this picture. Still we seem to know physics better than life. We know physics plays a crucial role in all of lifes fundamental processes. The ever interesting Richard Feynman expressed this as: "we now realize that the phenomena of chemical interactions, and, ultimately life itself, are to be understood in terms of electromagnetism". Very little of our knowledge in this cross-disciplinary field is transferred to students of today. At the same time we are witnessing a trend, where the position of Physics as the eminent primary discipline, uncontested for many centuries, might be succeeded by an era focusing on discoveries in the Life Sciences. This means changes, for example, the blending of historically separate traditions, norms and scientific subcultures. We must contribute to such a development with an in-house educational alternative and front-line research in the Life Sciences. In what follows this is called *Biological Physics*.

Biological Physics as an undergraduate education and research profile is the study of the physical processes governing living systems. There are many reasons why this is an important and worthwhile endeavor for the School of Physics and Engineering Physics:

- *interest*: we witness an ever increasing interest among young people in life sciences;
- *mainstreaming*: it gives women reasonable possibilities to access physics;
- *platform*: many physicists trained in fields other than biology, such as condensed matter physics, currently apply their thinking to biological problems, investigating living systems of any size and shape;
- *interdisciplinary*: biology, medicine and physics are becoming an interdisciplinary field where even complex biological materials are recognized as forms of "soft" condensed matter;
- *techniques*: from organs to cells and molecules, many different physical techniques are used at all levels of biological and medical research. These techniques require skilled engineers and physicists whom we can educate at our School of Physics and Engineering Physics;
- *information*: there is a growing demand to educate our students who can bridge the gap between scientists in life sciences and in physics;
- *common goal*: the School gets a major goal - something it lacks today - which will encourage several groups to join forces and make us more visible.

The field of *Biological Physics* encompasses statistical mechanics, kinetic theory, hydrodynamics, continuum mechanics, nonlinear dynamics, molecular functions, biomechanics, colloidal physics, animal studies, portions of physical chemistry and biophysics, etc. The field is not unlike astrophysics, where many different disciplines meet. New techniques such as micromanipulation (e.g. optical traps), microlithography (to create structured environments) and fluorescence methods (for direct visualization of living processes) will all play an important role. As biophysics has attained a special meaning, the term biological physics is today used for this type of broad approach by physicists. An important question is what physics can bring to this area? Or to phrase it differently: are there now questions in biological and medical science that cannot be addressed without the use of physics? Clearly, it is not productive for physicists to move into biology and simply copy the methods and adopt the paradigms of the biologists. To a much greater extent than is found in the biology or chemistry communities, physics is deeply connected with "model building" and testing, in which one makes contact with reality through a series of progressively more detailed physical and mathematical descriptions. At each stage, there is emphasis on consistency with established laws, introduction of dimensionless control parameters (related to time, length, energy, and force) to delineate the space of possible behaviors, establishment of scaling laws (expressing commonality or even universality of behavior), and some degree of logical and mathematical rigor regarding the results of those models. Biology in other words offer the physicist unique opportunities to learn new physics on elegant and complex systems.

We once again stress that *Biological Physics* as a field of research is primarily the study of and the utilization of the physical processes governing living systems. The enclosed table of contents (Appendix C) from the book *Biological Physics* by E.V. Mielczarek, E. Greenbaum and R.S. Knox shows a cross-section of contributions by leading physicists to biology during the last four decades. It provides an accessible introduction to a growing field. The papers are logically grouped into six sections: infrastructure, cells, energetics, information generation and transfer, experimental techniques and photosynthesis. The variety of problems, depth of theory, and sophistication of experimental techniques provides an understanding of the physical functioning of living systems and stimulates the curiosity of future students and researchers. An explicit exposition of topics in *Biological Physics physics* on different levels (from molecular to system level) can be found in Appendix D. In Appendix E we give a thorough listing of various working definitions of *Biological Physics physics*.

We want to stress a few sentences from the instructions to authors in Physical Review E; "Applications that apply traditional physical methods to biological problems and that have no new methods of analysis or interpretative theory, even though they contain important results for understanding the biology of the system, are usually more appropriately published in biophysical journals.", i.e. the main difference between biological physics and biophysics is that the former also has a responsibility of progressing physics in itself. In addition to this detailed description we have several general perspectives like that of P. Eisenberger and J.S. Langer from a recent Physics Today article (April 1995): "our recent glimpses into the physics of biological systems show us just a tiny corner of a vast new world of scientific inquiry" or "there are unrecognized needs and possibilities for doing real physics working closely with biologists" according to V.A. Parsegian in Physics Today, July 1997. Just another relevant perspective is expressed by R.H. MacArthur (Geographical Ecology (1972)) "But not all naturalists want to do science; many take refuge in nature's complexity as a justification to oppose any search for patterns...Doing science is not such a barrier to feeling or such a dehumanizing influence as is often made out. It does not take the beauty from nature".

In the next sections we give a brief introduction to the local history at Chalmers/Göteborg University, we present inventories of what is going on in Sweden and abroad in academics (teaching and research) and we describe industrial activities. The final sections discuss future trends in *Biological Physics* and suggestions for a program in *Biological Physics* at Chalmers University of Technology and Göteborg University. These sections also include a detailed project plan for the educational program *Biological Physics*, and suggestions for possible research profiles.

II. HISTORY AND BACKGROUND

Within the School of Engineering Physics and Physics there have been many discussions about focusing efforts in areas bordering Biology and Medicine. Several reports during the last 20 years, from different boards of the School, have pointed out that this field of research is one of great potential for the future.

In the sixties interested individual students went into biophysics but it was not until the end of the seventies before a more general initiative was taken to offer the students to replace their fourth year with courses having a "bio"-profile. Also during the eighties students were offered such schemes. In this connection the board of Engineering Physics made contacts with Henry Wallman and Bob Magnusson (Division of Medical Electronics in the School of Electrical and Computer Engineering) to include more technical applications with a biological profile. Two recent initiatives have been; the intention of the board of Engineering Physics to start an educational branch of Engineering Physics devoted entirely to biophysics and the definite commitment by the board of our School in its last development plan to "investigate what courses can be developed on the basis of the increasing research volume within *Biological Physics*. The goal is to offer a branch of Engineering Physics in Biophysics. Such a branch would be of such a nature that it should be of particular interest for our female students".

The faculty board in Chalmers has advised the pursuit of more connections to the medical and the philosophical faculties and explicitly suggested actions to make life-sciences a part of the Chalmers curriculum. There is presently direct talks between the faculties of medicine, science and Chalmers to create common graduate courses in "hot" areas, e.g. biological physics.

Why *Biological Physics*? Why not Biophysics? We give in Appendix E a few examples of definitions of *Biological Physics*. The basic distinction between *Biological Physics* and Biophysics is a matter of "roots". People doing *Biological Physics* generally come from a purely physics background and have switched interests toward biology. People doing *Biophysics* generally come from biophysics or biochemistry graduate training. This is consistent with the distinction made in the US that *Bio-*

logical Physics is a division of American Physical Society (APS) as distinct from the stand-alone Biophysical Society. In this context it is important not to let definitions hamper efforts going in the general direction of *Biological Physics*: **Our proposal is meant to reinforce all efforts of the university in this regard**. The proposed project in *Medical Physics* will also go in this direction of merging the strength we can find in different departments rather than every department having their own version.

III. ACADEMIC INVENTORY

This section is an inventory of what is going on at Chalmers/Göteborg University, other places in Sweden and what the rest of the world is doing. Section 3.1 surveys education and Section 3.2 surveys research. Any University not having a web-page is left out of this survey.

A. Current profile - education

We have two major groups of students; engineering students in Engineering Physics at Chalmers University of Technology and physics students in a multitude of programs and courses at Göteborg University. The Engineering physics students must elect an individual profile. They have 60 elective points out of 180 (one academic year = 40 points). The physics students are more constrained by the nature of the programs and courses chosen, however they usually acquire profiles having more depth. In Appendix F is a more detailed description what is currently available today in the form of packages of courses which are of relevance under the broad umbrella of *Biological Physics*.

1. Engineering Physics

The first three years of engineering physics education provides a firm base in mathematics, physics and technology. The last 1.5 years includes a master thesis and elective courses. The student can elect any mix which suits him/her. To aid students in selecting topics and profiles in order to achieve a greater depth there are suggested tracks. The ones in Biophysics and Radiation Physics, of most relevance here, are described in detail in Appendix F. Within the group of elective courses there are ones which are not directly geared towards *Biological Physics* which nonetheless can be of importance. The Engineering physics students (and others having a B.Sc. in Physics (or equivalent)) also have the possibility of getting a Master's degree in the International program *Physics and Engineering Physics* - *Nanophysics* (Appendix F) which has one recommended track (out of three) called *Biological Physics*. This is Chalmers' first biorelated program leading to a master's degree. We will comment on the simultaneous use of resources for all these different branches in section 7. However already now we want to stress that a sensible use of resources means that students will be adviced to take part in the master's program. Possibly within a few months there will also be a decision of starting a new master's programme in physics called Complex Adaptive Systems. More information about this in Appendix F.

2. Physics and Mathematics - Göteborg University

Within Göteborg University there are several programs covering different branches of mathematics and physics of interest to a Biological Physics program. Furthermore Göteborg University has a strong curriculum in environmental sciences. A good basic physics training is offered with branchings in the directions of experimental physics, theoretical physics, astronomy/astrophysics, radiation physics and oceanography. The most interesting one for our intentions is the one in *Radiation physics*.

Mathematics is a three or four year program. In the second year one specializes in applied mathematics, computer science or statistics. Within the statistics branch there is a group of courses in bio-statistics. This is a very interesting area for students within *Biological Physics* who are more mathematically inclined and wants to specialize in this direction.

3. Göteborg University - other

Within Göteborg University there are also other programs available, covering areas related to *Biological Physics*:

- *Chemistry* is a three or four year program. The last year(s) can be fully devoted towards biochemistry or biophysics. This is the traditional route to biophysics.
- *Biology* is a four year program including cell biology, botany, zoology, ecology and evolution. It has courses which can be of general interest if one wants to couple the proposed *Biological Physics* program to general biology.
- *Molecular Biology* is a four year program with a chemical base and a strong focus on a molecular approach. It is biochemical in its nature.
- *Pharmaceutical Bio-medicine* comprises 4.5 years with a base in chemistry and cell and molecular biology. It is strongly focused towards a research profile. Depending how much our proposed program will include *Medical Physics*, courses here is of potential interest.

- *Radiation Physics* treats different aspects of radiation sources, the nature of the radiation and its environmental impact. A large part of the activity is directed towards use in medicine but also radiation sources in our environment and transport of radioactive material in biological systems is of interest. Most courses are based on that the students have a formal education in physics corresponding to a Bachelor's degree.

The University environment also offers many courses in adjacent areas which are of interest like informatics, philosophy, ethics, theory of science and research, etc.

4. Chalmers - other

At Chalmers we have an engineering branch within the School of Chemistry called Bioengineering (4.5 years) where biology, chemistry and technology is combined (see enclosed curriculum, Appendix G) for the use in industrial processes and medical applications. An engineer in Bio engineering should be able to formulate and solve biotechnical problems from a knowledge base in chemical technology, biochemistry and molecular biology. As can be seen it differs in spirit from our intentions to the same extent that the regular undergraduate chemistry and physics educations differ in general.

The School of Environmental Sciences are planning an engineering education in Environmental Technology for all branches of Chalmers. The department of Environmental Physics is doing a similar planning for a branch of the Engineering Physics education. The measurement technique courses planned could be of interest for medical physics as well as a general course in basic biology.

The School of Mechanical and Vehicular Engineering are offering a one semester block of biomedical engineering - mainly focusing on biomechanics.

The School of Mathematical and Computing Sciences has just started to plan a master's programme in Bioinformatics (see Appendix F).

5. Sweden

Here follows a short summary of the main undertakings in this area at other places in Sweden. A general search in ASKen (*asken.hsv.se*), listing ALL courses and programs in Sweden shows that Biotechnology is often incorporated as an elective branch within chemistry programs, whether at Universities or at University Colleges. A search for Biochemistry or Biology give entries which dominates completely over Biotechnology, Technical Biology or for that matter Biological Physics (no match). Medical Technology is dominated by educations in electronic engineering, radiation physics and more clinical ones (e.g. at Karolinska Institutet, Sweden's only university for medicine). Karolinska Institutet have also agreed to cooperate within the area of biomedical technology with Royal Institute of Technology . It amounts to half a year of courses for most engineering branches at the Royal Institute. Finally University of Skövde has interesting stuff in bioinformatics and biocomputing.

Right now the three programs which has any relationship to physics beyond the trivial are Uppsala (Molecular Biotechnology; started as a separate program 1991), Linköping (Technical Biology; 1994) and Umeå (Engineering Physics with Molecular Biophysics; 1995 (Technical Biology starting 1998 has no physics)) (for more details see Appendix H).

6. International

In Europe, Italy has a very strong (theoretical) profile in *Biological Physics* (e.g. Università delgi Studi di Milano and Università delgi Studi di Firenze). In United Kingdom, Glasgow and Cambridge (Trinity) have signs of a dedicated effort to *Biological Physics.* In Denmark, the Technical University (Lyngby), has a theoretical effort in Biological Mathematics (www.imm.dtu.dk). ETH (Zürich) which includes both technology and agricultural units, have strong experimental and theoretical programs and educational programs tied to those. Imperial College of Science, Technology & Medicine (London) is another collaboration partner with Chalmers which has a broad coverage of the areas we are interested in.

In Asia many institutions are building up rapidly in the life sciences, for instance in Japan, the Tokyo University of Agriculture and Technology, has a very detailed program directed towards Chemical and Biological Physics Science and Technology with a substantial group of courses in "Bio" subjects, including *Biological Physics.* For a more detailed account of this, see Appendix I. Another representative example is Indian Institute of Technology in Mumbai, India, which has a School of Biomedical Engineering as well as Schools for Engineering Physics and Biotechnology. The schools admit students from various backgrounds including Engineering, Medicine and Life Sciences. The faculty is interdisciplinary.

The area of *Biological Physics* is one of the most rapidly expanding ones in higher education in US and we will within a few years time see several new places coming up. Traditionally there are many places with a good education within the field, for example Massachusetts Institute of Technology, University of Washington, University of Delaware (interdepartmental major in *Biological Physics*), Clarkson University and Cornell University.

Massachusetts Institute of Technology has a well-structured course by G. Benedek (Alfred H. Caspary Professor of Physics and *Biological Physics*) and F. Villars called *Biological Physics* designed to provide seniors and first-year graduate students with a quantitative, analytical understanding of selected biological phenomena. MIT

Biological Physics is seen as one of the major players in US.

University of Washington, Seattle, is historically very strong in biological sciences. The department of Physics, Biochemistry, Chemistry, Biological Physics Structure, Physiology and Biophysics, and Bioengineering are co-operating in a program that provides special courses and seminars to students with an interest in molecular biophysics. Ph.D. degrees are awarded through the participating departments whose thesis research is in an area encompassed by the molecular biophysics program. Biomimetics and biocompatible materials are two major research areas in the field. University of Washington is very strong in Bioengineering. Bioengineering (sometimes called biomedical engineering) began to emerge as an interdisciplinary field some thirty years ago and describes a wide range of activities in which the disciplines of engineering and biological or medical science intersect. Representative areas include: design of diagnostic and therapeutic devices for clinical use; development of biologically compatible materials; application of state of the art technology to answer biological questions; and many others.

Clarkson University offers physics majors an early focus in their curriculum with a *Biological Physics* option. To cite a few words: "To solve outstanding problems of today's biology a synthesis of several disciplines is needed. As a consequence *Biological Physics* has become one of the most rapidly growing domains of physical sciences. In addition to basic courses in physics, students are offered a solid foundation in biology, including laboratory experience". It should be mentioned in this context that Clarkson University also has a branch in Engineering physics, like ourselves.

Cornell University: The College of Engineering at Cornell University is composed of eleven schools and departments that house specialists in traditional engineering disciplines. Additional, interdisciplinary programs focus on bioengineering, environmental engineering, and the science of earth systems. Bioengineering, as practiced at Cornell, involves the application of engineering principles and approaches in conjunction with biological systems. It is carried out at the interface between traditional engineering disciplines and the knowledge and techniques developed in the life sciences. To cite from the Cornell home page:"The emphases that drive these activities may come from various directions. For example, engineers may use biological systems in the design of new processes to produce a drug, destroy a hazardous compound, or construct artificial skin. Or they may design new devices intended to work in a biological context, such as pacemakers, artificial joints, and equipment to diagnose disease. Or engineers may simply use biological systems for inspiration in designing nonbiological processes, as when an understanding of natural polymers leads to better synthetic materials, or an understanding of how the brain works leads to better computers. Different subareas within bioengineering are sometimes referred to as biomedical, bioenvironmental, bioprocess, biomaterial, biomechanical, etc. But the boundaries between these subareas are often indistinct, and the rapid rise of molecular biology has made them increasingly artificial, since solutions to fundamental problems affect multiple areas. For example, how cells adhere to a surface is a fundamental question that can be understood through a knowledge of cellular structure combined with a knowledge of how the cell's molecules recognize surfaces, how changes in recognition alter cellular physiology, and how attached cells respond to mechanical forces. Once cell adhesion is understood, this knowledge can be applied in various subareas. In medicine, it may aid in the design of artificial organs; in biomaterials, it has implications for the design of surfaces that can manipulate cell physiology; in bioprocess engineering, it can affect the design of bioreactors for the production of pharmaceuticals; in bioenvironmental engineering, it may imply processes that use cell adhesion to remove and contain contaminants; and in biomechanical engineering, it may affect the way artificial joints are designed to interact with surrounding tissue. Since bioengineering may include activities in all the traditional engineering disciplines, the Cornell program puts the emphasis on the engineering side of the interface. Before all else, bioengineers have to be good engineers. The Bioengineering Option allows undergraduate students to major in any of ten engineering fields and learn enough biology and bioengineering to apply their skills to a targeted set of bioengineering problems. With faculty guidance, students use their elective courses to acquire a basic mastery of biology and bioengineering".

Perhaps one of the most interesting broad approaches to integrating biology in engineering can be found at Cornell: see the home page www.cs.cornell.edu/cv/UgradBio/biology.htm

B. Current profile - research

We describe in this section research activities in Göteborg, Sweden and abroad of relevance to our work plan; i.e. they touch upon different aspects of *Biological Physics* . Recently an international evaluation group visited the natural science faculty of Göteborg University and stated that there should be a closer collaboration with the medical faculty within the biological area.

1. Chalmers/Göteborg University - Physics

The School of Physics and Engineering Physics is the largest joint research and educational unit for physics in Sweden. This is because most of the departments are shared by both Chalmers University of Technology and Göteborg University. All the basic traditional scientific areas are represented: astrophysics, particle physics, nuclear physics, atomic and molecular physics, and condensed matter physics. In addition, there are activities in physical resource theory, radiation physics and reactor physics. Thus research activities are extensive and include both theoretical and experimental projects of both a basic and an applied nature. Several evaluations have confirmed the high quality of this research. The most extensive research is conducted in condensed matter physics and spans several areas with the emphasis on material science. For example, research is conducted on polymer materials and glasses, in particular energy-related materials such as polymer electrolytes for batteries and fuel cells. Several groups work with phenomena on surfaces, including studies of molecule-surface reactions, ranging from two-atomic molecules to biological macromolecules. Research on semiconductor materials includes: synchrotron radiation-based basic studies of surfaces, material fabrication using molecular beam epitaxy techniques and ion implantation, and investigations of nanostructures for microelectronics. Both fundamentals and special applications of antiferroelectric and ferroelectric liquid are being studied. The properties of metallic and ceramic materials are studied as a function of the manufacturing parameters using microscopy and microanalysis. The instrumentation is extensive and includes a national nanometer laboratory. A new building for microelectronics is under construction in cooperation with the School of Electrical and Computer Engineering. Several research areas are of an inter-disciplinary nature. They include radiation physics, physical resource theory and environmental science.

These different research groups collaborate with some twenty companies within and outside Sweden. For example, within the field of metal physics, cooperation has been established with Sandvik Coromant, Sandvik Stål, SECO (Fagersta), Volvo and the Swedish Institute of Production Engineering Research (Mölndal). Contacts in both research and development of superconductors and microelectronics have been established with Ericson, ABB, Siemens, NKT and Oxford Instruments. Research on biocompatibility is conducted together with Nobelpharma. Consortia and competence centers focus on superconductivity, high-speed electronics, photonics, biomaterials and catalysis.

Several groups in Göteborg, both at Chalmers University of Technology and at the Göteborg University already do research, or plan to do so, which can contribute significantly to a base of education in *Biological Physics*. Not all of it is *Biological Physics* in a strict sense but it never the less belongs to the general area. Our main strength seems to be in the interface between dead and living matter. Several groups do research which relates to the theoretical and experimental foundations of *Biological Physics Physics* without directly mentioning Biological Physics applications in their projected plans for the future. In Appendix J we have especially cited those groups with an explicit reference to "Bio". There are in all eleven such groups. Several of the external contacts we have used in the course of making this work plan have pointed out that this means that we already now have a very strong effort within *Biological Physics*. Once again we want to point out that groups which do not directly work in Biological Physics will also strengthen the base and fundamental knowledge needed within the faculty for a strong program in *Biological Physics*.

2. Chalmers/Göteborg University - outside physics

Chemistry (bioscience research areas): The departments of Physical Chemistry, Chemical Reaction Engineering, Biochemistry and Biophysics, Bioengineering and Food Science collaborate within this research area. State of the art Nuclear Magnetic Resonance and Mössbauer Spectroscopy, specialized equipment for the growth of single crystals, and an excellent X-ray diffractometer, are just some of the important facilities located in this school. Other major research areas are synthesizing model systems for enzymes and studies of single protein crystals. The departments which are primarily active within Natural science chemistry are Physical Chemistry, Biochemistry and Biophysics, Organic Chemistry, Inorganic Chemistry, Nuclear Chemistry, and Analytical and Marine Chemistry. Of these we find of particular interest to us Physical Chemistry and Department of Biochemistry and Biophysics:

- *Department of Physical Chemistry.*

  By tradition physical chemistry includes the theoretical basis of chemistry, especially interactions between energy and matter. Within this context classical thermodynamics, electrochemistry, reaction kinetics and photo chemistry have been developed. Studies in these subjects were previously restricted to macroscopic properties of matter. However modern research exploits spectroscopy and quantum mechanics to obtain molecular information about the underlying mechanisms of these properties. The research profile of this department includes Biophysical chemistry; experimental studies of DNA systems with respect to structure, dynamics, interactions in solution, and mechanisms of electrophoretic separation.

- *Department of Biochemistry and Biophysics.* The research activities of the department are directed towards basic research on the structure and function of proteins, dynamics of electron-transport proteins, and proton-pumping proteins. Other important projects include studies on photosynthetic proteins, DNA-structure, the interaction of DNA with proteins, the biochemical basis for toxic effects of ozone and UV-light on plants, and collaborative projects with the pharmaceutical industry.

A variety of biochemical/biotechnological, biophysical and theoretical techniques are used.

The so called *Lundberg Laboratory* of Göteborg University houses four Departments in Natural Sciences: Biochemistry and Biophysics (described above), General and Marine Microbiology, Genetics and Molecular Biology. It will be a major center for cellular and molecular research at Göteborg University. Its goal is to provide a stimulating atmosphere which promotes scientific interaction and cooperation among the departments as well as with other national and international research groups. The Lundberg Laboratory also provides an educational program including advanced courses, lectures and seminars for students and researchers.

- *General and Marine Microbiology.* In this department the physiology, ecology and molecular biology of bacteria, yeasts and algae are studied. Part of this institute is the *Biointerface and Biofouling Laboratory* which was established in 1995 by the Faculty of Mathematics and Natural Sciences at Göteborg University. Its purpose is to advance the basic knowledge and education required to increase the understanding of interface biology and biofouling. Current work is on some novel concepts of how to prevent and control the proliferation of microorganisms on surfaces that are used in different industrial applications, including medical implants.
- *Department of Molecular Biology.* The functioning of genes are being studied experimentally. The major emphasis is on the human genome and understanding of genetic diseases. The work is carried out using biochemical and molecular genetic methods, in addition to standard cloning techniques. Experimental systems include yeast cultures, cultured mammalian cells, and transgenic animals. The main projects focus on enzymes involved in human lipid metabolism, on tissue-specific transcription factors, and on cell-cycle control.

Hasselblad Laboratory. The Hasselblad laboratory has been built to house the Swedish Nuclear Magnetic Resonance center. Göteborg University is a host for this center. Three-dimensional pictures of molecules are obtained and show how atoms are distributed in space. This is important for discovering the structure of biomolecules and their interactions with other molecules; a key process in the assimilation of drugs. The laboratory is authorized to conduct both research and teaching.

Center for Biotechnology is a scientific center at Chalmers. Chairman is Professor Gunnar Bjursell, Molecular Biology, Göteborg University. The center gives general courses for the public about biotechnology or structure and function of biomolecules.

Centre for Biomechanics. Foundation chairman C. Högfors (department of polymeric materials, division biomechanics). Deals with research and product development.

Advanced Study group on Biophysics and Biomaterials
(coordinator Mikael Käll, condensed matter physics) The Advanced Study group on Biophysics and Biomaterials has just started. The aim is to increase the general interest, and competence in the area of biophysics and biomaterials at Chalmers/Göteborg University, with the specific goal to stimulate interdisciplinary collaborative projects and contacts between the groups. The main activity to start with is seminars by either invited prominent international experts in relevant fields or by members of the participating groups. The first kind aims at stimulating the general interest in particular areas and the second kind is to stimulate local collaboration and contacts.

Material Science Committee
(coordinator Lars Börjesson, applied physics) On Chalmers initiative this group has as its task to develop a strategic plan for all Chalmers research in material science. Material Science is a key area at Chalmers and the collaboration with Göteborg University makes this even more so. Several different Schools are involved with many interdisciplinary projects. The aim of the group is to describe the present situation and to discuss possible future scenarios. One such is of course in the direction of *Biological Physics*, concerning biomaterials.

3. Sweden

Swedish University of Agricultural Sciences. Historically based dividing lines between disciplines becomes less and less important. This is very evident in the structure and functioning of the Swedish University of Agricultural Sciences. It represents about a third of all Swedish research in Biology. It has had a long interest in Biotechnology which is of importance for our own efforts in *Biological Physics* at Chalmers/Göteborg University, and offers an education in Biotechnology and is a partner in the new Technical Biology program at Umeå University. There is also a graduate school in *Metal Biology* with emphasis on the chemistry, biology and physics of metals which attracts undergraduate students from science, medicine and pharmacy.

