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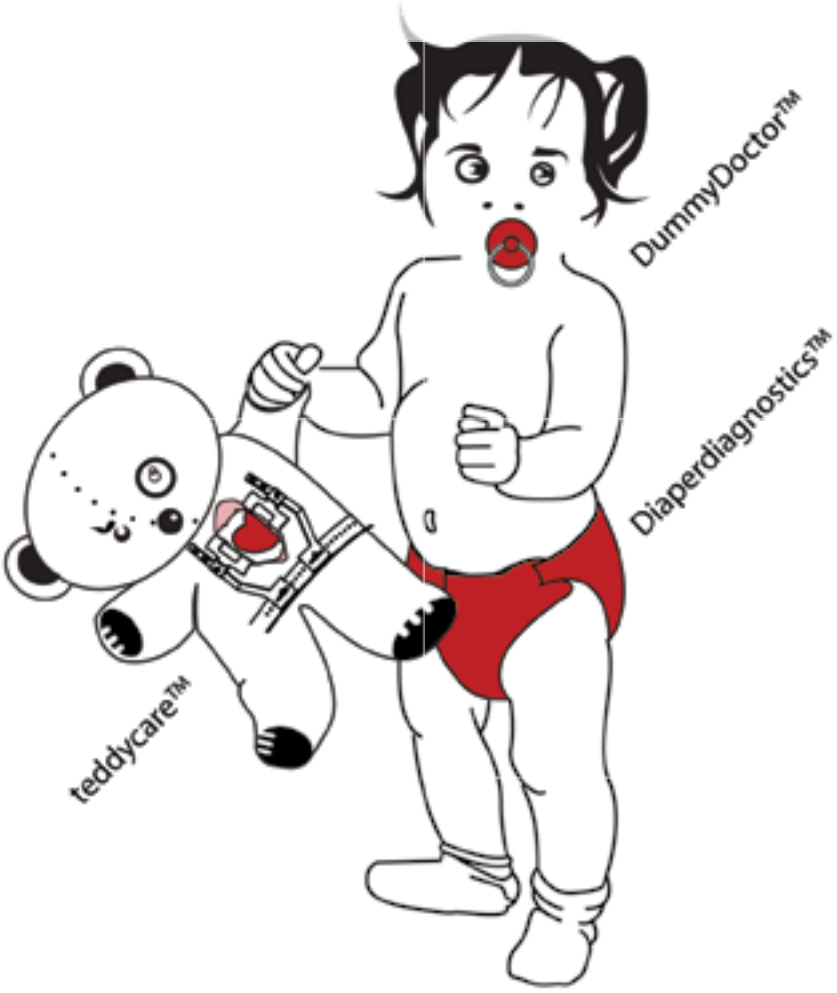
Foresight Biomedical Sensors



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Nordic Innovation Centre (NICe) project number: 04247		
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Abstract: The foresight study on biomedical sensors has addressed different approaches with future use of biomedical sensors in the health care sector, like: How will biomedical sensors shape the healthcare systems of the future? How can they impact the quality and cost of healthcare and what are the business opportunities in the Nordic region? The project revolved around a series of workshops in the Nordic countries during the autumn 2005 and spring 2006. Nordic experts at different areas from leading companies, research institutes and universities took part in the discussions. FOBIS has studied four different perspectives of future use of biomedical sensors: Home care, Doctor's office, Hospital and Defence/Public space. The foresight scenarios point out that: o The health care system will face an enormous challenge in the near future due to e.g. ageing population, well-fare diseases and new technology. Thus, development of biomedical sensors technology will be crucial. o Biomedical sensors will be a central unit embedded in several health related applications and scenarios. By using micro- and nanotechnology it will be possible to design small, smart, robust and cost effective sensors with a wide functionality. o Biomedical sensors will monitor important body functions and status (i.e. blood sugar level, heartbeat rate, presence of toxic agents), and advanced algorithms adapted to each individual may trigger alarms when non-normal values are encountered. o Technologically there is a tremendous potential, especially related to converging technologies, however technology alone does not create business. o Nordic industries are major vendors of medical sensors, and the region is leading in relation to the use of medical sensors for the benefit of health care and well being. This creates great opportunities for Nordic companies to find international markets for biomedical sensors and take leading positions.		
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Executive summary:

Within the public health service the Nordic countries will face a growing amount of elderly in the years to come and it will be important to offer high quality cost effective health care services to them. Demographic changes will inevitably require a change in health care procedures. Monitoring, diagnostics and therapy must become much more closely coupled than it is with current procedures. In addition to this fact there will be a strong pressure for improved services. On the other hand it is unlikely that the societies will tolerate drastic increases in healthcare costs. It is inconceivable that this will be feasible without an extended use of biomedical sensor systems.

Biomedical sensors will be a central unit embedded in several health related applications and scenarios. By using micro- and nanotechnology it will be possible to design small, smart, robust and cost effective sensors with a wide functionality. Biomedical sensors will monitor important body functions and status (i.e. blood sugar level, heartbeat rate, presence of toxic agents), and advanced algorithms adapted to each individual may trigger alarms when non-normal values are encountered.

The Nordic countries also have a tradition as key players in peace-keeping missions and humanitarian aid support, where telemedicine, exposure of personnel to unknown chemical or biological exposures is a major hazard. Biomedical sensor can provide significant improvements in this area, too.

The biomedical sensors foresight project, FOBIS, has focused on three important aspects of health care – home based care, emergency medicine and chemical hazards.

FOBIS has studied the implications of the applications of biomedical sensors on cost and quality of health care; both in civilian and military scenarios. Focus has been on generic solutions with a large degree of reusability.

Main conclusions from the work have been:

- The health care system will face an enormous challenge in the near future due to e.g. ageing population, well-fare diseases and new technology. Thus, development of biomedical sensors technology will be crucial.
- Technologically there is a tremendous potential, especially related to converging technologies, however technology alone does not create business.
- Nordic industries are major vendors of medical sensors, and the region is leading in relation to the use of medical sensors for the benefit of health care and well being. This creates great opportunities for Nordic companies to find international markets for biomedical sensors and take leading positions.

Some of the important research challenges identified in the project:

- Usability; biomedical sensors must be easy to wear, easy to use
- Implants; chips implanted in the body meet a number of challenges, both technical and ethical
- Low power issues, low power electronics and efficient batteries must be developed to provide solutions with an acceptable battery lifetime suited lifestyles of modern people

- Wireless technology; user friendly biomedical sensors require wireless communication solutions
- Reliability; the solutions must operate at all time under all conditions specified
- Security; sensor data may be sensitive personal information and the solutions must provide personal integrity
- Scalability and flexibility; the system must accommodate different users, environments and usage
- Communication infrastructure; monitoring applications require an established communication infrastructure between patient/biosensor host and healthcare personnel in charge.

The purpose of the project was:

1. To enable a strategic understanding of the possibilities and implications of the use of biomedical sensors for healthcare purposes by establishing likely scenarios for technology, applications and markets.

The project has clarified the current state-of-the-art and identified likely technological developments during the next 5-10 years. The most likely areas of applications in the health-care sector have been discussed. Further, main drivers and the most severe barriers for use and commercial exploitation have been identified. The project consortium has also tried to provide recommendations for future initiatives.

2. To provide a framework for commercially viable exploitation of biomedical sensor penetration in the Nordic region by enhancing a network of competencies relevant to technology and applications.

FOBIS has identified specific areas of current and potential importance to the Nordic countries and specific areas where the Nordic countries have natural, existing or potential advantages. The project has also created an environment for successful collaboration between Nordic actors in the area, demonstrated with the acceptance of follow-up activities involving the partners.

This project has had ambitious objectives relative to the small resources available, and has focused extensively on a small number of crucial tasks in order to be successful.

At the project closure, most of the key success criteria for the project defined at the beginning have been reached:

- To mobilize key players throughout the value chain within the Nordic biomedical sensor arena

  ⇒ More than 130 experts from all Nordic countries took part in the five workshops organized bye the project. They covered the whole value chain of interest, from development of biomedical sensors to clinicians using the sensors at hospitals.

- To connect the project work to similar ongoing European and international activity

⇒ Key partners in European research projects within biomedical sensors and e-Health has presented their view and current state-of-the-art in some of the workshops.

- To facilitate a series of first-class workshops and intermediate work processes

  ⇒ A lot of people from all Nordic countries have been enthusiastic about the project and given valuable input through their participation in the workshops. Some of them has also assisted the project partners in the preparations to the workshops, and even contributed with valuable written input.

- To disseminate the project results to decision makers within all important sectors; i.e. the government, health care, research and business sectors

  ⇒ The FOBIS project has been innovative in the way results are disseminated to different stakeholders. A multimedia presentation available on internet[1] encourages people interested to get ideas of like future scenarios themselves. More traditional dissemination tools, like publicity in different media, have also been used. Both TV and radio features have been made covering the project activities, and a lot of articles have been written.[2] Five newsletters have also been published as part of the dissemination strategy. These have been spread to more than 500 people in all Nordic countries with a common interest in the project results.[3]

Method/implementation:
The foresight study had two main objectives, which simultaneously should be fulfilled. The first was to collect information and establish possible scenarios. The second was in parallel to disseminate information about medical sensors. This fact implied a deviation from the traditional foresight process, where information is collected first, scenarios are then established and the information is finally disseminated possibly with feedback for an update of the scenarios.

In this project both information collection, establishing scenarios and dissemination were done in conjunction with a series of workshops complemented by desk research and individual visits to companies and health care institutions.

The project has revolved around a series of workshops, the first being held in Copenhagen 6 - 7th October 2005, the second in Oslo 2nd November 2005, the third in Stockholm 3rd March 2006 and the fourth in Tampere 7th June 2006. A dissemination workshop was held in Oslo 31st October 2006. The objectives of the workshops have been to establish status, needs and perspectives for sensors in relation to health care and in particular the need for biomedical sensors. This has been done through presentations from leading experts, targeted discussions in groups and moderated panel discussions. In addition to this, the project group have described some scenarios and created a SWOT analysis on the business perspectives for biomedical sensors in the Nordic countries.

[1] See www.orgdot.com/fobis
[2] See http://www.sintef.no/content/page1____12810.aspx for a list of the main activites.
[3] The Newsletters are available at http://www.nordic-fobis.net

Concrete results and conclusions:
The health care system will face an enormous challenge in the near future due to e.g. ageing population, well-fare diseases and new technology. Thus, development of biomedical sensors technology will be crucial.

Biomedical sensors will be a central unit embedded in several health related applications and scenarios. By using micro- and nanotechnology it will be possible to design small, smart, robust and cost effective sensors with a wide functionality.

Biomedical sensors will monitor important body functions and status (i.e. blood sugar level, heartbeat rate, presence of toxic agents), and advanced algorithms adapted to each individual may trigger alarms when non-normal values are encountered.

Technologically there is a tremendous potential, especially related to converging technologies, however technology alone does not create business.

Nordic industries are major vendors of medical sensors, and the region is leading in relation to the use of medical sensors for the benefit of health care and well being. This creates great opportunities for Nordic companies to find international markets for biomedical sensors and take leading positions.

It is recommended, to include a first phase with focus in information gathering and subsequently a dissemination and feed-back phase, in future foresight studies of this kind.

Recommendations:
A Nordic program that specifically addresses research and development in small businesses in relations to commercialization and national needs (like the SBIR/STTR[4]-programs in the United States) should be established. Such a program based on interaction between industry, research, and public needs could provide substantially to the development, application and commercialization of biomedical sensors.

The FOBIS consortium supports the recommendations from The National IST Research Directors Forum[5] entitled "Pre-commercial Procurement of Innovation – A missing link in the European procurement cycle". In this report it is proposed that the European Commission start to explore the interest of a limited number of procurers. We would suggest that biomedical sensors are included in one of these topics, which could be *e-Health*.

The FOBIS project should be followed up by a number of collaboration projects involving Nordic companies and researchers. These projects should stimulate the development of new biomedical sensors targeted towards important application areas in the healthcare sector. In parallel, projects focusing system aspects like wireless sensor networks in hospital environments and implementation of new healthcare services.

[4] http://www.sba.gov/SBIR/indexsbir-sttr.html

[5] The National IST Research Directors Forum (NAT IST RTD Directors Forum) brings together National IST (Information Society Technologies) Research Directors to discuss key policy and implementation issues related to the development of a European Research Area in IST. The forum complements the bottom-up approaches supported by the Framework Programme. http://www.cordis.lu/ist/about/era.htm

Content

Preface

The FOBIS project has demonstrated how valuable Nordic collaboration is. A common Nordic competence has created a unique insight in the future use of biomedical sensors and their potential impact on the health care sector. Managing a project with enthusiastic people from four different countries with input and contributions from leading Nordic experts has been a pleasure.

The FOBIS team thanks all the people that have contributed to the project. Speakers and participants at the workshops have given a valuable input to the project, and companies, research organizations and individuals have responded to our work and shared their knowledge with others.

A special thanks to Dorothy S Olsen, University of Oslo, Stein Sørlie, Orgdot AS, og Lars Hagsholm Pedersen, Bioneer A/S, for valuable input, fruitful discussions and contributions to the project methodology, dissemination and business perspectives.

Oslo, September 11 2007

Dag Ausen
Project leader

1 Introduction

Challenges in health care are huge. The number of elderly people is increasing, with a corresponding rise in the use of healthcare resources. So-called welfare diseases are increasing. There is large potential in technologies that can give more cost-efficient services.

FOBIS has illustrated that biomedical sensors will be a central unit embedded in several health related applications and scenarios. By using micro- and nano-technology it will be possible to design small, smart, robust and cost-effective sensors with a wide functionality. Biomedical sensors will monitor important body functions and status (i.e. blood sugar level, heartbeat rate, presence of toxic agents), and advanced algorithms adapted to each individual may trigger alarms when non-normal values are encountered. Chips implanted in the body will function as a constant on-board doctor, detecting diseases early and delivering drugs directly into the bloodstream. We define a biomedical sensor as a device that provides information about the state of the human body or elements affecting the state of the human body. A biomedical sensor may be a biosensor. However, other sensors may also serve as biomedical sensors.

The biomedical sensors foresight project has focused on three important aspects of health care – home based care, emergency medicine and chemical hazards.

1. Home based care / monitoring of patients with chronic diseases

Advanced body-wearable biomedical sensors combined with remote monitoring and telemedicine open up for a whole new range of new health care services. Persons with chronic diseases (i.e. diabetes, rheumatism, heart defects) may be monitored for better treatment and response for changes in the illness development. Automatic diagnosis and medication may result in better quality of life. Today there are large costs associated with hospitalization. Biomedical sensors combined with telemedicine will be a cost efficient way of providing health services.

2. Emergency medicine / monitoring of injured and acute ill patients

Biomedical sensors measuring vital data may improve the quality of treatment by enabling health care personnel to respond quicker and more accurate to a given injury or illness and critical changes thereof. Possible scenarios may span an acute illness at home to large accidents or terror acts with lots of injured people. With the latter, biomedical sensor information can be crucial to improve survival rate, e.g. to ensure that critical changes in a patients status is detected.

3. Monitoring humans for the presence of toxic agents (bio-warfare)

The risk of harmful exposure to chemical agents is increasing. This is especially true for personnel engaged in military or peace keeping operations but applies also to the society as a whole through the general increased risk of terrorist attacks. For the most appropriate medical treatment it is important to find the specific biomarkers for the toxic agents as early as possible.

This foresight project has studied the implications of the applications of biomedical sensors on cost and quality of health care; both in civilian and military scenarios. Focus has been on generic solutions with a large degree of reusability.

1.1 Methodology

The FOBIS project has used discussions in cross disciplinary expert panels as the main methodology. The discussions during the workshops have been focusing emerging and converging technologies related to biomedical sensors, philosophical and ethical dilemmas, commercial potential and policy implications and addressed major trends and drivers and future uncertainties and challenges. Facilitated visionary brainstorming, knowledge sharing, analyses of technology trends and identification of major challenges (especially in the man-machine interface area), cultural and social contexts and possible products and services, have also been part of the foresight methodology. This approach is a way of how to "see" what you can't see. In retrospect, it's clear that this has been the basic methodology for the workshops FOBIS has revolved around.

