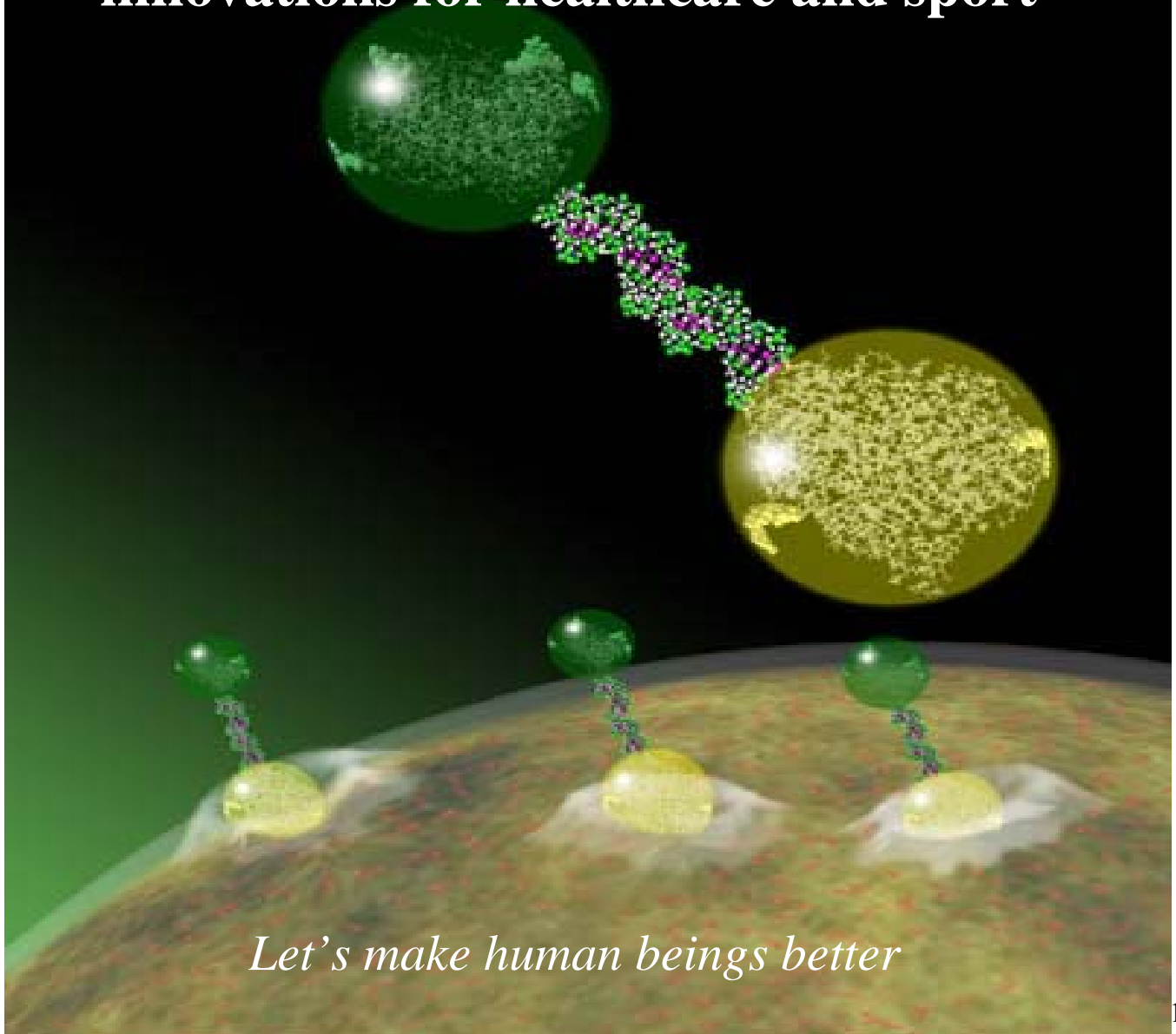


TNO S&I innovations for healthcare and sport



Let's make human beings better



Preface

After a century of industrialization and materialization that has lead the world to a considerable rise in living standard, the society seems to recognize that the time has come to focus technology more on personal values such as health and wellbeing. Not only for ethical reasons. The western economy has evolved into a very consumer centric system where consumers drive the demand. With the upcoming living standard, consumers demand it all: housing, food, pleasure, comfort, mobility, connectivity, entertainment, spiritual enrichment and last but not least health and sport. With focus on improving his performance and wellbeing, of course against affordable costs that fits the consumer budget. The credo “let’s make human beings better” will address the future consumer demand and will impact strongly the macro economic performance both by consumption as well as by productivity.