The Swedish Foundation for Strategic Research (www.stratresearch.se): One main emphasis of this Foundation is directed towards biomedicine and to some extent biotechnology. An increased integration of modern biology and biotechnology into medical and pharmaceutical research has been the major goal. To stimulate cross-disciplinary science, effort has been put into bioinformatics and a graduate school in biomedicine. The latter is a common graduate school for the medical, science and technical faculties. During 1996 the Foundation decided to support Neuroscience in order to increase our understanding of the working of the brain; especially incorporating molecular biology technology. Together with the

Swedish Natural Science Research Council it also supports basic science. Of relevance to this report are the two programs Cellular signal systems and Medical Technology:

- *Cellular signal systems* is a cross-disciplinary area with research on how information is transferred and integrated in biological systems on all levels, cellular, molecular and structural.
- *Medical Technology* is a rapidly growing area of importance for the future hospital care and thrives on technical inventions within information technology, materials technology, chemistry and biotechnology. Whether one works with X-rays, ultra sound, magnetic resonance imaging or laser analysis pictures are generated and have to be interpreted. Medical informatics and bioinformatics are also developing rapidly, as is sensor technology.

The Swedish Foundation for Strategic Research furthermore supports a number of materials consortia of which the Swedish Biomaterial Consortium is the most interesting for *Biological Physics*. The purpose of this consortium is to obtain an increased knowledge of surface properties and their correlation with interfacial biological processes and to contribute to the development of new and better surfaces for medical applications (implants, sensors, etc).

The Swedish Foundation for Strategic Research also supports research programs in different areas in biomedicine of special relevance to *Medical Physics*.

Finally two other noteworhty entries are the Royal Institute of Technology which has a Theoretical Biophysics group whose fiels of research are Biological physics, theoretical biology and molecular dynamics and Lund University has a group on Complex Systems among other things addressing biological information processing.

4. International

In section 3.1 we already touched upon interesting research efforts. We give in this section a broader account for international research in *Biological Physics*.

To the east of us both Finland and Estonia have strong profiles in Bioengineering. There is a large institute of *Biological Physics* at the Pushchino center for Biological Physics Research in Russia. In Europe one of the strongest units are ETH (Zürich) with many interesting theoretical and experimental programs and Imperial College of Science, Technology and Medicine (London). Since we already have close ties with these two universities through student exchange we look a bit closer at what they can offer in *Biological Physics*.

ETH: In theory we find interdisciplinary work between physics, neurobiology and information science; Sensorimotor systems: eye movements, multidimensional coordination of vision and manipulation; Modeling of biological neural networks. In experimental physics the interest is towards Functionalized surfaces for improved biocompatibility of titanium alloys, Structure and motion of lipids in bilayers and biological physics membranes, Atomic force microscopy for biological physics probes, and X-ray irradiation sterilization of pharmaceuticals. There is also a strong environmental component as expressed by projects like Combined biological physics-physical treatment of waste air, Fluxes of nutrients in wastewater treatment plants, and Biological physics phosphorus removal in activated sludge systems. It is definitely the best collaboration partner in Europe right now considering our own profiles at Chalmers and Göteborg University.

Imperial College with its Medicine component will be of great interest to us, especially its Centre for Biological Physics and Medical Systems: "There has been multidisciplinary research over many years at Imperial College relating to the application of physical science and engineering to biology and medicine. This research has traditionally been conducted within small discrete groups, whereas much of the research currently undertaken in basic medical sciences requires larger groups and sophisticated equipment. The establishment of a Centre for Biological Physics and Medical Systems is the College's response to this need. There are two key factors for its success. The first is that for many years a large number of academics from Britain and all over the world have been attracted to work at the Centre. They have been individual graduates from medicine and the biological sciences seeking a deeper knowledge of physical science as a means of advancing their careers, as well as physical scientists seeking an introduction to biological sciences. In addition, a large number of leading research workers in the fields encompassed by the Centre have either visited and/or taken sabbaticals at Imperial College. The second area of activity has been the establishment of major collaborative research projects with many of the world's leading academic institutions. Major areas of interest of the Centre are the cardiovascular, respiratory, connective tissue and nervous systems. Detailed analysis of the function of these systems is a key component in understanding important diseases such as atherosclerosis, thrombosis, bronchitis, arthritis, cancer and Alheimer's disease. These diseases comprise the most disabling medical conditions in a large and increasing proportion of the world's population. An important point of the Centre strategy in the solution of these problems is that a truly multidisciplinary approach essential. In this regard the academic staff of the Centre comprises individuals who are leaders in a broad spectrum of fields including basic medical science, physical science, engineering and mathematics. The Centre for Biological Physics and Medical Systems includes individuals from a wide range of departments in the College, and much of the research is carried out in a wide range of medical institutions. However. this section concentrates primarily the Postgraduate opportunities offered by two of the constituent groups: the Physiological Flow Studies Group and the Biomedical Systems Group of the Department of Electrical and Electronic Engineering. Nevertheless, the nature of the Centre's work is such that all students are likely to be involved in conjoint activities with other groups either in the College or in other institutions. Indeed, a major aim of the Centre is to foster communication and interaction between workers in different disciplines".

In north America we find three national institutes and several universities of interest.

The *National Science Foundation* in US has a directorate for Mathematical and Physical Sciences. It stresses that "nature knows no boundaries". The physics division, in cooperation with other divisions, has begun small-scale initiatives in *Biological Physics*.

National Institutes of Health has a Laboratory of Structural Biology which is a branch of the Division of Computer Research and Technology, under V. Adrian Parsegian, physicist and biophysicist. It has four sections: Analytical biostatistics (especially structure prediction), Center for molecular modeling and molecular modeling interest group, molecular graphics and simulation and osmotic stress, and Measurement and theory.

Oak Ridge National Laboratory has a Life Science division which captures very well a situation we can accomplish ourselves if we want to integrate the environmental efforts of Göteborg University and the engineering profile of Chalmers: "The Division was created in February 1997 by merging the Biology and Health Sciences Research Divisions. It continues the ORNL tradition of excellence in biomedical research that started 50 years ago. Building on strong and often unique competencies and special facilities in Biological physics and Chemical physics, Bio informatics, Biomedical technology, Biotechnology, Environmental assessment technologies, Mammalian genetics, Molecular biology, Risk analysis, Structural biology, and Toxicology, the Division is continuing to pursue research and development addressing important and high-impact problems at the intersection of the Biological Physics, Physical, Medical, Engineering, and Computational Sciences." A particularly interesting section is the "Chemical and *Biological Physics* Section": its activities span the fields of physics, chemical physics, biophysics, and biochemistry. This diverse, interdisciplinary group applies both theoretical and experimental approaches to problems arising from the harmful effects from the production, distribution and consumption of energy. Basic studies of the chemical and physical processes relevant to radiological and chemical pollutants and their interactions with other chemical and biological species include photoexcitation and photoionization processes, molecular clustering phenomena, ion-molecule reactions, biochemical processes, and studies of chemical kinetics in gas- and liquid-phase systems. These studies are related to problems of atmospheric chemistry and physics, pollutant characterization and detection, and to radiation chemistry and biology. Major portions of these studies are aimed at development of new principles for advanced analytical instrumentation for very low level environmental pollutant detection. Other major efforts include the development and application of new microscopies, properties of superconductors, genome sequencing methodologies, and issues of chemical warfare stockpile reduction." Thus this division has a lot in common with the emphasis at Göteborg University on environmental sciences.

Prominent university institutions in the US are Vanderbilt University, University of Virginia, Wake Forest University, Carnegie-Mellon University, Massachusetts Institute of Technology, Cornell University, Princeton University, University of Rochester, Syracuse University, University of Illinois at Urbana-Champaign, California Institute of Technology and Washington University in St. Louis. In Appendix K we give first person descriptions from the departments home pages of the current activities.

We end this section with perhaps the most interesting of all the programs found: at the Tokyo University of Agriculture and Technology (see Appendix I) where there is a graduate program *Bio-Applications and Systems Engineering.* Downloaded from the web:"A graduate school of Bio-Applications and Systems Engineering (BASE) was founded in 1995 as the first interdisciplinary graduate school in Tokyo University of Agriculture and Technology. Applications of well-organized biological systems to the large-scale production as well as mimicking the efficient functions for the designing of sophisticated materials have been absorbing keen interests for human society, in particular, for industrial fields of medicine, foods, chemistry, mechatronics, electronics, energy, environment, and so on. In order to respond this social trend, Tokyo University of Agriculture and Technology has organized an *interdisciplinary* faculty, twenty-four professors with great expertise in the fields of agriculture and engineering." The program has its base in three departments:

- *Department of Chemical and Material Systems.* "Designing of new materials, chemical processes, and energy production systems, which are friendly to the global ecosystems, and tolerable to the recycling. Fields of education and research are functional designing of materials, advanced materials, energy and materials engineering, and dynamics of molecular systems."

- *Department of Bio-Mechanics and Intelligent Systems.* "Pursuing a new artificial system which consists of biological intelligence, perception, motion, transport and transformation. One example is the realization of intelligent robots composed of new artificial intelligence and perception functioning by neural network models. Fields of education and research are transport and transformation in bio-systems, neural information processing, biomodeled sensory system and Intelligent motion control systems."

- *Department of Environment Symbiotic Production Systems.* "It is very important for our mankind to ensure our natural resources, energy and provisions for the 21st century. The department tries to create environmental symbiotic production systems by learning from living things or organisms. The staff intends to educate graduate students for making the new production systems so that all various forms of life can live together on the earth. Fields of education and research are science and engineering for sustainable agro-production systems, molecular mechanism of bio-interaction, molecular biology of plant production and microbial transformation, biological physics and environmental sensing system."

C. Graduate programs

If we undertake an undergraduate program in *Biological Physics* we should also provide the possibility of achieving a PhD, especially since we conduct research in the area. This section lists some of the PhD programs around which are of interest for us.

The division of *Biological Physics* of the American Physical Society has listed universities in the US where one can make Graduate studies in Biophysics and/or Biophysical research leading to a physics PhD. The list comprises about 100 institutions. Out of these 10 have a clear profile in *Biological Physics Physics* (see aps.org/DBP). Appendix K contains more details since they are all intimately connected to ongoing research programs. Furthermore we remind the reader about the excellent graduate program at Tokyo University of Agriculture and Technology as described above (end of section 3.2.4) and in Appendix I.

Among the Swedish programs the most interesting is the one supported by the Swedish Foundation for Strategic Research; *Graduate School in Materials Science.* It is a graduate school in materials science at Chalmers (physics, chemistry and mechanical engineering) and Göteborg University (medicine, dentistry and natural sciences). The graduate school is coordinated with the two ongoing Foundation research programs in Molecular Engineering of Polymers and Biocompatible materials. The purpose is to strengthen the research in material science at Chalmers/Göteborg University and to stimulate cross-disciplinary contacts. Part of the program is allied with industry. Already from the start it is clear that the majority of the students are interested in biorelated matters. !998 four courses are offered: Introductory course in Biomaterials (1), Biomedicine for materials science graduate students (4), material science for biomedical students (4) and advanced course in biomaterials (6) One program within the graduate school, *Biopolymers and Biocomposites as structured materials*, takes examples and inspiration from biological systems to create future materials. The US National Materials Advisory board in its report *Hierarchical structures in Biology as a Guide for New Materials Technology* stresses: " Many material systems found in nature exhibit a combination of properties that is not found in synthetic systems. The unique performance of natural materials arises from precise hierarchical organization over a large range of length scales. These materials display unique properties that are affected by structure and generative processes at all levels of biological structural hierarchy". Another branch of the school is devoted to *Biocompatible materials.* Within the area of biomaterials and medical implants there are several different project of relevance to *Biological Physics.* A few examples are, optimization of material surfaces for a more effective healing or functioning, new methods for production and evaluation of material surfaces to obtain functionality in a biological environment and bioadhesion.

Forum Scientum, based at Linköping University, is a broad multidisciplinary graduate school - encompassing natural sciences, technology and biomedical sciences. 15 departments from three different faculties are involved. The aim is to graduate students 1-2 years earlier than normal with no change in quality. The research program within Forum Scientum is based on sensor technology aiming at new applications within medicine, biotechnology and environmental technology. It concentrates on three overlapping strategic research areas: analysis of technical and environmental systems, physiological measurements including blood flow engineering, and biological physics receptors, and biosensors. Main support for this research is from the Swedish Foundation for Strategic Research.

Finally we have the *Göteborg Graduate School in Biomedicine* which is one of six local biomedical graduate schools also financed by the Swedish Foundation for Strategic Research. It is a collaboration between Chalmers and Göteborg University (science, medical and odontological faculties). The aim is to provide a year in between undergraduate and graduate studies in biomedical research and with close collaboration with relevant industries.

IV. INDUSTRIAL INVENTORY

This section contains a regional, national and to some degree international inventory of interesting companies and government (federal and local) undertakings which could be of interest for students graduating from *Biological Physics.*

Already from the outset we should stress that a physics education as well as the Engineering physics education at Chalmers has never been constructed or intended to work in such a way as to satisfy direct needs of companies or other employers. Instead a very strong profile of the education has been the training of basic (time-independent) skills (to solve new problems in technology and science, mathematical modeling, approximations and estimates and analysis; all with a strong base in mathematics and physics) coupled together with a large degree of freedom for the individual to compose his/hers own program the last year(s). We see no reason why this concept should not be succesfull also with the new direction towards *Biological Physics* as we suggest. This does not mean, however, that we do not consider such contacts useful and fruitful. In fact many of our boards at the School of Physics and Engineering physics have industrial representatives. The School of Physics and Engineering Physics is also in the process of building up an Alumni network which will further strengthen those ties. Moreover diploma works and other arrangements imply that we keep close tabs on what the industrial development is like. Physics and Engineering physics students are now found in almost all kinds of industrial and government undertakings. In this context it should also be mentioned that the branch Engineering Physics has supplied 25% of all Chalmers PhD from its start 1956. We foresee that the new branch in *Biological Physics* also will be a source of good graduate students for physics and biomedical research.

A background in biomedical engineering provides students with great flexibility after graduation. They can find employment in industry, go to graduate school, or go to a professional school in medicine or business. Since they have a good training in a traditional engineering fields, they have the same employment opportunities as classmates who did not pursue the bio option–but they have additional opportunities in biotechnology-oriented industries. The rapidly growing pharmaceutical, environmental, and biomedical-devices industries have increasing numbers of positions available to such graduates. The job market for someone graduating from *Biological Physics* therefore looks positive even if it takes some time in the beginning to advertise the competence. Areas such as environmental technology, engineering biology, medicine, clinical science, pharmaceutical Research and Development, biomaterials, and sensor technology as well as an academic career in physics or related fields in medicine or biology are in need for students with our suggested profile. It is even stressed by leading people within the field that "please provide us with a general problem-solver rather than someone who is tailor-made for an industry which will not be the same when they graduate". There are several companies in the region which are interested in students graduating with such a profile. To name a few: Astra Hässle AB, Cinventa AB, Sahlgren Hospital, Stena Line AB, Svenska Telemedicin System AB, Wallenberg Laboratory, Östra Hospital, Nobel Biocare, Mölnlycke Clinical, Kronan, etc. On top of this we can then add the rest of the country. Our students will also be very effective to compete on a European level - especially if they follow the international master's program we have, where they would train their social competence in an international atmosphere.

In connection with the new branch we also hope to stimulate entrepreneurial interests among the students so they can actively go and work at the Chalmers Science Park or at the newly started "Sahlgrenska Biomedical Innovation Center" which is set up in order to support small and medium sized companies, or satellites to large companies, with research facilities and marketing support. The key focus is on pharmaceuticals, biomedicin and medical technology since these are three rapidly growing areas today. In the Götegorg area there are approximately 200 such companies (1994) with around 5500 employees (1997).

The Göteborg region is the fastest growing of Sweden's three medical metropoles. The largest company is Astra Hässle (2000 employees). Others are Art in Plant, Astra Tech, Beiersdorf, Ciba Geigy, Chromogenix, Elos Industri, Glaxo Wellcome, Höron, Janssen-Cilag, Nobel Biocare, Nova Medical, SCA Mölnlycke, Kronan, Zeneca, Ada and Meda. A number of small companies like Scandinavian IVF, Medi Team and Qualysis are also said to have a very large potential growth. "Medicine tomorrow in West Sweden" and "Operating Theatre 2000" are just two of many inter-disciplinary projects underway to develop tomorrow's medical-surgical therapies and techniques.

Even a traditional company as Volvo has interests close to this area, in particular topics related to the behavior of drivers and customers. This area has for a long time been dominated by "soft" methods and there is a clear need to complement these psychological methods with more hard core physics knowledge about topics like the study of brain waves and cellular signals. There is already a small nucleus of researchers active in these fields in the Göteborg area.

We have also solicited the opinions from other departments within the science faculty and the medical faculty. They all welcome the suggested education. Monitoring the interest from prospective students and companies both in Göteborg and surrounding areas, shows a very positive response. They also agree on that the strong component in our concept is a small group of students within an established physics education which will have the chance to also meet the biology side - learning concepts and terminology - hence being better communicators in future project groups including physicists, biologists and medical professionals.

The European biotechnology sector is expanding rapidly (see "European Life Sciences: Continental Shift" by Ernst & Young). 1997 there was 1036 biotechnology companies in Europe employing some 39.000 people. This is an increase by 45% in one year. The increase in company research was 27%, to 1.9 billion ECU. The investors are primarily interested in Germany, Switzerland, Denmark and Sweden. In those countries, and France, the biosector is increasing more rapidly than in US.

Let us close this section with a real life example of the meeting between biology and silicon technology as one example of many of the interesting and rapid developments taking place in a way making any prediction of possible job markets failing quickly. A California based company *Affymetrix* uses technology for creating silicon computers chips to create DNA probes that scientists can use to identify various genes and mutations. This simulator allows Netscape users to "build" DNA probes, using the combination of laser technology and chemical reactions that create a gene chip. Is is an amazing blending of silicon technology with biology (New York Times, March 1997).

V. CURRENT TRENDS IN *BIOLOGICAL PHYSICS*

This section starts by citing from recent conferences to give a flavor of interesting areas:

In Trieste in August 1997 there was an Adriatico Research Conference on Nonlinear cooperative phenomena in Biological Physics Systems. The conference board describes interests in this field as follows: "Living matter is condensed. Without correlations on membranes, on cytoskeletal and receptor proteins, in DNA and RNA molecules, the cell could neither differentiate nor proliferate. No signals would be transduced; there would be no life. Biological Physics events and functions associated with life, however, also depend on nonstationary conditions because living matter always defines chemically open systems. Thus, it is also time to consider the origin and driving mechanism of biological events, and to try to understand the difference in this respect from inanimate matter. Nonlinear modeling of biological systems have in the last years mainly been focused on protein folding, solitons and neural networks, each of which has become a field of its own. This has given rise to fields like, random boolean networks, percolation processes and self-organized criticality, spin glass models in biological systems, dynamics of proteins, DNA and membranes, the cells "quantal" decision to replicate DNA and dynamical models of morphogenesis. The bank of molecular biological data, however, is rapidly growing in many areas of interest. Extended studies are therefore devoted to other processes where especially cooperativity plays a large role".

In December 1997 the conference *Molecular Electronics: Science and Technology* took place:"The trend of miniaturization of electronic circuits has progressed unabated since the invention of the integrated circuit by Noice and Kilby in 1959. The number of transistors in a state of the art microchip has steadily grown and by the end of the century it will reach the one billion mark. At the sam time, the size of features on a microchip has declined to 0.25 microns, and the prospect are that it will shrink even further. However, it is feared that once the size of printed lines on an integrated circuit shrinks below 0.1 microns, the performance of the silicon device will suffer because of crosstalk and other quantum limitations. It is entirely possible that at those small dimensions and below, a new technology will emerge based on properties of some molecules that act as electronic components. This new technology is *Molecular Electronics*.

Theoretical proposals for molecular scale devices have appeared as early as 1974. Since then, hundreds of publications have appeared. The attractive features of molecular electronics are that it offers to scientists an opportunity to study and understand a new class of materials, on the molecular level and in isolation, while offering to engineers a whole new microelectronics technology. The unique properties of molecular devices would be high density and high switching speed. The high density is inherent in the size of molecules, and the speed is implied from the short electronic transition lines that occur in molecules.

The conference will cover theoretical and experimental aspects of molecular electronics. It will also concentrate on the techniques that are currently employed for future molecular circuits and the techniques needed to be able to interact with single molecules and research their characteristics. Invited titles are: Molecular wires, Interconnections to a single molecule, conductivity of molecules in isolation, molecular electronic switches and devices, the chemical synthesis of molecular devices, measurement of molecular devices, self assembly, nanoscale materials and devices, and the interaction of molecular devices with light."

The Second conference on Evolvable Systems: From Biology to Hardware (Lausanne) earlier this year stated: "The idea of evolving machines, whose origins can be traced back to the cybernetics movement of the 1940's and the 1950's, has recently resurged in the form of the nascent field of bio-inspired systems and evolvable hardware". Topics covered were evolving hardware systems, evolutionary hardware design methodologies, evolutionary design of electronic circuits, self-replicating hardware, self-repairing hardware, neural hardware, adaptive hardware platforms, autonomous robots, evolutionary robotics, bio-robotics, applications of nanotechnology, biological- or chemical-based systems and DNA computing.

In addition to the conferences another visible trend of Biological Physics being a more mature field is the appearance of a new book series: AIP Press (transferred to Springer Verlag, April 1997) recently announced *The International Series in Basic and Applied Biological Physics*. "Its goal is to provide scientists, engineers and interested lay readers with textbooks, specialty monographs, reference works, guided reprint volumes, and works of cultural and historical significance. The composition of the editorial board reflects that *Biological Physics* is broad, challenging, and multi-disciplinary. Accordingly the series will emphasize frontier areas of science including: molecular, membrane, and mathematical biophysics; photosynthetic energy harvesting and conversion; information processing; physical principles of genetics; sensory communication; automata networks, neural networks, and cellular automata. Equally important will be coverage of current and potential applied aspects of biological physics such as biomolecular electronic components and devices, biosensors, medicine, imaging, physical principles of renewable energy production, and environmental control and remediation."

There are several areas of research which border *Biological Physics* or are at its heart. Many facets which indicate new developments and which stir the imagination are:

- *Nano-Macro Interface*
- *Biomagnetism*
- *Bioelectronics and Scanning Probe Microscopy manipulation*
- *Optical Biological Physics Spectroscopy*
- *Evolutionary (bio)technology* (breeding engineering systems)
- *Medical engineering*
- *Computational Bioscience*
- *Bio-inspired systems and Bio-informatics* (growing hardware, see Nature classified, **389**, 25 September 1997)

To be more explicit other examples are:

- *Biosensor Design Technology and Applications.* Biosensors are small devices that use biological recognition properties for selective on-site, real-time analysis. The aim is to biologically produce a signal that is quantitatively related to the concentration of the target analyte. For this purpose, a biospecific reagent is immobilized at a suitable transducer, which converts the biological recognition event into a quantitative response. Biosensor design and technology is a rapidly growing area, see the book *AIP Handbook of Modern Sensors, Physics, Designs and Applications* by J. Fraden (AIP 1993, New York). Current research efforts on biosensors are proceeding on many types of sensor principles. A high level of sophistication and state-of-the-art technology are employed for producing easy-to-use, compact, and inexpensive devices. This could be an area where there is a direct coupling between the *Environmental* profile of Göteborg University and the more *Biological Physics* profile of Chalmers. In Appendix L we give an interesting account of the role of sensors as the driving force in the next technological revolution after the microprocessor and the laser.

- *Tissue Engineering: technology and applications.* The ultimate goal in this area is to develop living tissue that can be used to replace or repair damaged tissue in the human body. With the recent advances in cell biology, biotechnology, biomaterials development and bioengineering, the capability to construct new tissues is now a reality. Central to this field is the development of biocompatible materials that provide casings for cell transplants, materials for tissue repair, and scaffolds that facilitate cell growth and tissue formation. Bioengineering has provided tools for the analysis of complex, living tissues.

- *Artificial life* (see, e.g.,

  www.krl.caltech.edu/avida/home/intro.html)

  "Historically, life and the physical world have been studied in parallel, with little overlap. While this has changed with the advent of modern microbiology, there can be no doubt that we have a much better understanding of physics than we have of life. Life is so diverse and complex that it seems impossible to extract the general principles governing each individual living system. The physical world, on the other hand, also displays diversity and complexity in its phenomena, yet yields to analysis, mainly because we can deconstruct complex physical systems and study specific aspects in isolation. For example, the global weather system is an extremely complex system which we do not need to study in its entirety to gain insight into basic properties of gaseous dynamics. Rather, we study aspects like turbulence and convection in model systems, ideally in their most simple occurrence, to apply what we have learned about them to the full system later. Such an endeavor appears to be fruitless as far as living systems are concerned. In almost all cases, a deconstructed living system is no longer living, and hence the property in which we are most interested has disappeared. On the other hand, the simplest living system (that which has been a precursor to all living systems) has been replaced by much more complicated ones over four billion years ago. Attempts to reconstruct it are as yet unsuccesful and will probably remain so for some time. Fortunately, it appears that the unrelenting growth of the power of modern computers we are witnessing has opened up an entirely unexpected avenue: the construction of an *artificial* living system. This has created the possibility to design and conduct dedicated experiments with these systems that could otherwise only be performed with much hardship if at all. Moreover, such artificial living systems have also generated interest in the idea of formulating a set of "general principles of the living state" which are quite independent of a particular implementation. Such a "theory of simple living systems" should equally well predict the outcome of experiments performed on the protean living system which gave rise to life on earth, e.g. an RNA world, and those worlds in which information is coded in binary strings compiled to programs that have the ability to self-replicate: an instance of "Artificial life". There is no question that this new field of Artificial life will necessarily be an inter-disciplinary one, straddling the "classical" fields of Biology, Chemistry and Physics, as well as the more recent field of Computer Science."

- *Biomimetics* (the imitation of natural design). The book *Biomimetics, design and processing of materials* by M. Sarikaya and I. A. Aksay gives a good overview of this field. From the index we can pick a few titles which gives insight into the main areas of this field: Soft biomaterials and structures, collagen composite systems, crystallography, morphology and formation, the inorganic-organic interface, microstructure of an insect cuticle and applications to advanced composites, artificial membrane interfaces, macromolecular design of spiders' silk, role of molecular genetics in polymer material science. Whereas the now mature area of medical engineering (bone prostheses, heart valves, replacement eye lenses and artificial blood vessels) has developed from a microscopic focus, biomimetics borrows approaches from the biological microscopic world and has its origin in research in biochemistry and in the mechanical properties of natural materials, especially fibers, tendons, bone and exoskeletons. Thus the study of biomimetics is firmly based in materials science (to read more see Imitating nature's design by R. W. Cahn in Nature **382**, 684 (1996)).