The traditional use of scenarios is to analyze future situations with several potential outcomes and assume that groups of people who have considered future situations will react better when they occur[6]. This methodology has been used as a tool to assist planning of future requirements in public services, and usually analyses the probability of scenario occurring. Direct results of this kind of foresight and scenario building are action plans, enlargement of personal networks and a good overview of on-going activities and state-of-the-art technology. The indirect results, perhaps the most important ones, are that people taking part get new ideas, often not measurable at the time. It also gives a comprehensible way of communicating with the public and with political decision makers and creates a valuable new network of potential contacts.

The scenario approach used by FOBIS has been based on existing research and product development projects, the sharing of ideas and information between people of different backgrounds and interests, generation of ideas on future uses of technology, discussions of possible consequences of new technologies and future challenges of further development.

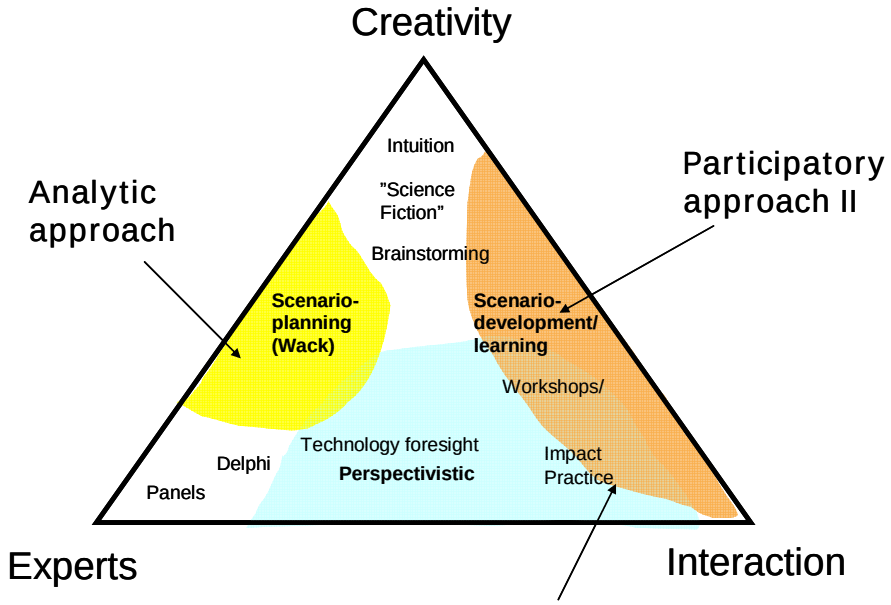


Figure 1 FOBIS methodology; building scenarios based on existing research and products[7]

[6] Examples from Van Der Heijden and the oil industry
[7] Dorothy S Olsen, Institute of Educational Research, University of Oslo

Foresight is a matter of statistical forecasting, interpretation of multiple facts - and feelings - and operations of fantasy. There are many valid methods within the discipline called foresight;

- Trend spotting and weak signal monitoring
- Delphi and survey methods
- Expert panels
- Scenario based organizational learning
- Wild Cards
- Visioning and brainstorms
- Triangled conversations (technologists, politicians, lay people)
- Games and narratives
- Backcasting
- Foresight as tool in innovation processes
- Foresight as part of strategic decision making processes (road maps, path matrices)

There are also many definitions of what foresight is about; basically everyone agrees that it is not about getting it right, but getting better prepared. A few of them are presented below:

"Foresight is a systematic, participatory, future intelligence gathering and medium-to-long term vision building process aimed at present-day decisions and mobilizing joint actions".[8]

Spyros Makridakis states that "foresight is to provide business executives and government policy makers with ways of seeing the future with different eyes and fully understanding the possible implications of alternative technological/societal paths".

Robert Chia emphasizes the importance of wisdom and deeper collective insight in foresighting, where the "innocence of the eye", scanning of the unconscious and tacit knowledge play a serious role: "Foresight is a unique and highly valued human capacity that is widely recognized as a major source of wisdom, competitive advantage and cultural renewal within nations and corporations". This modern perspectivistic definition, urge us to be professionally naive and open-minded and look for what's in the corner of our eye.

Another definition of "foresight as invention" is one that views the future as the unpredictable outcome of myriad interactions between complex agents. The dynamic environments we live and interact in are moving targets characterized by constant flux, where small and trivial events can cause major consequences. Actors, both individuals and organizations also create contexts. The future cannot be predicted, the best we can hope for, is to improve our ability to act when changes occur and establish better real-time-planning or real-time foresight. This kind of sense-making and action takes place in a mixture of improvisation, learning and imagination.

[8] FOREN - a guide to regional foresight (EU:2001)

2 Biomedical sensors – definitions and technology

Medical sensors and BioMEMS is a rapidly growing field. The development in microsystems is a key driving force: cost per function decreases with 25% every year, no. of bits per chip grow by a factor of 4 times every 3 years, processing speed is increased by a factor of 5 every 10 years.

Future medical sensors will require small low cost, low power sensors, remote power generation, wireless communication, nanotechnology and advanced functional and bio-compatible materials.

High research activity for medical MEMS is expected in the Cardiovascular area (e.g. sensor systems for rate adaptive pacing, cardiac well-being monitors) in Drug delivery (e.g. oral ticking tablets for timed delivery) and in Endocrinology (e.g. minimally invasive glucose monitoring).

2.1 Background and definitions

The technology of biomedical sensors is rapidly expanding. This is due to the increasing demands of a more efficient health care and to the driving forces in a number of important fields, such as information and communication technology, the new biology and micro and nanotechnology.

To be consistent in the following unless otherwise convinced, it is useful to introduce a set of definitions.

> ***A sensor*** *is a device that provides information about the physical, chemical or biological state of a system. This can be key physical parameters like temperature, pressure, velocity or acceleration. It can also be the concentration of a particular substance in e.g. a blood vessel or cardiac nerve potentials. The sensor is often very compact and robust. However, the key element is that a sensor is tailored to operate in the environment where the sensory information is to be obtained. Taking a sample and doing an analysis remotely – in space and time – in a laboratory is contradictory to the operation of a sensor. However, this fact does not imply that the sensor physically has to be present at the location where the sensing takes place. The sensing may be done remotely. Very well known examples are our eyes and ears: sensors that probe what either light patterns or sound signals from locations that are remote to the sensors.*
>
> ***A medical sensor*** *is a sensor that in one way or another is incorporated in health care.*
>
> ***A non-invasive*** *sensor is a sensor that obtains its information without a physical penetration of the protecting membranes of a living object.*
>
> ***A biosensor*** *is a sensor that incorporates at least two processes. One is a biochemical reaction defining the specificity of the sensor; the other is the physical part that – as a consequence of a biomedical reaction – provides for a readout signal. A medical sensor may – or may – not be a biosensor.*

or according to IUPAC[9]:

*"**A biosensor** is a self-contained integrated device, which is capable of providing specific quantitative or semi-quantitative information using a biological recognition element (biochemical receptor) which is retained in direct spatial contact with a transduction element. Because of their ability to be repeatedly calibrated, we recommend that a biosensor should be clearly distinguished from a bioanalytical system, which requires additional processing steps, such as reagent addition."*

To illustrate these concepts we can consider small pressure sensor in a hearing aid device. The sensor is sensitive to small fast pressure fluctuations given by a remote acoustical signal. The sensor is outside the protecting membranes and no biochemical reaction is involved in the sensing.

Another example is a glucose sensor, which may be based on a chemical reaction with the glucose in the blood. The chemical reaction may give rise to fluorescence. This is an invasive sensor: it has to penetrate a protecting membrane to get access to a blood vessel. The sensor is also a biosensor: both a (bio-) chemical process and a physical process are involved.

In diagnostics it is customary to distinguish between *in vivo* and *in vitro*. In vivo implies diagnostics performed inside the patient, whereas in vitro is tests performed outside the patient on samples taken from the patient. This could be body fluids or tissue samples. In vivo is often associated with imaging e.g. by magnetic resonance (MRI). Such systems are not considered to be sensors. Ultrasound systems are on the borderline and are also considered here.

2.2 Existing technologies

Biomedical sensors have today a limited impact in health care. In the intensive care, continuous monitoring of heart activity, blood pressure, temperature, oxygen levels, etc is prevalent. In the home care, disposable test strips for a number of analytes are available, such as for testing of urine for albumines, bacteria, urea, pregnancy, glucose etc. In the doctor's office, also a number of tests for bacteria, viruses, allergenes and the most common physiological compounds are available. The development of simple, disposable test for glucose has been very important for people suffering of diabetes.

Most of the chemical tests are based either on the action of an enzyme or an antibody, making the tests very specific and sensitive. The emerging DNA technology has lead to genetic diagnosis.

The development of new biomedical sensors is growing rapidly, and many Nordic companies have launched new products on the market during the last years. This report does not present a state-of-the-art overview for biomedical sensors, but gives instead examples of existing products from Nordic companies to illustrate the potential with such sensors. Many of the products and technologies presented below have not yet been

[9] IUPAC "Recommended Definitions and Classification" Pure Appl. Chem., Vol. 71, No. 12, pp. 2333-2348, 1999.

adapted by the healthcare sector, but will find their way to the international market within a few years.

Novo Nordisk A/S manufactures and markets pharmaceutical products and services that make a significant difference to patients, the medical profession and society.

Novo Nordisk is a healthcare company and a world leader in diabetes care. The company has the broadest diabetes product portfolio in the industry, including the most advanced products within the area of insulin delivery systems. Biosensors are a vital part of their products. In addition, Novo Nordisk has a leading position within areas such as haemostasis management, growth hormone therapy and hormone replacement therapy.

Mobidiag Oy develops the innovative Prove It™ DNA diagnostic solution for the detection of microbes and antibiotic resistance. The key benefits of Mobidiag's new biochip technology for clinical laboratories are speed, accuracy, and ease of use.

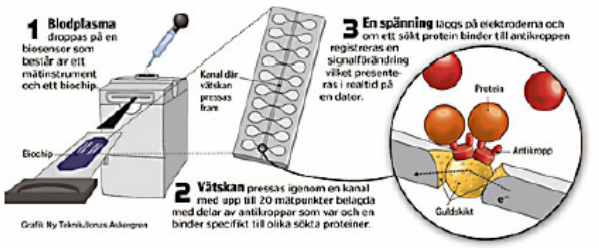
Axis-Shield AS is focussed on the development and manufacturing of key in vitro diagnostic tests for use in the hospital laboratory and at the point of care. In the former environment their products are available as stand-alone tests and also on the menu of many high throughput analysers marketed by the large global companies which dominate this marketplace. At the point of care their products include NycoCard and the new Afinion system. They specialise in the identification of increased risk of cardiovascular and neurodegenerative diseases.

Afinion™ Point-of-care instrument from Axis-Shield

Midorion AB develops and markets analytical biosensor systems for life science applications.

The lab-on-a-chip technology enables medical researchers to acquire unique information previously beyond reach, in order to create better understanding of human diseases. The technology platform can be adapted for numerous different applications. Midorion work with an extensive license program to position quantum detection methods as standard to which all other biosensor instrument suppliers will be compared.

Midorion has invented and developed a new analysis system including a new, sensitive, patent-pending detection method. MEMS technology is used to measure quantum electrical phenomena in real time through changes in electric fields. This analysis system makes possible the study of individual molecules in parallel trials with answers in real time, which produces faster and more cost-effective results.



Analytical biosensor system from Midorion

Biacore AB is a global supplier of systems for protein interaction analysis which are used in key areas such as antibody characterization, proteomics, lead characterization, immunogenicity, biotherapeutic development and production. The Company offers a range of products to meet specific application needs. Customers include leading life science research centres, all of the leading global pharmaceutical companies, and a large number of companies in the emerging biotechnology sector.

Surface Plasmon Resonance (SPR) enables the real time measurement of interactions between two or more molecules by immobilizing molecules (e.g. antibodies, receptors) on the surface of a unique, proprietary "sensor chip" and passing solution containing possible interactants over the surface under controlled conditions using proprietary microfluidics. Any binding to the target molecules can be detected in real time, producing extremely detailed kinetic data.

Biacore A100 - unmatched productivity for protein interaction analysis.

For medical and biomedical fields, the company MEMSCAP AS offer two main products families based on biomedical MEMS pressure sensors, namely the multi-purpose AE800 sensors family which main commercial applications are flow sensing in medical ventilators, as well as muscular force pressure, and the SP840 sensors family, dedicated to physiological pressure (including blood pressure).

2.3 System aspects

The concept of wireless connections is very important in a healthcare context.

A wireless sensor simply means that no wires are connected to the sensor from an external device. This is of course important for implanted sensors, but is also essential for many other sensors that may be mounted on e.g. the skin. The sensors may be operated by a small battery and fitted with a miniature radio transmitter. However, the sensor may also operate without an internal dedicated power supply. The sensor is then defined as being:

> ***A passive sensor*** *that relies on the power obtained from a remote reading device (a transceiver) through e.g. electromagnetic radiation (radio frequency or optical). The device may also obtain power from local movements, chemical reactions or temperature gradients.*

Sensors may be connected in a network:

> ***A wireless sensor network (WSN)*** *is a computer network consisting of spatially distributed autonomous devices using sensors to cooperatively monitor physical or environmental conditions at different locations. In addition to one or more sensors, each node in a sensor network is typically equipped with a radio transceiver or other wireless communications device, a small microcontroller, and an energy source, usually a battery. The size of a single sensor node can vary from shoebox-sized nodes down to devices the size of grain of dust.*

Remote reading of implanted sensors is essential. A number of techniques exist for this, such as optical, acoustical, radiofrequency, microwave, inductive or capacitive. The use of implantable sensors will dramatically change the understanding of a treatment.

2.4 Enabling technologies

There are many biomedical sensor technologies that already has left the test and approval stage. Breakthrough in the area of microtechnology has enabled the manufacturing of miniaturized devices for a number of physical and chemical parameters. This includes the growing area of micro-total analytical systems (μ-TAS) and micro electro mechanical systems (MEMS), where total analytical systems are integrated on a chip.

The ability to perform laboratory operations on small scales using miniaturized (lab on a chip) devices has many advantages. Designing and fabricating such systems is extremely challenging, but physicists and engineers are beginning to construct highly integrated and compact labs on chip with exciting functionality. Recent advances include the application of microfluidic-chip-based technologies such as chemical synthesis, the study of complex cellular processes and medical diagnosis.

The microtechnology had also enabled developed sensors for continuous monitoring, pressure sensors mounted on the tip of an optical fiber has been used for the monitoring of cardiac vascular blood pressure, respiratory monitoring, and urology, and also miniaturized 3-D accelerometer has been developed for monitoring of cardiac activity. Wireless, disposable ECG-sensors have also been developed.

There is a large interest for non-invasive monitoring, examples includes a glucose watch based on iontophoresis and wireless measurements of sweat activity based on skin conductometry.

There is a large development in biomedical sensors based on the landmarks in genetic engineering, DNA techniques, genomics and proteomics. This has enabled genetic diagnostics based on DNA-biochips, sophisticated diagnostic assays for e.g. cancer or heart diseases based on antibodies.

2.5 Future trends

The driving force in the development of biomedical sensors will be strongly directed by the demands in many medical fields. The need for home care is expected to increase drastically which will necessitate an increased use of simple disposable sensors, telemedicine and remote consultation. Screening of patients, implantable devices for continuous, wireless monitoring, will also be increasingly important. Thus, due to these demands, future medical sensors will require small size, low cost, low power consumption, remote power generation and wireless communication. It is generally expected that the R&D from related fields (e.g. nano and microtechnology) will spill over and push developments in the field.

Future important technological fields have thus been identified:

Implantable sensors have a large potential in many parts of the body for continuous monitoring. It may be intracranial, retina, or even acceleration and rotation sensors in the limbs. Remote reading of implantable sensors will be essential; another important issue is the biocompatibility of the sensor.

Microtechnology will be very important in the future, since key drivers for the biomedical sensor development is miniaturization. The production cost will be low since it is possible to massfabricate single sensor chip. For the “lab-on-a-

chip", the microtechnology enables the possibilty to integrate several functions, also making it possible to measure several biomarkers in human samples using multianalyte systems.