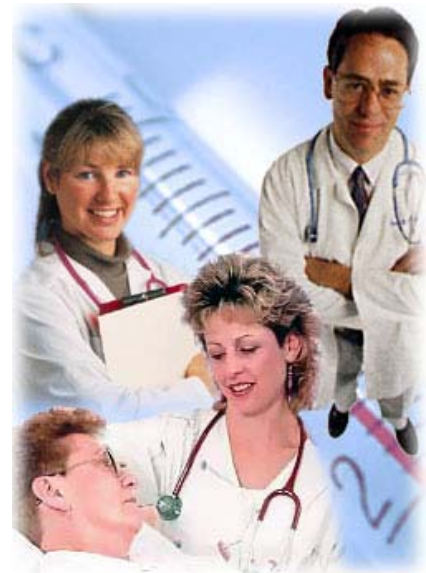
This document has been compiled in order to find answers on the following questions:

- how does the market for health and sport evolve
- what are the main market demands
- which technologies, or set of technologies, can fulfill these demands
- how can this be implemented, concepts
- what barriers need to be overcome

TNO Science & Industry
portal Medical and Sport



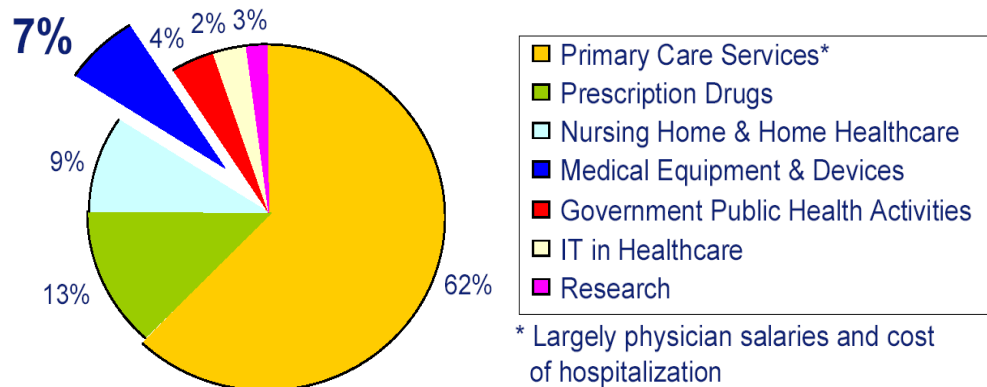
human performance



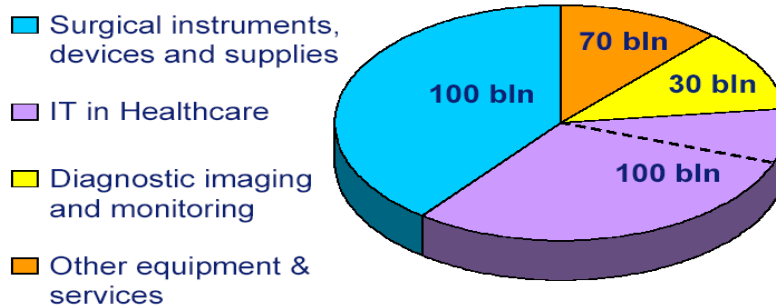
cost reduction

Contents

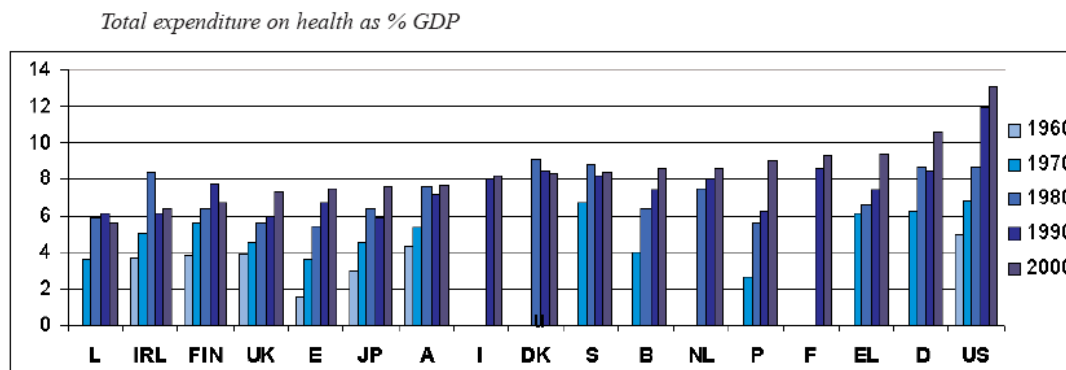
Preface	2
Market	
Overall market analysis	5
Trends	7
Issues	9
Growing markets	11
Industrial playing field health, NL	13
Industrial playing field health, NL	15
Technology section	
Technology radar health(care)	16
Nano for healthcare and wellbeing	17
Technology radar sport/wellbeing	18
Health in EU 7 th framework program	19
Emerging health technologies	21
TNO S&I section	
Technology base	23
Technology roadmap Healthcare	25
Technology selection	26
TNO profile in health	27
Concepts	
Future surgery room, assistive environment	28
Health ICT	29
Sample preparation on chip, DNA extraction	30