- *Device physics and learning systems* (www.vxm.com/21R.58.html, F.T. Hong)

  "Can a single molecule possess intelligence? The answer depends on what one means by intelligence. One tends to associate intelligence with what a human brain can do: perception, memory, thinking, problem solving, learning, innovation, creativity, etc. A personal digital computer can do some of these tasks and, in performing certain types of tasks, appears to surpass the human brain. But in terms of the more sophisticated aspects of intelligence such as pattern recognition in an ambiguous situation and creativity, a personal computer is no match even to a modest human brain. The recognition of these ultimate limits has inspired computer scientists to seek inspiration from biology. This is because a living organism operates with functional elements which are of molecular dimensions (about one thousandth of the size of a transistor) and which actually exploit quantum and thermal fluctuation phenomena. The hope of breaking the barrier of miniaturization seems to lie in the utilization of organic and biological materials, and the exploitation of their chemistry, and in the utilization of radically different computer architectures. This line of thinking has ushered in a new science and technology: molecular electronics, which is sometimes also referred to as nanotechnology. The new science and technology calls for research and development in three related areas: novel materials, novel fabrication technology, and novel computer architectures. These three aspects actually go hand in hand; the progress in one area depends on that made in the other two areas. Novel computer architectures require materials with extraordinary properties to implement, and new techniques to assemble the required "hardware." The entire field of molecular electronics thus requires joint, integrated efforts of scientists and engineers of different backgrounds; it is truly an interdisciplinary and multidisciplinary endeavor. Until recently, biomaterials have not been seriously considered for device construction because they were perceived as too fragile and not durable enough. A number of years ago, Nikolai Vsevolodov and his colleagues in the Institute of Biological Physics, Pushchino, Russia, excited the biomedical research community by producing the first imaging device and microfilm made primarily of biological materials and entirely organic materials (named the "Biochrom" film). The key substance in this device is bacteriorhodopsin. More recently, Robert Birge's group at Syracuse University has devoted considerable efforts to developing a high-speed optical random access memory based on bacteriorhodopsin. With the advent of genetic engineering, the intelligence of a biomolecule originally acquired through evolution can be further improved by breeding it in the laboratory in a much shorter time. Thus, molecular engineering will fast become one of the key technologies for the implementation of molecular electronics." For more on nanotechnology see *Nanofabrication of Biosystems*, eds. H.C. Hoch, L.W. Jelinski and H.G. Craighead (Cambridge University Press 1996).

- *Biological Physics Surface Science:* The rapid recent developments in molecular biology, biochemistry and biophysics provides new and challenging opportunities for surface science. Interfaces between simple inorganic or organic solid surfaces and biological systems are rich both in number and in their properties and phenomena. A systematic research approach in this field becomes extremely cross-disciplinary: it needs expertise from biology, medicine, chemistry, physics and materials science. Surface science plays a major role for the preparation, characterization and functionalization of surfaces to be used in the biological environment, but also to understand and describe interfacial properties and phenomena. When a piece of a solid is just placed in a living tissue a complex scenario develops at the new interface. The understanding and control of these processes are central to the successful development and use of medical implants and biosensors *in vivo*, advanced drug delivery systems, etc.

- *Nanotechnology for Molecular Manufacturing* (from RAND corporation home page www.rand.org)

  Nanotechnology–a term introduced in 1974 to describe ultrafine machining of matter–has come to be applied to a wide scope of small-scale engineering. With nanotechnologies, two activities are possible–nanomeasurement and nanomanipulation. Molecular manufacturing is the willful use of these two activities to create objects. Proponents of the application of nanotechnology to molecular manufacturing suggest that environmentally clean, inexpensive, and efficient manufacturing of structures, devices, and "smart" products based on the flexible control of architectures and processes at an atomic or molecular scale of precision may be feasible in the near future (i.e., 10-20 years from the present). The ambitious goal is to produce complex products on demand using simple raw materials; e.g., inserting the basic chemical elements in a molecular assembly factory to yield a common household appliance, perhaps with sensors and actuators built-in to respond to commands or environmental conditions. The question of whether it is possible to achieve a stage in the foreseeable future when such extreme capability might be viable, and if so how to develop the field, is a point of contention in both scientific and policy circles.

  The concept of manufacturing at the "nano" or atomic scale dates to more than three decades ago. Many developments in biotechnology, chemistry, computational tool building, electrical engineering, and physics have moved the scientific and engineering community closer to operating on the nanoscale. In addition to extensions of micromachining–with production methods such as lithography, commonly encountered for microelectronics or microelectromechanical systems (MEMS)–there have been recent developments in scanning force microscopes (SFM), using probes that can position atoms or molecules to nanometer scales, and interest in investigating the means by which complicated molecules with desired properties can be modeled, synthesized, and perhaps even self-assembled. These recent developments have motivated advocates of a "bottom-up" approach for manufacturing molecule-by-molecule.

  Exclusive use of this approach however, misses the longer-lived history and some of the benefits being achieved through the more familiar "top-down" approaches. The top-down approach is one in which macroscale components are utilized to create nanoscale structures. This differs from the bottom-up approach, which uses nanoscale components to create structures. In particular, top-down structures and methods might help with the interfacing of bottom-up structures into a system. Cases to support this position include chemical sensors that use microelectronics technology, biosensors that use enzymes and electrodes, and the potential of protein-based memory in an optical holography system.

  Useful means of positioning and interconnecting molecular structures might be created in the near term that could serve as a proof-of-principle that more ambitious molecular manufacturing may be possible. If meaningful molecular assembly (or more extensive modeling tools for rational molecular design) is not demonstrated in the next decade, then the field of molecular nanotechnology may well have encountered an impasse that will challenge the credibility of the practicality of molecular nanotechnology for a revolution in manufacturing concepts.

  Extensive molecular manufacturing applications, if they become cost effective, will probably not occur until well into the far term. However, some products benefiting from research into molecular manufacturing may be developed in the near term. As initial nanomachining, novel chemistry, and protein engineering (or other biotechnologies) are refined, initial products will likely focus on those that substitute for existing high-cost, lower-efficiency products. Likely candidates for these technologies include a wide variety of sensor applications; tailored biomedical products including diagnostics and therapeutics; extremely capable computing and storage products; and unique, tailored materials (i.e., smart materials using nanoscale sensors, actuators, and perhaps controller elements) for aerospace or similar high-cost/high-capability needs. The current development of MEMS devices may open avenues for incorporating molecular nanotechnological components into widely used systems, such as automotive parts.

  As indicated by the large number of U.S. research centers involved in molecular manufacturing and nanotechnology, the United States is a leader in this field. The majority of these centers are in academia and often consist of a few investigators in one or two departments. Identified activity represents a diverse set of basic or applied studies in materials properties. This is vital to providing the building blocks for a technology development. However, this is being done largely without a plan representing an organized, embracing systems-development goal of molecular nanotechnology.

  A key observation is that a number of countries are engaged in some level of effort relevant to the foundations of molecular nanotechnology. Although the United States has many groups performing work related to nanotechnology and molecular manufacturing, there are several strong competitors and potential collaborators. Japan has large efforts that are funded individually at a significantly higher rate than their U.S. counterparts and are coordinated by a dedicated national effort. Other nations with strong research centers include China, Denmark, France, Germany, Russia, Sweden, and the United Kingdom.

It is unclear which fabrication method will best succeed–multiple research paths should be left open at the basic and applied research level. Areas that are important to the future of molecular nanotechnology-based advanced manufacturing, and in which successful discoveries could serve other applications in the interim, include the following:

- Macromolecular design and folding
- Self-assembly methods
- Catalysis (inorganic, enzyme, and other)
- Dendrimers, fullerenes, and other novel chemical structures
- Bioenergetics, nanobatteries, and ultrasound-driven chemistry
- Semiconductor-organic/biological interfaces
- Miniaturization and massive parallelism of SFM
- Molecular modeling tools.

The potential is enormous and could lead to extreme miniaturization in space systems, capabilities in human performance enhancement and medical treatment, as well as ability to manufacture a wide variety of sophisticated products on demand. It might be expected that if sufficient applied science checkpoints are passed, then manufacturers would be motivated to pursue development of applications.

Past experience with translating science into practical engineering provides cautionary examples as well as successes. In principle, civilization can make use of controlled nuclear fusion as an immense source of energy in analogy with nature's application of various fusion reactions to power stars. However, the reality of achieving this has been much more difficult than originally anticipated. Similarly, achieving the manufacture and control of sophisticated molecular nanodevices from current conceptual designs may be more difficult than anticipated.

A fully credible assessment of how far molecular manufacturing will progress in the next two decades is not possible until incremental steps have been undertaken, although tentative indications appear positive. At present, modeling and theoretical underpinnings need to be further developed. Demonstration of assembly, control of chemistry, and practical component creation and integration are important. The laboratory development of several steps should be closely followed for indications that milestones can be expected:

- Produce material parts at the nanoscale.
- Process material parts into components at the nanoscale.
- Order molecular components into structure and interconnect.
- Interface system components with the macroenvironment.
- Control a massive collection of miniature parts and systems.
- Provide a power system.

The many laboratory steps needed indicate that a careful decision on development policy, if any, should be made. There are several options:

- Maintain a laissez-faire policy toward coordination of research efforts and resources.
- Conduct a detailed, objective working group technology assessment of the state of the art of relevant molecular nanotechnology research and potential applications.
- Establish a coordinator or program to oversee research and developments.
- Create a national or international cooperative effort.

To prevent the possibility of technological surprise, yet not prematurely enact policies that commit funds and valuable resources, a prudent course of action would be to create a working group of biotechnology experts, chemists, computer scientists, electrical engineers, materials scientists, mechanical engineers, and physicists. This group's assessment of a laissez-faire posture versus coordination and cooperation should then be implemented as a basis for a rational policy about support for molecular nanotechnology.

Although there has been much encouraging theoretical and conceptual study of the advanced manufacturing potential of molecular nanotechnology (and panel reports and surveys of expert opinions), a comprehensive, detailed technical assessment by a multidisciplinary, objective expert working group is lacking and should be conducted to determine engineering feasibility. The role of ultrafast phenomena in manufacturing methods and the issue of what applications these could address can be included in conjunction with an assessment of nanoscale technologies (as a secondary focus of how to exploit extreme-scale phenomena).

A positive finding from such an assessment would indicate that cooperation at the basic and applied research level beyond the present situation should be organized. Increased coordination of research funds may improve the cost-effectiveness by reducing redundancy; however, such increased organization should be done in incremental steps so that it does not come at the expense of healthy competition. A negative finding from such an assessment–such as low engineering feasibility; low potential for viable, near-term application; or limited prospects for critical research progress–would strongly indicate that the current levels of funding and structures for basic scientific research in molecular-based nanotechnology is appropriate and that extensive resources should not be dedicated to developing specific pathways."

A section on nanomanufacturing would not be complete without mentioning the fundamental work by K. E. Drexel: Nanosystems: molecular machinery, manufacturing and computation. The space is to limited here to give it full justice. Appendix M contains a detailed index of the book and we give here only the major chapter headings to give a full flavor of the breadth of the approach (www.zyvex.com):

- Preface
  - Chapter 1 Introduction and Overview
- PART I PHYSICAL PRINCIPLES
  - Chapter 2 Classical Magnitudes and Scaling Laws
  - Chapter 3 Potential Energy Surfaces
  - Chapter 4 Molecular Dynamics
  - Chapter 5 Positional Uncertainty
  - Chapter 6 Transitions, Errors, and Damage
  - Chapter 7 Energy Dissipation
  - Chapter 8 Mechanosynthesis
- PART II COMPONENTS AND SYSTEMS
  - Chapter 9 Nanoscale Structural Components
  - Chapter 10 Mobile Interfaces and Moving Parts
  - Chapter 11 Intermediate Subsystems
  - Chapter 12 Nanomechanical Computational Systems
  - Chapter 13 Molecular Sorting, Processing, and Assembly
  - Chapter 14. Molecular Manufacturing Systems
- PART III IMPLEMENTATION STRATEGIES
  - Chapter 15. Macromolecular Engineering
  - Chapter 16 Paths to Molecular Manufacturing
- Appendix A. Methodological Issues in Theoretical Applied Science
- Appendix B Related Research
- Afterword
- Symbols, Units, and Constants
- Glossary

VI. MEDICAL PHYSICS

Medical Physics began to emerge as an interdisciplinary field some thirty years ago and describes a wide range of activities in which the disciplines of engineering and biological or medical science intersect. Representative areas include: design of diagnostic and therapeutic devices for clinical use; development of biologically compatible materials; application of state of the art technology to answer biological questions; and many others. The use of free electron lasers (using electrons not bound to atoms as in a conventional laser) is growing in the field. Such a free electron laser is planned to be part of a new material analysis laboratory at our School of Physics and Engineering Physics and a good idea is that this could be an important device to merge the interests of our faculty and the medical one and others doing biosciences.

Medical Physics is a field which is much more vast than Biological Physics (Altavista gives a hit-ratio of 8:1). Biomedical engineering is taught at more than 70 U.S. colleges and universities. We have concentrated on Biological Physics in our report since this is the area of closest interest to us and one which should mature within our own organization. Medical Physics takes a much larger coordinated effort and rightly so. It is in fact a wonderful chance for Chalmers University of Technology to find an area of close collaboration with the Medical Faculty at Göteborg University as we suggests in this report and to unite efforts from all directions rather than each section having their version of a similar education or trend in research. Such a program has also the potential for a wonderful cross- fertilization between different levels and cultures. Just look at the impressive list of areas covered by the 45 professors associated with The Institute for Medicine and Engineering (IME) at the University of Pennsylvania, in Philadelphia, US:

radiology, biophysics, medicine, neurosurgery, mechanical engineering, applied mechanics, bioengineering, electrical engineering, microbiology, computer and information science, rheumatology, materials science, pathology, laboratory medicine, biochemistry, biophysics, chemical engineering, applied mechanics, pharmacology, psychiatry, anesthesia, genetics, biology, environmental medicine, physiology, pediatrics, orthopedic surgery, chemistry, neurosurgery, cell biology, developmental biology, physics and electrical engineering.

Right now we have in the Göteborg area several activities with a physics content which could participate in forming such a common educational and research effort in *Medical Physics* together with the School of Physics and Engineering Physics and the Medical Faculty:

- *Department of Medical Biophysics (Medicinsk Fysik)*, Medical Faculty. Main activities are studies of function and properties of ion channels in lipid bilayers and in cell membranes, synaptic plasticity, regulation of hormone secretion and cellular response to (low frequency) electromagnetic fields.

- *Department of Radiation Physics* School of Physics and Engineering Physics, has been thoroughly covered in section 3.1.3 and this department would be a key player in coordinating a medical physics venue.

- *Polymeric Materials division of Biomedical Engineering* in School of Mechanical and Vehicular Engineering.

- *Biostatistics group* in School of Mathematical and Computing Sciences. See section 3.1.2 and Appendix F for more details.

- *Department of Injury Prevention* in the School of Technology Management and Economics. Within this area one studies the conditions for human interaction with technology. Courses given have titles associating with this: Man-machine systems, Human factors in production, Risk management and safety, and Man and technology in the industrial environment. The goal is to find the optimum conditions where human preferences, needs and capacity is of importance. The modern engineer has to be able to handle technical systems and products and to tailor them to human capacity and needs. Two typical research projects are Development of a mechanical dummy for measurement of violence and Research about accidents and risks in technica systems.

- *Electrical and Computer Engineering (bioengineering)* at Chalmers: The biomedical engineering group applies systems engineering techniques to clinical medicine. One key effort in this area is to tackle real world problems which challenge engineering tools and methods. Research activities focus on human motor system modeling and identification, respiratory system modeling and control, robust dynamic distributed information handling and adaptive signal conditioning in hearing aids. The main actor is the Medical Electronics group within Department for Applied Electronics. They mainly deal with Human motor system (pathological tremor; identification and modeling, motor strategies in simple and complex movements and motion analysis for diagnosis and as therapeutic control tool), Neonatology (lung function monitoring during respirator treatment and lung mechanics; non linear modeling of the most immature lungs), Neurology (real time fluorescent imaging-based analysis of astrocyte functions and neuromagnetic based studies of brain functions), Bone anchored hearing aids (optimizing the hearing aid for bone conducted sound and noise cancellation techniques for hearing aids), and Imaging and image analyses (three dimensional reconstruction of heart structures based on echocardiographic signals). Methods and techniques are oriented towards system identification, adaptive signal processing and modeling, and signal parameter estimation. Certain courses in this department are open to both undergraduate and graduate physics students.

  Closely associated with this group is

- *Foundation for Biomedical Engineering* (kaj@ae.chalmers.se) which was established in 1985. The role of the foundation is to promote clinical use and commercialization of the biomedical research at Chalmers University of Technology and University of Göteborg. The ways to accomplish this varies, ranging from knowledge transfer via partnership in development projects, to full responsibility for creation of spin-off companies. Since 1994, the Foundation has a special focus on medical systems engineering, medical informatics, and telemedicine. Current projects in this area are: Health emergency care through telematics operational resources and Signal archiving and communication system.

- *Medical Physics and Engineering* a division at Sahlgren Hospital. Contains the following sections: Terapeutic Radiation Physics, Diagnostics, and Medical Engineering Department. They form a link between radiation physics, technology and clinical work.

When it comes to medical physics several university colleges in Sweden have started with biomedical engineering education in collaboration with health colleges. Royal Institute of Technology and Karolinska Institutet has agreed to cooperate within the area of biomedical technology. It amounts to half a year of courses for most engineering branches at the Royal Institute. Also Stockholm University is involved in this project. However we do not have to look far away to already find an embryo of such an education in the context of three year engineers at University of Borås: The program started 1997. First year is common with other engineering educations to give a solid science basis, a second year is added with specific basic courses and a specialization towards electronics and biomedicine during year three.

As stated above there are many venues for starting a broad effort in Medical Physics. One way would be to study in depth someone who is just about to start or is close to us in spirit or way of working. University of Pennsylvania is such a partner where we already have the possibility of exchanging students on a small scale. It is therefore of interest to take a closer look at its educations in Biomedical Engineering (Engineering Faculty) and the Master in Medical Physics (School of Arts and Sciences) as well as its Institute for Medicine and Engineering (IME).

The IME was established in 1996 jointly by the School of Medicine and the School of Engineering and Applied Science. Its focus is on interdisciplinary research and education fundamental to the application of advances in the treatment of disease. Emphasis is on the integration of the engineering/computational/technological sciences into biomedicine, particularly at the cell and molecular levels, and the application of interdisciplinary studies to clinical medicine.

Biomedical engineering at Penn prepares students for leadership in bioengineering enterprise in industry, government and non-profit organizations involved in the development and sale of advanced biomedical technologies. The Program's flexibility allows students to shape the curriculum to their career goals in industry, government or health-care systems. Courses are drawn from four different areas:

Biomedical engineering fundamentals: These courses cover how to: Build, test, and validate analytical models of biological systems. Measure biological events and activities. Design experiments. Process and analyze experimental data. One course in biomedical engineering fundamentals is devoted to analytical methods and modeling; and one is devoted to experimental methods and data analysis.

Biomedical science: Biomedical engineering research requires deep knowledge of living systems and organisms. Each student takes an advanced cell biology course in biomedical engineering in addition to an elective that matches the student's interests and intended career path.

Biomedical technology development: Specially designed professional business courses set this program apart from other biomedical engineering masters programs. These courses provide students with a full understanding of the process involved in taking a new technology from the laboratory to the marketplace and a complete awareness of the procedures and strategies needed to develop a company around that new technology.

Engineering: Each student can tailor his or her biomedical engineering applications courses to their interests and intended career path.

Bioengineering research includes programs in the Department of Bioengineering, the School of Engineering and Applied Science, and the new Institute for Medicine and Engineering (IME); in the University's medical, dental, and veterinary schools; and in four research oriented hospitals, all of which are located on campus.

Major facilities located within the department and the School include laboratories for biotransport, biointerfaces, tissue engineering and biomaterials, cellular biomechanics, computational neuroscience and neuroengineering, vision studies, electron optics, materials testing, surface analysis and extensive computer facilities. Special purpose laboratories in the health and life sciences exist throughout the University. Those most involved in bioengineering research include the Auditory research laboratory, Rehabilitation engineering, Hyperbaric chamber facility, Neuroscience laboratories, Ocular measurement and laser laboratories, Medical imaging laboratories, McKay orthopaedic research laboratory, Cardiothoracic surgery research laboratory and Anesthesia research laboratories.

Another way of obtaining a degree in the biomedical field at Penn is to take a Master of Medical Physics. The School of Arts and Sciences is establishing a new professional degree, the Master of Medical Physics. The purpose of the Master of Medical Physics degree is to meet the academic and career interests of a class of technically prepared college graduates who seek to combine their interests in graduate physics with career opportunities in the medical research and clinical environments. Medical research and clinical treatments at Penn and other top medical schools and hospitals utilize and concurrently develop advanced technology. The field of medicine now requires a supply of highly educated and well trained problem solvers to aid in research, help develop new technologies and maintain existing high technology clinical equipment. The Master of Medical Physics program will aim to provide the graduate students with a rigorous graduate physics training in essential graduate physics courses, balancing classroom and laboratory experience, as well as more traditional coursework in medicine and biology. The traditional problem solving techniques emphasized in physics graduate training will enable students to address a wide variety of problems encountered in modern medicine and to evolve as the field of medicine continues to change at a rapid pace. In conjunction with the Departments of Radiology and Radiation Oncology in the medical school, the Master of Medical Physics program will aim to train students in the essentials needed for a physicist to function in a medical environment comprising doctors and medical professionals. The program will introduce them to research and bring them into contact with state-of-the-art medical technologies. Students will be admitted to the program if they have a Bachelor's degree in physics, chemistry, mathematics, biophysics or engineering, or if they have a Bachelor's degree in another discipline that provides enough background training such that graduate physics courses could be sucessfully completed after one or two semesters of undergraduate courses at Penn.

Each student will choose courses from the following list. The additional course requirements will be chosen in consultation with the student's advisors.

Eight *required courses*: Quantum mechanics I, Electromagnetic theory I–II, Advanced laboratory, Mathematics for medical imaging, Quantitative human physiology, Medical radiation engineering, Diagnostic and biomedical imaging and Applied radiation dosimetry. Additional suggested *optional courses* include: Advanced cell biology, Genetics and biology, Physical and quantitative biochemistry methods, Current biochemical topics, Topics in biological physics, Measurements (electronics) laboratory, Nuclear medicine physics, Mechanics, fluids, chaos, statistics for biologists, Modern optical physics and spectroscopy, Introduction to solid state physics, Computer methods in mathematical science I and Gross human anatomy.

During the first year, the student will be required to attend a non-credit seminar series called Introduction to Medical Physics. The series will be clinically oriented and will survey the Imaging Areas and Radiation Oncology. The purpose of the seminar series is to introduce the student to the possible areas of concentration and the faculty involved in those areas. It is through these seminars that the student pairs up with a faculty member who will direct the student in Practical Training. There are two periods during which the student receives exposure to the clinical setting and advanced medical technology in use in the hospital. Independent study during the summer will allow the student to concentrate on a particular Imaging technique or on Radiation Oncology in one of the following areas: Ultrasound, CT, MR, PET/SPECT, X-ray or Radiation Oncology. Each student will have two advisors, one in the Department of Physics and Astronomy and one in either the Departments of Radiology or Radiation Oncology.

We see how close the Penn structure is to our own of dividing very similar educations in an engineering version and a physics version. Appendix N give more details about the course content.

Another representative example to study more closely is the School of Biomedical Engineering at Indian Institute of Technology, Mumbai, India. This is a school having engineering physics as ourselves and is one of the leading technology universities in a land of 960 millions. It also has a School of Biotechnology. The schools admit students from various backgrounds including Engineering, Medicine and Life Sciences. The faculty is interdisciplinary.

The program in Biomedical Engineering routinely admits students with backgrounds in Engineering, Life Sciences, Medicine and Physical Sciences. They are required to go through core courses on Engineering Mathematics and Linear circuits and systems while the students with background in physical sciences and engineering go through courses on Physiology for Engineers. All students are also required to present a seminar on a topic related to Biomedical Engineering under the guidance of a faculty member. In the second semester students with backgrounds in Physical Sciences and Engineering go through a core course on Clinical Physiology. Besides this all students has to go through a core course on Biostatistics and Design of Experiments. Students start on their M.Tech Project and finish their first stage in the second semester itself. In the third and final semester the students are not required to go through any course work and devote their full time for the MTech Project.

All Student read Physiological measurements and quantitative physiology, Cell physiology and biopotentials, Signals and systems for biomedical engineering, Medical imaging physics, Electrodiagnostics, therapy and electrical safety, Biomaterials, Medical sensors, Biostatistics, Biorheology, Introduction to medical informatique, Molecular basis of disease processes, Medical instrumentation, Physiological system modeling, Bioelectricity, Biomedical fluid dynamics and ergonomics. (see Appendix N for more details).

VII. EDUCATIONAL PROGRAM - PROPOSAL

This section contains the motivation for and the direct proposal for an undergraduate program in *Biological Physics*. We outline a possible scenario for starting up such a program and we give recommendations for the special characters it should have.

A. Important factors

It is our definite view that the program has to start on all levels simultaneously (undergraduate - graduate - research). The program as such must have a strong physics profile; it is a physics education after all. Furthermore the program shall provide a good training in three disciplines (mathematics, physics and biology) and at the same time provide the students with a good feeling for "Biology" as a science in itself. All this has to be done with intellectual rigor and it has to lead to an intellectual leap for the students. Any choice the students can make to create their own profile has to be tied to major research directions in the School of Physics and Engineering Physics or at other departments at Chalmers or Göteborg University. The education must include experimental techniques and new ways for developing interpersonal skills. We have to be especially careful about the notion among biologists that many physicist think that once the structure is there - function is implicit. We rather have to stress the interplay between those two aspects. Over-lap with medicine, biomedicine, pharmaceuticals and classic biology has to be chosen according to maximum benefit within the structure at Chalmers/Göteborg University. Furthermore we need to provide the students with an understanding of molecular biology concepts from a physics standpoint. We thus need to create a common platform for the description of e.g. model systems, cell communication, transport and diffusion. We should furthermore combine molecular biology, mesoscopic systems and self-organizing systems to fully benefit from the research we already have in place. Special considerations should be taken with respect to the explicit profile of Göteborg University stressing environmental physics.

B. New ways of learning and teaching; the third culture and the fifth discipline.

A bald step in creating a new educational program would be to take as a starting point *The Fifth Discipline* (The art and practice of the learning organization) by Peter M. Senge (Currency Doubleday, New York 1990) and *The Third Culture* (beyond the scientific revolution) by John Brockman (Simon & Schuster, New York (1995)) in order to figure out new and important ways of enhancing the learning experience and the construction of a new organization within an old one. Synge stresses five items in order to create a good learning organization which we see as important also for a new education in *Biological Physics* :

1. *Personal Mastery* (personal mastery is the discipline of continually clarifying and deepening our personal vision, of focusing our energies, of developing patience, and of seeing reality objectively, to focus and to be devoted). Emphasis on personal development.

2. *Mental Models* (mental models are deeply ingrained assumptions, generalizations, or even pictures or images that influence how we understand and how we take action). To understand how we learn.

3. *Building shared visions* (One is hard pressed to think of any organization that has sustained some measure of greatness in the absence of goals, values, and missions that become deeply shared throughout the organization). Create such an atmosphere.