Nanotechnology has a very large future potential, since it is working on atomic and molecular level to design, manipulate, develop and use materials to produce new mechanical, functional, chemical and biological properties. Nanomedicine is defined as the application of nanotechnology for health. It exploits the improved and novel physical, chemical and biological properties of material at the nanometer scale. It is regarded to have a very large impact on the prevention, early and reliable diagnosis and treatment of diseases.

Biotronic can be defined as an integration of biological, mechanical, optical and chemical techniques for hybrid system with specific functions. The development is directed towards more general system based on bioMEMS, and "lab-on-a-chip" technology. The most important applications will be found in medicine, such as drug delivery and control of biological processes. In the long term perspective, there should be advanced interfaces which make it possible to connect natural and artificial biological systems with microelectronical systems.

DNA-and biochips offer diagnosis of microbes and antibiotic resistance. It will also offer future diagnosis of genetic disorders. Their goal is to revolutionize the way DNA and antibody/antigen information is used in diagnosis.

Surface science has been identified as an important future technology area, which is the playground for many of the promising activities attributed to nanotechnology. This includes aspects such as biomaterial immobilization, and biocompatibility aspects, important for in-vivo sensors. Surface science is central for chip manufacturing, biosensor development, atom manipulation, etc.

Disposable systems will in the future be more sophisticated for a large number of different and medical very important analytes, they can be made either as simple sticks or more complicated "lab-on-a-chip". This also includes hand held systems possible to be linked wireless.

Communication and information technology will be one of the more important areas in health care. Pervasive system, having the ability to be present throughout all steps of the health care, include computing technology for health care and wellness management, making health care available anywhere. Information based systems within the health care of today that treat symptoms will move to predisposition testing and to personal health care. The information technology also entails the ability to handle large amount of information and to search for structure and correlation in the data, making it possible to make predictive diagnosis.

Certain point areas of future importance have also been identified, these include markers for different cancer forms, viral infections, heart infarcts, and biomedical sensors for insulin levels and for evaluating shock effects of on patients involved in accidents.

2.6 Research challenges

There are significant challenges to be solved before biomedical sensors technology is commonly used. The list below indicates some of the aspects of this:

- Usability; biomedical sensors must be easy to wear, easy to use
- Implants; chips implanted in the body meet a number of challenges, both technical and ethical
- Low power issues, low power electronics and efficient batteries must be developed to provide solutions with an acceptable battery lifetime suited lifestyles of modern people
- Wireless technology; user friendly biomedical sensors require wireless communication solutions
- Reliability; the solutions must operate at all time under all conditions specified
- Security; sensor data may be sensitive personal information and the solutions must provide personal integrity
- Scalability and flexibility; the system must accommodate different users, environments and usage
- Communication infrastructure; monitoring applications require an established communication infrastructure between patient/biosensor host and healthcare personnel in charge.
- The need for surface modifications in order to obtain specificity, proper transport, and long term stability has to be emphasized
- Molecular medicine and imaging
- Surface science and design; tissue engineering, membrane technology, synthetic imprints, artificial receptors
- Body interaction - biosensing materials, biomaterial coating
- Biomimetic - the interface natural/artificial is a blurred - fluid interface, artificial organs/organ growing
- Particle therapy, gene surgery
- Pervasive health design - wireless implants, wearables and embedded solutions; remote reading (optical, acoustic, radio, microwaves etc.
- Mass production (disposables) - safe, cheap - and personalised
- Technology tolerance - in the human body - and in the human culture
- Interdisciplinary focus in R&D - innovation, design and product development - activity system design, networks, arenas, incentives
- Political issues - priorities and ethics
- Ethically sound and risk willing venture capital in the Nordic countries - public-private cooperation/co-creation

Methods for detecting a large number of medically relevant data do exist. However, to do this with non-invasive sensors is currently only possible in very few cases. It is recommended that the key focus here is on non-invasive sensors and sensors with a high level of specificity.

Biosensors have a large potential, but widespread has only emerged in very few areas. It is recommended that a strong focus is given to bio-chemical processes and surfaces that provides for very good specificity and can be fabricated at a low cost.

Wireless technology is becoming well developed. Useful technologies do exist, but the power consumption is the main issue. Her several technologies are being developed, but no clear winner can be identified at this point in time. Standards represent an important issue. This is especially the case for so-called body area networks for very short range information transfer. In relation to wireless technology for medical sensing it is recommended that the key focus is on energy consumption (her it is not for CO2 reasons) and so-called passive sensors requiring no batteries.

3 Future health care system - applications & use of biomedical sensors

Within the public health service the Nordic countries will face a growing amount of elderly in the years to come and it will be important to offer high quality cost effective health care services to them. Demographic changes will inevitably require a change in health care procedures. Monitoring, diagnostics and therapy must become much more closely coupled than it is with current procedures. In addition to this fact there will be a strong pressure for improved services. On the other hand it is unlikely that the societies will tolerate drastic increases in health-care costs. It is inconceivable that this will be feasible without an extended use of biomedical sensor systems.

Early detection using biosensors, enabling the patient to read and monitor the health status, will shorten hospital stays and contribute to a better life quality. Today many decisions in a hospital are taken on the basis of samples that have been analyzed in the laboratory on a manual basis. The introduction of biosensors to automate the whole or part of these manual processes will reduce the hospital costs considerably. Implanted biomedical sensors and actuators will also make a huge impact in the years to come; examples are glucose sensors for diabetics, cardiovascular ventricular assist devices, pressure sensors for post-surgery leakage detection, and on-demand drug delivery pumps.

The pressure on faster and more efficient developments of drugs as well as the need for improving health care without increasing costs makes it extremely important to provide likely scenarios for technology and application. Biomedical sensors will be one of the main driving forces for a high quality cost effective health care system.

The Nordic countries also have a tradition as key players in peace-keeping missions and humanitarian aid support, where telemedicine, exposure of personnel to unknown chemical or biological exposures is a major hazard. Biomedical sensor can provide significant improvements.

The European Community has made health and wellbeing one of its top priorities, not least in view of EU enlargement. Three lines of action have been suggested:

1) Improving information for the development of public health;
2) Creating an EU surveillance, early warning and rapid reaction capability;
3) Health promotion and disease prevention, screening and testing of target populations.

Main objectives for the e-Health society to implement better healthcare in Europe[10]:

1) Putting people more in control of their own health and care
2) Enabling and supporting health, independence and well being
3) Rapid and convenient access to high quality, cost effective care

[10] European i2010 agenda

3.1 Perspective 1: Home care

Needs and opportunities

The need for home care will most likely increase drastically. This will necessitate an increased use of medical sensors, telemedicine, remote consultation, diagnostics and decision making. Home care can be classified either as an extension of the general health care system or as a part of what could be called self care. Self care may be in conjunction with the authorized health care system or it may be without interaction with the health care system.

Self care is increasing rapidly as a consequence of a more affluent community, a greater awareness about health and diseases and simply because the availability of commodities for both diagnostic and therapeutic use is increasing and is being marketed aggressively. As an example it is noted that the market for home blood pressure sensing equipment is now close to 40% of the total market for blood pressure equipment (see section 4). The private market for health care services will most likely increase and health care and so-called well being will often merge. Home care is currently the largest market for low-cost medical sensors and this will most likely also be the case in the future.

Home care as a part of the general health care system will increase for two reasons: (1) Diagnostics and treatment can often be improved considerable if diagnostics can be performed continuously during normal activities (e.g. work and sleep) and (2) new possibilities for remote diagnostics are emerging and can reduce the burden on the health care system. This is especially the case for hospitals and to some extend also for the general practitioners.

The medical community is not unanimous about how increased home diagnostics and care will affect the cost of the whole health care system, and there are also some reservations about the quality of home care. However, there seems to be no doubt about the fact that sensors and especially biosensor systems will become an increasingly important part of home care diagnostics and that home care will become much more common in connection with a more widespread introduction of telemedicine.

The public system as well as individuals will have to face a number of difficult problems in relation to defining priorities and this will certainly also involve home care.

The organization and market will most likely become even more chaotic than what currently is the case. This fact may call for a strengthening of the regulatory conditions.

Cardio-vascular diseases (CVD) are the leading cause of death in the west. In Europe over 20% of all citizens suffer from a chronic CVD and 45% of all deaths are due to CVD. Europe spends annually hundreds billion Euros on CVD. With the upcoming aging population, it is a challenge for Europe to deliver its citizens healthcare at affordable costs.

It is commonly accepted, that a healthy and preventive lifestyle as well as early diagnosis could systematically fight the origin of CVD and save millions of live-years. The MyHeart mission has been to empower citizen to fight cardiovascular diseases by preventive lifestyle and early diagnosis.

The starting point is to gain knowledge on a citizen's actual health status. To gain this info continuous monitoring of vital signs is mandatory. The approach is therefore to integrate system solutions into functional clothes with integrated textile sensors. The combination of functional clothes and integrated electronics and process them onbody, we define as intelligent biomedical clothes. The processing consists of making diagnoses, detecting trends and react on it. Together with feedback devices, able to interact with the user as well as with professional services, the MyHeart system has been formed.

The MyHeart system is suitable for supporting citizens to fight major CVD risk factors and help to avoid heart attack, other acute events by personalized guidelines and giving feedback. It provides the necessary motivation the new life styles. MyHeart have demonstrated technical solutions. The outcome opens up a new mass market for the European industry and it will help prevent the development of CVD, meanwhile reduce the overall EU healthcare costs.

www.extra.research.philips.com/euprojects/myheart

Technology

The development will involve sensor for cardiovascular conditions, e.g. blood pressure and vascular compliance with wireless sensing, electrocardiograms also with wireless reading, glucose sensing, which already has a big market, sensors for the respiratory system, both for the functioning and for the composition of the exhalation gas. Sensors for home tests (e.g. pregnancy) are already in widespread use and will expand tremendously. Sensors may also become integrated wound healing bandages and with ostomy bags.

Implantable devices where sensing and therapy are combined have a great potential, but poses a number of legal and ethical issues. Sensing of glucose concentration coupled to automatic insulin injection is an obvious case.

For home care it is essential that the equipment is simple to use, is accurate, reliable, robust and that the cost is low. Accuracy and reliability are often conflicting with ease of use and low cost in currently available equipment.

ISTVivago®WristCare is a wrist-worn smart social alarm device from the company ISTInternational Security Technologies Oy. The initial goal with the product was to develop a smart social alarm system. A panic button and automatic alarms in case of emergencies where the user is not capable to raise the alarm manually was the basic product functionality. In the next generation, sensors and intelligence were added to enable automatic alarms. The sensors monitor movements, temperature and skin conductivity. Energy consumption, optimization, intelligence, manufacturing issues, durability, robustness, etc have been challenges that are overcome in the product development. Today's product focuses on long-term wellness monitoring. The product integrates different biomedical sensors with wireless RF communication (range 30-60 meters) and has a battery lifetime of 6-12 months. The sensors are in daily use by more than 10.000 users in several countries.

Drivers

Healthcare is one of the most potent application areas for ICT. Pervasive healthcare is application of pervasive computing technologies for healthcare, health, and wellness management making health care available everywhere, anytime –pervasively.

Pervasive healthcare addresses those technologies and concepts, which integrate healthcare more seamlessly to our everyday life, wherever we are.

Efficient diagnostic tools are a key element in the EU FP7 and especially in the work programme *Health*, which was also laid out in the document NanoMedicine, Vision paper, Sep 2005[11]. In the US several professional societies within health care as well as the National Institute of Health are promoting continuous low cost diagnostic tools.

Europe is facing the challenge of delivering quality healthcare to all its citizens, at affordable cost. The increasing demand by citizens for best quality healthcare, the costs of managing chronic diseases, and the need for prolonged medical care for the ageing society are major factors behind this challenge. Personal Health Systems can create opportunities for everybody, including the elderly population, to receive the best available healthcare. State-of-the-art in Personal Health Systems includes areas such as wearable

Personal Health Systems empower citizens to become involved in healthcare processes and enjoy better interaction and relationship with healthcare providers.

Personal Health Systems encourage preventive lifestyle, enable early diagnosis of diseases and facilitate the provision of personalised care at the point of need.

Personal Health Systems offer effective means to contain the rising healthcare costs.

Personal Health Systems 2007 – conference, European Commission, February 2007

[11] www.cordis.lu/mamotechnology/nanomedicine

and portable health monitoring systems, and ICT-supported personalized services for extended healthcare, including home care.

Another area that drives the technology development is the need for better cancer cure. In the near future, cancers are not 'cured' but 'managed'. One of the major areas of progress with cancers, such as breast cancer, is the benefit of long term therapies for reducing growth rates. This approach requires regular monitoring such that the efficacy of maintenance therapy is rapidly noted and different therapy can be initiated as required. This necessitates regular testing for cancer load. People wish to avoid hospital yet want results interpreted expertly and communicated rapidly. They want tests that do not miss problems yet avoid unnecessary worry.[12]

The economic impact of new diagnostic systems are potentially very considerable with the future technologies that will facilitate improved healthcare provision, from improved centralized screening systems, through to fast and flexible point of care systems. Expenditure for diagnosis generally represents less than 1% of total healthcare expenditure, thus increased testing cannot significantly increase healthcare costs but can significantly contribute to the quality of health care as it:

- Allows earlier and more appropriate and therefore less costly treatment.
- Helps to rule out expensive treatments.
- Reduces costs of treatment of complications.
- Potentially shortens the length of hospital stay by making therapies more effective and therefore more cost-effective.

3.2 Perspective 2: Doctors office

Needs and opportunities

It has been concluded, that the General Practitioner medical doctor (GP) will face a more market driven situation, thus the patients will be more active and demanding. This calls for quicker and more reliable services, which again implies more "on the spot" sensing and diagnostics.

- Screening of patients will be an increasingly important task.
- Preventive health care will most likely become even more important than it currently is.
- Insurance companies will play an increasingly important role even in countries with "social medicine".
- Tasks that are currently allocated to hospitals will be transferred to GPs.
- In relation to medical sensors, GPs represents a very large potential market for low-cost reliable medical sensors.

[12] FP6-project: Smart Integrated Biodiagnostic Systems for Healthcare, SmartHEALTH, www.smarthealthip.com

Technology

Some technology trends identified[13]:

- Point-of-care laboratories will be available at every GP's office. Increased skills in relation to so-called distributed diagnostics would become more important. Distributed point-of- care systems puts pressure on the user friendliness and security of all patient information transferred within the data systems.
- Since space is a limiting factor in the doctor's office, the technology used should be simple and small.
- Interoperability is a problem today. Standardization, all the way from signals from home cared patients to interoperation between devices in the Doctors office will be standardized.
- DNA testing will not happen for a while (it is still costly, but as prices gets reasonable, the DNA screening of patient could be as standardized as blood samples).
- Overall number of tests will increase from 2005 to 2020. Biggest increase will be in doctor's office.
- New ways of testing will open up for new markets. Genetic profiles opens up for new test that makes many of the old tests obsolete.
- The slide does not include scenarios sensors for monitoring purposes, e.g. invasive blood pressures.
- User friendliness is very important of solutions are to be moved out from hospital with high skilled personnel.

Biodiagnostic sensors and diagnostic systems/platforms usually employ traditional chemometric methods for signal treatment – typically to translate the "bare" measurement into the concentration of a biomarker. For multianalyte screening applications, multivariate calibration methods such as partial least squares (PLS), multiple linear regression (MLR) principal components regression (PCP) and alternative multi-way methods are used. The high specificity and selectivity inherent to many biological assays based on DNA technologies, together with the large volume of biological sample (such as blood) available, means that these basic signal evaluation algorithms suffice, particularly for tests performed by highly qualified professionals in the controlled environment of the central laboratory in a large hospital. Diagnostic instruments are generally 'stand-alone' though means exist to enable the data from the instruments to be electronically transferred to a Laboratory Information System and then to patient records. In many cases the results are simply printed out and stuck in the patient's paper notes. Little effort has been put into ensuring integrity, checking and data confidentiality. Many of the instruments use entirely propriety interfaces (if any). However a range of new developments is seeking to change this situation.

[13] 1st FOBIS workshop, Copenhagen, 6-7 October 2005

Drivers

Economic incentives are a main driver for change. The technical aspects will be secondary.