Systems biology, prognostic biomarkers	31
Targeted drug delivery	32
Telemonitoring, body sensors	33
Non invasive treatment	34
Minimal invasive surgery	35
Regenerative medicine, tissue engineering	36
Custom fit, 3D scanning	37
Biosensors	39
Nanomedicine	41
Nanosensors	43
Implantable sensor, optical sensor	44
FMCW radar	45
Diagnosis with vision systems	46
Evaluation quality of healthcare	47
Future sport training	49
TNO healthcare innovation program	50



3500 billion \$ spending in Healthcare annually, sources Medistat



300 billion \$ spending in medical equipment, sources Medistat



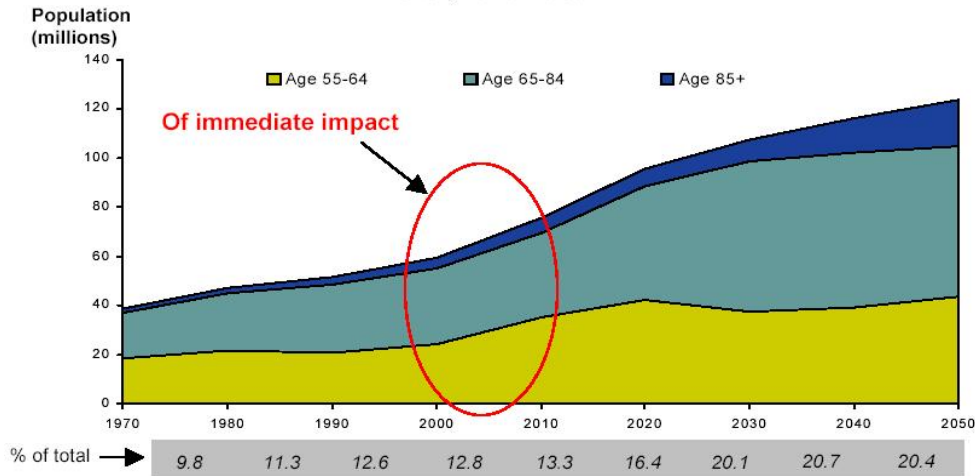
Market analysis, trends and issues

Healthcare is world largest service sector, growing from 8% to 10% GDP (Europe) in 2010. Per capita in US \$ 5300 is spent on healthcare, in Europe \$ 2500 annually. Hospitalisation costs are quite dominant: 62%. The healthcare market is estimated to 3500 mld \$ (2005) whereas the sport market is estimated to a 1000 mld \$ market worldwide. European countries spent nowadays about 8% of their GDP on health, in the US already 12%. The health expenditures increase more rapidly than the GDP's.