4. *Team learning* (when teams are truly learning not only are they producing extraordinary results but the individual members are growing more rapidly than could have occurred otherwise). Balance between this and individual mastering.

5. *Systems Thinking* (systems thinking is a conceptual framework, a body of knowledge and tools that has been developed over many decades, to make the full patterns clearer, and to help us see how to change them effectively). Notice emphasis on over-view and control.

It is vital that the five disciplines develop as an ensemble. This is challenging because it is much harder to integrate new tools than simply apply them separately. But the payoffs are immense. This is why systems thinking is the fifth discipline. As the five components of learning disciplines above converge they will not only enhance the learning organization but also create a new wave of experimentation and advancement.

" *The third culture* is about the transition taking place today where scientist and other thinkers takes the place of traditional intellectuals in rendering visible the deeper meanings of our lives, redefining who and what we are. In the past few years, the playing field of e.g. American intellectual life has shifted, and the traditional intellectual has become increasingly marginalized. A 1950's education in Freud, Marx, and modernism is not a sufficient qualification for a thinking person in the 1990's. In 1963, C. P. Snow suggested that a new culture, a "third culture", would emerge and close the communications gap between the literary intellectuals and the scientists. But literary intellectuals are not communicating with scientists. Scientists are communicating directly with the general public. What we are witnessing is a passing of the torch from one group of thinkers, the traditional literary intellectuals, to a new group, the intellectuals of the emerging third culture. The ideas presented in *The Third Culture* are speculative; they represent the frontiers of knowledge in the areas of evolutionary biology, genetics, computer science, neurophysiology, psychology, and physics. Some of the fundamental questions posed are: Where did the universe come from ? Where did life come from ? Where did the mind come from ? Emerging out of the third culture is a new natural philosophy. There is a new set of metaphors to describe ourselves, our minds, the universe, and all of the things we know in it, and it is the intellectuals with these new ideas and images who drive our times". It is necessary for our new education to reflect upon this dramatic change in the role of science and its interaction with the common man."

It is our intention to weave in those more philosophical questions in the curriculum and at the same time develop the individual itself and in collaboration with others. We therefore suggest that time is also devoted to such topics as group dynamics, communication knowledge and conflict management. Especially since the students of *Biological Physics* will interact with people from other scientific disciplines. This could either be provided by School of Technology Management and Economics or made together with the new branch at Chalmers devoted to Technical Communication, starting 1999. The latter will have courses such as Knowledge, communication and multimedia (5 credit units), Project Management (5), Human-computer interaction (5) and Professional writing and oral presentation (4). Another alternative is a collaboration with the education in Management of medical technology at Södertörn University (economy/medical technology/applied physics). It would also be possible, and highly interesting, to include such a program within an actual course on human physiology which touches upon the brain and consciousness.

Another important aspect to add to the program is to be able to encourage entrepreneurial instincts, overview and total responsibility though extensive projects and a curriculum which is holistic rather than divided into tiny units that makes any overall understanding impossible. There is an old and well developed way of doing this, originating at Massachussetts Institute of Technology in the 60's called UROP which stands for Undergraduate Research Opportunities Program. It was the first program in US to have issued undergraduates a broad and open invitation to participate in research as the junior colleagues of faculty. It was created in 1969 by the late Margaret L. A. MacVicar, Professor of Physics and MIT Dean for Undergraduate Education, UROP was inspired by Edwin H. Land, inventor of instant photography, who believed in the power of learning by doing.

Undergraduates may participate for credit, receive stipends, or work as volunteers. All projects must be worthy of regular MIT academic credit, regardless which mode is chosen. UROP projects, which students can begin any time during the term and continue full time in the summer, frequently last up to a year or more. Opportunities exist in all MIT's academic departments and interdisciplinary laboratories.

Students choose UROP projects to learn about a potential major, investigate an interesting area outside a major, gain practical skills and knowledge for a possible career or graduate school experience, to get to know faculty, to find out what research is like, or because they find a particular area to be exciting and challenging. At Chalmers we have previous experience of this and the engineering physics students are already today doing this, however on a very small scale compared to what we have in mind.

Finally, in line with the reasoning above, a proposal should be submitted to the Council for the Renewal of Undergraduate Education for a study related to the implication of a management technique and a new vision of the role of science in society when starting a new venue of research and education within an old organization.

While designing a new program we should also utilize the possibility of merging students entering either from Engineering Physics side or from the Physics program side. We should also stress the possibilities of entering a PhD program before finishing the under-graduate program in order to both shorten the total study time as well as bring out younger PhDs than we presently do. This task is most easily accomplished by integrating the program within the international master's program at the school of Physics and Engineering Physics - Nanophysics, with its special branch in Biological Physics.

C. Proposal

We list in this section the different items which we would like to propose based on the discussions above and the material presented in this working plan. We first summarize the overall structure in the form of a table shown below. Six crucial factors for our proposal are:

- we do not seek a multi-disciplinary education. We want students fully trained in mathematics and physics to be able to meet as qualified students in medicine and biology, in their disciplines.
- we want to see younger PhDs coming out of our system.
- the basic courses should be developed as a collaborative effort between physics and medicine/biology teachers.
- most work is done in the way of projects.
- every student should be assigned a research group to participate in.
- the curriculum in *Biological Physics* should avoid fragmentization.
- the whole approch is based on an atomistic view of the world

Table 1. A plan for the combined branches of Engineering Physics and Physics Education to meet in Biological Physics following the master's program in Nano-physics at the School of Physics and Engineering Physics.

Year	*Chalmers*	Common	*Göteborg Univ.*
1-3	physics, techn. and math.	- -	physics and mathematics
4a	electives (PhD courses)	master's prgrm (PhD courses)	electives (PhD courses)
4b	electives (PhD courses)	biol. physics (PhD cour./MSc)	MSc thesis (-)
5a	MSc Thesis	MSc Th.(PhD c)	PhD courses
5b	PhD work	PhD work	PhD work
6	PhD work	PhD work	PhD work
7	PhD work	PhD work	PhD work
8a	PhD work	PhD work	PhD work
8b	PhD in physics	left or right	PhD in phys.

B.Sc corresponds to 1.5 years of physics courses and a thesis corresponding to 1/4 year. M.Sc. corresponds to 2 years of physics courses and 1/2 year thesis work (or 1/4 + 1/4).

Detailed proposal:

1. In the information material for *Biological Physics* it should be stated very explicitly that it is primarily a physics education (this is also a definite demand on all courses entering the program), where biological and medical systems forms an important area of study. This implies the students must have a solid and deep base in mathematics and physics

2. It is absolutely necessary to have a close pooling of resources between the three programs in Engineering Physics, Physics and the International Master Program (Physics and Engineering Physics - Nanophysics) and our graduate school(s). We achieve this goal best by having the students following the international master's program in Nanophysics.

3. One year of *Biological Physics* is offered to students being in their fourth year of study. It should be on such a level that it can be the basis for a thesis work. With their solid training in basic physics as a base the graduates from such a *Biological Physics* training should have a very different profile from Biotechnology graduates, both very useful and badly needed. In order to avoid fragmentation the core of these courses are under the heading of *Living State Physics* (15 credit units) whose major components are introductions to Biophysical chemistry, Molecular Biology of the Cell, Human physiology, and Spectroscopies, Sensors and Actuators (see Appendix P). The course is supposed to give a good balance between experimental, engineering and theoretical aspects. This will all take place within the framework of the branch Biological Physics within the international master's program offered at our School of Physics and Engineering Physics.

4. For a *Medical Physics* education we suggest the students follow the courses offered by the Department of Radiation Physics, in waiting for an overall study being undertaken incorporating all of Chalmers and Göteborg University, especially the medical faculty to create a common program in *Medical Physics*.

5. The basic block in *Living State Physics* is to be complemented by elective courses where at this moment we would like to stress choices in the following areas: Biostatistics, Radiation Physics, Biomaterials, Biosensors and -electronics, and Dynamical Systems since those are the ones having the best research facilities, potentials and what is most important a direct coupling to *physics*.

6. It is important in this new education set up to also stress social competence and learning to work in a group environment. This will be achieved by introducing courses from School of Technology Management and Economy and the international environment provided by the master's eduction it is attached to.

7. It would be useful for other teachers if examples and problems from *Biological and Medical Physics* were made accessible also to other courses in the first three years.

8. Every student is assigned to a research group which will be hers/his *home* during the studies at Chalmers and Göteborg University.

9. A strategic alliance with other major international players in the field of *Biological Physics* should be investigated. Right now we have in mind Imperial College (London), ETH (Zürich), University of Pennsylvania (Philadelphia), Tokyo University of Agriculture and Technology and Indian Institute of Technology (Mumbai).

10. At the outset we should start the planning of a complete education leading to a Master in *Biological Physics*. In such a way we can both offer highly trained Biological Physics Physicists within 2 years from now (now entering Engineering Physics or Physics) and at the same time we can build up a new branch of Engineering Physics and the Natural Science School combined, where the first genuine Biological Physics Physicist (starting 1999) will graduate 2003. We imagine that the classes are a mixture of physics minded and engineering minded students. Another solution would be separate programs but shared courses.

11. In the new program mentioned in (10) the students will basically have the mathematics and physics of the Engineering students replacing technology with biology. The present Engineering Physics courses will be grouped into larger units than presently and more of the material will refer to examples and references taken from biological and medical systems.

12. At the same time as we offer our own physics students a deeper insight into Biology and Medicine we should offer a course in Physics for biological and medical students at Göteborg University (see Appendix P).

Once the board of School of Physics and Engineering Physics have made a commitment of that we should go in the proposed direction, more detailed course and program plans will be set up.

VIII. RESEARCH PROGRAM - PROPOSAL

In this section we give some major points about how a research program in *Biological Physics* should be supported and how it should be able to develop freely.

A. Important factors

The true foundation for research in this area is a strong belief that physics can make impact in life sciences and that it has something new to contribute. This means that we do not see it as a realistic platform to enter this field based on the suspicions that Biology will eventually be stuck without physics techniques and that the theoretical development is hampered because of that the biologists do not have the necessary math. This might be the case but cannot be the foundation for our research efforts. For us it is the interplay between structure and dynamics and the intriguing complexity which draws our attention as physicists. Of course this does not mean that our biology friends will welcome us with open arms. The biggest barrier is probably their inability to see what we can offer or that we cannot present clearly what we offer. The only way to progress is then to establish contacts with well established researchers in biology (who can see opportunities rather than threats) or very young ones. We have a responsibility in the educational part of the program to train our student to speak "bio language". We have not found it important to already from the outset discuss and speculate about some major common directions for the program, even if this was one of the tasks given to us. Rather we think that a development of the present basis in *Biological Physics* together with a dialogue with Biology, Chemistry, Physics, Mathematics, Computer Science and Information Technology will slowly evolve our research efforts in a way like the development of an organism.

B. Research

In this section we specify our direct suggestions and proposals.

1. Graduate school

Our graduate program should be complemented in such a way that a reasonable volume of graduate courses are available in *Biological Physics*, totally coordinated with all the other graduate programs and schools around. We do not suggest a separate PhD in *Biological Physics and Medial Physics.* The graduate students we have will be Physics PhDs working in the traditional groups and departments we already have.

2. Proposal

1. To have a sucessfull academic education in *Biological Physics* a research program is necessary to give sufficient depth and support when entering higher levels.

2. The competitive edge we have at Chalmers and Göteborg University will automatically progress an area which is the *meeting place between molecular biology, condensed matter, surface physics and mesoscopic physics.*

3. We suggest that instead of announcing a new professor in *Biological Physics* we should start from the activities already present and supplement them with dedicated young people.

4. Other faculty should be encouraged to join groups working in the area. Invited key persons, post-docs and guest scientist will keep the activities at a high international level.

5. The area of *Biological Physics* will be an identifiable branch of research and teaching within the School. This requires dedicated, long-time, support.

6. There is probably no need for a new Phd or Licentiat in *Biological Physics.* Existing graduate programs will, however, offer new courses in *Biological Physics* to all PhD students and research projects are performed in already existing groups. The time for obtaining a PhD should not be longer than eight years.

7. Any coordination of the present resources and interest in *Biological Physics* will develop best if left alone without unnecessary umbrella organizations or the creation of new departments at this stage. The start-up of the program is best made in the form of a project with continous follow-up and evaluation.

8. Based on this work plan we will need resources of the order of 82 (48) millions during a five year period.

9. We suggest that the school of physics and engineering physics approach the Chalmers foundation for a large scale support of *Biological Physics.*

10. Strong areas within our section in the area of *Biological Physics* are biomaterials, surface biophysics, complex systems, polymer- and nanophysics.

In the interplay between these points a program in *Biological Physics* will grew in an organic way and any umbrella organization or alike will naturally occur when the time is ripe; perhaps even a professor in Living state physics. The only constraint we would like to impose is the existence of a good home page under the School of Physics and Engineering Physics describing our common efforts in the area of *Biological Physics*.

IX. BUDGET AND TIME-PLAN (1999-2003)

In this section follows a short overview of the main resources needed in order to have the program to fly by itself after five years. The main funding source is supposed to be the Chalmers Foundation capital. Especially since the statures of this indicate that the money shall be used for investment in new programs, changing faculty structure and research renewal. All those aspects can be coupled to our proposed program in *Biological Physics*. The program is already underway by the research activities we have in the field and the work plan we are presenting.

Alternative 1

This alternative allows for a quick pace in developing the program. It will take about four years. Main components are:

1. six new graduate students per year during four years.
2. number of post-docs in the system during the first four years: 2, 4, 6 and 8.
3. number of research assistants in the system: 1, 2, 4 and 4.
4. number of guest scientists: 1, 2, 2 and 2.
5. a formal start of a new program in *Biological Physics* fall of 1999 or 2000 (20 students, 800 kkr per year; total of 8 millions)

For researchers with cost for equipment and maintenance this alternative will need a budget of about 8, 14, 18 and 22 millions for the first four years. The necessary infrastructure development cost is estimated to 5 millions per year on average. The total amount needed is then 82 millions. This budget should possibly be used over a little longer period depending on hiring capacity.

Alternative 2

This is less expensive and is under-critical like most of our earlier projects in physics:

1. A formal start of a new program in *Biological Physics* fall of 1999 or 2000 (20 students, 800 kkr per year; a total of 8 millions).
2. A guest professor and four post-docs (14 millions).
3. During 1999-2002 8 PhD positions are announced (total cost 19 millions).
4. The hiring of 3 young researchers (1999-2001; 7 millions).
5. Invite guest scientists/lecturers to take part in this study and offer a pilot course in *Biological Physics*. Secure a quick start, which is urgent. (150 kkr - already allotted).

   The total estimated cost for initiating this program is thus 48 Mkr, distributed as 5 Mkr (1999), 8 Mkr (2000), 11 Mkr (2001), 12 Mkr (2002) and 12 Mkr (2003). Part of this money will be coming from the regular student money within the system.

   The program should be evaluated continuously. After 2003 we should be able to completely absorb all the costs associated with the *Biological Physics* education and research program within the regular (enlarged) financial program of our own section.

Questions to be further analyzed

The basic proposal is a start in the fall of 1999 for engineering physics, physics, masters program and graduate studies. This proposal also implies such a heavy investment in basic research that external funds have to be considered. Especially Chalmers Foundation capital. A number of questions need more deliberations before we can embark on the new program:

1. The name *Biological Physics* have to be discussed further. Of marketing reasons it could be important to include "engineering" in the name, e.g. Bioengineering physics for our engineering students.
2. The amount of biological physics during the first years has to be large enough to give the students a substantial insight into the area. At least a couple of courses per year is needed.
3. The research profile we eventually end up with has to be a careful balance between what we have, what we want to have and local synergetic effects with other sections and faculties at Göteborg University, and international networks.
4. Any money applied from Chalmers Foundation has to be focused on a) positions limited in time (guest scientists, research assistants, post-docs and graduate students) and b) infrastructure.
5. How will we cover our costs when the initial investment phase is over ?

ACKNOWLEDGMENTS

Discussions with Eugenie Mielczarek, Göran Niklasson, Lars-Göran Rosengren, Elias Greenbaum, Robert S. Knox, Russel K. Hobbie, Mort Sternheim, George Benedek, L. Jelinski, Anders Vedin, Göran Wendin and Bengt Lundqvist, were most helpful.

APPENDIX A - MISSION AND PROJECT GROUP

The Board of the School of Physics and Engineering Physics decided at its meeting May 21, 1997 to form a project group to implement its earlier decision of April 23, (1997) that the area Biological Physics should be one of the profiles of the School with a forceful and long term effort for its realization. The group has to its disposal 150.000 SEK to produce a detailed project plan, to invite guest scientist and lecturers and to initiate research and courses within Biological Physics. The dean decides the following project group:

- Magne Alpsten, Radiation Physics (magne.alpsten @radfys.gu.se)
- Peter Apell, Applied Physics (apell@fy.chalmers.se).
- Lars Brink, Theoretical Physics and Mechanics (tfelb@fy.chalmers.se).
- Maj Hanson, Experimental Physics (maj.hanson @fy.chalmers.se).
- Claes Holmberg, WermTec Gothia AB. (claes.holmberg@mediteam.se)
- Bengt Kasemo, Applied Physics (kasemo @fy.chalmers.se).

To include views from students, other sections at Chalmers and to allow for a larger flexibility, the group is later extended (after hearing with the dean) to include also:

- Peter Jagers, Statistics (jagers@math.chalmers.se).
- Fredrik Dicander, Engineering Physics (f93frdi@dd.chalmers.se [SNF]).
- Axel Svensson, Problem solving in Science (asdf@mdstud.chalmers.se).
- Lars Jacobsson (Eva Forssell Aronsson) Radiation Physics (to substitute for Magne Alpsten; lars.jacobsson@, evafa@).

APPENDIX B - CONTACTED

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- Mort Sternheim (sternheim@phast.umass.edu) [author, General Physics, J. Wiley and Sons 1986 (premed. students)].
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– Olle Vogel (ov@iva.se) [royal swedish academy of engineering sciences].

– Marina Voinova (voinova@fy.chalmers.se) [TFR guest professor, applied physics, Chalmers].

– Tore Vänngård (tore.vanngard@bcbp.gu.se) [biophysics].

– T.F. Weiss (umech.mit.edu/weiss/home/html, tfweiss@mit.edu) [author Cellular Biophysics].

– Göran Wendin (wendin@fy.chalmers.se) [prefect, microelectronics and nano-physics, director international master's program]

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APPENDIX C - TABLE OF CONTENTS
BIOLOGICAL PHYSICS

Here follows the contents of Mielczarek, Greenbaum and Knox book *Biological Physics*:

7. Evidence for conformational and diffusional mean square displacements in frozen aqueous solution of oxymyoglobin [*Phys. Rev. Lett.* **45**, *68 (1980)*] H. Keller and P.G. Debrunner
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5. Energetics of initial charge separation in bacterial photosynthesis: the triplet decay rate in very high magnetic fields [*Biochim. Biophys. Acta* **934**, *253 (1988)*] Richard A. Goldstein, Larry Takiff, and Stephen G. Boxer

- Author Index

APPENDIX D - TOPICS IN *BIOLOGICAL PHYSICS*

Molecular level:

- molecular energy transfer dynamics,
- enzyme physics,

- nonlinear mechanisms of molecular energy coupling and transport,
- fundamental mechanisms of bioenergetics.

Supramolecular level:

- dielectric phenomena,
- cooperativity in molecular function,
- membrane biophysics,
- physical principles underlying the genetic code and replication,
- origins of life,
- physio-chemical origins of disease.

System level:

- sensor receptor principles,
- automata networks, neural networks and cellular automata,
- electromagnetic effects in biology

Instrumentation and Analysis:

- radiological, ultrasound and NMR imaging techniques,
- new processing and display and representation methods in biological and medical science,
- new methods in spectroscopy
- data analysis techniques
- new nonlinear mathematical and engineering methods applied to biology and medicine,
- new approaches to physio-chemical understanding.

APPENDIX E - DEFINITIONS OF *BIOLOGICAL PHYSICS*

This appendix contains some different ways of defining *Biological Physics Physics*.

American Physical Society

The American Physical Society has a division called *Biological Physics*. It is composed of individuals who are interested in the study of Biological Physics Phenomena using Physical techniques. As such they are usually members of Physics departments, but in addition have many contacts with others in *related* fields such as Biophysics, Biochemistry, Chemistry, Mathematics and Computer Science.

European Physical Society

European Physical Society has an International Union of Pure and Applied Physics with a subdivision called Commission on *Biological Physics* (chairman Nobuhiro Go (Japan)). The Commission on *Biological Physics* has the following Article 1 in its Mandate:

"To promote the exchange of information and views among the members of the international scientific community in the general field of *Biological Physics*. *Biological Physics Physics* deals with the concepts and laws that underlie the structure and function of biological systems. Scientific activities in *Biological Physics* include experimental, theoretical, and computational studies of biomolecules and other biological systems of interest to physicists."

Journal of Biological Physics

Journal of Biological Physics is an international journal for the formulation and application of physical and mathematical models in the biological sciences. It is devoted to the physical understanding of biological phenomena by the experimental and theoretical exploration of the physical principles underlying biological functioning, both normal and abnormal. Experimental techniques and results are included, viewed as means of gaining greater physical insight.

Physical Review E

Physical Review E welcomes biologically inspired physics papers for publication in Section 5 on *Biological Physics*. Appropriate papers should report on innovative Physics, which may involve:

- advances in physical understanding of biological processes or the materials that are involved in biological systems.
- better methods of physical analysis of experimental data or better theory.
- advances in physical instrumentation to be applied to biological problems.
- new phenomena of a primarily physics nature in a biological system.

Appropriate topics range from conformations of biological macromolecules to the properties of neural networks. Applications that apply traditional physical methods to biological problems and that have no new methods of analysis or interpretative theory, even though they contain important results for understanding the biology of the system, are usually more appropriately published in biophysical journals. Many biomedical projects that result in multiple publications involve both basic physics and applications to a subfield of biology. It is the purpose of Physical Review E to provide a publishing home for the physics component.

APPENDIX F - EXISTING COURSES

This section contains an overview of the major current possibilities for students within the School of Physics and Engineering Physics to get courses related to *Biological Physics*. (1 year = 40 credits).

Göteborg University - Physics

Here is a list of general courses at Göteborg University which should be of interest to the Biological Physics or Medical Physicist (1 year = 40 credits):

- Atomic and Molecular Spectroscopy, FY0290 (5).
- Applications of Physics in Chemistry, Biology, Medicine and Technology, FY2900 (5).
- Computational Physics, FY4190 (5).
- Elementary Radiation Physics, RF3100 (40) consisting of elementary atomic and nuclear physics (10), interaction of ionizing radiation with matter (5), radiation detectors and measurement methods (5), radiation dosimetry (10), environmental radiology and radiobiology (5) and radiation protection (5). The last five are also open for students from engineering physics.
- Clinical Radiation Physics, RF8000 (40) consisting of non-ionizing radiation (5), X-ray physics (5), nuclear medical physics (5), physics of radiation therapy (5) and a diploma project (20).
- There is also a group of courses in measurement techniques which could be important for the medical physicist (selected FY-courses).

Biophysics for Engineering Physics

This is a group of courses in biophysics. Biophysics is the science which describes and do research about *phenomena within biology with a physical insight* as base. Experimental and theoretical methods from physics and related areas such as physical chemistry are used. This package is designed to give an increased insight and orientation in the cross-disciplinary area between biology, biochemistry, physical chemistry and physics. It also aimes at giving a research methodology using physical, physical-chemical, theoretical and experimental methods when solving biological problems. Main division responsible is the one in Biophysics at the department of Biochemistry and Biophysics at Göteborg University. The specialities are electron transfer in photosynthesis and catalytic reaction mechanisms for enzymes. The following courses are recommended:

Course	Credits
LEVEL 1	
Physical Chemistry	3
LEVEL 2	
Medical Electronics ETI010	2+2.5
Organic Chemistry KOK050	3
Biochemistry KBB021	2
Atomic and Molecular Spectroscopy FFY290	3
LEVEL 3	
Biochemistry (Göteborg University)	10
Biochemistry (Chalmers) KBB031	6
Applied Quantum Physics FTF120	3
Biological Physics effects of e-m fields EMI130	3
Medical Electronics	2.5+2.5
Biophysical Chemistry KFK020	4
Structural Biochemistry KBB055	6
Applications of Physics in Chemistry, Biology, Medicine and Technology FTF010	3
Biophysics KBB060	3
Molecular Biotechnology KBB070	5

Course	Credits
Condensed matter physics FKA090	4
Surface physics FTF080	3
Organic chemistry F KOK050	3
Het. catalysis and other surf. react. FTF090	3
Biomaterials and biophysics at surf. FKA125	4
Liquid crystals FFY070	2.5
Mesoscopic physics of soft matter FTF070	3
History of mathematics and science UIL020	5
Chaos and dynamical systems FFM370	3
Fourier- and wavelet analysis TMA461	4
Part. diff. eq. - non-linear problems TMA481	4
Nanoscale science and technology FKA130	4
Symmetry analysis FFY350	2.5
Complex systems theory FFR 050	3
Material theory FTM100	2
Applied quantum physics FTF120	3
Artificial neural networks FFM380	3.5
Biomechanics and injury prevention	3.3
Headship - leadership XFU010	3
Group psychology UPI010	5

Master's program - elective part

The Master's program *Physics and Engineering Physics - Nanophysics* is directed towards students aiming at careers in research and development in University or Industrial environments. The program assumes that all students have a B.Sc in Physics (or equivalent) and have passed introductory courses in Electromagnetic Field Theory, Quantum Physics, Thermal Physics and Solid State Physics. The backbone of the program is six compulsory courses (Quantum Mechanics FKA080 (5), Condensed Matter Physics FKA090 (5), Statistical Physics FKA100 (5), Computational Physics FKA120 (5), Advanced Experimental Physics FKA110 (4) and Living State Physics (4) for a total of 28 credit units). This is the foundation for three elective programs of which one is called *Biological Physics* (12 credit units). The programs are concluded with a Master's Thesis (20 credit units).

Available courses for *Biological Physics* are:

Course	Credits
Advanced Problem Solving 1/2 (FKA060/70)	5+5
Biomaterials and Biophysics at surf. FKA125	4
Bioelectronics - see FKA060/070	5
Electron Microscopy and Microanalysis FFY040	4
Surface Physics FTF070	2.5
Biophysical Chemistry KFK020	3
Applied Quantum Physics FTF120	3
Materials Theory FTF100/105	2+2
Complex Systems Theory FRF050	3
Chaos and Dynamical Systems FFM370	3
Electron Microscopy and Microanalysis	4
Mesoscopic Physics FTF070	3
Liquid Crystals FFY070	2.5
Appl. in Chemistry, B, M and T FTF010	3
Artificial Neural Networks FFM380	3
Biophysics KBB060	3

In this context we shall also mention the plans for a new master's program of much interest to *Biological Physics* which is the one called *Complex Adaptive Systems*. It is close to theoretical and computational biology as well as bioinformatics. It is at the junction of biology, physics and computer science. Apart from courses already mentioned above there are plans to give Evolutionary computation (5), Autonomous agents (5), Computational Biology (molecular biology (5) and modeling biological systems (5)) and Modeling and simulating complex systems (5):

Artificial neural networks (5)

Neural networks are distributed computational models inspired by the information processing in the human brain, consisting of many simple analog processing elements connected in a network. Neural networks are increasingly used in many different fields of engineering for tasks such as pattern recognition, prediction, and control. The theory of neural networks is a crossdisciplinary field which includes both neurobiology, computer science and statistical physics.