The GP still needed to diagnose and give patient care. GP is the first meeting point for patients- hence screening is important. We will always need the GP for the personal assessment and expertise (in order to handle the increased volume of information of deceases).

As long as there is a market; the Medical Device Companies will supply new testing devices to GPs who will buy because the pressure is on from their patients.

Other factors driving the development:

- Politics can be a driving force, hence all GP offices will do some type of screening in 2010.
- Patients get more enlightened and informed; they will shop around for the best services.
- In 2020 we will have probably have more implantable devices.
- More elderly people are a mega-trend which will create new challenges for the GP.
- Home monitoring will be increasingly important combined with therapy. Thus simple at home diagnostic techniques combined with central solutions at the GP's office will find increased use.
- Problem that home tests provide more information for the patient, giving rise to more questions and need for contact with the GP e.g. not necessarily reducing the cost and efficiency of health services

Cross-validation and consistency – important that say home care does not develop separately from the rest of the healthcare services.

There are trends in favour of personal health checks being made easily available, but stressed that these should be voluntary. The risk of obsessionalism is very real and may cause more problems for the health services that it removes.

Diseases as diabetics, continuous monitoring might make real treatment possible in comparison with today's "treatment" of diabetics with insulin which does not of course cure the patient.

What do the public want at the GP's office?

Electronic storage and easy access to personal health data for individuals will be demanded. This makes the integration of test, therapy and historical data, available whenever and wherever the individual goes, necessary.

Various cheap types of monitoring may become attractive to younger and otherwise healthy people who are interested in technology. However some self-testing kits are available today like cholesterol test-kits, but they do not sell very well. It would appear that the public do not actually want to know the status of their health.

The problem of safety of Alzheimer relatives for family, who may not live nearby is considered more pressing. Solutions for monitoring of patients movement and activities so that they do not get injured in traffic for example would be useful. The idea for an "Intelligent Environment" for Alzheimer patients or other elderly to live in was mentioned as a possible area of application, but again this would probably have to be financed by national health authorities.

What does the GP want?

Reduced time between testing and certain treatments e.g. with some cancers, doctors want markers to be measured on the day, so that they can take the decision on treatment on the same day. There are traditions for certain types of monitoring and certain turnaround times on test results. Any solutions improving what is already perceived, as a problem should meet with interest among doctors, however other factors are also important and it is not enough to simply offer improvements, the economic benefits should also be obvious. There are other tests of serious conditions where the doctor wants the data quite quickly.

Generally people will demand more preventative medicine at all levels and for all kinds of diseases and health problems.

New wireless sensors and measurement systems have a huge market potential for communicating with the GP. Wireless implantable sensor technology is the only way to realize reliable long-term monitoring of physiological signals.

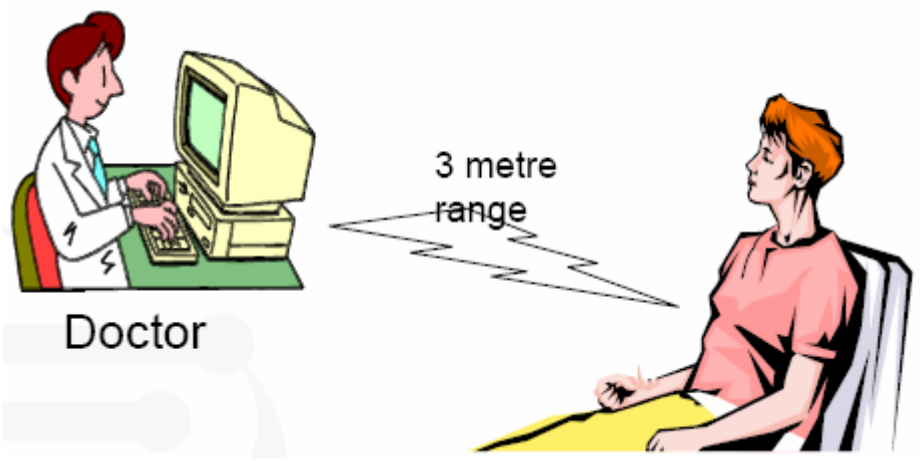


Figure 2 Future scenario for people with pacemaker visiting their local doctor for the yearly status. (Zarlink Semiconductors Ltd)

3.3 Perspective 3: Hospital

Needs and opportunities

They should be more service and production oriented! Greater attention to individuals would be required in the future.

Point-of-care vs. central laboratories was discussed. Both would be needed in the future. However, more diagnostics must be performed at the point of care.

Increased skills in relation to so-called distributed diagnostics would become more important. Distributed point-of- care systems puts pressure on the user friendliness of the systems.

Technology

Except for EKG, we do not have real-time detection of organ injury. Most organs reveal symptoms late. In the anesthetized patient and the ICU patients, symptoms are absent.

Reliable biosensors are badly needed, for early detection and continuous measurements.

Example of area of need is Ischemia. This is the most prevalent cause of mortality and morbidity in the Western world (myocardial infarction, stroke, trauma)

Alertis Medical AS is a medical device company with a new and unique technology for biosensors that will help save patients health and lives by providing early warning about critical changes in blood perfusion and respiration. The miniaturized biosensors are easy to use and will save health care expenses.

The technology of miniaturized biosensors addresses a considerable need in modern medicine by providing early warning of life threatening conditions, by measuring tissue pCO2, real time, on-line, as an indicator of adequate tissue oxygenation. There are no reliable, cost effective and user friendly methods available for this purpose today. Alertis unique biosensor technology will enable early warning and thereby early intervention of critical conditions related to changes in blood flow and respiration, providing a new tool for reducing mortality and morbidity as well as medical expenses.

This is a universal monitoring tool in modern medicine, with numerous potential applications, which are about to be explored.

Some key clinical areas for the biosensors will primarily be postoperative monitoring for the first 2-5 days following:

- *Orthopaedic surgery*
- *Plastic surgery*
- *Cardiac surgery*
- *Vascular surgery*
- *Solid Organ Transplantation*

and general monitoring to detect critical conditions such as:

- *Sepsis*
- *Shock*
- *ARDS (Acute Respiratory Distress Syndrome*

IscAlert™ from Alertis Medical AS

3.4 Perspective 4: Defence and Public Safety

3.4.1 International Crises Management and International Peace Keeping

Needs & Opportunities

The Nordic countries have a long tradition and a solid reputation for successfully negotiating and mediating between parties in conflicts worldwide.[14] The Nordic countries participate in various international peace keeping and crisis management missions worldwide within the framework of primarily UN and EU initiatives. It is expected that the Nordic countries will be even more engaged in future conflicts and other global crisis. This is further emphasized by the commitment to deploy the Nordic battle group in 2008.

Figure 3 Future Nordic military engagements will involve international crisis managements and participation in international peace keeping missions, where there is an explicit need for mobile, wireless sensors for rapid medical diagnosis and monitoring of the health condition of deployed personnel (Collage: Hjelt, G. FOI; Photography: Sandberg, K., Welter, J., Karlsson, A., Thulin, E., Eckervad, J. Haglund, S Å, Försvarets bildbyrå).

Modern international crises management involve both civilian rescue workers and military personnel deployed in high risk areas. From a health viewpoint, the risk to be exposed to or contaminated by infectious agents, radiation or toxic chemicals is a well-known problem under such circumstances. The exposure may be by accident, but also as a result of an act of hostility. Often the infrastructure is disrupted or even completely destroyed, which accentuates the problem with malfunctioning electricity net, sewerage, water supply, water cleaning, transportation networks, etc.

Pre-deployment risk assessment and risk management during these missions are especially important for personnel deployed in hostile chemically contaminated environments. Furthermore, capabilities for rapid assessment are important for prevention or mitigation of exposures. If there is no acute medical reaction but rather a latent disease or disability in the years after the deployment, it is equally important to have appropriate

[14] Å. Sellström, Director of FOI NBC Defence, Sweden, Fobis workshop, Copenhagen, Oct 2005.

tools for rapid assessment of exposures. Obviously, dedicated sensors is urgently needed to full-fill the needs for monitoring specific biological or chemicals either in the environment or directly on (or even inside) individuals. We foresee that by using new risk assessment strategies, and employing risk scenarios broken down even to the molecular level, the fundamental threats and needs can be defined and appropriate counteractions can be implemented at an early stage or even beforehand. These preventive actions may even be made on an individual basis, with personalized sensors, prophylaxis, drugs, and drug-delivery systems. Similarly, rapid post-analysis of human samples is important to verify or deny potentially hazardous exposures after completed missions. Specific biomarkers[15] (or biomarker patterns) should rapidly and accurately be traced to an exposure event at an early stage to enable appropriate medical treatments.

Figure 4 Deployment of UN personnel (Photography: Haglund, S. Å. Försvarets bildbyrå*)*

In general, there is a need for biomedical sensors to detect macromolecules in harsh and complex environments or in demanding medical applications. The ultimate goal is the fast, reliable, specific and cost-effective detection of a few molecules (or even a single molecule) in a complex, non-amplified and unlabelled biological sample. The improvement of in vitro diagnostics, and in particular biomedical sensors, toward this goal depends on several factors:[16]

- Nanoanalytical instruments of the highest spatial resolution, sensitivity and range of information, and integrated, combined instruments;
- Better sensitivity of screening methods, enabling the sample size to be decreased, or for the early detection of low concentrations of disease markers;
- Higher specificity, for quantitative detection of markers in complex samples.
- Stronger reliability, simplicity of use and robustness;

[15] We referred to molecules that are specific to the exposure as biomarkers. Typical biomarkers include DNA and protein adducts.
[16] NanoMedicine, Vision paper, Sep 2005, www.cordis.lu/mamotechnology/nanomedicine.html.

- Faster analysis;
- Integration of different technologies to provide data for complementary multi-parameter analyses.

The long term goal is to create miniaturized and integrated sensor systems that are wirelessly connected to an intelligent user interface, which have the capability to detect a large number of chemical and biological agents simultaneously with zero false alarm rates. These sensors could be used in surveillance systems and or directly on individuals. A further vision, which probably is beyond a 2020 perspective, is to have biocompatible sensors implanted in deployed personnel, which are individually adjusted for in vivo detection of specific biomarkers, which are similarly connected to a wireless communication network.

Technology

The current technology trends in biomedical sensor research portend a rapid development where we in a 10 to 20 year perspective can have solutions (products) that meet many of the demands discussed above, which can facilitate operation in unknown and unsafe environments. It may be so that some of the basic concepts or even technical solutions already have been developed, but that we have not yet appreciated them, or implemented them in the right context[17]. However, from current research several conclusions can be made. In the near future, disposable, colometric (i.e. naked-eye sensors) will be used to monitor water quality. Recent reports of chemosensors nanosized based on ion-selective dye particles,[18] and synthetic supramolecules[19] promise sensitive (ppb level) detection of a wide range of functional reagents in highly competitive aqueous environments.

In a 20 year perspective, it may be anticipated that nanotechnology will provide new materials that open up the window of opportunity for functionalizing nanoscale materials with improved sensitivity (large surface-to-volume) and selectivity (specific binding sites tailored from a bottom-up approach). Miniaturization will also allow for fabrication of arrays for multiple agent detection, which coupled with pattern recognition, microsystem integration and smart and fast computer algorithms have the potential to completely avoid positive false responses. It is clear that integrated microsystems housing arrays of many thousands of specific sensors will pave the way for portable or wearable sensors. Advances in microfluidic technologies show great promise towards the realisation of a fully integrated device that directly delivers full data for a medical diagnosis from a single sample. Combined with appropriate software this will lead to more reliable readouts with faster response time. Already today, advanced 'lab-on-a-chip' prototypes are available, where sample preparation; distribution (microfluidic handling); concentration; and analysis are integrated on microfabricated chips (made of silicon or polymer)[20]. Similarly, 'cells-on-chips' use cells as their sensing elements, and are employed in many cases for pathogen or toxicology screening. Integrated devices based on these detection principles

[17] B. McCraith, Dublin City University, Ireland, in Fobis workshop, Stockholm, March 2006.
[18] Y. Takahashi and T. M. Suzuki, AIST, Sendai, Japan (Angew. Chem. Int. Ed. Dx.doi.org/10.1002/anie.200503015).
[19] P. E. Kruger, T. Gunnlaugsson and co-workers at Trinity College Dublin, Ireland (J. Org. Chem. 2005, 70, 10875).
[20] Ralph W. Bernstein, SINTEF ICT, in Fobis Workshop, Oslo, Nov 2005; Wolfgang Rossner, Siemens, in Fobis Workshop, Tampere, June 2006.

can be used in the early diagnosis of disease and for monitoring the progress of therapy. It will be possible to prepare functionalized carbon nanotubes either for in vivo[21] or in vitro sensing; possibly integrated in clothing and protective armours.

Within a shorter time span, the recent advancements in nanophotonics and waveguide spectroscopy will allow for portable and even wearable biomedical sensors.[22] Coupled with pattern recognition and chemometrics these new spectroscopic techniques can function as fast, predictive sensors for screening. In fact, synergetic research efforts between optoelectronic and biotechnology may be a future Nordic R&D area with large potential, where current materials and surface science research can channel in new concepts and ideas.

Developments of new nanostructured materials will allow new types of robust sensor surfaces to be made, which are suitable for field operation. Recent advances include nanocrystalline diamond (NCD) materials, which can be functionalized by a fairly straightforward organic approach using covalently bonded amine linkers to under-coordinated C atoms at the NCD surface.[23]

Further developments will employ synthetically designed receptors such as molecular imprinted polymers or dendrimers, which are robust enough to be suitable for outdoor use. 'Lab-on-a-molecule' sensing principles, where multiple substrate interactions trigger a fluorescent response have recently been demonstrated, and promise developments of specific biomarker sensors.[24] For disease screening, in vivo detection using e.g. quantum dots may 'report back' by fluorescing on contact with diseased cells. At the same time it may be envisaged that other function can be incorporated on such nanoscale devices; for example nanomagnetic particles may 'report back' by providing increased contrast and also take part in the therapeutic process (controlled, localized drug delivery).

The need for remote communication for rescue workers, UN troops, and other personnel deployed in unknown environments cannot be underestimated. A common understanding among researchers, entrepreneurs, industry and end-user is that wireless communication and networking is central in future sensor systems. It is even suggested that wireless implantable sensor technology is the only way to realize reliable long term monitoring of physiological signals.[25] "Linking the molecular world to the Internet would be the next big thing…" says, D. Diamond, Dublin City University, Ireland in an interview for C&EN.[26] Diamond envisions a vast distribution of sensors that would relentlessly sniff the environs for molecular signs of weapons, disease, pathogens, and contaminants. He also argues that they would need to be maintenance-free and to power themselves by harvesting energy from their local environment. In human bodies, glucose molecules might provide the energy, but such sensors also would have to include the trait of biocompatibility. In the realm of public safety and home defense, such system of networked sensors could detect and track attacks with chemical and biological agents.

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[21] C. R. Betozzi, A. Zettle and co-workers, Lawrenec Livermore National Lab, Berkely, California, USA (J. Am. Chem. Soc. 2006, 128, 6292).
[22] Lars. H. Pedersen, Fobis Workshop, Copenhagen, Oct 2005; www.nano.dtu.dk/Forskning/Nanofotonik.aspx
[23] A. Härtl et al., Nature Mat. 2004, 3, 736.
[24] A. Prasanna de Silva and co-workers, Queen's Uni, Belfast, Ireland, JACS, March 28, 2006: dx.doi.org/10.1021/ja05295+.
[25] J. Lekkala, Institute of Measurement and Information Technology, Tampere University of Technology, in Fobis workshop, Tampere, June 2006.
[26] I. Amato Chemical & Engineering News, 9 Oct 2006.

One step forward in this direction may be the proposed Computer Screen Photo-assisted Technique (CSPT) for global monitoring of environmental and sanitary parameters.[27]

3.4.2 Public spaces

Needs & Opportunities

The threat that terrorists use biological, chemical or radiological agents (so called CBR agents) on civilians has become a major concern following the incidents of the 'anthrax letters' in 2001. The need for preventive opportunities to counteract terrorist attacks and mitigating causalities and secure areas for increased safety, comfort and well-being of citizens has motivated an extensive research aimed at finding new technologies for CBR warning and detection. Simultaneously, these developments also open the possibility for preventing and mitigate chemical accidents by early warning and rescue planning. Quite generally, there is a general need for ultra-fast response (real-time) with high detection sensitivity and probability and low false positive rate.

Figure 5 Stand-off and point detection equipments are used at the Superbowl events (Dolphin stadium, South Florida, www.superbowl.com).

A terrorist attack might take place anytime and anywhere. Even though it is not probable that a terrorist attack will have opportunities or the skill to use the most advanced and lethal chemical or biological agents, it is wise to be prepared for a worst-case scenario. Moreover, even rather limited incidents may have dramatic consequences.[28] Likely targets are areas where a large number of people gather. Such places include railway stations, airports, theatres, city centres and sport stadiums. International sport events typically include a large number of peoples. The spreading of infectious diseases may become particularly effective because of the large international participation. Today the protection of such an event has become a major under-taking costing hundreds of millions Euros.

Actions and activities should minimise the number of exposed persons if an incident take place. In order to obtain correct information on for example the need for evacuation, detection of a release has to be in real time. Moreover, the detection has to be reliable, i.e. to avoid false positive and/or negatives alarms. Small concentrations of aerosolized

[27] I. Lundström, Linköping University, in FOBIS workshop, Stockholm, March 2006.
[28] Ltc. Per Lausund, Norwegian Defence Research Establishment, in Fobis Workshop, 31 Oct 2006.

biological agents that are able to provide significant risk of infection will remain undetected by the present most advanced, or even future, significantly refined real time biosensors.[29] This means that improved real-time methods, especially for airborne biological particles are needed. Additional requirements are simple and robust systems for continuous monitoring.

Different detection strategies are required for the protection of open and of indoor spaces. A large out-door area has to be covered and scanned for contamination using stand-off (remote) detection technology or/and point detectors (local detectors) placed strategically. Optimally the detectors should be connected in a network and data fed into a decisions support system.

Buildings, such as airport terminals, could probably be well protected by strategically located detectors. A future integration of sensors in the buildings ventilation system could become as common as today's smoke detectors. We may also see walk-through detection systems that penetrate cloths, similar to what we today used for metals (realized in e.g. the emerging Teraherz technologies).

Following a terrorist incident, hospitals may become overwhelmed by contaminated people. This may eventually cause the health system to collapse. Not all individuals will be exposed or contaminated; this means that there is a need for sensors that rapidly can diagnose and discriminate between exposed or not exposed individuals.

Technology

The technology needed for public space detection go hand in hand with the technology development discussed above, but differ somewhat in that fairly large, immobile units for point and stand-off detection may be appropriate or even suitable in some circumstances. Even though their present status do not strictly place them per se in the area of biomedical sensors, future R&D is likely to bring these ideas and concepts into new devices for medical diagnosis, e.g. for quick, non-invasive breath monitoring or blood analysis. Point detection and stand-off devices are already implemented today at air ports and larger sport events,[30] which for example are capable of detecting chemicals (explosives) and biological aerosols (B agents). Although these devices do not meet the criteria of the 'magic bullet' in Figure 6 (see below), they are rapidly becoming increasing more sophisticated and reliable. For example, researchers at Lawrence Livermore National Laboratory, Berkely, California, USA, have developed an advanced mass spectrometer prototype, BAMS (Bio-Aerosol Mass Spectrometer) that was deployed in November 2001 to the postal sorting facility in Florida to scan the billions of pieces of mail for any detection and identification of harmful biological or chemical aerosol particles. Individual airborne particles can be identified at the single-cell level in about 100 milliseconds. BAMS identifies signatures for different spores and the difference between harmful and benign spores. So far, it has identified the spore for an anthrax surrogate. "Some day, when the system is perfected for field use, BAMS could be smaller than a breadbox and detect particles in about a millisecond", says Eric Gard, team leader. "In the future, BAMS could also be used in medical diagnosis".

[29] A. Sabelnikov, V. Zhukov, R. Kempf. Probability of real-time detection versus probability of infection for aerosolized biowarfare agents: A model study. Biosensor and Bioelectronics 2006, 21 2070.
[30] M. Lindgren, Deputy Research Director FOI NBC Defence, Umeå, Sweden, Fobis Workshop, Oslo, Oct 2006.

It is recognized that various spectroscopy techniques coupled with chemometric analysis is a way forward to develop better point and stand-off detection devices.[17,31] Fluorescence spectroscopy, Light Detection and Ranging (LIDAR), and infrared spectroscopy are currently investigated for this purpose. A general scheme for a point detection device is depicted in Figure 6.

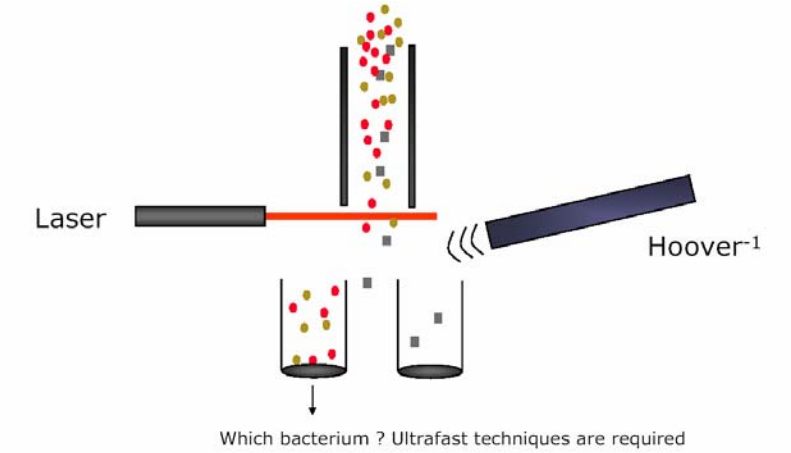

Figure 6 Principle sketch of a point detection device, which is capable of rapid detection of biological agents. (Lars H Pedersen, Bioneer, in Fobis Workshop, Copenhagen 6 Oct 2005).

New concepts will emerge for point detection that will merge biodefense and medical applications. Various approaches utilizing photoactivated localization techniques and optical stimulated emission depletion methods have been reported[32]. These techniques are among a wave of innovations that are poised to usher optical microscopy into a new era of finer vision. The once seemingly ineluctable limit on the resolving power of optical microscopy (the diffraction limit) is proving to have been more a state of mind than an unbeatable constraint founded on theory. These advances in nanoscale imaging show that it is in principle possible to simultaneously detect and chemically identify individual biomolecules. Given the strong foothold for optical microscopy in life science, these techniques will rapidly gain acceptance in wide range of medical applications.

In close analogy with the anticipated technology development in the previous section, nanotechnology will bring new sensor capabilities suitable for public space surveillance. Again, a vast deployment of wireless such sensors would yield both improved detection capabilities and dispersion profiling. This will aid risk assessment and rescue planning. Metal oxide based sensors may be one viable route, due to their easy of preparation (cost-effective) and stability. Recent reports include multi-striped metallic nanowires suspended within cavities of porous mineral solids with antibodies of specific pathogens attached to the different metal stripes. These nanowires are reported to rapidly identify sensitive single and multiplexe immunoassays that simulated biowarfare agents[33]. Covalent and non-covalent linking schemes to couple probe DNA strands to ZnO

[31] Ltc. John Carrano, Study Chair, Program Manager, Microsystem Technology Office, Chemical and Biology Sensor Standards Study, 2004, DARPA; L. H. Pedersen, Fobis Workshop, Copenhagen, Oct 2005; B. McCraith, Fobis workshop, Stockholm, March 2006.
[32] See e.g. Science, doi:10.1126/science.1127344; Nat. Methods, doi:10.1038/nmeth929; Phys. Rev. Lett. 2005, 94, 143903; C&EN Sep 4 2006.
[33] J. B.-H. Tok et al Angew. Chem. Int. Ed. 2006, 45, 6900)

nanostructures (unique for B. Anthracis) have also been reported[34]. When combined with automatic sampling and fluorescence detection these and similar systems have the potential to be signal enhancing platforms for rapid, multiplexed, high-throughput, highly sensitive, DNA sensor arrays.

3.4.3 Ports-of-entry

Needs & Opportunities

Large volumes of hazardous material are in circulation in various part of the world. Barrels of toxic waste, infectious material and/or radioactive sources are all examples of material, which are traded with or shipped illegally.[35] The globalization of trade and the recent political changes within the Nordic countries and our neighbouring states accentuates this problem. In particular the development in Eastern Europe following the collapse of the Soviet Union, with the Baltic States approaching the Nordic countries, and the entry of Sweden and Finland in the European Union has opened new trade routes into the Nordic countries. In order to deny dangerous goods entry, border control has been reinforced with a variety of detection devices in all Nordic countries. This development will continue in the near future.

Figure 7 Ports-of-entry: Sensors are needed to detect goods to prevent spread of diseases, toxic and radioactive materials. (Photography: Nyström, H. Försvarets bildbyrå)

Consider efforts has been undertaken to secure the traffic of passengers and gods at most airports, a similar control of ports and harbours is still lacking. A night-mare scenario

[34] N. Kumar et al, nanotechnology, 17, 2875.
[35] NBC International, 34-36, autumn 2006, www.defenceinternational.co.uk.

involves the smuggling of for example nuclear material in a standard container destined for some vulnerable target.

Detection technology for radioactive material is well established, while the detection technology for chemical and in particular biological compounds is much more complicated. Using today's technology an effective screening that allows an intelligent interception of dangerous material is impossible. Future development should produce technologies by which containers could quickly be pre-screened for hazardous materials. It is likely that we will see the development of smart and secure containers that may contribute to a decreased risk for illegal shipment of dangerous materials.

Technology

The ensuing technology development in this area follows closely that for public spaces discussed in the previous section. Today, there is no practical solution for complete and rapid CBR, pathogen (disease) or drug screening of humans, cargo, planes and ships that cross country borders. The BAMS instrument discussed above represents state-of-the-art at present for point detection, but can at present only fill rudimentary aspects of the actual needs. There are a number of shortcomings with the technology being used today. For example, detection of radioactive materials is currently of limited use due to high background levels in e.g. cargos containing food (e.g. bananas contain high concentrations of potassium). However, it may be foreseen that e.g. radio frequency identification (RFID) or other wireless communication labelled containers and goods with ICT integrated sensors will also emerge for these types of applications. Current limitations for point detection using e.g. X-ray imaging may create synergetic effect with in invasive imaging concepts developed for medical diagnosis.

3.4.4 Pandemics (single bacteria or virus detection and verification)

Needs & Opportunities

A pandemic is the spreading of a contagious infectious disease to a large portion of the world's human population. Influenza may become pandemic, when a new strain of influenza virus emerges. Since there is little or no immunity in the human population to a new influenza strain, a pandemic influenza can spread from person-to-person to most places on the planet in only a few months. The rate of spread is larger today than it was century ago (during e.g. the Spanish Flu) due to global travelling and more dense population distributions. Provided that sensors at various ports-of-entries or public spaces cannot prevent the spread, it is expected that the rate of dispersion increases in the future.

Recent experiences with highly pathogenic avian influenza, H5N1, have given the world its first advance warning that yet another type of influenza pandemic may be imminent.[36] Given the serious consequences of past pandemics, such as the Spanish Flu, this advanced warning has stimulated a search for preventive measures. The elements of such discussions unambiguously advocate an increased preparedness, rapid response and swift

[36] WHO pandemic influenza draft protocol for rapid response and containment. Updated draft 30 May 2006 http://www.who.int/csr/disease/avian_influenza/guidelines/protocolfinal30_05_06a.pdf.

containment. The rapid response and containment strategy aims at stopping, or slowing the spread of the pandemic. At best this will stop the influenza at the source of its emergence. If the spreading is slowed down, this will allow more time for preventive measures such as vaccination.

The outbreaks cannot be predicted. They are a function of mutations in an already existing virus. Hence, early detection and early diagnostics of the new virus are cornerstones in the successful response and protection strategy. Sensitive virus detectors with the capability to continuously monitor first signs of changes in the behaviour of the virus are needed. The possibility to detect the disease in animals before it reaches the human should be investigated. For example the control of airborne organisms of diseases in chicken farms has a high priority. Sensitive detection system will also assist when an infected area is to be declared free from infections.

Improved diagnostics is also essential to manage the outbreak and monitor its development. Combined diagnostic data can be used for risk assessments and refine monitoring strategies.

Technology

Again we see clear synergetic effects in the sensor developments for other applications. These include advanced point detection and stand-off detection systems; mass distributed wireless sensors, etc. However, it is unlikely that all threat scenarios can be met and in vitro and vivo medical diagnosis of infected individuals is necessary. Fast, reliable screening methods are needed. Monoclonal antibodies (mAb) have the potential to offer a method beyond PCR procedures to confirm positive screening results, which can provide quick and ease-of-use screening. Recent results demonstrate that small differences in the carbohydrates on the cell surfaces can be used to obtain specific immune reagents and can be a basis for development of anti-pathogen vaccine candidates.[37] 'Lab-on-a-cip', 'cells-on-chip' or 'lab-on-molecule' and variations of these concepts can be used for pathogen or toxicology screening. Combined with Microsystems and ICT, integrated devices can be used in the early diagnosis of disease and for monitoring the progress of therapy. Dendrimer and supramolecular chemistry show great promise as substrates to attach a variety of functional molecules, such fluorescent molecules, which can be used to construct from molecular level functional, artificial antibodies and synthetic biomarker receptors.[38] Again, it is a challenge to track appropriate target molecules in a highly competitive environment and various molecular-scale pattern recognition strategies will probably be used to alleviate this problem. Using a biomimetic approach E.V. Anslyn and J.T. McDevitt and co-workers at Uni Texas, Tx, USA, use the concept of 'differential binding' by analogy with the human sense of taste to make a biochip that determines the immune function of HIV patients.[39] The idea here is that a group of generalized characteristics, none of which are necessarily specific or even very selective, create a composite signal or pattern which can be interpreted by pattern recognition. Variations of the latter approach may provide a way to make rabid and robust biomedical screening.

[37] P. H. Seeberger, ETH, Zurich, Switzerland and co-workers, Angew. Chem. Int. Ed. DOI:10.1002/anie.200602048
[38] S. A. Edwards, The NanoTech Pioneers, Wiley-VCH (2006); NanoMedicine, Vision paper, Sep 2005, www.cordis.lu/mamotechnology/nanomedicine.html
[39] Chem. Soc. Rev. 2006, 35, 14; Angew. Chem. Int. Ed. 2005, 44, 6375.

3.4.5 Drivers

To analyze specific drivers for future development is a complex matter. In focus is the relationship between security, politics and economic incentives. In two areas i.e. pandemic and border control this relationship is relatively direct. Increased internationalization and open borders is a major driver. With the increased sensing and surveillance capabilities envisioned in this chapter, governments, non-governmental organizations and e.g. WHO (World Health Organization) have several opportunities during the pre-pandemic phase to mitigate the risk for proliferation of pandemic viruses to spread globally. WHO, FAO (Food and Agriculture Organization) and OIE (World Organisation for Animal Health) will facilitate in these activities, through their research networks.

Reinforcement or restrictions in border control will have serious consequences on the world economy, due to limitations in delivery times, accessibility and logistic planning. Ninety percent of the worlds trade occurs via container cargo shipped in and out of seaports.[40] However, this trade is highly vulnerable and the global economy depends upon it. CSI (Container Security Initiative) is a program that was started by the U.S. Custom Service in order to protect the world's shipping network from dangerous cargo and nuclear materials.[41]

A successful control of security in public spaces and internationally peace keeping operations are also profoundly important for the world economy. Here political forces attracting strong voter groups have profound influence. Changes in the near future that affect the Nordic countries include collaborative efforts within Europe to form a united European political platform that balances US and Chinese powers. This involves deployment of pan-European defense forces[42].

A major driver will in a 20 year perspective be an increasing ambition from politicians to protect their citizens in a world with increasing global activities (politics, economy, trade, work force, etc.). Pore preparedness for protection and management may create widespread distrust among citizens and is therefore politically sensitive. Common to the identified drivers is an increasing demand for rapid and reliable information of imminent threats. Improved warning-, defense-, diagnostic systems will all contribute to a larger security. The resulting increase in economic and political stability will results in improved comfort and well-being for the individual. However, the strategy to achieve an increased preparedness against e.g. bioterror is currently different between different countries, also within the Nordic countries.[43] We foresee a political development, where international agreements and collaborations will supersede and guide national decisions and action plans.