The course gives an overview and a fundamental theoretical understanding of the most important neural net algorithms. These include models of associative memory (e.g., the Hopfield model), algorithms for learning from examples (e.g., perceptron learning, backpropagation, temporal difference learning), and models of self-organization (e.g., Hebbian learning, self-organizing feature maps). Through comparisons with methods from statistics and computer science students can develop an understanding of when neural networks are useful in application problems.

COURSE CONTENT AND ORGANIZATION

- Introduction to neurobiology.
- Associative memory. The Hopfield model. Optimization problems.

- The perceptron.
- Multilayer perceptrons. Back-propagation and other learning algorithms. Radial basis networks.
- Introduction to learning theory. Generalization.
- Reinforcement learning — learning in situations with infrequent information from the environment.
- Recurrent networks.
- Self-organization in neural networks. Hebbian learning. Self-organizing feature maps.
- Neural network applications.
- Classification and prediction using methods from statistics and machine learning.

To develop an thorough understanding of the basic neural networks algorithms, students are expected to develop their own implementations (in a language of their choice), and apply them to simple application problems. This is done through a sequence of small projects and a larger exam project, which form an essential part of the course.

COURSE LITERATURE

J. Hertz, A. Krogh, R. G. Palmer: Introduction to the Theory of Neural Computation (Addison-Wesley, 1991). S. Haykin, Neural Networks: A Comprehensive Foundation, Maxmillan/IEEE Press, 1994. Lecture notes and articles. Additional recommended reading: P. S. Churchland and T. J. Sejnowski, The Computational Brain, MIT Press, 1992.

Evolutionary computation (5)

The course provides basic knowledge of new methods in computer science inspired by evolutionary processes in nature, such as genetic algorithms, genetic programming, and artificial life. These are both relevant to technical applications, for example in optimization and design of autonomous systems, and for understanding biological systems, e.g., through simulation of evolutionary processes.

COURSE CONTENT AND ORGANIZATION

The course consists of the following topics:

- Evolutionary algorithms: Fundamentals of genetic algorithms, representations, genetic operators, selection mechanisms. Theory of genetic algorithms. The schema theorem and extensions. Genetic programming: representation and genetic operators.
- Applications of evolutionary algorithms: Optimization problems. Data mining. Evolving neural networks. Design of autonomous systems. Cognitive models, such as classifier systems; the credit assignment problem.
- Artificial life: Self-organization in evolutionary processes. Game theory and multi-agent systems. Models of coevolution. Collective behavior.

The course consists of lectures and a large project which includes both model building and programming, where students use the techniques from the course to study an application problem.

COURSE LITERATURE Melanie Mitchell, Introduction to genetic algorithms, MIT Press, 1996. Wolfgang Banzhaf, Peter Nordin, Robert E. Keller, Frank D. Francone, Genetic Programming – An Introduction, Morgan Kaufmann, 1997. Articles from the research literature.

Modelling and simulating complex systems (5)

The aim of the course is to teach students methods for modeling and computer simulation of complex systems, in particular systems where the behavior of many individuals is relevant. Methods for analyzing and presenting data from simulations are also included. Applications studied will include large-scale traffic simulations, simulations of economic markets, models of Internet use, industrial organization, and environmental applications.

COURSE CONTENT

In particular the course will treat the following topics:

- game theory for modelling of interactions between individuals or agents in biology, economics, and computer science.
- simple models of human learning and behavior; adaptive agents based, e.g., on neural networks.
- problem solving in systems of cooperating agents.
- simple modelling techniques for dynamical systems with spatial extension — cellular automata and coupled map lattices.
- visualisation of simulation results, virtual reality.
- simulation of complex technical and societal systems, industrial applications.
- simulations on parallel computers.

Invited lecturers will describe simulations in industrial applications. The course contains a large modelling and simulation project where the students build models of complex systems of adaptive agents and carry out simulations.

COURSE LITERATURE

Lecture notes and articles from the research literature.

Computational biology A (5)

The aim of the course is to give a basic understanding of computational biology directed towards molecular and cell biology, and in particular of algorithms used for storage, search, prediction and analysis of information from biological experiments. It also gives an introduction to molecular and cell biology for students with a background in physics, mathematics or computer science. In particular, the course deals with how information theory, adaptive algorithms such as neural networks and genetic algorithms, and the theory of complexity of algorithms can be used in computational biology.

COURSE CONTENT AND ORGANIZATION

The main topics of the course are

- introduction to molecular and cell biology.
- algorithms for database search and sequence alignment.
- protein structure.
- molecular evolution.
- existing databases och Internet resources for biological information.
- applied molecular evolution.
- modelling and simulation in molecular and cell biology.
- DNA computing.

The course is designed around a sequence of small projects, where students have the opportunity to use the concepts and techniques from the course.

COURSE LITERATURE:

Joao Meidanis och Joao Carlos Setubal, Introduction to Computational Molecular Biology, PWS Publishing, 1997. Internet resources, e.g., the course Principles of Protein Structure Using the Internet (Birkbeck College). Articles from the research literature. Additional reading: C. Bränden och J. Tooze, Introduction to protein structure, Garland Publishing, 1991. B. Alberts et al, Molecular Biology of the Cell, Ingram International, 1994.

Computational biology B: modelling biological systems (5)

The course concentrates on biological systems rather than the molecular level, and at how these can be studied using mathematical modelling and computer simulation. An understanding of this kind is essential to make the transition between genome sequences and the function of cells and organisms, and it will in a longer perspective be necessary for applications in biotechnology. Modelling and simulation are also essential tools for understanding biological systems at the scale of ecosystems, with applications for example to bioconservation.

COURSE CONTENT

The course will in particular contain the following topics:

- evolutionary models.
- gene regulation, models and data analysis.
- models of morphogenesis.
- biological pattern formation.
- models of the function of the immune system, in particular HIV infection.
- computational neuroscience (biologically realistic neural network models).
- models and simulations in ecology — population dynamics, bioconservation.

The course contains a project where students model and simulate a biological system.

COURSE LITERATURE:

Articles from the research literature. Recommended reading: S. A. Kauffman, The Origin of Order, Oxford University Press, 1993. J. D Murray, Mathematical Biology, 2nd ed., Springer-Verlag, 1993. P. Yodzis, Introduction to theoretical ecology, Harper & Row, 1989.

Information theory for complex systems (3)

The course provides an understanding of fundamental concepts used to describe complex systems, in particular dynamical systems such as chaotic low-dimensional systems, self-organizing systems, and simple discrete spatially extended systems such as cellular automata. Many of the concepts, are based in information theory.

COURSE CONTENT AND ORGANIZATION

- Basic concepts of information theory.
- Information theory and statistical mechanics.
- Geometric information theory — randomness and complexity in spatially extended systems.
- Information flow. The relation between microscopic and macroscopic levels.
- Introduction to computation theory and formal languages. Algorithmic information theory (Kolmogorov complexity).
- Cellular automata.
- Applications in nonlinear dynamics, computational biology, chemical self-organizing systems, and statistical mechanics.

COURSE LITERATURE

K. Lindgren, Information theory for complex systems. Articles from the research literature.

Autonomous agents (5)

The course aims at giving the students an understanding of design principles for autonomous systems, both robots and software agents, and also gives students the opportunity to apply their knowledge in practice by constructing a simple autonomous robot. The course contains a major construction project, where students collaborate in groups to build simple robots that take part in a competition to solve a problem.

COURSE CONTENT AND ORGANIZATION

The course consists of a lecture part, which includes the following topics:

- software agents, applications in information gathering and entertainment.
- technology for autonomous robots.

- design paradigms for autonomous systems, e.g., subsumption architecture, neural networks.
- learning algorithms, reinforcement learning.
- evolutionary robotics.
- biological analogies from behavioral ecology, designing simple behaviors, Braitenberg vehicles.
- collaboration among groups of agents, collective problem solving.
- evolution of communication.

The lecture part is intended to give the students a solid theoretical understanding of autonomous agents and how they can interact. The project part is carried out in small groups, and is intended to give students an opportunity to apply their knowledge to a real engineering problem.

COURSE LITERATURE:

D. McFarland och T. Bösser, Intelligent Behavior in Animals and Robots, MIT Press, 1993. J. L. Jones och A. M. Flynn, Mobile robots: Inspiration to Implementation (A. K. Peters, 1993). Articles from the research literature.

Chaos and dynamical systems (3)

Simple deterministic systems can give rise to complex and unpredictable behavior. In a chaotic system, the distance between two close initial states grows exponentially with time, which makes the long-term behavior of the system impossible to predict.

The purpose of the course is to give an understanding of basic theoretical aspects of nonlinear dynamical systems, in particular iterated maps in one and two dimensions. We also consider questions such as: How is chaos measured and characterized? What are the effects of spatial degrees of freedom in chaotic systems? How can one detect deterministic chaos in an experimental time series? How can one control and predict chaotic systems?

Applications in physics (e.g., detecting chaos in experimental time series), biology (e.g., population dynamics), and economics (prediction and nonlinear time series analysis) are also considered.

COURSE CONTENT

- One-dimensional iterated maps: Symbolic dynamics, in particular for the logistic map. Circle maps. Introduction to ergodic theory: Kolmogorov-Sinai entropy, Lyapunov exponents. Bifurcation theory. Structural stability.
- Iterated maps in more than one dimension. Attractors.
- Complex dynamics. Julia and Mandelbrot sets.
- Fractal dimensions. Fractals in physical systems.
- Space-time chaos. Cellular automata and coupled map lattices. Self-organized criticality.
- Non-linear time series analysis. Algorithms for detecting deterministic chaos in a time series. Time series prediction.
- Control of chaotic systems.

COURSE LITERATURE

R. L. Devaney: An Introduction to Chaotic Dynamical Systems, 2nd ed., Addison-Wesley, 1989. E. Ott, Chaos in Dynamical Systems, Cambridge University Press, 1993.

Biostatistics

Biostatistics is used in biological research and many applications are in pharmaceutical and food processing industries, for instance when testing new drugs or analyzing survivability after certain medical treatments. Another area is to calculate how an epidemic disease spreads and decays. In the food processing industry it is important to know how bacteria develop in a certain product to be able to use the right kind of heat treatment.

In Göteborg we have the first graduate school in Sweden in Biostatistics. Most of the graduates have gone to pharmaceutical industries and the majority of problems treated in the biostatistics group have a background in pharmaceutical and medical applications even if most of the work is of such a general character that the methods are applicable also within other areas. Recently the focus has been towards statistical methods in conjunction with genetic problems.

There is presently a suggestion to start a master's program in Biostatistics at Chalmers University of Technology. Students with a background in engineering physics, electrical engineering, computer engineering, biotechnology or university studies in mathematics, statistics and computer science are supposed to be able to apply. The program is also open to students with a background in biology. In their case the biology block (14, introduction (2), biology (4), molecular biology (4) and genetics (4)) is replaced by courses in mathematics (6), statistics (4) and computer programming (4). Apart from this the program has a mathematical statistics block (12, statistical inference (4), stochastic structures (4) and multivariate statistical analysis (4)), a computer science block (12, algorithms (Data and Program structures)(4), data bases (4) and algorithms for machine learning and inference (4)) and a computational molecular biology block (12, fundamentals of computational molecular biology (4), algorithms, software and data bases in computational biology (4) and statistical genetics (4)). The diploma project work is 12-20 credits.

Computer Science

Here we also find interesting courses which should be possible to relate to bioinformatics (course points; 1 year = 40):

- Artificial Intelligence TIN170 (3,7)
- Cryptography TIN250 (3,5)
- Human Computer-interaction TIN 600 (3,5)

APPENDIX G - BIOENGINEERING CURRICULUM

Students in the new branch Biotechnology (under the School of Chemical Engineering at Chalmers) are right now into their third year. Even if they encounter topics which would be of interest for the students we have in mind this Biotechnology branch is as remote in spirit and intents as the difference between the regular physics and chemistry programs, as can be seen from the following list of courses:

Course	Credits
Math. Analysis in One variable A+B	4+4
Introductory Biotechnology	2
Introductory Chemistry	4
Linear Algebra	3
Biochemistry 1+2	3+3
Math. Analysis in Several variables	4
Mechanics	3
Physical Chemistry A+B	3+5
Biology	4
Introduction to Electricity	2.5
Scientific Computing and visualization	4
Organic Chemistry	6
Numerical Analysis	4
Applied Mathematics	3
Transport phenomena	5
Mathematical Statistics	3
Chemical reaction engineering	4

Course	Credits
Applied microbiology	4
Automatic control	3
Chemical apparatus engineering	5
Bioprocess engineering	4
Analytical Chemistry	3
Molecular Biology	4
Experimental Design	4
Macromolecular engineering	6
Molecular Biotechnology	4
Environmental science	3
Surface Chemistry	4
Electives	40
Diploma work	20

APPENDIX H - OTHER PROGRAMS IN SWEDEN

- **University of Umeå** has a branch of Engineering Physics called Molecular Biophysics. It has an emphasis on spectroscopies (e.g. NMR) and contains courses from chemistry in one end (e.g., protein technology) to experimental/theoretical physics in the other end (e.g., radiation detectors/simulation of biological systems). The goal is to educate engineers entering companies within the pharmaceutical and surface chemistry areas, as well as forestry. (see www.phys.umu.se/education/teknfys/)

  1998 started a new program called Technical Biology which is at the meeting point of technology, environmental science and biology. It contains however no physics and only one semester of mathematics. The last year branches out in medical biotechnology, plant biotechnology and environmental technology. (see info.adm.umu.se/utbkat)

- **University of Linköping** recently started a branch called Technical Biology. The motivation was that biology and technology have to go hand in hand in dealing with the major problems of our time: energy, population and the environment The biological part is directed towards ecology and biomaterials. There is also a good base of mathematics, physics and technology. The last year gives the possibility of branching out into environmental science, biomaterials, protein engineering, gene technology and technical biomedicine. The job prospects are like those in Umeå. (see www.lith.liu.se/kurskatalog/tb/html)

- **University of Uppsala** has a 4.5 years education in Molecular Biotechnology. It has a strong emphasis on the molecular and atomic level. The students will in their last year branch into three major directions: protein engineering, protein biotechnology or neural nets and complex adaptive systems. (see www.uth.uu.se/civing.html)

Notice that the three programs above and the one at Chalmers have started a close collaboration giving the students a chance of reading elective courses at the other places.

APPENDIX I - TOKYO UNIVERSITY OF AGRICULTURE AND TECHNOLOGY

Graduate school of Bio-Applications and Systems Engineering (BASE) has been founded in 1995 as the first interdisciplinary graduate school in TUAT (www.tuat.ac.jp). Applications of well-organized biological systems to the large-scale production as well as mimicking the efficient functions for the designing of sophisticated materials have been absorbing keen interests from the human society, in particular, from industrial fields of medicine, foods, chemistry, mechatronics, electronics, energy, environment , and so on. In order to respond this social trend, TUAT has organized an interdisciplinary faculty, twenty-four professors with great expertise in the fields of agriculture and engineering.

Master's Program Courses for School of Bio-applications and Systems Engineering:

- Bio-Science and Modeling. General introduction of biological and bio-ecological flexibilities related to the functional materials, moleculardynamics, biological information, biological interrelationship, and biological resources.
- Systems Science. General introduction of biological and bio-ecological self-controlling mechanistics related to the materials designing, energy systems, neuro and bio-ecological functions, intelligence systems, and measurements.
- Applied Chemical and Materials Science. Conceptual and practical topics on the artificial products created by using intermolecular interactions.
- Biological Information and Science. Explaining about mechanisms of biological intelligence, perception, motion, transport and transformation.
- Science on Environment-symbiotic Production Systems. Giving topics and approaches to sustainable bio-production systems associated with molecular biology, bio-technology, bio-interaction, ecosystem dynamics and bio-information and instrumentation.
- Functional Designing of Materials I. Fundamentals for the synthesis of macromolecules, their reactivities and physical properties, and development to organic functional materials.
- Functional Designing of Materials II. Analytical methods of molecular conformation, and the variation of molecular cohesive states under the influence of tension, electrical field, and/or magnetic field.
- Application of Materials I. New catalysis and process involving homogeneous or heterogeneous catalyst, reaction mechanism, and chemical analysis of solid surface.
- Application of Materials II. Synthetic process of functional chemicals using enzymes and microorganisms as biological catalysts.
- Energy and Materials Engineering I. New design concepts of energy and resource utilizations with the preservation of global environment, behaviors of meso-scale materials, and etc.
- Energy and Materials Engineering II. Concepts of resources-energy transformation systems including biospheres from the stand point of chemical engineering.
- Dynamics of Molecular Systems I. Intermolecular interaction in molecular complexes, and environment dependence of molecular structure and dynamics.
- Dynamics of Molecular Systems II. Structure, property, and function of molecular clusters, metal clusters, and supermolecules as the models of biosystems.
- Transport and Transformation in Bio-Systems I. Heat transfer by convection, radiation, and phase change which is relevant to biological sustainment of body temperature.
- Transport and Transformation in Bio-Systems II. Lecture on biosystem mechanism in systematical reaction and information propagation fields as a bio-essence.
- Neural Information Network I. Basic mechanism of brain neural system and theory of its information processing model.
- Neural Information Network II. Advanced image processing based on shape and size and its applications
- Lecture on Bio-Modeled Sensory System I. Advanced lecture on introduction to characteristics of human sensory system, and its application to design and implementation of artificial systems.
- Lecture on Bio-Modeled Sensory System II. Architecture, programming language and application of parallel computers.
- Intelligent Motion Control System I. Linear control systems (classical, modern, and robust control systems), nonlinear control systems I (adaptive, and sliding mode control systems), nonlinear control systems II (fuzzy, neural net, and genetic algorithms).
- Intelligent Motion Control System II. Mechanisms, structures and sensors for bio-mechanical robots, and their control and application.
- Science and Engineering for Sustainable Agro-Production Systems I. Plant growth model, Dynamics in ecological system, and bio-production system on the basis of systems engineering.

- Science and Engineering for Sustainable Agro-Production Systems II. Sustainable agro-production avoiding land constraints.

- Special Lecture of Molecular Mechanism of Bio-Interaction I. Molecular biology of bio-interaction in disease. Especially, molecular mechanisms of host defense of insect and infection by insect-pathogens.

- Special Lecture of Molecular Mechanism of Bio-Interaction II. Organic chemistry analyzing the mechanism of bio-interaction which was established through an evolutional process.

- Production and Utilization Systems of Biomass I. Biochemistry and organic chemistry of process of biomass production and the breakdown metabolism process.

- Production and Utilization Systems of Biomass II. Production of biomass, balance of biomass energy, chemical and biological utilization of biomass, and comprehensive conversion systems of chemicals derived from biomass.

- Biological and Environmental Sensing System I. Acoustic remote sensing technique for biological tissues and living environment (underground, ocean, atmosphere).

- Biological and Environmental Sensing System II. Biological, medical and environmental measurement about plant, human body and other their environment.

Doctoral Program Schedule for Graduate School of Bio-applications and Systems Engineering:

- Lecture on Design of Functional Materials. Transformation from raw substances to designed materials, and architecture of cohesive- and macro-molecules for introducing particular functionalities.

- Development of Material Functions. Electroconductive, piezoelectric, and nonlinear optical organic materials; their electric properties and correlation with cohesive superstructure.

- Functional Catalysis. Adsorption, reaction kinetics and mechanism in homogeneous and heterogeneous solid catalysis, preparation of new catalysts of molecular dimension.

- Designing of Functional Materials. Synthesis of polymer colloids, and various techniques to introduce functionalities.

- Material and Energy Systems. Designing, evaluation, and processing of the material systems essential for the construction of high temperature-level energy systems.

- Chemical Reaction Engineering. Broad dimensions of reaction engineering, new process, development of environment and energy, accomplishment of the most advanced research projects.

- Designing of Molecular Systems. Property and dynamics of molecular complexes, and designing of functional molecular complexes.

- Lecture on Molecular Spectroscopy for Biology. Optical chemistry and physics, interactions between light and mass, mechanism of bioluminescence, and etc.

- Transformation between Optical and Thermal Energy. Heat transfer phenomena in energy transformation process between optical and thermal energy like laser processing.

- Photo-biophysics Lecture on photochemical and photophysical properties of materials in bio-systems.

- Topics on Biological System and Theory Model of information representation and processing in brain memory system, and its relation to real brain. Application of brain memory theory to memory based neuro computer.

- Topics on Neural Computing Advanced lecture on pattern recognition and neural signal processing

- Topics on Visual Information Processing. Lecture on introduction to approaches for design and implementation of application systems based on human sensory models.

- Topics on Parallel Computers. Computer vision algorithms derived from human visual perception models.

- Micro-Vibration Control Mechanism of micro-vibration control, hardware and software design of the micro-vibration control devices.

- Numerical Motion Control Dynamics and control of computerized numerical controlled machine tools and robots, and evaluation of their performance.

- Topics on Phytotechnology. Modeling the Soil-Plant-Atmosphere continuum complex system and its application to agricultural field management.

- Soil Resource and Ecosystem Diversity and functions of soil ecosystems for sustainable production.

- Special Lecture of Molecular Structures and Biological Functions of Receptors Molecular structures and biological functions of some proteinaceous receptor of mammal or insect which give rise to specificity of bio-interaction.

- Special Lecture of Chemical Communication in the Biological World Complexity, diversity and specificity of semiochemicals, and their applications for sustainable agro-production.

- Molecular Biology of Biomass Production. Lecture on molecular mechanism of biosynthesis process of lignin and polysaccharide from point of view of control of gene expression.

- Conversion System of Biodegradation-Resistant Substances. Chemical structure of biodegradation-resistant natural polymers, biological conversion and degradation mechanisms of these polymers by microorganisms, enzymes and genes.

- Special Lectures on Biological and Electrical Measurements. Measurement of bio-electrical phenomenon, visualization of biological information, biological modeling, signal processing and feature extraction.

- Biological Sensing System. Biological, and medical intelligent sensors or measurements and their devices.

APPENDIX J - GÖTEBORG RESEARCH IN *BIOLOGICAL PHYSICS*

Department of Experimental Physics

- *Atomic Physics*

  A new project has been initiated in which an optical tweezer will be set up to study biological surfaces. It is a collaboration with Halina Rubinsztein-Dunlop at the University of Queensland. With an optical tweezer small particles can be trapped in a focused laser beam. Using such an optical tweezer one can sort a mixture of bacteria. The group has collaboration in this area with department of microbiology at Lund University called Bacterial Viability.

- *Solid State Physics*

  Dielectric and thermal properties are studied for inorganic ionic conductors, polymers and inhomogeneous isolation materials. This group developed equipment for measuring the dielectric properties of materials over a range of frequencies from 10^{-4} to 10^{10} Hz. The main purpose is to investigate the validity of theoretical models for dielectric relaxation in amorphous and inhomogeneous materials, colloids and biological systems.

- *Electronic Structure of Condensed Matter*

  Free electron laser planning in progress.

- *Materials Physics*

  Materials science is central to a technically advanced society. The development of materials is largely concerned with functionalization, i.e. the molecular engineering of systems to obtain specific mechanical, electrical, optical or magnetic properties. In the development of materials researchers from widely differing fields are involved in everything from molecular physics and molecular modeling to macroscopic processing techniques and system modeling. Among the new groups of materials, special attention focuses on what are known as soft materials with a disordered amorphous structure such as glasses, polymers, liquid crystals, gels and so on.

- *Microscopy and microanalysis*

  The research in this group focusses on the micro structure of materials. This means everything from grain boundaries in ceramic materials to the distribution of basic elements in biological structures. All of this demands competence to handle analysis down to the atomic level. Added to this is their experience with industrial materials like steels, ceramic materials and powder materials for electronic applications. Using microbeam X-ray analysis biological materials will also be studied.

- *Environmental Physics*

  A part of the group develops physical measurement techniques for trace element analysis in biological materials of environmental interest, e.g. trees, plants, and human tissue. This group is able to use non-perturbative analysis down to the level of pico grams, using Total Reflection X-Ray Fluorescence Spectrometry. Further development of this probe will make it possible to scan through trees finding seasonal variations of nutrients, and correlations with damage in the forest from various pollutants.

- *Molecular Physics*

  A knowledge of various properties of molecules and clusters is essential in basic and applied science. In molecular physics, electronic structure, reactivity of molecules and clusters are studied experimentally and theoretically. Examples of investigated problems are the role of radicals in catalytic reactions and the way the electronic structure of clusters determines their reactive and catalytic properties. Research activities consist of a theoretical program for the investigation of the electronic structure of atoms, free molecules, fullerenes, atomic clusters and surfaces and an experimental program for studies of clusters, surfaces, non-linear optics and catalysis using laser spectroscopy.

- *Subatomic Physics* no entry at present.

Department of Theoretical Physics and Mechanics

- *Astrophysics* no entry at present.
- *Elementary Particle Physics* no entry at present.
- *Solid State Theory*

  Research in dynamical systems is applied to a broad range of practical problems such as medicine, biology, computation and analysis of financial and economic models.
- *Applied Mathematical Physics*

  Mathematical physics is the development of mathematical models describing physical phenomena: Formulation of a mathematical model for the phenomenon, theoretical analysis of the properties of the model, choice of a suitable approach to obtain its solution, analytical treatment and numerical calculations within the model, analysis of the results, and evaluation of the model. The group has several projects in the mathematical modeling of biological systems. These exploit a web of interconnected reactions and subprocesses. These include diffusion, fluid transport and other physical processes. Initial planning of experiments on such biological systems and the analysis of experimental data requires a mathematical modeling of the system.

Department of Applied Physics

- *Chemical Physics*

  During the past 20-30 years, surface science has been one of the most dynamic and expanding scientific areas. Surfaces and interfaces play a central role in a large number of technological, biological and medical applications. Examples of application areas include; semiconductor technology and microelectronics, electrochemistry, corrosion, catalysis, surface coatings, medical implants, chemical sensors, tribology and photochemical processes in the stratosphere. Major application areas, with active industrial collaboration, are heterogeneous catalysis, biomaterials/medical implants, (BIO)chemical sensors and photoinduced surface processes.