The R&D activities related to detection and identification of hazardous chemical, biological and radioactive (CBR) substances is currently dominated by the US military funded initiatives. Following the US initiatives to fight back the "terror threat" the goal for the US initiatives is clear: to develop the 'magic bullet' (Figure 8).

[40] http://www.nnsa.doe.gov/megaports_initiative.htm
[41] NBC International, autumn 2006; Chemical Biological warfare Review, 2006, published by GDR Publications Ltd, London, UK. www.cbwreview.com.
[42] WHO pandemic influenza draft protocol for rapid response and containment. Updated draft 30 May 2006. http://www.who.int/csr/disease/avian_influenza/guidelines/protocolfinal30_05_06a.pdf
[43] In Fobis bioterror and biodefense workshop, Oslo, 31 Oct 2006

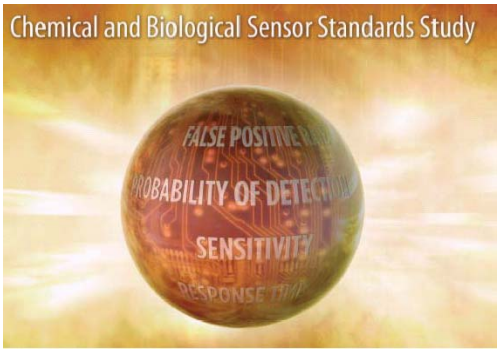

Figure 8 The 'magic bullet'. From Chemical and Biology Sensor Standards Study, 2004, DARPA, Ltc. John Carrano, Study Chair, Program Manager, Microsystem Technology Office

Today the military spending on R&D amounts to more than ca $70b compared to less than $30b in medical R&D.[44] The US pushes B detection hard, and this will probably result in significant spill-over into civilian biotechnology applications, including biomedical sensors. From a Nordic perspective, this results in a push and pull scenario, where in a short term national objectives and global activities influence R&D strategies. At the same time, the military spending in the US and elsewhere is anticipated to spill over to civilian R&D since much of the work is conducted at Universities and research institutes (and not only in the US). In Sweden a comparable example can be made with the company Biacore.[45] This is one of the few examples of a Nordic biosensor company based on basic R&D, which now is a global, prosperous company. In the early stage (beginning of 1980s) the founders did basic work and scientific publishing possible concepts to do real-time and no-label detection at University of Linköping and the Swedish Defense Research Agency (FOI). This work led to the defining concepts for the detection (SPR) and surface immobilization technology, which later was commercialized by Biacore (initially within the company Pharmacia). Can we anticipate similar spill-over from the ensuing security research programs, launched e.g. within the forthcoming EU framework programs? Yes, and we believe that this will occur even within a rather short time span. The needs created by an increased commitment of the EU member states to contribute in international crisis management and peace keeping operations, augmented by domestic border and ports-of-entry control, will spur activities in primarily CBR detection and analysis. The changed focus towards crisis management will lead to further need of Environmental and Industrial Health Hazards (EIHH) detection and analysis capabilities in order to minimize acute or long term exposure to hazardous substances. For certain, these trends will also lead to developments of ideas and concepts that will benefit biomedical sensor R&D in general.

[44] American Association for the Advancements of Science (AAAS); D. Kammen, University of California, Berkely, USA.
[45] Ulf Jönsson, former founder and CEO Biacore, Fobis Workshop, Copenhagen, Oct 2005.

4 A Nordic Business Perspective for Medical Sensors

This section addresses the business potential of medical sensors in a Nordic context. However, it is initially emphasized that any business in this area will inevitably have to be seen in a global context. Only addressing Nordic markets is unlikely to produce a profitable business in this area. By the same token it is so that the technology used may be based on important Nordic contributions. However, most likely any product will be based on technologies developed around the globe.

4.1 Introduction

The Nordic countries all have well-developed and extensive health care systems. There are strong industries within pharmaceutical development, production and marketing as well as strong companies in medical diagnostics. Micro-and nanotechnology and telemedicine are also areas where the Nordic countries have strong competence. In order to take advantage of the needed symbioses of these technology fields, Nordic industry need to create collaborative networks and strategic alliances. The region is in an excellent position to exploit potential benefits of biomedical sensors both as users and as vendors of sensors and systems.

The Nordic Countries is a MedTech cluster, carrying 30% of the European investment in medical technology.

The Nordic Countries have a good basis for the exploitation of the market for medical sensors. This is related to a well developed health care sector, both in relation to the health care system and in relation to the industry. A very good knowledge pool exists. However, there are barriers related both to the structure of the health care system in Europe that is less adaptive to new technology than what is seen in North America and in some Asian countries. The environment for new knowledge based business is generally better than in the rest of Europe, but not as good as in The United States. Pre-competitive governmental procurement is an instrument that especially in the sector addressed here could have a dramatic effect on the development of new technologies.

4.2 Market Segmentation

In order to access the business possibilities we found it useful to partition the applications and the market into several subgroups. They are as follows:

4.2.1 Diagnostics

Diagnostics is the process of identifying a medical condition or disease based on signs, symptoms and measurements. Sensors are generally used for in-vivo measurements. They may be instantaneous or provide for a temporal history. The latter is often very important, since it may minimize the effects of uncontrollable instantaneous conditions that should have no or only a minor impact on the diagnosis.

Prognosis denotes the prediction of how a patient's disease will progress. Diagnostics is here a key element.

In vitro is currently the dominating market in relation to sensor technology. The total turnover is estimated to be in the range of USD 30 billion.

In vivo diagnostics is primarily performed with equipment, which is not considered as medical sensors and includes X-ray systems, NMR scanners etc. However, we do find that there is a trend towards sensors also for in vivo diagnostics. They may be implanted or may be non-invasive.

4.2.2 Aid to improve the quality of life

This is a very important area. For the Nordic countries and in particular Denmark the hearing aid industry is by far the largest with a turnover in the area of EUR 6 billion. The area exhibits a reasonable steady growth of 4-6% annually. It is dominated by relatively few companies and may become even more consolidated. This is a mature market and the opportunities for new players are somewhat limited unless a radical new technology is introduced and that this technology implies a substantial improvement in ease of use and hearing quality.

Other areas related to the general health condition appear to be much more open to new enterprises. This has e.g. been illustrated by the rapid growth in blood pressure measuring equipment for home use. Sensors incorporated in sports equipment is emerging[46]. Sensors that detect health related properties are anticipated to be incorporated in clothes, beds etc. and is already incorporated in soldiers outfit.

4.2.3 Drug discovery and development

Drug discovery is the process of finding substances or molecules that has a particular desired biological effect. Drug development is the subsequent process of preparing a substance that can actually be used in humans. These are very important areas both in relation to health care and in relation commercial exploitation. Although only indirectly related to health care, we have included this topic because it is found that sensors can play an important role both in drug discovery and in drug development in particular in high throughput screening.

High throughput screening is an approach for finding new drugs which looks for chemicals that act on a particular enzyme of molecule. For example, if a chemical inactivates an enzyme it might prove to be effective in preventing a process in a cell which causes a disease. High throughput methods enable researchers to try out thousands of different chemicals against each target very quickly using robotic handling systems and automated analysis of results. However, it is still one of the most expensive and time-consuming parts of developing new drugs. Sensor methods compatible with the current robots and microtiter plates (arrays of small wells) may provide for a significant reduction in development time.

[46] Companies like Nike jointly with Apple, and Adidas have products where wireless sensors are incorporated in shoes. See e.g. http://www.apple.com/ipod/nike/gear.html and http://www.adidas-polar.com/.

4.2.4 Security and safety

This area has unfortunately attained very much increased importance. The relevant sensors cover a whole range like intrusion detection, detection of explosives, of biochemical substances, weapons etc. An overview of the area has recently been published by The US National Science Foundation.[47]

4.2.5 Environment

This has been considered a very important area. Application areas are in water recovery, waste water, in- and outdoor climate, particle concentrations, volatile gasses etc. A number of companies are active in this sector. There is a considerable overlap with both health care and with safety and security. There are a number of commercial operators in this sector. However, according to the information we have collected the growth is relatively slow and it has been difficult for new companies to establish a business. The actual use of sensors and measuring instruments is very much dictated by regulatory conditions. Only a very small part of the measurements are done by sensors *on-line*. Most types of analysis are done on samples in a laboratory.

Sensors and measurements for industrial processes are considered to be outside the scope of this project despite the fact that they may have important impact on human health, but they are not considered to be medical sensors.

4.2.6 Other relevant areas

Sensors and measurements for industrial processes are considered to be outside the scope of this project despite the fact that they may have important impact on human health, but they are not considered to be medical sensors. Likewise are sensors used in transportation equipment like automobiles and airplanes not included and neither are sensors for detecting the structural integrity of buildings and other large structures. This is despite the fact that these sensors can also be of considerable important to human health and welfare.

4.3 Business Structure

Addressing the market it is particularly important to realize the following:

- Who has a need?
- Who decides about the purchase of medical sensors?
- Who is paying?
- Who sets the rules?

Who has a need for medical sensing can be summarized as follows as shown in Table 1.

[47] http://www.nsf.gov/news/special_reports/sensor/safety.jsp

Table 1 A number of different actors in the health care system have a need for medical sensors

Who	Need
Hospital	Clinical routine tests
	Monitoring critically ill patients during e.g. surgery
	Monitoring of critically ill patients during intensive care
	Monitoring of (critically ill) patients at point of care
Medical centers/practitioners	Routine tests
	More advanced tests (cell counting)
Diseased individuals at home	Testing for development of non-cronical disease while at home in order to be in a non-hospital milieu.
	Testing for cronical disease (diabetes)
	Testing for infectious disease
	Sensing of device function/function of device (implant)
Healthy individuals (home care)	Self testing (blood pressure, pregnancy, testing of children)
Soldier biosensing	Medical care testing as stated above
	Remote and self testing in the (battle) field (infectious agents, explosives)
Legal authorities	Doping (sport)
	Drugs

Who decides to purchase medical sensors?

The major decision makers are the physicians, but not necessarily those who actually use the sensor equipment. The customers are mainly MD's (in a managing position) from the public hospital environment, private hospital environment and possibly decision makers from military agencies. Purchasing for hospitals is often organized by special joint operations. General practitioners do also have joint purchasing organizations. For home-care products the patients/consumer may decide about what to purchase. However, it will very often be under the influence of professional health care personnel. Overall it must be concluded, that the decision process is rather complicated and far from as straight forward as in many other businesses.[48]

Who sets the rules?

Although most countries have national regulatory agencies the American Food and Drug Administration is setting world wide de facto standards. In addition to this many countries do also have professional bodies that set standards for “good practice” (in some case there are even separate bodies for hospital uses and for uses at the general practitioner). The structure of the health care sector is very much a political issue (Europe) or may be defined by insurance companies. How and who is doing what is generally determined by national health care bodies.

Who is paying?

This varies very much between countries and continents. Of special relevance is the

[48] An detailed discussion about the topic in relation to the hearing aid industry is given by S. Kochkin from Knowles Electronics Inc. (http://www.knowleselectronics.com/pdf/presentations/MarkeTrak6.ppt#257,1,MarkeTrak%20VI:%20Hearing%20Aid%20Industry%20Market%20%20Tracking%20Survey%201984-2000)

difference between North America – in particular The United States – and Europe. Europe is very much based on a public health care system, where governmental or public institutions provide for much of the funding of health care costs. In the US private insurance companies have a dominating role in relation to "who pays". Hospitals and GPs in the US have purchasing organizations that very much sets the standards in terms of performance, price and vendors. In Europe it is very much hospitals, regulatory bodies and organizations that defines the business rules.

Medical sensors have a primary application in the area of *diagnostics*. Therefore we shall elaborate on some of the key features of this segment.

In relation to needs for diagnostics the differences are relatively small between the affluent parts of the world. The US is leading in relation to so-called welfare diseases with Europe right behind and Asia still less affected. In all affluent countries welfare diseases is considered to be the major health care problem. It is estimated that currently about 300 million people suffer from diseases related to poor eating habits and inadequate exercise. A recent trend is that these diseases are also appearing in many less affluent countries[49].

The decision making in relation to acquiring specific sensor products is either done by physicians (as described above) or by the consumers themselves. It is anticipated that decision making will become more decentralized in relation to the increase in demand for decentralized diagnostics.

It is interesting to notice that the market for self-care/consumer may be similar in size to the market where physicians are the decision makers. This is illustrated in Figure 9. The consumers are in this case the user, the decision maker (possibly aided by physicians), and the ones who pays for the devices. This market is addressed very much in the same way as it is done for other consumer products.

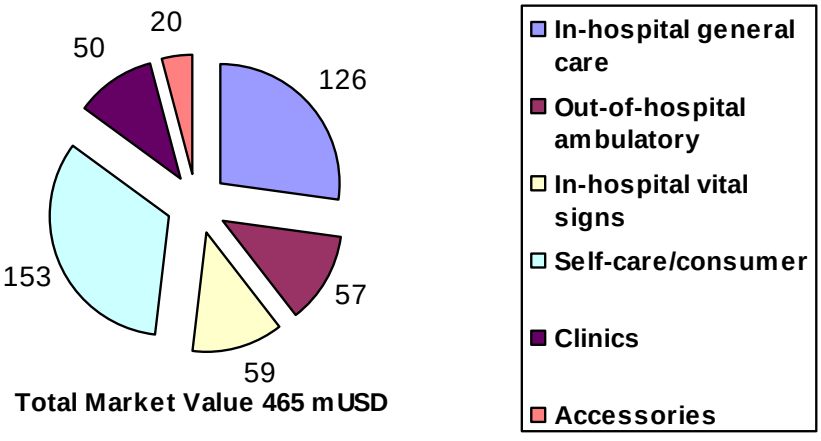

Figure 9 The US Blood pressure market[50].

In order to assess business perspectives it is important to realize *what*, *where*, and *how* diagnostics is performed. We have partitioned the area into *home care*, *doctor's office*,

[49] http://www.who.int/dietphysicalactivity/publications/facts/diabetes/en/; http://www.who.int/mediacentre/news/releases/2004/pr68/en/
[50] Susanne Friis: Blood Pressure Sensor Market MBA-thesis, Copenhagen Business School 2004

and *hospitals*. The hypothesis is that in order to maintain a well functioning health care system a shift must occur so that a larger fraction of the testing/sensing is done in homes and in doctor's office rather than in hospitals[51]. This has been the basis for quite a large number of companies that develop products for *point-of-care* in some cases based on *lab-on-a-chip* systems. A number of market reports address this sector[52]. Quite a large growth has been stipulated with a double digit figure for near-patient applications (doctor's office and hospitals) and somewhat less for home care. This has been expressed as follows:

> *Over the last few decades, there has been a strong trend toward POC testing because of an increasing demand for near-patient testing that provides rapid results. More tests are being performed at the hospital patients' bedsides, in physicians' office laboratories, outpatient clinics, emergency rooms and intensive care units. Critical care instruments combining selected important chemistry, hematology and hemostasis parameters have entered the market for POC testing in the emergency and operating rooms. The trend toward greater POC testing is driven by the faster diagnostic benefits it provides.*

However, until now it appears to be the home care market that has grown fastest. Of what could be called certified sensors (FDA and/or doctor approval) diabetes sensors have obtained the largest market share, which currently is estimated to approx. USD 4 billion annually out of a total biosensor market of about USD 7 billion.[53]

Characteristic of the *home care market* was summarized at the first FOBIS workshop[54] as follows:

- The need for home care will increase drastically. This will necessitate an increased use of medical sensors, telemedicine, and remote consultation, diagnostics and decision making.
- It is not obvious whether this development will increase or decrease the burden on the rest of the health care system.
- Implantable devices where sensing and therapy are combined have a great potential, but poses a number of legal and ethical issues.
- Equipment must be developed in the form of simple, robust, and reliable kits.
- The private market for health care services will most likely increase and health care as well as so-called well being will often merge.

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[51] Lasse Larson, "Point-of-Care Testing in Sweden", Blood Gas News vol. 8, no. 2 1999.

[52] Point of Care Diagnostics BCC Research February 1, 2006 156 Pages - Pub ID: WA1260727
The Global Market for Point of Care Diagnostics: Major Players and Key Issues, Espicom Healthcare Intelligence, une 9, 2006 440 Pages - Pub ID: ESPI1317800

[53] This number is based on the report Medical Biosensor Applications and Market to 2008; Takeda Pacific 2005 and compilations performed by Sensor Technology Centre.

[54] The first FOBIS workshop, Copenhagen, October 2005, see the second FOBIS Newsletter Jan 2006., www.nordic-fobis.net

- The public system as well as individuals will have to face a number of difficult problems in relation to defining priorities.
- The organization and market will most likely become more chaotic than what currently is the case.
- Home care is currently the larges market for low-cost medical sensors and this will most likely also be the case in the future.

4.4 Estimates of market size and growth rates

The Nordic countries have very good possibilities for exploiting the markets for medical sensors: They are affluent countries with well developed health care systems, they have very good research activities and they do already have a strong health care industry – especially in pharmaceutical products, hearing aids and diagnostic equipment.

Figures that describe the current status in Denmark have been collected and partitioned according to the segmentation given here. Estimates of the potential for the different sectors are also given. The Danish figures cannot be directly extrapolated to the whole Nordic region. However, we believe they provide for a good indication.

Table 2 Estimated revenue, number of companies, and potential for medical sensors within the different sectors

Sector	Revenue billion EUR 2005	Potential (+10 years) EUR	Number of companies (2006)	Comments
Diagnostics	2	5	51	A few large companies are dominating. Infectious and cardio-vascular
Quality of life	3	6	15	Hearing aid is the dominating industry: Three main companies, one major component manufacturer + several smaller
Security and safety	Very low	2	3	A growth area
Drug discovery	not available	0.5	2	EUR 13 billion.
Other	?			The sensor market for *well being* products may exceed the recognized health care market

Some comments in relation to the different sectors may be in order.

Diagnostics

The projections for this area are that it will most likely exhibit a double digit growth figure over quite a long period. Three main factors will drive the market:

1. A shift towards home care and doctor's office diagnostics partly in conjunction with telemedicine.

2. An increase in so called welfare diseases, which has a strong impact on diabetes monitoring and cardio-vascular diagnostics.
3. The emergence of large markets in the developing world and especially in Asia.

The market developments imply both major opportunities for existing manufactures of diagnostic equipment, which will shift towards sensor-oriented products as well as for start-ups.

Most of the current diagnostics market is performed *in vitro* (outside the body) and in most cases in laboratories with measuring instruments, which are not considered to be medical sensors. Rather well established data for the in vitro diagnostics market do exist.[55] We have tried to estimate how large a fraction of the in vitro diagnostics market that currently is performed with medical sensors and how large a fraction that could be performed 10 years from now. This is illustrated in Table 3.

Table 3 Estimated percent of the IVD market where micro fluid/sensor systems are essential. The total IVD market in 2005 is estimated to USD 26 billion.

	Percent of total 2006	
	2006	2016
Hospitals		
Central labs.	85	90
Operating theater	2	4
Intensive care	2	4
Bed-side	3	9
Doctor's office	5	15
Home care	3	10
Total	100	132

The total world wide market is estimated to USD 28 billion. The Nordic market currently is estimated to account for approximately 2.5% of the world market.

The drivers and issues that determine the future of the diagnostics market can be summarized as shown in Figure 10.

[55] Se e.g. www.datamonitor.com

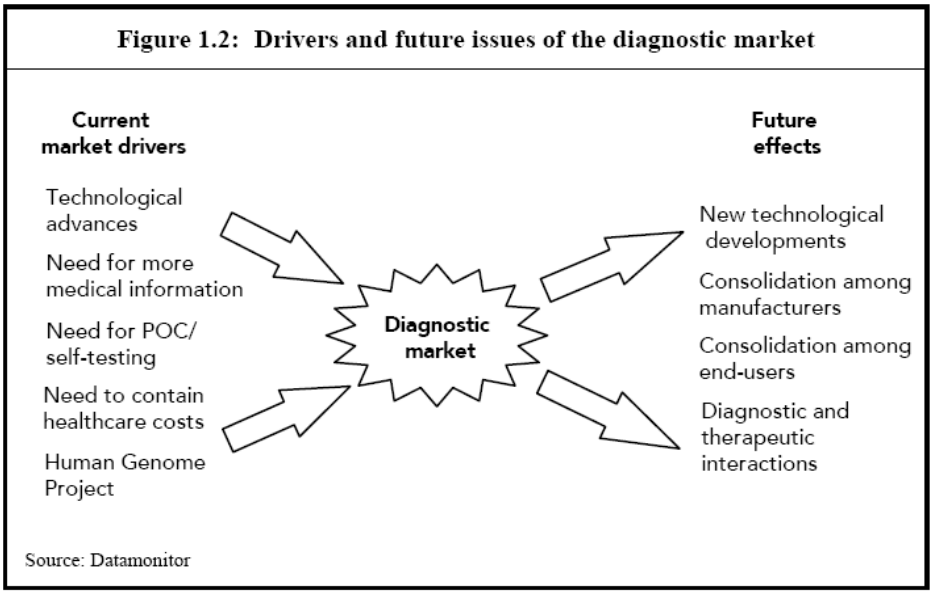

Figure 10 Drivers and future issues that determine the future of the diagnostics market (from *Datamonitor*).

Quality of life

We do not have numbers for the whole area. However, the hearing aid industry is very important to especially Denmark. The following figures are extrapolated from an American investigation pertaining to The US.[56] About ten percent of the population in the affluent parts of the world suffer from hearing impairment. The percentage of these who actually have a hearing aid is about 22%. The decisions about which make of hearing aid to acquire is primarily affected by physicians and audiologists. However, the decision process appears to be rather complicated and is not well understood. This is very likely the case for other sensors that can improve the quality of life.

Implanted sensors do still represent a relatively small market. However, the increased knowledge about the functioning of the neural system and the increase in average age implies a large potential for growth.

Drug discovery and development

The major broadly defined enabling discovery technologies are outlined in the figure below. These technologies are used in combination with *in vitro* cell screening assays and *in vivo* analysis of animals to assess the potential of new therapeutic candidates. The global market for the hard ware technologies associated with the drug discovery process is estimated to be in the order of USD 1 billion and we estimate that less than 1% is related to sensors.

The Swedish company *Biacore*[57] is relevant to consider. Originally establish in order to exploit surface plasmon resonance biosensors to high-throughput screening it has developed into a world leading company for used in connection with drug discovery. However, the actual use as a sensor in conjunction with high-throughput screening is till to be demonstrated. A somewhat different technology will most likely be needed.

[56] http://www.knowleselectronics.com/pdf/presentations/MarkeTrak6.ppt#379,38,Conclusions
[57] www.biacore.com

High throughput screening is currently a bottleneck – time wise – in drug development. A fast sensor system compatible with the microtiter well format appears to be a viable market. The company Bioneer A/S and STC have jointly estimated the potential of this market based on the following assumptions:

- A 20-times reduction in analysis time is feasible compared with current methods based on so-called radio immunoassay and/or optical fluorescence.
- An extrapolation to world figures can be done on the basis of the size and needs of the Danish pharmaceutical industry assuming that the industry in terms of turnover per capita here is about three times larger than the average for the affluent part of the world (approx. one billion people).

We found that there is a potential for the following:

- About 500 units sold per year
- 30 million disposable "sensor heads" per year

This could form the basis for a billion dollar industry!

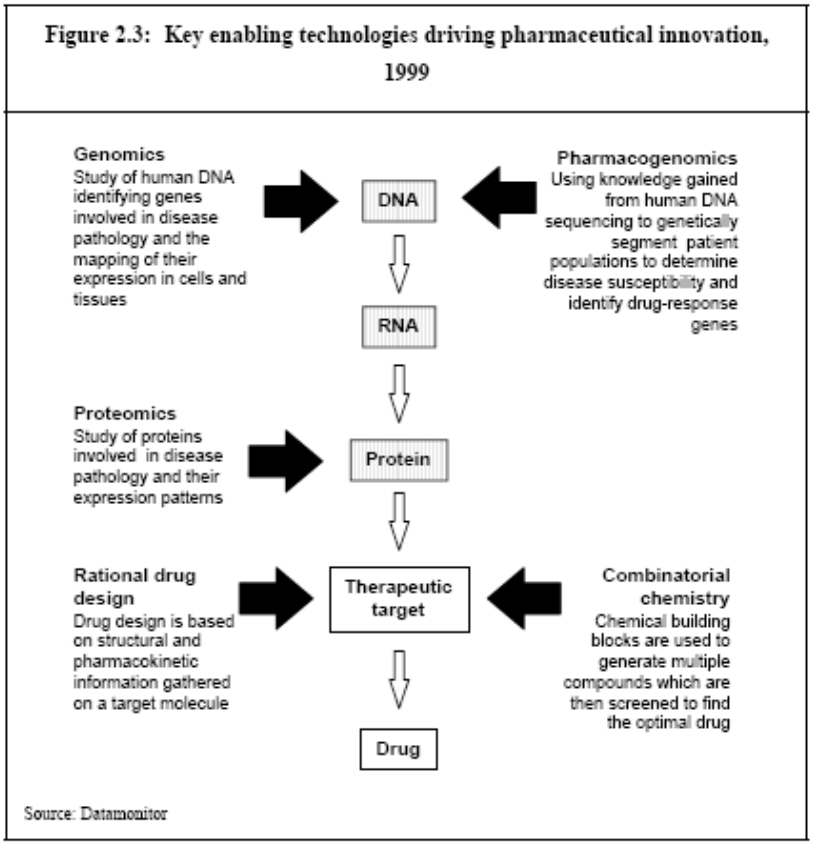

Figure 11 Key enabling technologies for pharmaceutical innovation. (From Business Insights, The drug discovery outlook, 2000)

Safety and Security

This sector is one of the fastest growing sectors. The sector does cover areas far beyond medical sensors (e.g. acceleration sensors for air bags in automobiles). We have not

obtained detailed market information on medical sensors in the course of this project but a valid market guess 2007 may be in the range of USD 200 - 400 millions. The area can roughly be partitioned into the following sectors: Defence and military systems, public services (e.g. transportation by airplanes) and home security. It is expected that the market will grow considerably in the forthcoming years due to the research efforts in the defence and homeland security areas where the focus is put on personal soldier surveillance and area surveillance.

4.5 Main opportunities and barriers

The opportunities and barriers in relation to the exploitation of medical sensors by the Nordic countries can be considered by a SWOT (Strengths, Weaknesses, Opportunities, and Threats) analysis. A useful SWOT analysis does require clearly defined objectives. In relation to the present analysis the objectives can be defined as follows:

- Nordic industries are major vendors of medical sensors.
- The growth of Nordic companies in the field is considerably larger than the world average.
- The Nordic countries are leading in relation to the use of medical sensors for the benefit of health care and well being.

A SWOT diagram could then be as shown in Table 4.

Table 4 SWOT table in relation to Nordic exploitation of medical sensors.

Strengths: • A competitive and well established research environment • A strong health care industry in general with several world leading companies • A health care system that can provide very good statistics in relation to needs and effects of measures • A good record with respect to companies working with sensors • Educational skills	**Weaknesses:** • Inadequate seed and venture capital • Inadequate market access (Test markets are small) • Regulatory conditions that limits the use of medical sensors – especially in Europe • High overall costs
Opportunities: • A very good potential for improvements of health care systems • An ageing population and increase in lifestyle diseases requires increased point-of-care and at home diagnostics • Access to novel technologies due to a strong research environment • A non-bureaucratic business environment	**Threats:** • The US and the Far East continues to demonstrate a larger agility to innovate (transform knowledge to business) • A slow and complicated decision-making within health-care systems • A consumer basis that is less adaptive to new health care technology than encountered in the US and the Far East • Shortage of adequately qualified personnel • A world market that does not develop as predicted

In order to assess the barriers we may consider a value chain[58] illustrating the avenue from *problem to product*. The *avenue* is confined by external factors that only to a very limited extend can be affected. On one side it is the system that defines the market: the needs of the patients, the organizational structure (hospitals, GPs, home care etc.) and the legal and regulatory conditions under which the system operates. On the other side are external factors that are decisive for the ability to *progress along the avenue.* This is illustrated in Figure 12.

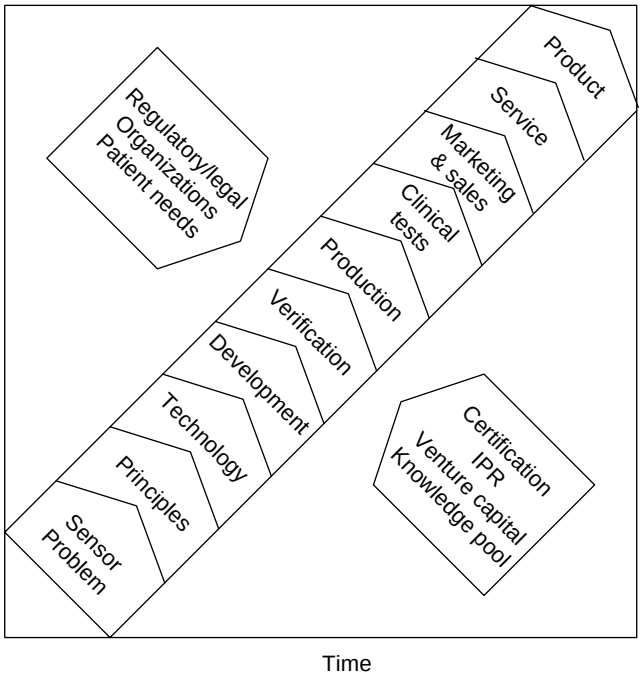

Figure 12 A value chain illustrating the *avenue from problem to product*. The steps on the avenue can very much be controlled. However, the overall conditions are very much influenced by external factors that only to a very limited extend can be affected.

The two main barriers in the present case are identified to be the following:

- Regulatory conditions that seriously limits the use of sensors particularly in hospitals.
- Shortage of venture capital especially to finance the stage between the research stage and the development phase

The first barrier is of course particular to the present topic. The second barrier is rather general to the development of new knowledge-based companies.

[58] A *value-chain* may be defined as a series of value-adding functions that connect through governed transactions and result in the supply and sale of products (modified from M. E. Porter, Competitive Advantage, 1980)

4.6 Recommendations

A few important recommendations have been identified during the course of this project. They are of course based on the justified assumption that medical sensors can contribute significantly to an improvement of health care and the quality of life.

The United States has a program that specifically addresses research and development in small businesses in relations to commercialization and national needs (SBIR/STTR[59]). The program has been very successful in relation to its objectives. To our knowledge, an equivalent program does not exist in Europe. However, we find that such a program based on interaction between industry, research, and public needs could provide substantially to the development, application and commercialization of medical sensors.

A recent report has been published by The National IST Research Directors Forum[60] entitled "Pre-commercial Procurement of Innovation – A missing link in the European procurement cycle". It is here pointed out that other regions - especially The United States and major Asian economies – uses pre-commercial procurement as active instrument for innovation in industry. This instrument is almost absent in Europe. The report recommends that this state of affairs is changed. It is proposed that the European Commission start to explore the interest of a limited number of procurers. We would suggest that medical sensors are included in one of these topics, which could be *e-Health*.