  The activities of the group focus on basic and applied research in surface and chemical physics. Basic research includes the properties of adsorbed molecules on surfaces and gas-surface dynamics with the emphasis on energy and charge transfer mechanisms in gas surface collisions, as well as the kinetics and mechanisms of catalytic reactions, non-thermal surface processes (photo reactions, collision-induced processes), combustion, adsorption of biomolecules on surfaces and metal hydrides. The application-oriented research includes energy-related surface processes (catalytic combustion, catalytic gasification, exhaust cleaning, tribology, metal hydrides), biomaterials and implant surfaces, and nanofabricated surfaces.
- *Condensed Matter Physics*

  Research in this group is directed towards three main areas: soft matter, high temperature superconductors, and complex biological molecules and membranes. The area of soft materials includes polymers, glasses, liquid crystals, colloids, gels, biological macromolecules and membranes, i.e. materials which are characterized as disordered or complex as opposed of to being crystalline. This group intends to tailor materials with specific applications; "molecular engineering". This area of physics is cross-disciplinary, combining chemistry, materials science, biology and electronics. By its nature it propels the development of new theoretical models and experimental techniques. With the expertize developed by the study of disordered materials the group has initiated projects on structure, dynamics and function of biomolecules and membranes. Because these projects are in the initial phase they are to a large extent of a fundamental nature. However, one long term goal is using the knowledge acquired from applied projects, in for example the pharmaceutical industry. The group is also active in the new graduate school for material science where one important area is biomaterials.
- *Condensed Matter Theory*

  Present research and future plans for this group include investigation of mesoscopic composite structures containing magnetic, superconducting, and biological materials. Such materials will have a large impact on future materials technology. Collaboration with Chemical Physics will increase for the biological component. This latter area will be the major undertaking of the group. Other lines of research include structure, dynamics, and the functioning of biomolecules, membranes, and biomolecular sensors.
- *Materials and Surface Physics*

  The research within our group covers large parts of the condensed- matter theory, with focus on materials physics, surfaces physics, simulations, and surface-field interactions. Investigations on antenna properties of bacterial photosynthesis. Light scattering studies of red blood cells.
- *Surface Physics*

  The activities of the surface physics group focus on basic research in surface and chemical physics. During the past 20-30 years, surface science has been one of the most dynamic and expanding scientific areas. Surfaces and interfaces play a central role in a large number of technological, biological and medical applications. Examples of application areas include; semiconductor technology and microelectronics, electrochemistry, corrosion, catalysis, surface coatings, medical implants, chemical sensors, tribology and photochemical processes in the stratosphere. Major application areas, with active industrial collaboration, are heterogeneous catalysis, biomaterials/medical implants, (BIO)chemical sensors and photoinduced surface processes.

Department of Microelectronics and Nanoscience

- *SIMS-laboratory*

  (Secondary Ion Mass Spectroscopy) This group will cooperate with other materials research groups within geology, biological materials and dental composites. The latter two in collaboration with Odontological departments in Sweden and abroad.

- *Physical Electronics and Photonics*

  Packaging of semiconductor components.

- *Applied Quantum Physics Theory*

  Molecular electronics, bioelectronics, artificial intelligence and theory of computing.

- *Applied Solid State Physics*

  Molecular electronics.

- *Applied Semiconductor Physics* no entry at present.

- *Liquid Crystal Physics*

  The groups activities focus on theory and experiments for a deeper understanding of the phenomena of liquid crystalline ferroelectricity and antiferroelectricity as such, in both monomeric and polymeric materials. Underlying symmetry requirements prescribe the use of chiral, left-right-asymmetric, substances, in order to achieve the desired ferroelectric or antiferroelectric phases. Part of the work involves molecular engineering and organic synthesis (undertaken in close cooperation with chemists elsewhere), the analysis and physical characterization of the new substances, the production and testing of simple and more complex electro-optical devices and, in a feed-back process, the improvement of evaporation and other surface preparation techniques.

Department of Physical Resource theory

The research in this department is the application of thermodynamics to industrial and societal energy needs and material flows. They also study the coupling between thermodynamics, statistical mechanics and information theory. Information theory is an important tool in analyzing complex systems. It unites research from different disciplines such as physics, chemistry, biology and economics. One project is to develop models for evolutionary systems, such as using a classical example from game theory to model interactions between individuals. Even though the model is simple it succesfully shows several characteristic phenomena associated with biological evolution. This group is part of an international network and is a member of the External Faculty at the Santa Fe Institute, New Mexico, USA.

Department of Reactor Physics

Experimental and theoretical techniques used in reactor physics can be adapted to diagnose and treat patients. To name two: measurement of blood circulation (*in vivo* in blood vessels by a correlation method applied with X-ray microbeams). Calculation and measurement of the neutron field in the human body in order to design an optimum energy spectrum and geometry for an irradiation treatment. Most of these projects will be done jointly with the Radiation Physics Department.

Department of Radiation Physics

Research within radiation physics is related to phenomena associated with ionizing and non-ionizing radiation, and problems in medicine and environmental studies. During recent years the projects have developed a biomolecular and biophysical profile. Traditional natural radioactive techniques, X-ray, Magnetic Resonance, and neutron activation are used to measure the molecular content of different tissues in the *living* human. This is very important for medical research.

APPENDIX K - MAJOR US RESEARCH IN BIOLOGICAL PHYSICS

Here follows a first person description of the major undertakings of some large Universities in US with efforts within *Biological Physics*

Department of Physics and Astronomy at *Vanderbilt University* has a group in *Living State Physics*: "Living State Physics merges research at the forefront of physics with exciting and significant biomedical investigations. It is an interdisciplinary field that draws upon the tools, methods, and theories of physics, biology, engineering, and medicine to increase our understanding of biological systems and phenomena. Living State Physics merges research at the forefront of physics with exciting and significant biomedical investigations. It is an interdisciplinary field that draws upon the tools, methods, and theories of physics, biology, engineering, and medicine, as well as computational physics, to increase our understanding of biological systems and phenomena. Physicists have already made significant contributions to medicine and biology, primarily in medical physics, which emphasizes the application of radiation to diagnosis, imaging, and therapy; and in biophysics, which is concerned largely with the properties and behavior of biological molecules. There are, however, innumerable, unexplored biomedical applications of physics. Hence, the term Living State Physics is both an excellent name for this broad field and an appropriate parallel to the more familiar field of solid state physics, which applies numerous techniques and theories to study solids. Living State Physics elucidates, as no other discipline does, living functions and mechanisms, biological states, and pathological conditions. Just as the turn of this century brought rewarding and advancing applications of chemistry to the life sciences, today medicine and biology are ripe for the wider application of physics. Ophthalmology, neurology, cardiology, surgery, physical therapy, and audiology are examples of medical specialties that can benefit from new understandings gained through Living State Physics. Apart from contributing to progress in biology and medicine, the knowledge that flows from Living State Physics simultaneously advances the physical sciences, particularly polymer physics, molecular dynamics, and solid state physics, as well as engineering fields such as electronics and materials science. The Living State Physics Group at Vanderbilt utilizes a three-pronged approach to solving problems of biomedical interest: the development of new instrumentation that ranges from high resolution superconducting magnetometers to free electron lasers, the use of these instruments to make fundamental measurements on biological systems, and the development of analytical and numerical models that probe the depth of understanding of both the relevant biophysical mechanisms and the theories that describe them. To interpret data, mathematical models have been developed which provide new insights into the behavior of nerves, and cardiac and skeletal muscle. Much of the instrumentation, mathematical models, and analysis developing in this effort is also applied to non-biological problems such as non-destructive evaluation of structures such as aging aircraft".

Department of Molecular Physiology and Biological Physics at *University of Virginia (Health Sciences Center)*: "The biophysical sciences are vigorously pursued at the University of Virginia. Pure and applied research in biophysics is carried out in many departments, including Biochemistry, Biology, Chemistry, Microbiology, Physiology, and Physics. Interdisciplinary collaborations and the organization of colloquia and special lectures by faculty with common interests in biophysics, contribute to research programs in biological physics in the Department of Physics. Quantum mechanical models, incorporating the effects of low symmetry and electron delocalization, are being developed to provide a unified electronic structural basis for magnetic, optical, and magneto-optical data taken together".

Wake Forest University has programs in *Biological Physics*: "Electron paramagnetic resonance (EPR) techniques are being used to study irradiation damage in keratin proteins, defects in ionic solids, and structural phase changes in polymeric chains containing metallic ions. The conformation and dynamics of biological macromolecules in solution is another major focus. The roles of molecular orientation and molecular packing on the Circular Dichroism of DNA. Experiments have also been conducted on cell membranes, intact viruses and cholesteric liquid crystals. A theoretical and experimental approach to the understanding of how light interacts with matter (and, in particular, how matter changes the polarization state of light) is taken to gain structural information not readily obtained by other biophysical methods. Measurements of the absorption, scattering and fluorescence of macromolecules have been made".

Carnegie-Mellon University (has also a branch in Biomedical engineering): "Biological Physics is one of the most exciting frontiers in physics today. In this field, we are challenged to explain the mechanisms by which complex biological molecules and assemblies operate. At the same time, biology offers the physicist unique opportunities to learn new physics on elegant, complex systems. Problems we presently study at Carnegie Mellon include the structure of lipid phases, which are the essential components of biomembranes, the folding of proteins and the three-dimensional structure of cells. We use traditional tools of physics including Monte Carlo calculations, molecular dynamics simulations, x-ray scattering, optical microscopy and nuclear magnetic resonance."

Massachusetts Institute of Technology, Department of Biological Physics: "Physics concepts and methods, both experimental and theoretical, can be uniquely useful to biological and medical systems. In turn, the latter are complex systems that provide ultimate testing grounds for physics concepts and methods. This symbiotic relationship continues to be nurtured in the Department of Physics. MIT physicists are currently studying phase transitions and critical phenomena in binary and ternary protein-water solutions, as well as studying the ways chemically and genetically engineered modifications of the proteins shift the location of these phase boundaries. These experiments, combined with their quantitative theoretical analysis, are providing an understanding of the molecular basis of cataract formation in the lens of the eye. Additional studies are focusing on phase transitions and critical phenomena in polymer gels. The physical principles of these phenomena reveal how molecules in polymers interact with each other, helping to elucidate the most fundamental of biological problems: protein folding and protein functions of molecular recognition, catalysis, and motion. The study also enables the technological applications of gels as artificial muscles, actuators, sensors, controlled delivery systems, chemical memories, and separation matrices. Medical physics research at the Spectroscopy Laboratory spans the full range from basic to applied problems. Research areas include light scattering and photon migration in biological tissue, the physics of ablating tissue using laser light, and spectral signatures of tissue components".

Cornell University. "New York State Center for Advanced Technology in Biotechnology The Cornell Biotechnology Center focusses on five major areas of research and technology development: 1) biocontrol (biological alternatives to chemical methods of disease and pest control), 2) gene isolation and enhancement (identifying and altering particular genes to enhance the traits of plants and animals for disease resistance, crop yield, and nutritional quality), 3) bioremediation (the use of biological systems for environmental stewardship), 4) diagnostics (tests for health, safety, and other conditions, with applications in humans and animals, in food, and in the environment) and 5) health care (structure based drug design; vaccines for human and animal health)".

Princeton University: "Theory of "soft" condensed matter: We are interested in stochastic and dynamical phenomena underlying the behavior of various molecular systems, such as fluctuating membranes, self-assembling polymers or molecular machines. Theoretical investigation of these systems are done by using analytical methods of statistical mechanics and field theory, and are reinforced by numerical simulations. We are also using methods of statistical mechanics to study the collective behavior of the so-called networks in which many components (e.g. enzymes, genes or neurons) interact in a dynamical fashion. All this theoretical work is closely related to experiments performed in our laboratory. Experimental physical cell biology: We are interested in the collective behavior of cellular components which assemble to large, highly organized and regulated structures. For instance, we study how the mitotic spindle forms, how it spatially organizes and separates the chromosomes, how its formation is connected with the action of biological "clocks". In addition, we study the action of molecular motors, their stochastic character and the process of energy transduction in these proteins. We are also interested in the phenomena of signal transduction such as chemotaxis in bacteria. Experimental techniques include fluorescence and video microscopy, the use of micromanipulation devices (optical and magnetic tweezers), laser (in)activation methods and others. Applications of Microlithography to Biology: Recently we have realized that the optical lithography techniques of the semiconductor industry can be used to attack problems of biological interest. For example, we have recently constructed micron-sized "obstacle courses" on a silicon chip to mimic (and improve upon) the complex topology found in gels. We have shown that it is possible to image megabase long DNA molecules moving through these arrays and that the arrays can fractionate very long (chromosomal length) DNA molecules. We are pursuing this technology to sequence DNA, and are also now running red blood cells through larger arrays to study the influence of membrane rigidity on cell mobility. Further applications await our imagination".

University of Rochester Biological Physics; Most research of this group involves the interaction of radiation with biological systems, studied primarily at the molecular level. Prof. Foster's interest centers on photodynamic therapy a method of cancer treatment. During photodynamic therapy, laser light is absorbed by exogenously administered, tumor localizing molecules, and the resultant photoproducts include an excited state of oxygen that causes cell death. Using both theory and experiment, Foster's group studies the balance between the oxygen- consuming photochemistry and the diffusional supply of ground state oxygen in tissue and in model multicell systems in vitro. Recent work includes studies of light propagation in highly scattering media. Prof. Knox's research interest is photosynthesis, the process by which plants and other organisms convert solar energy into chemical energy. His group studies the physical processes by which the energy of absorbed photons is transported to the initial site of chemical reactions. The theory of excitons is applied to predict photosynthetic efficiences, to establish the effect of coherent excitation, and to evaluate proposed structures of the "photosynthetic antenna".

Physics Department, *Syracuse University*: "*Biological Physics physics* is the fourth major research group at Syracuse, and has since the 1960's grown to involve several distinct research efforts. An important concentration of this research is upon sensory phenomena, from single cells to neural networks. In Biophysics: Molecular orbital theory and molecular dynamics of primary photochemical events in light transducing proteins with experimental studies of sensory processes in vision; combined system analysis and genetic analysis of light responses of a microorganism; medical imaging with antiproton beams, application of high performance computing and communication to telemedicine and medical image processing."

University of Illinois at Urbana-Champaign: "The Theoretical Biophysics Group was founded by Professor Klaus Schulten in 1989 and is located at the Beckman Institute of the University of Illinois at Urbana-Champaign. Over the years the group has grown in size and scope into the equivalent of a small academic unit with external funding above 1.5 million/year, a large computational laboratory, 35 members (faculty, students, postdoctoral associates, staff), a regular seminar series, a record of impressive graduates, and many visitors. The mission of the Theoretical Biophysics group is to promote scientific knowledge, to expand the realm of scientific computing, and to provide service to the biomedical community. Present research activities, led by Professor Klaus Schulten (Physics, Biophysics, Chemistry) with Professors Robert Skeel (Computer Science) and Laxmikant Kale (Computer Science), can be classified into two broad categories: The study of the structure and function of biopolymers and biopolymer aggregates by theoretical and computational means: researchers focus on molecular dynamics and quantum chemistry studies in collaboration with experimental laboratories in universities, research institutions and industry across the U. S. and around the world. This research is complemented by theoretical studies designed to improve data analysis and general understanding. The development of tools to employ high performance parallel computers and high end graphics for research in structural biology: since July 1995, the group has been distributing its molecular modeling program MDScope, for large scale and long time simulations on serial and parallel computers, and for interactive molecular dynamics. MDScope combines a highly developed molecular graphics application VMD, a molecular dynamics program NAMD, and a communication package MDComm that allows VMD and NAMD to be linked over wide area networks. New features and improved algorithms, such as efficient force evaluation and long time integration, are regularly added to the program. The group operates a National Resource Center in Computational Biology funded by the National Institutes of Health and leads a multi-campus Grand Challenge Application Group grant awarded by the National Science Foundation. Other sources of support include grants from Roy J. Carver Charitable Trust , on- and off-campus fellowships, University of Illinois matching funds, and industry. The researchers in the Theoretical Biophysics Group represent a spectrum of disciplines, each of which contributes a meaningful piece to the intricate fabric of goals the group has set for itself. Local researchers are affiliated with the departments of Physics, Computer Science, Biophysics, Chemistry, Mathematics, Nuclear Engineering and Electrical and Computer Engineering. The Center for Complex Systems Research is an interdisciplinary group (typically, Biology, Chemistry, Engineering, Mathematics, and Physics) of faculty and graduate students. They employ theoretical and experimental methods in the study of the dynamic properties of complex systems, many of which are related to the Main Research Themes of the Beckman Institute. The common focus of this Center for complex systems research is in addressing the designs, controls, and communications within strongly coupled networks. Within the Biological Physics Intelligence area, several studies deal with the organization and dynamics of biological networks. One study concerns understanding how information and short-term memory processes can occur in biological neural networks. Related to this are studies of the formation and controls of spatiotemporal patterns in neural networks, that relates to medical research to control epileptic seizures and migraines. Another study involves the design of networks of enzyme-catalyzed biochemical reactions, in order to accomplish specific functional tasks. The long-term goal of this study is to develop a theory for the organization of biological networks at different hierarchical levels. A global form of biological intelligence involves the ever-increasing networks of global information exchange. A search for new strategies for managing international relations and local crises within a global-brain concept of distributed information servers is being pursued in the Center for Complex System Research. Some dynamic studies have an impact in the Biological Physics Intelligence area, on solid-state systems, and in the Molecular and Electronic Nanostructures Beckman Research Area. Thus the studies of how systems can adapt to environmental conditions is closely associated with learning processes, which are fundamental for biological survival. Adaptive dynamics can also be usefully applied in solid-state devices, and may have future applications at the nanostructure level. Presently, a dynamic process, involving coupled quantum dots has been patented by Toshiba Corporation in Japan. Extensions of this process are being explored in conjunction with the Beckman group. The Center for Complex System Research is a leader in the field of general controls of complex dynamic systems. This knowledge is presently being applied to provide various types of interfacing software for human-computer interactions, in connection with the Beckman Human-Computer Interaction projects. One basic contribution is in control methods needed to explore the dynamic origins of complex physical phenomena. This requires the development of programs which can be manipulated in real time from the keyboard, and which control or reliably influence complex dynamic systems. Such controls have a range of applications, from use of "model-resonance" methods developed, to the generation of both graphic and sonic representations of dynamic information. Extension of this latter activity has been adapted to the exploration of chaotic-based musical compositions within the School of Music. The application of these controls of complex systems is also being studied experimentally in electrical circuits, and in chaotic chemical systems, with potential applications in industrial processes in the future. Other research concerns the impact of the changing informational foundations of science, and related new "scientific methods", on scientists' search for new unifying principles of all natural sciences, which will replace the "theory of the everything" views developed during the past century. These evolving foundations of science are a basic legacy of our deeper understanding of the dynamics of complex systems".

California Institute of Technology: Has a very strong program in basic biological physics with strong connections to other fields. "There is an interdisciplinary graduate program for studying the biological and engineering aspects of sensory-motor processing, learning and memory, leading to a PhD in "Computation and Neural Systems". Part of this includes large research projects to understand how the brain computes so effectively, using six orders of magnitude less energy than human-engineered computers. Our current working hypothesis is: "In order to achieve a global optimum, evolution simultaneously optimizes both structure AND function." To study how structure and function are optimized, we draw on both scientific and engineering disciplines. This multidisciplinary research paradigm, which includes both analysis and synthesis, is at the core of neuromorphic engineering. On the scientific side, electronic VLSI systems, based on the structure and function of the nervous system, are built to test hypotheses about how the brain works, and are analyzed to understand the tradeoffs involved in the brain's design. Since these tradeoffs arise from physical limitations, they can only be understood in the context of real physical models; the abstract models used in computer simulations shed no light on these issues. On the engineering side, our understanding of these tradeoffs is used to synthesize more effective and energy-efficient computer designs for performing biomorphic tasks, such as dynamic prediction and self-organization, real-time sensory-motor control, adaptive sensing and multimodal associative learning (we are pursuing these goals as part of the National Science Foundation sponsored Center for " Neuromorphic Engineering"). To the extent that we are successful, the neuromorphic approach will advance neuroscience—the study of the most energy-efficient information processing systems in existence today—as well as advance VLSI system design, the effort to build more powerful computers in the face of severe power-density limitations. Caltech also has a keen interest in life itself as reflected in the avida group consisting of researchers interested in the foundations of those processes which make living systems appear "alive". We use auto-adaptive genetic systems to make quantitative and qualitative statements about evolution, adaptation, and the emergence of complexity. Auto-adaptive genetic systems (such as tierra and avida) have a self-reproductive system combined with a versatile genetic basis. We believe that these systems represent minimal living systems. Avida is the name of the Artificial Life "platform", or experimental testbed, which we use in most of our experiments. In order to characterize the processes of living systems, we have tried to construct the most simple system which displays properties of being alive. Simply put, avida is a population of self-replicating strings of code subject to random mutations, adapting to a complex information rich landscape".

Washington University at St. Louis "The Institute for Biomedical Computing, is an independent faculty unit of Washington University engaged in research and training. We are affiliated with the Schools of Medicine and Engineering and Applied Sciences at Washington University in St. Louis, Missouri. The Institute for Biomedical Computing is composed of three independent research units. Biomedical Computer Laboratory, Center for Computational Biology and Center for Molecular Design. Our mission is to advance biology and medicine through the development of novel computational methods, and where necessary hardware. We are dedicated to the solution of challenging problems with a multidisciplinary approach. Current activities include molecular sequence and genome analysis, biochemical databases and information retrieval, molecular design and computational biophysics, real time 3-D microscopy, wide field computational optical sectioning microscopy, and model based quantitative image restoration. Contact us for more information. Graduate training in Computational Molecular Biology and Bioinformatic. The Biomedical Computing Institute and Washington University are establishing graduate training programs in computational molecular biology and genome analysis. These are multidisciplinary training programs drawing upon faculty in computer science, genetics, biochemistry, pharmacology and biology departments".

APPENDIX L - SENSORS: THE NEXT WAVE OF INFOTECH INNOVATION

[By Paul Saffo, Institute for the Future (www.iftf.org/sensors/sensors.html)].

The infotech revolution is fifty years young, for despite all the innovation and surprises served up to date, it is quite clear that far greater change lies ahead. We marvel at how computers have insinuated themselves into every corner of our lives, knowing all the while that in a few years today's marvels will seem quaint compared to what follows. Amid all this change, a half-century of history provides us with one important constant–a clear trajectory of innovation and consequence that reveals important insights about the nature of surprises to come.

It turns out that about once a decade a new technology comes along that completely reshapes the information landscape. Just before 1980, that key enabling technology was the microprocessor, and its arrival set off a decade-long processing revolution symbolized by the personal computer. In a classic confusion of cause and effect, we called it the "Personal Computer Revolution," but it was really a processing revolution, a decade during which we were utterly preoccupied with processing everything we could stuff into our machines.

Then just as the 1980s were closing, another new enabling technology came along to displace the centrality of the microprocessor–cheap lasers. Much as the microprocessor slipped into their lives hidden in PCs a decade earlier, lasers slipped into the lives of ordinary citizens hidden in everyday appliances–compact disc music players, CD-ROMs, and long-distance optical fiber phone lines. Lasers delivered bandwidth–huge volumes of storage on optical disk and high-quality communications bandwidth over optical fiber.

The consequence was a shift in emphasis from processing to access. In the 1980s, the processing decade, our devices were defined by what they processed. In the 1990s, the access decade, our devices are defined by what they connect us to. The advent of cheap lasers completely reinvented our desktop environment. Machines on the desk outwardly looked the same but changed profoundly in function, from stand-alone devices defined by what they processed to networked devices defined by what they connected us to, from 1980s-era "data laundries" to 1990s network windows on a larger information world.

Just as the PC symbolized the 1980s processing revolution, the centerpiece of today's laser-enabled access revolution is the Internet in general and the World Wide Web in particular. Web surfing would be an outlandish impracticality but for massive amounts of laser-enabled fiber-optic bandwidth.

Note one important detail. The arrival of each successive new technology does not make the older technology obsolete. Microprocessors did not become irrelevant in the laser decade. In fact, lasers and the access they enabled led to demands for new kinds of access-oriented microprocessors such as digital signal processor (DSP) chips. The communications tail is now wagging the processing dog, but cheap lasers created enormous demand for microprocessor innovation.

We are approaching the end of the laser decade, and even though a few laser-enabled surprises are still waiting in the wings, we are beginning to see diminishing returns from merely adding more bandwidth to our access-oriented world [1]. It is now clear what will replace lasers as the foundational technology of the next decade.

Hints are lurking in many areas, but one of the most intriguing indicators appeared in Los Angeles in the last two years. What is the most popular item to steal out of automobiles in Los Angeles today? Air bags–because they contain an expensive and not-entirely-reliable accelerometer trigger. The consequence has been a booming market for replacement airbags, which thieves are happy to fulfill.

Air bags are about to become too cheap to steal, however, because, using MEMS (MicroElectroMechanical systems) technology, one can build an accelerometer on a single chip for a couple of dollars, creating a device that is not only cheaper than today's sensors, but also smarter and more reliable. Today's systems dumbly explode whenever they sense an abrupt acceleration, whether or not a passenger is present. Future systems will incorporate sensors capable of identifying not only the presence of a passenger, but their weight and size as well, and adjusting the force of inflation accordingly.

Such new devices–cheap, ubiquitous, high-performance sensors–are going to shape the coming decade. In the 1980s, we created our processor-based computer "intelligences." In the 1990s, we networked those intelligences together with laser-enabled bandwidth. Now in the next decade we are going to add sensory organs to our devices and networks. The last two decades have served up more than their share of digital surprises, but even those surprises will pale beside what lies ahead. Processing plus access plus sensors will set the stage for the next wave–interaction. By "interaction" we don't mean just Internet-variety interaction among people–we mean the interaction of electronic devices with the physical world on our behalf.

For example, the next big surprise will occur on the World Wide Web. At the moment, the Web is defined by people accessing information. Over the next two years, look for the Web's focus to shift away from this to a new model of people accessing other people in information-rich environments. In other words, the Web will go from being an information environment to an interpersonal environment in which information plays an important role supporting human interactions.

What Are Sensors? A suite of technologies underlie the rise of sensors, including MEMS, piezo-materials, micromachines, very large scale integration (VLSI) video, and a handful of other technologies.

MicroElectroMechanical Systems (MEMS) are by far the most important of the technologies enabling the rise of sensors in the near term. In concept, MEMS technology is simplicity itself: it amounts to nothing more than using semiconductor manufacturing techniques to create analog devices. But underlying MEMS technology is an interesting mind-shift in chip design.

Traditional chips are little more than intricate race tracks for electrons built up through an elaborate process of etching and deposition. One of the worst bugs a traditional chip can have is a "released layer"–in effect, a loose piece of circuit material hanging out in microspace above the chip surface. That loose layer interferes with the smooth flow of electrons because it interacts with the surrounding analog environment. In the MEMS world, however, that "bug" is a crucial feature because such released layers can serve as analog sensors, sensing everything from acceleration and temperature to pressure and fluid flows.

MEMS research has been underway for over a decade [2], and MEMS-based devices are already finding their way into the marketplace. The automobile industry is a major consumer of MEMS devices, and is likely to be the single largest early market, as carmakers add them to everything from emissions systems to tire hubs.

The fact that MEMS is not a "new" technology underscores an important point about how each successive decade unfolds. What defines each decade is not the underlying technology's invention, but rather a dramatic favorable shift in price and performance that triggers a sudden burst in diffusion from lab to marketplace. Thus, like MEMS, both the microprocessor and communications laser were "old" technologies from a research perspective by the time their respective decades began. The novelty was that the devices suddenly were cheap enough to put into ordinary products in the marketplace.

Piezo-Materials are materials (typically ceramics) that give off an electrical charge when deformed and, conversely, deform when in the presence of an electrical field [3]. Put a charge in, the material deforms; deform the material, it sends out a charge. Piezos are particularly useful as surface-mount sensors for measuring physical movement and stress in materials. But more importantly, piezos are useful not just for sensing, but for effecting–manipulating the analog world. This is an indicator of the real significance of the sensor decade. Our devices won't merely sense and observe. They will also interact with the physical world on our behalf.

Like MEMS, piezo-materials have been around for some time, and there is no shortage of interesting work underway. Researchers at the Georgia Institute of Technology are engaged in one of the most whimsical applications: creating a piezo-augmented "smart guitar" that mimics the sound of a high-end traditional guitar at much lower cost. As is discussed below, such research is bringing us to the verge of creating new classes of "smart materials"–materials that actively sense and respond to the surrounding analog environment.

Micromachines are semiconductor cousins to MEMS technology. Like MEMS, Micro-machines are built using semiconductor manufacturing techniques, but unlike MEMS, they are more complex in design, incorporating in some instances micrometer-scale gears and other moving parts. At the bleeding edge of this field, in 1996, an affiliate of Toyota Motor Corporation, Nippondenso, constructed a "microcar" not much larger than a grain of rice–a replica of an early Toyota complete with electromagnetic motor and tiny ring-gear drive.

Micromachines exploit the often overlooked structural qualities of silicon: a low coefficient of thermal expansion, high thermal conductivity, a strength-to-weight ratio more favorable than aluminum, and elasticity comparable to that of steel. At the same time, the process of manufacturing micromachines is in its infancy, and it will be some years before elaborate micromachines are anything more than lab curiosities. Simpler devices will arrive slightly behind MEMS devices.

VLSI Video: today, a videocam with all the attendant circuitry required to attach it to a computer costs approximately $9 a unit in OEM (manufacturers' price to other manufacturers) quantities. Expect this to drop precipitously as the next generation packages everything on a single chip: the charge-coupled device (CCD), all the circuitry needed, and even the lens will be glued directly to the chip. Cheap video translates into cheap "eyes" that can be used for a myriad of applications, including surveillance, security, and even party games.

Other Sensor Technologies A host of other technologies are being pressed into the service of mediating between the analog and digital worlds. One example is Micropower Impulse Radar (MIR), a recent invention of Lawrence Livermore National Laboratory. Personal radar sounds like an unlikely consumer hit, but consider the following applications, all under commercial development: "intelligent" oil dipsticks for autos, handheld wall stud sensors, bulk tank level sensors, land mine detectors, and nondestructive testers for concrete structures. Global positioning system sensors are also undergoing radical reinvention, lowering cost and increasing performance. Systems once costing tens of thousands of dollars can now be had in a handheld package for under $500. In the not-too-distant future, integrated sensor/GPS modules will be small and inexpensive enough to integrate into courier parcels in order to track the location and treatment of valuable cargoes. Cheap laser technology is also rapidly changing gyroscopic technology as ring laser gyros (RLGs) displace traditional spinning-mass systems in aircraft, delivering dramatically increased performance in cheaper, more reliable packages. In the long run, it is likely that advanced MEMS accelerometer arrays will in turn displace RLG technology.

Implications: From Sensors to Effectors

The impact of sensors will be as surprising in the decade ahead as that of microprocessors in the 1980s and lasers in the 1990s. And the surprises will be additive because of the synergistic interaction among the generations of technology. Some of the most interesting applications of sensing technology will be applied to solving existing information technology problems. One such problem created by lasers is switching. Data moves along fiber-optic threads as photons traveling at the speed of light, far faster than the fastest of electronic switches can switch it. Thus the performance of fiber-optic communications systems are often "switch-bound"–limited by the speed of switches rather than the cable itself. Modest micromachine/MEMS technology could break this impasse. Researchers are working on a micromirror deformable diffraction grating "switch" theoretically capable of 20-nanosecond switching speeds.

MEMS technology could also deliver interesting storage packages or a MEMS-augmented optical disk system with capacities orders of magnitude larger than that of a conventional CD-ROM.

But these examples merely touch the most prosaic of possibilities. Casual inspection of prior forecast and subsequent reality of the microprocessor and laser decades makes it clear that the scale of surprise will be enormous even for professional forecasters. But the good news is that hints of what is to come are already occurring. As novelist William Gibson once observed, "The future's already arrived; it's just not evenly distributed yet."

One place to look is the World Wide Web. In 1995, a home page of the California Department of Transportation posted a pointer to a Web-based map of the San Diego freeway system. The map displays traffic speeds and densities in real-time by means of sensors embedded in the asphalt that send data to a Sun workstation.

What's more certain is that the most expected of futures will–as always–arrive late and in utterly unexpected ways. Even as telecommunications executives continue to try and sell tired old notions of videoconferencing, the interaction of cheap video and laser-based Web bandwidth has already delivered a hint of what the future will really hold. Recall the "Cambridge Coffee Pot," which became an early curiosity on the Web: researchers in a research lab in the Computer Science Department of Cambridge University aimed a networked camera at the coffeepot down the hall in order to know when there was coffee fresh enough to make a trek to the kitchen worthwhile. A world of ubiquitous video is not a world of people looking at each other via videoconferencing. Rather, it is a world of cameras aimed at everything everywhere, watched over by machines, and only occasionally examined by people.

But the impact of sensors doesn't stop at mere sensing. What happens when we put eyes, ears, and sensory organs on devices? Inevitably, we are going to ask those devices to respond to what they "see," to manipulate the world around them. The sensor decade will really be a sensor/effector decade, where devices will not only observe things, they will also manipulate them.

This has profound implications. Two parallel universes exist today–the everyday analog universe we inhabit, and a newer digital universe created by humans, but inhabited by digital machines. We visit this digital world by peering through the portholes of our computer screens, and we manipulate it with keyboard and mouse much as a nuclear technician works with radioactive materials via glovebox and manipulator arms. Our machines manipulate the digital world directly, but they are rarely aware of the analog world that surrounds their cyberspace.

Now we are handing sensory organs and manipulators to the machines and inviting them to enter analog reality. The scale of possible surprise that this may generate over the next several decades as sensors, lasers, and microprocessors coevolve is breathtakingly uncertain.

Scaling Change: Orders of Impact

Such change seems overwhelmingly uncertain because we tend to compress outcomes into a telephoto view of the future–just as a telephoto lens compresses distance, creating the illusion that distant objects are close to nearby objects, our expectations lead us to compress chronology and overlook the logic of orders of impact as early developments contribute to later innovation. The way to make long-term sense of sensors and their place in the digital technology complex is to think explicitly in terms of first-, second-, and third-order impact, and beyond.

The history of the internal combustion engine provides a good example of orders of impact and their predictability.

The first-order impact was the "horseless carriage," and that was no surprise to anyone for the simple reason that it was precisely what everyone was trying to build. The process of invention and subsequent diffusion was chaotic, but the outcome was clear.

The second-order impact–the traffic jam–came as something of a surprise, but only to idealists and others who had not taken the time to anticipate consequences. In fact, traffic jams were not unfamiliar to city dwellers in the horse and buggy era, so it was all but a foregone conclusion that the same would happen with cars.

But the third-order impact–suburbs–was rather more surprising, even though the first suburbs had already been around for decades on a small scale [4]. But the mobility afforded by the automobile led to the reinvention and dramatic spread of suburban life.

The biggest surprise though was the fourth-order impact–the rise of huge regional conurbations, such as the Atlantic Seaboard and the Los Angeles basin. This was unexpected in 1900 because everyone assumed that by conferring mobility, the auto would lead to the dispersal of populations, rather than their further concentration.

Sensors' Orders of Impact

What assumptions are now blinding us to the impact of cheap and ubiquitous sensors? Notice the interesting pattern of alternating tension between expansion and constraint in each of the successive orders of impact for the internal combustion engine. The horseless carriage gave us sudden expansion locally, yielding a new constraint–the traffic jam. Early adopters responded with a third order expansion–moving to the suburbs. This in turn led to a new fourth order constraint–megacities.

Look for the same pattern of surprising consequence and interplay between expansion and constraint as sensors assume center stage in the information revolution in the decades ahead. And keep in mind that just as microprocessor and laser innovations continue today, sensor advances will have reverberating consequences well beyond the next decade. While the leading edge of sensing is with us today, the trailing edge will be felt as far out as 50 years from now, just as we're still getting reverberations from earlier advances in lasers and microprocessors–not to mention the internal combustion engine.

Like the evolution of automobiles, the evolution of sensing technologies will pass through several orders of change.

The first-order impact of sensors is quite obvious–cheap input-output (I/O) for networks and computing devices, plus modest levels of effecting - actual computer controlled modification of the analog world - and the creation of simple "smartifacts" (defined below). A few examples include:

- Sensor-augmented heating ventilation and cooling (HVAC) systems, delivering dramatic improvements in performance and energy savings
- "Smart" courier boxes with sensors embedded in the cardboard skin that sense accelerations and box treatment en route
- Disposable video cameras as a consumer fad.

The second-order impact is more interesting. As effecting becomes richer, look for sensor/effector arrays to mature into simple classes of "smart-stuff"–smart materials and intelligent artifacts–smartifacts [5]. In addition, cheap sensors will contribute greatly to making old notions of hyperautomated manufacturing - cyber - manufacturing a practical reality. The block in the past has been one of measurement and control granularity: the available sensors and effectors have been too coarse to really deliver the requisite levels of control over the materials. MEMS-scale devices radically reduce the scale of control, and make true automation practical.

The possibilities of smartifacts will lead to important third-order consequences, such as the advent of mass-customization. Ever since Stan Davis popularized this concept in the late 1980s, the philosopher's stone of manufacturing has been finding a means of combining the appeal of unique one-purchaser customization with the economies of scale associated with mass manufacturing [6]. The scale-change triggered by sensors and effectors could set the stage for this to become a reality across a broad segment of industries, from autos to consumer apparel.

But there are even more interesting third-order impacts. One of the most important will be an acceleration in the decay and centrality of Von Neumann computing architectures. Consider a research initiative already underway to build turbulence-damping "smart-skins" for fighter wings [7]. This work contemplates a leading-edge array of myriad 0.2 millimeter-sized silicon microflaps, interspersed between equally small MEMS turbulence sensors.

This array is comparatively buildable today, but computational control is another matter. Even if one had an infinitely fast supercomputer controller in the fuselage linked by fiber-optic network to the array elements, the limits of the speed of light alone would make it impossible for the flaps to respond quickly enough to sensor data sent downwire to the computer and then back out as a control instruction. The only option is to create radically new hyperdistributed computational architectures, in effect a community of processors interspersed throughout the array, where each element is a triad of processor, sensor, and effector. This kind of development opens the information world to a host of way-radical exotica: from theories based on ecology and symbiosis to, in one case, models built around economics [8].

At the fourth-order level, we will witness a generalized substitution of computation for stuff, and possibly the erosion of the entire digital order that we now take for granted. We will literally dematerialize objects, substituting, as Nick Negroponte likes to observe, "electrons for atoms." Using arrays of sensors and effectors, one could take a structure (say, a bridge truss or aircraft spar) that in inert form lacks the intrinsic structural strength to support a given load, and dynamically sense and align its elements to yield the desired strength at a fraction of the weight of a traditional structure [9].

The essence of this fourth order is that we will be connecting two previously parallel universes–the digital universe of our creation and the preexisting physical analog universe. The two worlds are in collision, and the biggest surprises will come when the boundaries between the two blur beyond recognition. Warriors fighting "virtual war games" over networks may discover after the fact they were killing real opponents [10]. Autonomous smartifacts, successors to today's military UAVs (unmanned aerial vehicles), will become annoyingly commonplace. And just as the first biplanes were quickly turned from reconnaisance to battle, these new autonomous smartifacts will inevitably be pressed into service as "warbots" of unprecedented lethality. The Advanced Research Projects Agency (ARPA) recently commissioned research on micro UAVs–autonomous flyers smaller than a dollar bill using micromachine engines to sustain a one-hour flight time and a 16-kilometer range. Just the thing for a 21st century James Bond–or a terrorist bent on assassinating a well-guarded head of state.

As the foregoing example implies, things get especially interesting as device size shrinks. If one shrinks the device sufficiently, it becomes possible to dispense with batteries entirely and allow the gizmo to run off ambient energy–sunlight, vibration, or perhaps even breezes flowing over tiny MEMS cilia. And cost shrinks with size, opening the door to what researchers refer to as "MEMS dust"–tiny, disposable devices used in a "toss-out-and-forget" manner for any number of applications from environmental sensing to surveillance.

Digital Is Dead?

The impact of ubiquitous sensors on the digital computing order could be especially surprising. In the short term, the challenge is interfacing analog sensor devices with digital computers and networks. However, it is inevitable that there will come a point when it will seem obvious that the logical next step is to create analog computers and networks in order to more effectively interface with and exploit the growing sensor arrays. And it may prove likely that there are instances where it is simply impossible to accomplish a desired goal with digital technology at all. Perhaps the ultimate solution to controlling the aircraft wing smart-skin mentioned earlier is with distributed analog electronics rather than arrays of digital processors. A modest indicator of this trend is visible today in the audiophile world. CDs may have replaced phonograph records, but the most sophisticated audiophile stereo systems available today rely on old-fashioned vacuum tube technology to perform their magic. Audiophiles can tell the difference between sound that has been deconstructed into bits and reconstituted as an analog waveform and sound that has remained in analog form all along.

Thus, the long-term consequence of the coming sensor revolution may be the emergence of a newer analog computing industry in which digital technology plays a mere supporting role, or in some instances plays no role at all. At first, these new analog devices will probably occupy a place similar to that once occupied by supercomputers and parallel processing systems–specialized devices tailored to work on especially challenging tasks. But in the longer term, say 25 to 50 years maybe the digital order we take for granted will prove to be merely a transitional phase in a longer process of connecting symbolic universes of our creation with the preexisting physical world. Outlandish as this may sound, imagine telling information professionals in 1948 that one day they would do their work on then nonexistent digital electronic computers based on microprocessor descendants of the transistor invented in that year.

Digital Is Dull?

Yet as shocking as this sounds, one short-term surprise will prove even more startling to today's digital establishment. Ever since the invention of the transistor, digital has been cool, and analog has been the forgotten old-fashioned stepchild. That is going to reverse itself in the next decade. Analog is going to be the great new unexplored frontier, and digital will seem just a bit dull.

Three decades ago, a generation of graduate students quietly made fun of their professors, who were trained in a world of analog electromechanical devices. They thought, "Oh, those old fuddy-duddies, vacuum tubes and analog, how quaint. Digital is hip." Well, those professors will now have their revenge, for their once-arrogant students will be old fuddy-duddies now. The next generation will think of their digitally-steeped teachers: "You had it so easy. I mean, digital representations, it's so straightforward, it's so discrete, it's so easy to contain. Analog is messy and subtle and unpredictable, and that's where the big wins are, so get out of the damn way and let us assume the mantle of innovation."

Of course, reality will be subtly different. Analog will be the frontier, but in turn it will lead to new digital challenges. That said, researchers would do well to ask their departmental librarian to dust off some of those overlooked 1950s Ph.D. dissertations on then interesting, now seemingly irrelevant analog problems, because we may suddenly discover that a host of insights from the analog 1950s are going to be very relevant in the analog years after 2000.

Footnotes

1. For example, the next big surprise will occur on the World Wide Web. At the moment, the Web is defined by people accessing information. Over the next two years, look for the Web's focus to shift away from this to a new model of people accessing other people in information-rich environments. In other words, the Web will go from being an information environment to an interpersonal environment in which information plays an important role supporting human interactions.

2. It is noteworthy that the Advanced Research Project Agency (ARPA)–the same agency responsible for the initial research leading to the development of the Internet–has been a key player in catalyzing MEMS research. Just as ARPA's investments in the early 1970s led to huge 1990s commercial payoffs in the form of the Internet "revolution," its 1980s-era investment in MEMS could prove to be of crucial importance in the next decade.

3. Anyone who has used a disposable lighter has experienced piezo-materials in action–pushing down on the tab flexes a fleck of piezo-crystal, generating an electrical charge converted into a spark.

4. The first suburbs arguably appeared in the greater Boston area in the 1820s, and later experienced dramatic growth in the late 1800s, thanks to the advent of street car systems (see Henry C. Binford's The First Suburbs [University of Chicago Press, 1985]).

5. Smartifact is a term first coined by researcher Harry Vertelney at Apple Computer in the 1980s to refer to new forms of software-based agents. Smartifact is used here to connote something different: physical objects possessing rudimentary "intelligence" sufficient to be aware and affect the environment around them.

6. See Stan Davis's Future Perfect (Addison-Wesley, 1996, 1987).

7. This research is being led by Dr. John Kim at the University of California at Los Angeles, under a grant from ARPA.

8. Bernardo Huberman at Xerox's Palo Alto Research Center is doing especially interesting work on this front.

9. This research was performed by Andy Berlin, currently at Xerox's Palo Alto Research Center.

10. This is often referred to as the "Ender's Game scenario," a reference to a science fiction novel in which a group of kids are training in a computer simulation to eventually save Earth from invaders, only to learn that their graduation "simulation" was, unbeknownst to them, an actual war commanded by them (see Orson Scott Card's "Ender's Game" (Analog [August 1977]; TOR [1985]).

APPENDIX M - DREXEL'S NANOSYSTEMS

- 10.2. Spatial Fourier transforms of nonbonded potentials. Barrier heights and sums of sinusoids.
- 10.3. Sliding of irregular objects over regular surfaces. Motivation: a random-walk model of barrier heights. A Monte Carlo analysis of barrier heights. Implications for constraints on structure. Energy dissipation models. Static friction. Coupled sites.
- 10.4. Symmetrical sleeve bearings. Models of symmetrical sleeve bearings. Spatial frequencies and symmetry operations. Properties of unloaded bearings. Properties of loaded bearings. Bearing stiffness in the transverse-continuum approximation. Mechanisms of energy dissipation. Sleeve bearings in molecular detail. Less symmetrical sleeve bearings.
- 10.5. Further applications of sliding-interface bearings. Nuts and screws. Rods in sleeves. Constant force springs.
- 10.6. Atomic-axle bearings. Bonded bearings. Atomic-point bearings.
- 10.7 Gears, rollers, belts, and cams. Spur gears. Helical gears. Rack-and-pinion gears and roller bearings. Bevel gears. Worm gears. Belt-and-roller systems. Cams. Planetary gear systems.
- 10.8. Barriers in extended systems. Sliding of irregular objects over irregular surfaces.
- 10.9. Dampers, detents, clutches, and ratchets. Dampers. Detents. Clutches. Ratchets and reversibility.
- 10.10. Perspective: nanomachines and macromachines. Similarities between nanomachines and macromachines. Differences between nanomachines and macromachines.
- 10.11. Bounded continuum models revisited
- 10.12. Conclusions

- Chapter 11 Intermediate Subsystems
  - 11.1. Overview
  - 11.2. Mechanical measurement devices. Well partitioning and indicator latching. Force discrimination. Shape and position discrimination. Reliability through iterated measurements.
  - 11.3. Stiff, high gear-ratio mechanisms. Harmonic drives. Toroidal worm drives.
  - 11.4. Fluids, seals, and pumps. Fluid micromechanics. Walls and seals. Pumps and vacuum systems.
  - 11.5. Convective cooling systems. Murray's Law and fractal plumbing. Coolant design. Cooling capacity in a macroscopic volume.
  - 11.6. Electromechanical devices. Conducting paths. Insulating layers and tunneling contacts. Modulated tunneling junctions. Electrostatic actuators. Electrostatic motors.
  - 11.7. DC motors and generators. Charge carriers and charge density. Electrode charging mechanism. Motor power and power density. Energy dissipation and efficiency. Motor start-up. Speed regulation.
  - 11.8. Conclusions

- Chapter 12 Nanomechanical Computational Systems
  - 12.1. Overview
  - 12.2. Digital signal transmission with mechanical rods. Electronic analogies. Signal propagation speed.
  - 12.3. Gates and logic rods. Electronic analogies. Components and general kinematics. A bounded continuum model. Dynamics and energy dissipation in mobile rods. Dynamics and energy dissipation in blocked rods. Fluctuations in stored energy. Thermal excitation and error rates. Summary observations based on the exemplar calculations.
  - 12.4. Registers Kinematics of an efficient class of register. Device size and packing. Energy dissipation estimates. Fluctuations in stored energy.
  - 12.5. Combinational logic and finite-state machines. Finite-state machine structure and kinematics. Finite-state machine timing and alternatives. Fan-in, fan-out, and geometric issues. Signal propagation with acoustic transmission lines.
  - 12.6. Survey of other devices and subsystems. Gates for non-PLA combinational logic. Carry chains. Random-access memory. Mass storage systems. Interfaces to macroscale systems.
  - 12.7. CPU-scale systems: clocking and power supply. Clocking based on oscillating drive rods. A CPU-scale drive system architecture. Energy flows and clock skew. Power requirements. Power supply and energy buffering.
  - 12.8. Cooling and computational capacity
  - 12.9. Conclusion

- Chapter 13 Molecular Sorting, Processing, and Assembly
  - 13.1. Overview

APPENDIX N - BIOMEDICAL ENGINEERING AT PENN AND IIT

MEDICAL PHYSICS AT PENN:

Biomedical engineering at Penn prepares students for leadership in bioengineering enterprise in industry, government and non-profit organizations involved in the development and sale of advanced biomedical technologies. The Program's flexibility allows students to shape the curriculum to their career goals in industry, government or health-care systems. Courses are:

- Independent Study

  An opportunity for the student to become closely associated with a professor in (1) a research effort to develop research skills and technique and/or (2) to develop a program of independent in-depth study in a subject area in which professor and student have a common interest.

- Intro to Bioengineering

  Discussion of application of science and engineering to problems in biology and medicine. Includes design project.

- Intro to Biomechanics

  Application of statics and dynamics to do simple force analyses of the musculoskeletal system. Introduction to the fundamentals of strength materials. Biomechanics of soft and hard tissues: microstructure and mechanical properties. Biomechanics of injury and analysis of pathological material from the perspective of engineering mechanics.

- Intro to Human Physiology and Anatomy

  An introduction to quantitative aspects of human physiology. An emphasis will be placed on cellular, neural, cardiovascular, respiratory and renal physiology. Applications to clinical and bioengineering problems will be emphasized.

- Bioengineering Laboratory I

  First term of a two year sequence designed to integrate real world experiences into various Bioengineering and Bioengineering Science courses. Emphasis is on bioengineering aspects of mechanics, electricity and magnetism. Includes regular lab assignments and work with human material in the medical examiner's office.

- Bioengineering Laboratory II

  Second Bioengineering Laboratory - Emphasis on Bioengineering aspects of biomaterials, applied mathematics, and physical chemistry.

- Structure and Properties of Biomaterials

  An examination of the issue of biocompatibility of materials used in surgical implants and medical devices. Consideration is given both to degradation of materials by biological systems and to biological response to artificial materials.

- Physical Foundations of Electromagnetics

  The goals of this course are to introduce the physical principles of electrical charge, forces and fields and their relationship to living systems; develop principles of elementary circuit theory based upon linear field equations; and to introduce principles of quantum physics to enable a description of atomic and molecular structure with examples drawn from biological systems.

- Chemical Basis of Bioengineering II

  Critical concepts in physical chemistry essential to understanding function in living systems. Emphasis on applications of thermodynamics to living systems with topics in organic chemistry, cell biology and molecular biology introduced as needed.

- Bioengineering Systems

  Modeling of mechanical and electrical systems by means of ordinary linear differential equations, transient and steady state solutions, the transfer function. Laplace transform, Includes material on analog circuits and circuit theory.

- Bioengineering Laboratory III

  Laboratory with experiments in biophysical chemistry biomechanics, and biomaterials.

- Bioengineering Laboratory IV

  Hands-on instrumentation laboratory involving the design and construction of circuits used to measure and incorporate biopotential signals. Topics include EMG amplification and conditioning, force measurements using strain gage technology, and infra-red telemetry to measure joint-angle. Short lectures are followed by experimental workshops in which students work in small groups.

- Chemical Basis of Bioengineering III

  Advanced topics in physical chemistry including solution and colloid chemistry, electrochemistry, kinetics applied to biological systems.

- Introduction to Biotransport Processes

  Introduction to basic principles of fluid mechanics and of energy and mass transport, with emphasis on applications to living systems. Mass, momentum and energy conservation; mass diffusion; convective diffusion.

- Hemodynamics

  The structure and operation of the mammalian cardiovascular system will be discussed from a quantitative point of view, for both the normal and the abnormal case. Material includes relevant instrumentation and exposure to clinical situations.

- Advanced Transport Processes in Living Systems

  Modeling of momentum, energy, and mass transport processes in physiological systems. Boundary layer, penetration, and compartment models; interphase transport. Applications to respiratory, circulatory, and other systems.

- Seminar in Biomechanics

  The design and selection of engineering materials for the biomedical environment. Principles of fabrication processing, and clinical application. Examples include knee ligament, prosthetic external ear, bone rasp, etc. Students will carry out the design of a specific device.

- Seminar in Biomechanics

  The design and selection of engineering materials for the biomedical environment. Principles of fabrication processing, and clinical application. Examples include knee ligament, prosthetic external ear, bone rasp, etc. Students will carry out the design of a specific device.

- Biomedical Instrumentation

- Medical Radiation Engineering

- Human Visual Communication . An engineering approach to the visual system and comparison with man made image processing and manipulation techniques. Visual system performances in the spatial, temporal, and color domains and the interaction of these signal dimensions are studied. Basic image processing operations and their relation to visual system image coding and architecture are discussed.

Graduate Courses

- Quantitative Human Physiology

  Introduction to human physiology using the mathematical and quantitative methods of engineering and physical science. Emphasis is on the major organ systems at the macroscopic level. Includes analysis of cells and cellular content, cardiovascular system, respiratory system, renal system, neural systems, and other topics.

- Bioengineering I - Biomechanics and Biotransport

  Introduction to engineering principles applicable to the biomedical sciences. Biomechanics, including solids and fluids. Analysis of stress, equations of motion, strain, rate of deformation. Constitutive equations for solids and fluids. Applications to hard tissue stress analysis, biotransport in lung and circulatory system, heat transfer in human and animal systems.

- Bioengineering II - Biosystems

  Introduction to the theory of linear systems and control, with applications to the analyses of biomedical systems and transducers. Mathematical modeling of biomedical processes.