Conclusion from the panel discussion at the 4th FOBIS workshop in Tampere (June 2006):

> *Technologically there is a tremendous potential, especially related to converging technologies, however technology alone does not create business.*

[59] http://www.sba.gov/SBIR/indexsbir-sttr.html

[60] The National IST Research Directors Forum (NAT IST RTD Directors Forum) brings together National IST (Information Society Technologies) Research Directors to discuss key policy and implementation issues related to the development of a European Research Area in IST. The forum complements the bottom-up approaches supported by the Framework Programme. http://www.cordis.lu/ist/about/era.htm

5 Visions for biomedical sensors

5.1 Future health care

Some statements from different research groups about the future health care and biomedical sensors:

> *Increased longevity and larger population will require rapid development of all the health care sectors, with particular focus, on the development of fast and cheap methods in the pharmaceutical industry, the development of local and timely drug application-methods, the expansion of new methods in implant surgery as well as in the near-patient care and preventive diagnostics.*

Imego magazine, Future of biosensors- 10 years from now
(www.imego.com)

> *Current national studies show that patients provided with some form of home-based monitoring are hospitalized less, and when they are hospitalized are able to be discharged earlier than unmonitored patients.*

Carl Taylor, director of the Office of Emerging Health Technologies
(www.southalabama.edu/emergingtech/news/news-sybernet.html)

> *Being able to remotely monitor, collect and analyze biometric patient data in a dependable and scalable fashion and make this information available to healthcare providers via secure web technology has the potential to improve patient safety and dignity, and can lead to better outcomes and real time/cost savings. The healthcare industry has only begun to scratch the surface of this opportunity.*

Kenneth Kleinberg, vice president and research director Gartner Inc.
(www.southalabama.edu/emergingtech/news/news-sybernet.html)

Important factors affecting the future of healthcare are as follows:

- *The development of Finland's public health service will be determined by the EU's specifications of the pan-European welfare policy. Globalisation can bring new, significant challenges such as new epidemics, new disease spectra or multi-cultural customers.*
- *The coming changes in the needs of the ageing population are well anticipated. The changes, which are related to an urban life style, a higher education level, individualism and living alone, can cause unexpected pressure on social and health services.*
- *The transition of the large age groups (born between 1946 and 1953) to retirement causes serious recruiting problems for new staff.*
- *Bio-medical breakthroughs lead to new possibilities in examining and treating patients. Medico-technological developments will continue, cycles will accelerate and the expectations of the population will increase.*
- *Several routine services will be performed via electronic transactions (appointments, laboratory consultations, handling of prescriptions, consultation with medical experts)*
- *An open rationing will unavoidably be needed to restrict the increasing demand for services. All rationing systems must be transparent, fair for everyone and based on medical principles (mostly on the cost -effectiveness of the treatment). The Finnish 15D quality-of-life scale has become a national standard in measuring the effectiveness of health care.*
- *The number of multi-problem patients will increase, especially with children and adolescents. Their needs for medical, social and educational services will increase.*
- *Every citizen's own role and responsibility to his or her own health will increase.*
- *The financing of health care services comes from several different sources: state, municipal health care systems, KELA (the Social Insurance Institution), employers, insurance companies and the private sector). The financial system must be clarified.*

Skenaariot ja strategiat palvelujärjestelmän turvaamiseksi (2004)
(www.eduskunta.fi)

5.2 Small pictures of the future

To illustrate possible mini scenarios of future health care, the FOBIS team has described some pictures of the possible future.

Case 1 –Osteoporosis

Maria is a 60 year old Norwegian grandmother. Every week she uses a personal diagnostic screening instrument for common diseases for elderly people. She takes a blood sample (only a droplet is needed and it's very easy to perform) and puts it onto a lab-on-a-chip device (disposable of course). The plastic chip is the inserted into the instrument. The lab-on-a-chip contains markers for the most common diseases for elderly people. After a few minutes she gets a red light for the osteoporosis marker. She

immediately calls her local doctor at his office and gets an appointment at the local lab assisting the doctor for a validation of the result. The next week her local doctor verifies the test results. Then he initiates new and a more detailed tests using equipment at the local lab. He then sends her to a specialist who sets up a treatment strategy for Maria.

This unique lab-on-a-chip device, developed by a Nordic company, has once again demonstrated its effects; the early detection makes preventive medicine possible and prevented complicated breaks caused by falls for Maria in the future. It also gives a personal comfort and safety and the society saves money.

Case 2 – Diabetes

John is a 30 years old Danish guy. He visits his local doctor because he is not feeling well (he has all the typical symptoms on diabetes without knowing it himself). After listening to him, the doctor concludes that this most probably is diabetes. The doctor uses a lab-on-a-chip device at his office to verify his identification. He takes a blood sample of John and the test concludes that he suffers from diabetes, type 1. More sophisticated tests are then carried out in another machine to present a prognosis and suggest a personal treatment. The prognosis is based on statistical data from a national database (the doctor have access to this). The doctor sets up a treatment plan and John will come back after one month for a check.

Case 3 – Prostate

Frank is a 55 years old Swedish guy. He sees his local doctor for the yearly check-up. At the doctor's office he is screened for the most common diseases, mostly by taking a blood sample and put droplets onto different lab-on-a-chip devices, among them one for the most common types of cancer. The marker for prostate cancer is positive. The doctor then takes a new test for verification and estimation of how aggressive the cancer is. The test shows that it is an aggressive type, and Frank is immediately sent to the hospital for more tests and preparations for an operation. One week later Frank is operated at the hospital with a good chance of being cured.

Case 4 – Cervix cancer

This scenario is described by the EC FP6 project MicroActive[61].

Current situation

Anne visits her local doctor. It's time for her cervix cancer check, which she takes every three years. The doctor takes a sample with epithelial cells and tells her that if she does not hear anything within three weeks, it is OK. The doctor sends the pap-smear to a central laboratory where it is studied manually under a microscope. Some suspicious cell changes are seen. The results are mailed back to the doctor. He calls Anne and tells her that she will need to re-test in 6 months to see if there still are any cell changes. Anne spends 6 months anxiously waiting, but the second test shows no cell changes. The first

[61] www.sintef.no/microactive (2006-2008)

test was probably a false positive result; the number of false positive results for first time cytological screening is between 50 – 75%.

5-10 years from now
Anne visits her doctor again. Cervix samples may, if necessary, be analysed more often than before as costs are now much lower. The doctor mixes Anne's epithelial cells from the swab with a preservation solution and selects a polymer chip for cervix screening from his fridge. A droplet of the solution is applied to the polymer chip and the chip is inserted into the MicroActive instrument on his desk. The automatic test takes two hours, so Anne goes shopping and pops into the doctor's office on her way home. The doctor tells her that her test produced 5 green lights on the MicroActive panel and tells her that the test is negative; no mRNA activity was found for the 5 markers of high cancer risk human papillomavirus (HPV) types. This result is correct with 99% probability. If some of the markers had been positive, she would have needed to see a specialist for a thorough follow-up and suitable treatment.

10-15 years from now
Anne now considers it commonplace that tests for common conditions are carried out by her own doctor. A small, hand-held instrument lies at the doctor's desk. With this instrument he is able to test her for a wide range of diagnoses such as cancers. Anne even thinks of buying her own hand-held instrument for home checks. At home she can test for less serious diagnoses such as respiratory and sexually transmitted diseases (STD) and check the food in her kitchen for bacteria.

Case 5 – Future hospital

Lars is on vacation in Spain. He has crashed with his motorcycle and suffered severe injuries. Unconsciously he is admitted to the Central Hospital in Barcelona. Upon arrival he is automatically checked in to the Hospital with his personalized electronic health ID (e-HID). The e-HID is an integrated chip on his credit card and contains a personalized key which is activated by confirming his DNA profile. The e-HID thus provides access to Lars medical record including his complete DNA. The information accessed via the e-HID is copied to a chip (eID) which is strapped around Lars's wrist. The software which is used is an open source code and the Hospitals own database can readily read and store Lars' medical record which is transferred from Oslo when the e-HID is activated and gives access to the data, which is stored at the Rikshospitalet's server. The doctors at the emergency immediately find out that Lars cannot tolerate Analgesia and he must therefore be treated accordingly. Since Lars has suffered severe head and facial damage Lars is sent for scanning. He is scanned with the Siemens Multi-MedScanner™, which performs simultaneous CT, MR, ultra-sound and acoustic measurements. The results are directly transferred to Lars eID (wireless). The results show no major afflictions to Lars' brain. The facial wounds, however, are severe and the right eye must be surgically removed. Meanwhile, Lars' relatives have been notified by Lars' MD in Oslo whom automatically receives the current status of Lars through communication with Lars eID in Barcelona. Lars prognosis is being constantly monitored back home. The eye surgery has caused some concern, but Lars' MD has informed his relatives that a new eye is currently grown at Rikshospitalet on a host-mouse based on Lars DNA. The nerve fibres are have already been surgically connected to artificial fibres in Barcelona and can be connected to

his new eye when Lars is sent back home. The nerve transmission is constantly being monitored by a sensor externally attached to Lars' skull. The sensor is connected to the nerve fibres through a biodegradable electrically conducting polymer fibre. The signal from this sensor constantly sends the status to the eID. Other body functions such as heart beat, pressure, chemical composition of exhalation gas etc. are similarly send their status to the eID. The eID also continuously updates Lars' eHID. His relatives find this information very comforting.

When Lars' gets back home his new eye is ready and is implanted the very next day. Lars chooses to monitor his condition in the after-treatment period with his e-Pod, which he has uploaded with the data from the Hospital's database through his eHID. Otherwise his MD has offered him to monitor his condition during the whole after-treatment period. With his e-Pod he receives continuous on-line monitoring of his condition (nerve fibre signal transmission to his new eye and other body functions, which his MD and Hospital doctors jointly have recommended him to monitor). We note that Lars is quite fond of his e-Pod which also contains a multitude of sensors ranging from weather monitoring, smell and taste sensors. It serves as his personal communication central where he stores all his personalized information. As a historical remark we remind the reader that the e-Pod was initially introduced back in 2014 as a sensor to non-intrusively measure the testosterone and even the sexual arouseness of people with teenagers as the target group. Eventually the services and sensors associated with the e-Pod gradually developed and established a new, widely accepted platform for a personal health sensor.

Case 6 – Home care

Harry, a middle aged Scandinavian man who smokes and drinks too much, has bad eating habits and does not want to do anything about it. He is breathless one day after running for the bus; his wife suggests he goes to the doctor for a check-up, but of-course he refuses. He does, however, agree to go to the pharmacist and buy a pack of smart "We Men" plasters. These intelligent plasters have embedded sensors which pick up cardio-vascular markers, and send a wireless signal to the health service database and check the values and send an instruction to him by SMS:

- Go to doctor - in which case appointments are generated in both diaries
- Take medication – with instructions to be collected (non-prescription) at the pharmacist.
- Continue to monitor daily.

Case 7 – Personalized water

Saul is 21 years old and lives in Stockholm. One day he gets an offer he cant's refuse from the company Bluedrop AB. He is prescribed with safe bluedrop water, which can also be personalized with his own medication and vitamins. Saul has his own tap and pays installation costs and then a pay-as-you-use model afterwards. Sensors measure the water quality and checks with approved norms. He also gets a handheld device as a mobile sensor for testing water quality when out traveling.

Case 8 – New services

Rita from Denmark, checks bone mineral index via a sensor in a machine at the pharmacist. Her values are compared with national averages in a database. Based on pre-defined categories the system chooses the relevant vitamin and mineral supplements necessary. Rita gets an anonymous-looking bag of pills from the machine and a personalized diet is sent to her private e-mail address. She is billed via the mobile for this service.

6 Conclusions and recommendations

Main conclusions from the work have been:
The health care system will face an enormous challenge in the near future due to e.g. ageing population, well-fare deseases and new technology. Thus, development of biomedical sensors technology will be crucial.

Biomedical sensors will be a central unit embedded in several health related applications and scenarios. By using micro- and nano-technology it will be possible to design small, smart, robust and cost effective sensors with a wide functionality.

Biomedical sensors will monitor important body functions and status (i.e. blood sugar level, heartbeat rate, presence of toxic agents), and advanced algorithms adapted to each individual may trigger alarms when non-normal values are encountered.

Technologically there is a tremendous potential, especially related to converging technologies, however technology alone does not create business.

Nordic industries are major vendors of medical sensors, and the region is leading in relation to the use of medical sensors for the benefit of health care and well being. This creates great opportunities for Nordic companies to find international markets for biomedical sensors and take leading positions.

Ethical considerations:
As responsible beings in a democratic society, we have a duty to evaluate the foreseeable consequences of the biosensor technology we are developing and hope will be applied in a high number of commonly used applications. This does not necessary imply that you as a scientist, company leader or one with particular interests in the field should start on such an attempt on your own, but such initiatives should be encouraged.

A public debate regarding biosensors will facilitate the acceptance and even accelerate the rollout of this new technology. This will also play a role in making the technology more socially robust and thereby reducing the likelihood of long-term serious set backs during the early phases of this technology.

A public, ethical debate will also facilitate a more comprehensive debate regarding the needs and requests to the potential users and this might therefore even open new avenues for research and product development.

The right to know and the right not to know are considered a fundamental right particular in relation to human health. At first glance, it seems that the right not to know is unproblematic. However, it might not necessary be all that easy when working with biosensors because the biosensors might generate information that was not thought about when the patient started to use the biosensor. An example: a certain blood glucose measurement might also indicate a given genetic lipid disease. Thus, the patient receives more information than what he or she asked for and most likely consented to.

When debating an emerging, technologically advanced field in public it is of high importance to be sincere and avoid overselling the benefits of the technology. The recent history with gene therapy, xeno-transplantation and stem cells are only but a few examples of overselling and that patient groups wrongfully have got the impression that a technological fix, for their condition, is just around the corner.

There is no sense in sensing something you can not do anything about. This is the biosensor equivalent of the mantra in medical ethics that you should only diagnose conditions you either can treat or at least have something to offer the patient. I do not necessarily agree with this mantra because, in certain cases, it could be useful to contribute to the understanding of phenomena, which in the future may lead to possibilities for treatment.

Recommendations from the project:

A Nordic program that specifically addresses research and development in small businesses in relations to commercialization and national needs (like the SBIR/STTR[62]-programs in the United States) should be established. Such a program based on interaction between industry, research, and public needs could provide substantially to the development, application and commercialization of biomedical sensors.

The FOBIS consortium supports the recommendations from The National IST Research Directors Forum[63] entitled “Pre-commercial Procurement of Innovation – A missing link in the European procurement cycle”. In this report it is proposed that the European Commission start to explore the interest of a limited number of procurers. We would suggest that biomedical sensors are included in one of these topics, which could be *e-Health*.

The FOBIS project should be followed up by a number of collaboration projects involving Nordic companies and researchers. These projects should stimulate the development of new biomedical sensors targeted towards important application areas in

[62] http://www.sba.gov/SBIR/indexsbir-sttr.html

[63] The National IST Research Directors Forum (NAT IST RTD Directors Forum) brings together National IST (Information Society Technologies) Research Directors to discuss key policy and implementation issues related to the development of a European Research Area in IST. The forum complements the bottom-up approaches supported by the Framework Programme. http://www.cordis.lu/ist/about/era.htm

the healthcare sector. In parallel, projects focusing system aspects like wireless sensor networks in hospital environments and implementation of new healthcare services.

It is recommended to include a first phase with focus in information gathering and subsequently a dissemination and feed-back phase, in future foresight studies of this kind. This can be exemplified by the fact that initially it was the intention that the first workshop should establish the 'current state of affairs'. However, it was found difficult to make such a workshop interesting to industry. Therefore the objective was changed, so that it also included 'future perspectives' – given at a rather preliminary state of the project. On the positive side it is noted that this change in objective had the effect of also attracting a reasonable number of commercial companies and gave very lively and constructive discussions especially in thematic groups.

The FOBIS dissemination toolbox at www.orgdot.com/fobis, an interactive website that presents visions of how biomedical sensors may be used in the future, is recommended for inspiration and a look into the future. By searching around in the different "rooms", you may get ideas and questions for yourself, hopefully learning you more about how biomedical sensors will shape the healthcare system of the future, and their potential impact on quality and cost of healthcare. Hopefully business opportunities in the area will be made clearer also.

The FOBIS website at www.nordic-fobis.net documents all the workshops and other project activities, and is also recommended as a starting point for inspiration and new knowledge.

norden

Nordic Innovation Centre

Nordic Innovation Centre

The Nordic Innovation Centre initiates and finances activities that enhance innovation collaboration and develop and maintain a smoothly functioning market in the Nordic region.

The Centre works primarily with small and medium-sized companies (SMEs) in the Nordic countries. Other important partners are those most closely involved with innovation and market surveillance, such as industrial organisations and interest groups, research institutions and public authorities.

The Nordic Innovation Centre is an institution under the Nordic Council of Ministers. Its secretariat is in Oslo.

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