- Bioengineering III - Biomaterials

  Comprehensive background in biomaterials and groundwork for advanced specialty topics including: mechanical, chemical, and thermal properties of replacement materials and tissues. Implantation of materials in the body is studied from the point of view of biological response of tissues and evaluation of biomaterials as implants.

- Bioengineering IV - Cell Biology and Molecular Structure

  The objective of this course is to integrate structure with function at the molecular level. With emphasis on cellular structures, students are introduced to the major tissue types found in the human body and the kinds of specialized cells which comprise them. Specialized functions and proteins associated with each of these tissues are examined in detail at the molecular level. The cellular mechanisms associated with ion transport, cell adhesion, cell division, DNA, RNA and protein synthesis are explored in detail, as well as relevant control mechanisms involving signal transduction and intracellular signaling. The role of the immune system is investigated as well as its molecular regulation. The function of growth factors in altering cell behavior is examined with emphasis on the cellular response to these types of signals.

- Computational Neuroscience and Neuroengineering

  Analysis of current computational models of neural function. Introduction to simulation techniques for neural networks. Emphasis on models of cerebral cortex and visual perception.

- Rheology of Biological Fluids

  An introduction to the properties of deformation and flow of fluids of physiologic importance. Modeling measurement of non-Newtonian and viscoelastic properties of body fluids in health and disease. Fluids discussed include blood, synovial fluid, epithelial secretions, and others.

- Quantitative Image Analysis

  Most of the time will be spent on different kinds of analysis methods (e.g., intensity measurements and approaches to segmentation) along with brief reviews of necessary mathematical background (e.g., transforms) and examples of specific areas of application (primarily biomedical) While traditional image processing techniques will be reviewed, a means of preparing images for analysis, they will not be a principle focus of this course.

- Engineering Aspects of Neurophysiology

  Emphasis will be on quantitative analysis of neural phenomena. Topics include EEGs, synaptic transmission, physiology of nerve axons, biophysical principles, and biological effects of electrical fields on nervous tissue, body impedance, and electrical hazards.

- Biomedical Instrumentation

  Design of electronic instrumentation for the recording and analysis of physiological signals, with special emphasis on computer applications. Electrical properties of physiological transducers. Design and analysis of simple amplifiers and filters for signal conditioning, Electrical safety requirements. Extensive circuit and computer design work.

- Modeling Biological Systems

  This course will present a comprehensive account of the application of modeling methodology to the investigation of biological systems. The emphasis through will be on an organized overview of the tools and techniques rather than the detailed mathematical structures upon which they may rely. The course will draw examples widely from the current literature in an attempt to not only show the topical relevance of the subject matter but also to equip participants with an understanding of the diversity of domains to which the techniques and methodologies apply.

- Injury Mechanics

  A background in physiology and anatomy is also recommended. This course is intended as an introduction to investigating the mechanics of injury, from the organism to the tissue level. The students will be exposed to both formal didactic instruction and selected field work. The course will cover principles in continuum and analytical mechanics, and will use applications in injury research to illustrate these concepts. The course will be divided into three major units. The first will be an introduction to variational principals of mechanics and calculus of variations, and will apply these concepts to injury problems (e.g., occupant kinematics during a collision, vehicle kinematics, impact to padded surfaces). Special emphasis will be placed on converting a system input into a body response. The second unit of the course will be used to discuss the effect of gross body motions on tissue and organ mechanical response. Material models of biological tissue will be discussed, and examples relating body motion to tissue response will be reviewed. In the final unit of the course, students are required to research and review a problem of their choice and present a report detailing an engineering based solution to the problem.

- Medical Radiation Engineering

  This course starts with a careful consideration of basic radiation physics. Applications are made to Medical Radiological Science including Nuclear Medicine, Diagnostic Radiology and Radiation Therapy. Lectures and laboratories are located in the Radiology Research Laboratory in the Medical Education Building.

- Techniques of Magnetic Resonance Imaging

  Detailed survey of the physics and technology of magnetic resonance imaging as applied to medical diagnosis. Basics of magnetism and NMR. Fourier analysis, imaging pulse sequences, contrast mechanisms, chemical shift, and flow effects, with chemical applications.

- Lasers in Medicine

  Interaction of laser radiation with living systems. Application to physiological, medical and surgical problems, including hemodynamical investigations with laser Doppler techniques, retinal photocoagulation, and tumor detection. Laser hazards and safety. Selected topics including testing of neural components in vision, ocular refraction, and others.

- Ultrasonic Imaging

  Principles and technology of medical ultrasonic imaging. Fundamentals of wave motion; properties of ultrasonic fields; methods of measurements and mechanisms of attenuation and scattering; pulse-echo imaging; Doppler methods and color flow imaging; transmission mode imaging; clinical applications and image artifacts.

- From Biomedical Science to the Marketplace

  This course explores the transition from discovery of fundamental knowledge to its ultimate application in a clinical device or drug. Emphasis is placed upon factors that influence this transition and upon the integrative requirements across many fields necessary to achieve success. Special emphasis is placed upon issues of intellectual property and upon the FDA process of proving safety and efficacy.

- Entrepreneurship in Biomedical Technologies

  This course brings together elements of economics, business planning, engineering, and basic science in order to study the evolution and transfer of advanced medical technologies into the marketplace. Emphasis is placed on the interrelationships among the strategic factors that influence investment in this field: research and development of a health care product or service; marketing; manufacturing; management organization; and finance. The course utilizes the business plan development as the vehicle for integrating technology and business strategies required for entrepreneurial success. Actual devices and technologies currently in use or in the planning stage are discussed.

- Case Studies in Bioengineering Research

  This course focusses on the special nature of bioengineering research, including the definition of engineering goals based on needs of clinical medicine, and ethical and legal issues related to human and animal research and academic integrity. The course will provide an in-depth examination of three case histories of bioengineering research. These include: mammography; heart valves; and health and safety issues related to microwave radiation. The case histories will involve careful analysis of the pertinent technical literature, as well as lectures from outside experts in medical practice, technology assessment, and bioengineering.

- Engineering Principles of the Visual System

  Quantitative analysis of the engineering principles and design considerations of the human visual system including detection, coding, transformation and representation of images and their attributes. Examples include color coding and color constancy, spatial considerations of retinal image sampling and significance of image statistics and image features in human visual system processing and analysis.

- Biomedical Application of Fluid Mechanics

  Momentum, mass, and heat transfer of importance in human physiology. Low Reynolds number flows in the microcirculation, high Reynolds number flows in the respiratory system, peristaltic pumping, respiratory and circulatory mass transfer, motion of microorganisms, and heat transfer in the respiratory and circulatory system. Relevance of flow processes to human disease and medical diagnosis and treatment.

- Low Reynolds Number Flows

  Low Reynolds number hydrodynamics with emphasis on biological transport processes. Creeping motion, flow in porous media, and the motion of rigid particles in unbounded and bounded media. Pore theory and its application to biotransport.

- Biological Elasticity

  Large deformation mechanics of biological materials. Nonlinear elasticity theory, strain energy functions, constitutive laws of hyperelastic and viscoelastic biological materials. Applications to heart, lung, and arteries.

- Biomechanics

  Viscoelasticity and its applications to hard and soft tissue; viscoelastic stress analysis; finite element method in biomechanics; applications to dentistry and orthopaedics.

- Advanced Topics in Biomaterials

  The effect of nearly inert and bioactive materials on surrounding tissues; mechanisms of bone tissue growth enhancement with bioactive ceramics; elasticity and strength of porous coated and ceramic coated implants; tissue remodeling around coated implants.

- Circulatory System Dynamics

  Pressure and flow measurement; hemodynamics; wave propagation in blood vessels; the heart as a pump; the microcirculation; interaction of subsystems; models of the cardiovascular system; physiological and clinical studies.

- Biocontrol

  Quantitative computer-assisted analysis of a selected cardiovascular control system; group analysis of the pertinent literature and preparation of a paper.

- Methods in Engineering Education

  Concepts in preparation and presentation of lecture and laboratory courses. Topics include course development, setting of educational goals, classroom format including lectures and visual aids, preparation of examinations and assignments, and grading. Workshops and practice including participation in departmental undergraduate courses.

- Special Topics in Bioengineering

  Special Topics in subjects of interest to Bioengineering students.

- Summer Institute in Rehabilitation Engineering

  Rehabilitation Engineering is the multidisciplinary field in which technology is developed, applied, modified, specified and evaluated to directly assist people with disabilities (both temporary and permanent) in carrying out the roles and functions of everyday life. The Summer Institute of Rehabilitation Engineering is devoted to understanding how problems of daily living are translated into engineering problems: how the rehabilitation engineer translates human needs into design specifications; and how the rehabilitation engineer faces special constraints.

- Master Thesis

- Thesis/Dissertation Research

MEDICAL PHYSICS AT IIT

The program in Biomedical Engineering at Indian Institute of Technology, routinely admits students with backgrounds in Engineering, Life Sciences, Medicine and Physical Sciences. Courses are:

- Bio-mathematics

  Ordinary differential equations of the first order: exactness and integrating factors, variation of parameters; Ordinary linear differential equations of n-th order: solution of homogeneous and non- homogeneous equations, operator method, method of undetermined coefficients and variation of parameters; Sequence and series; Power series methods for linear ordinary differential equations. Laplace transform and its applications; Fourier series and Fourier transform and applications in biomedical engineering. Partial differential equations: models in physiology, introduction to solution techniques such as variable separation, product method and Laplace Transform method.

- Biostatistics and Design of Experiments

  The scope of statistics in biomedical data analysis; Statistical design of experiments for clinical and laboratory data: random allocation, methods of allocation without random numbers; Volunteer bias; Crossover designs; Selection and distribution of experimental unit; Case control analysis. Applications of probability and standard distributions: Estimation, standard error and confidence interval, testing of hypotheses; Correlation and regression; Analysis of variance; Factor analysis; Statistical method oriented and problem oriented illustrations for computer aided inferencing.

- Physiology for Engineers

  Basic cell physiology; Biochemical cycles. Systemic physiology: Neuromuscular system; Blood and lymph; Circulatory system; Gastro-intestinal system; Kidney and excretory system; Sensory systems- visual, auditory, vestibular; Endocrine-pituitary, adrenal, pancreatic, etc.

- Clinical Physiology

  Pathophysiology of disease processes-Infection, degeneration, neoplasm, trauma; General diseases: bacterial, viral, parasitic, tropical. Diseases of different organ systems; Cardiovascular: valvular, conduction defects, myocardial diseases, vascular episodes, investigative techniques; Respiratory System: infections, tuberculosis, occupational hazards, bronchitis, asthma, pleural diseases, spirometry, investigations; Disease of Gastro-intestinal tract: peptic ulcers, appendicitis, cirrhosis of liver, liver failure; Diseases of Central Nervous System: sensory organ diseases, cerebellar disorders, upper and lower motor neuron, cerebrum-vascular and other disorders, spinal cord, modern investigation techniques; Kidney diseases: Glomerulo and pylonephritis, nephrolithiasis, uti, renal failures, artificial kidney; Reproductive system disorders: menstrual disorders, sterility, family welfare techniques; Hormonal disorders: diabetes mellitus, thyrotoxicosis, myxoedema, gigantism, dwarfs; Disorders of blood: anaemia, polycythemia, leukaemia, agranulocytosis. Examination of a patient; Health Care delivery system; Primary Health Center; Indices of Health; Epidemiology; Structure of a modern hospital.

- Physiological Measurements and Quantitative Physiology

  Programming for Data Acquisition. Experiments on: Behavior of excitable tissue - Electrical characteristics, mechanical characteristics of muscles; Kidney / Dialysis; RBC Membrane Proteins, Haemoglobin - types and separation, Electrophoresis, ELISA; Spirometry and lung physiology; Characteristics of the cardiovascular system; Energy Expenditure and Energy Balance.

- Biorheology

  Concepts of stress and strain and their relationships; Rheology and rheological equations; Definition of biorheology, its connection with physics and biology; Need for biorheology and rheological concepts; Haemorheology: definition and clinical aspects; Haemodynamics, blood viscosity factors, cardiovascular haemorheology; Rheology of body fluids; Application of rheology in diagnosis, treatment and fundamental understanding of diseases; Experimental determination of blood and plasma viscosity.

- Introduction to Medical Informatique

  Data and information capture in health care management and clinical delivery systems; Multimodal data; Epidimeology and etiology data; Data quality; Importance of data organization. Organization and retrieval of health care and clinical data; Data base systems and implementation for medical applications; Multi-sensor data with particular relevance to the organization of images. Intelligent systems approaches in medicine; Paradigms of inferencing; Building of knowledge-based systems; Treatment of uncertainty; Learnability and adaptive systems. Networked systems and intelligent retrieval; Web-based inferencing. Building and use of decision support systems for clinical applications.

- Molecular Basis of Disease Processes

  General themes; Chromosomes; Metabolic disorders of carbohydrates, amino acids, organic acids, purines, pyrimidines, lipoprotein, lipids, porphyrins, heme, metals; Peroxisomes and lysosomal enzymes, hormones, vitamins; Blood and blood forming tissues, membrane transport systems, defense and immune mechanisms; Connective tissue, muscle; Basis of diseases related to the gross anatomy, AMI, etc.; Molecular expression of diseases; Disease diagnostics using molecular markers.

- Medical Instrumentation

  Medical measurands; Sensor characteristics and design for measurement of medical parameters like ECG, arterial flow, blood pressure, heart sounds; Biopotential amplifiers, charge amplifiers and other interfaces; Signal conditioning and display. Medical imaging considerations; X-rays, X-ray tube design, film and detector design; CT - scanners: generations and basic algorithms. Elements of electrical safety; Built-in safety features for medical instruments.

- Physiological System Modeling

  Introduction to modeling: biophysical models and black box models, interpretation of physiological signals using models, numerical methods and computer implementation; Experimental methods for modeling physiological systems, opening the loop in physiological systems; A systems view of the membrane of excitable cells, determination of impulse responses of the components of the membrane, need for the non-linear Hodgkin-Huxley model. Action potentials to macroscopic signals- a model of the electromyogram, electrode configurations, Motor Unit Potentials, voluntary EMG, applications of the model in EMG analysis; Modeling muscle contraction: Huxley's biophysical model, linearization of Huxley's model, applications of the linearized model in muscle control. Systems analysis of sensory receptors and physiological control systems, e.g., sensory receptor transfer functions, pupil control system, vestibular control system, simple models of the immune response to disease; Selected topics in applications of physiological models, e.g., aspects of cardiovascular modeling (fluid flow, cardiac rhythm and regulation), drug delivery control systems; Current topics.

- Bioelectricity

  Generation and maintenance of the resting membrane potential; Contribution of membrane ionic pumps and exchange processes. Action potential of excitable cells: Quantitative description, Hodgkin-Huxley model, significance of parameters in Hodgkin-Huxley equations; Voltage-clamp experiments: design, and analysis of results; Factors determining the initiation, amplitudes, and kinetic properties of action potentials. Passive membrane electrical properties: Cellular resistance, capacitance, time constant and space constant, methods of measurement; Importance in cellular excitation and signaling: Impulse propagation. Electrophysiology of synaptic transmission: Prejunctional and postjunctional electrical events; time courses of transmitter-activated membrane currents and potentials in skeletal and smooth muscle; Electrical models of the skeletal and smooth muscle membranes.

- Biomedical Fluid Dynamics

  Introduction to fluid mechanics; Fluid properties, basic laws governing conservation of mass momentum and energy; Laminar flow, Couette flow and Hagen-Poiseuille equation, turbulent flow. Flow dynamical study of circulatory system, heart and blood vessels, anatomy and physiological considerations; Components and functions of arterial and venous systems; Lymphatic system; Body fluids and their motions; Flow of Newtonian and non-Newtonian fluids in rigid tubes, flexible tubes and collapsible tubes; Blood flow through arteries and veins; Holt and Conrads experimental investigations. Kinetic energy, flow, pressure-flow relations in vascular beds; Cardiac cycle; Cardiac valve dysfunctions; Blood pressure, regulation and controlling factors; Coronary circulation, heart failure.

- Ergonomics

  Introduction to Ergonomics and its application; Man-Machine-Environment System; Anthropometry and joint motions; Work Posture, Environmental factors and human performance. Designing of Controls and Displays, Control panel Organization; Principals of product design; Problem solving; Seminar on ergonomics related issues in Medicine.

- Cell Physiology and Biopotentials

  Introduction to molecular and cellular Biology; Molecules, membranes and cells; Cell structure and function: organelles, cytoskeleton and plasma membrane; Metabolism and energy cycles; Synthesis of proteins and nucleic acids; Transport across cell membranes and cytoplasm; Cell to cell biochemical signaling: hormones, receptors and synaptic transmission; Cytoskeleton and movement, Actin and Myosin; Energetics of ion pumps. Origin of biopotentials; Resting membrane potential; The resting membrane as a potassium electrode; Nernst potential; Selective permeability and the Donnan equilibrium; Action potentials: ionic basis, properties of generation and conduction, examples in different cell types, relation to surface-recorded signals; Synaptic potentials: passive properties and integration.

- Medical Imaging Physics

  Review of atomic structure and atomic particles: electrons, protons, neutrons, positrons, neutrinos, etc.; Classification of elements as per the periodic table. Atomic transitions - electron transitions and the generation of x-rays; Nuclear transitions and radioactive decay of nuclei. Characteristics of x-ray beams; Interaction with matter; Attenuation and interaction of x-rays in the human body; Films and fluoroscopic screens; Detrimental effects of radiation; Radiation safety and dosimetry; Overview of generation of radioisotopes. Physics of Nuclear Magnetic Resonance and its application in the field of diagnostic medicine. Interaction of Ultrasound with tissue; Physics of ultrasound imaging; Uses in diagnosis.

- Biomaterials

  Structure and property relationships in materials, ceramics and polymers; Interactions of materials with the human body; Influence of microstructure and environment on fatigue and fracture of materials. Composite materials concepts and applications; Whiskers and fibres medical applications such as structures, orthopedic implants, artificial organs, dental materials, etc.; Implementation problems - inflammation, rejection, corrosion, structural failure.

- Elements of Circuits and Instrumentation

  Review of Basic Electric Circuits: Kirchhoff's laws, Thevenin's and Norton's Theorems; Complex impedance and phasors; Electronic Devices: PN junction diodes, diode circuits; Transistors: bipolar and field-effect transistors; Integrated circuit fabrication; Operational Amplifiers, amplifier circuits, non-linear circuits; Transfer functions, Bode plots, Filters. Boolean algebra; Logic circuits: Simple logic circuits, combinational logic, sequential logic, multivibrators, counters.

- Signals and Systems for Biomedical Engineering

  Essentials of continuous time signals and systems: convolution, Fourier transform, system transfer functions; Discrete time signals and systems: sampling and quantization, the sampling theorem and signal reconstruction; Frequency analysis of discrete signals and systems: the discrete Fourier transform, power spectrum estimation and system identification; Analysis of non-stationary processes: examples using Wavelet analysis and Time-series models; Systems with Feedback Control: stability analysis. Examples of physiological signals and systems including feedback systems.

- Electrodiagnostics, Therapy and Electrical Safety

  Review of biopotentials. Electrodes as bioelectric transducers: The electrode - electrolyte interface; Specification and selection criteria for electrodes; Surface, needle, implanted electrodes; Polarizable and non - polarizable electrodes; Practical considerations. Instrumentation for biopotential recording: Practical considerations for optimum performance; Reduction of interference, grounding, safety. Electrical Stimulation: Use in generating evoked potentials, and for therapeutic correction (ECT, pacemakers, defibrillation); Stimulation parameters; Safety limits and precautions. Safety: Hazards associated with the use of electrical / electronic instruments; Provisions for safety; Clinical safety norms. Commonly measured biopotentials and their clinical interpretation ENG, ECG, EMG, etc.; Sensory evoked potentials (visual, auditory, somatosensory).

- Medical Sensors

  Sensor architecture and Classification; Medically significant measurands, functional specifications of medical sensors; Sensor characteristics: linearity, repeatability, hysteresis, drift; Sensor models in the time and frequency domains. Sensors for physical measurands ; strain, force, pressure, acceleration, flow, volume, temperature and biopotentials. Sensors for measurement of chemicals: potentiometric sensors, ion selective electrodes, ISFETS; Amperometric sensors, Clark Electrode; Biosensors, Catalytic biosensors, immunosensors.

Reading in Medical Physics (IIT)

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APPENDIX O - READING IN BIOLOGICAL PHYSICS

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APPENDIX P - SUGGESTED PROGRAM IN BIOLOGICAL PHYSICS

As soon as the board of the School of Physics and Engineering Physics have decided to go for the program in *Biological Physics* this section will be the basis for building up the complete curriculum in all its details down to the level of courses and course plans.

As mentioned in the main text we seek to have all the students in *Biological Physics* to follow the international master's program in nanophysics at the School of Physics and Engineering Physics. This means the following layout:

- all students entering are assumed to have a B.Sc in Physics (or equivalent) and to have passed introductory courses in Electromagnetic Field Theory, Quantum Physics, Thermal Physics and Solid State Physics.

- the backbone of the program is six compulsory courses (Quantum Mechanics FKA080 (5), Condensed Matter Physics FKA090 (5), Statistical Physics FKA100 (5), Computational Physics FKA120 (5), Advanced Experimental Physics FKA 110 (4) and Living State Physics (4 + 8 elective) for a total of 28 credit units (the first five are described more thoroughly at the site www.fy.chalmers.se, *Living State Physics* is described in detail below).

- The elective program in *Biological Physics* contains around ten different courses in the major areas of research in this field present at the School of Physics and Engineering Physics.

- The programs are concluded with a Master's Thesis (20 credit units).

The following ingredients are necessary to complement the present master's program (and its base in physics and engineering physics):

- A special group of appointed professors are there to guide the students in Engineering Physics at Chalmers University of Technology and the Physics students at Göteborg University, in order to put together a good elective program. This is also the basis for assigning the students a research group as their home during the master's program.
- Material should be developed in order to provide teachers in courses during year 1-3 with examples and problems from the area of *Biological and Medical* physics.
- A new course *Living State Physics* should be developed to give the students a good insight in the world and terminology of *Biological Physics*. Its main components are Biophysical chemistry, Molecular Biology of the Cell, Human Physiology and Sensors and Spectroscopies. It is described in more detail below and consists of 4 compulsory and 8 elective points, the latter being a deepening of the understanding in the first part.
- As a reciprocity a course in Physics for Medicine and Biology should be developed (see further down for details).

Living State Physics

This course is aimed at equipping the students with the necessary language and tools for model building and problem solving on systems which come from the biological world. It is based on group work and projects interdispersed with basic lectures, guest lectures, laboratory work and computer simulations. The main reading material will be a number of books (below) and current articles. Important issues to illustrate in the course are

- concepts in physical chemistry essential to understanding function in living systems
- modeling of momentum, energy, and mass transport processes in physiological systems
- intermolecular interaction in molecular complexes, and environment dependence of molecular structure and dynamics
- structure, property, and function of molecular clusters, metal clusters, and supermolecules as the models of bio-systems
- cell structure and function coupled to synthesis of proteins and nucleic acids
- relevant control mechanisms involving signal transduction and intracellular signaling
- tools and techniques for modeling methodologies in the investigation of biological systems
- interpretation of physiological signals using models, numerical methods and computers
- experimental methods for modeling physiological systems such as magnetic resonance imaging as applied to medical diagnosis
- systems analysis of sensory receptors and physiological control systems
- human physiology using the mathematical and quantitative methods of engineering and physical science
- interaction of (laser) radiation with living systems
- analysis of the engineering principles and design considerations of the human visual system including detection, coding, transformation and representation of images and their attributes
- sensor characteristics

Suggested reading:

1. T.F. Weiss, Cellular Biophysics (Vol. 1 Transport and Vol. 2 Electrical Properties), MIT Press, Cambridge Mass. (1996). [The author bases the text on four questions: Which molecules are transported across cellular membranes and what are the mechanisms of transport? How do cells maintain their composition, volume and membrane potential? How are potentials generated across the membranes of cells? What do these potentials do? Answering these questions allows the author to teach about cells in a physical way]
2. G. Benedek and F. Villars, Physics with illustrative examples from medicine and biology, vols. 1-3 (1. Mechanics, 2. Statistical physics, 3. Electricity and magnetism.). Springer Verlag has bought the rights and is coming with a new version 1999. [Designed to provide seniors and first-year graduate students with a quantitative, analytical understanding of selected biological phenomena. Topics include: Experimental and theoretical basis for the phase boundaries and equation of state of concentrated protein solutions, with application to diseases such as sickle cell anemia and cataract.

Protein-ligand binding and linkage and the theory of allosteric regulation of protein function, with application to proteins as stores as transporters in respiration, enzymes in metabolic pathways, membrane receptors, regulators of gene expression, and self-assembling scaffolds. The physics of locomotion and chemoreception in bacteria and the biophysics of vision including the theory of transparency of the eye, molecular basis of photo reception and the detection of light as a signal to noise discrimination]

3. H. Flyvbjerg, J. Hertz, M. H. Jensen, O.G. Mouritsen and K. Sneppen, Physics of Biological Physics Systems: From Molecules to Species (Springer, New York 1997). [nucleic acids, proteins, membranes and microtubules, neurons and signal processing, micro- and macro-scale evolution]

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Physics for medicine and biology

Not only do we presently have the power of imaging atoms and molecules on surfaces we can also manipulate them and induce chemical reactions. It is evident from many areas that the microscopic, atomistic picture, is slowly moving into areas outside physics; biology and medicine being two examples. Any university with some pride will in such a situation provide for the students in medicine and biology (and other interested) a physics based course to meet the demand and to propel our own way of building models and develop experimental techniques. A good course book would be Intermediate Physics for Medicine and Biology, by Russel K. Hobbie (3d ed. (Springer 1997, ISBN 1-56396-458-9)).

This book bridges the gap between introductory physics and the more advanced topics needed to understand application to the life sciences. The third edition adds much new material, including advances in understanding the circulatory system, the logistic equation, countercurrent transport, nonlinear systems, image formation, sensory transducers, and more. The book is intended for advanced students in biophysics, biological physics, physiology, medical physics, cell biology, and biomedical engineering who have a background in physics and in calculus. Developed and updated over 25 years of rapid advances in physics, medicine, and biology, this book offers a unique and timely compilation of topics.

Contents: Mechanics. - Exponential Growth and Decay. - Systems of Many Particles. - Transport in an Infinite Medium. - Transport Through Neutral Membranes. - Impulses in Nerve and Muscle Cells. - The Exterior Potential and the Electrocardiogram. - Biomagnetism. - Electricity and Magnetism at the Cellular Level. - Feedback and Control. - The Method of Least Squares and Signal Analysis. - Images. - Atoms and Light. -Interaction of Photons and Charged Particles with Matter. - Medical Use of X Rays. - Nuclear Physics and Nuclear Medicine. - Magnetic Resonance Imaging.