Healthcare (mld \$, annually)	expenditures	growth %	trends
Total healthcare	3500	5	acceptable cost with more elderly
Primary healthcare (hospitalisation, physicians)	2000	4	reduced hospitalisation time shifting to homecare
Pharmaceuticals	500	10	targeted drug release, nanomedicine
Medical equipment & devices	300	5	early diagnosis, imaging, biochips, non/minimal invasive treatment
Homecare	350	8	rapidly increasing elderly population telemonitoring
Healthcare IT	80	11	electronic patient and medical dossier genotyping, bioinformatics
Public activities	150	3	prevention programs, sport promotion
R&D	120	3	50% in pharmaceuticals

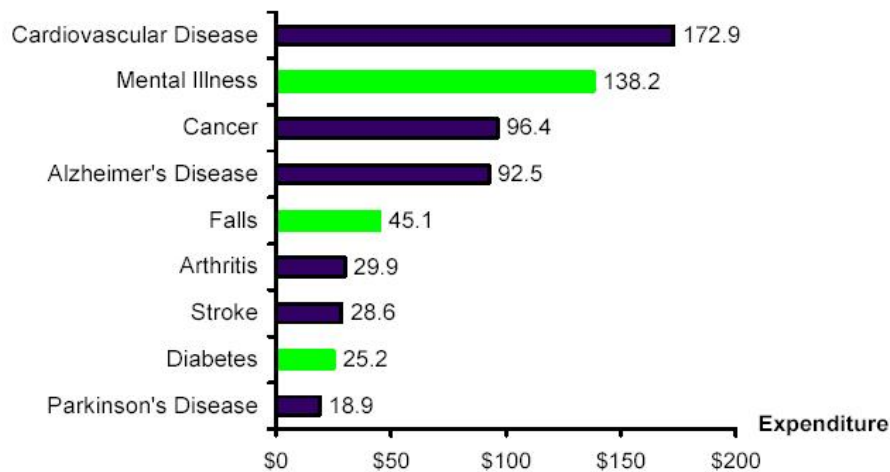
Sport (mld \$, annually)	expenditures	growth rate	trends
Total	1000		link with health, fitness + wellbeing
Facilities / accomodation, training	800		optimizing training conditions
Equipment	100		telemonitoring, (bio) model based training
Footwear	50		adaptive, custom fit
Apparel	50		sensor integration

Elderly and Upper Middle-age Population U.S., 1970-2050



Note: Data for 2010 – 2050 projections based on Census Bureau's "Middle Series" Scenario

Personal Health Expenditures on Select High-Cost Conditions - 2000



Trends

More elderly demanding care: in 2030 is 25% of our population is > 65 yrs (now 17%)

Reduction of hospitalisation time, need for high efficient, high throughput hospital or clinic

- non or minimal invasive surgery
- personalized medicine
- telemedicine
- after care via telemonitoring

Professional care shifts to homecare, need for efficient and professional homecare system

- care via IP
- diagnostic tools at the home
- self diagnostics and self treatment and rehabilitation
- telemonitoring

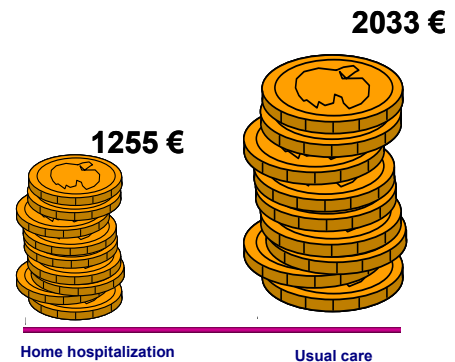
Cost reduction in healthcare system via:

- health IT
 - electronic patient dossier
 - electronic medical dossier
 - telemonitoring
- early diagnosis and treatment
 - molecular imaging
 - point of care diagnostics, lab-on-chip
- dedicated treatment of specific chronic diseases (cardiovascular, mental, cancer, Alzheimer etc)
 - targeted drugrelease
 - personalized medicine, genotyping of patients, bioinformatics
- prevention programs, sport and health promotion

Cost containment
home hospitalization program

Towards a consumer centric system:

- health shopping
- personalized medicine
- cosmetic surgery
- sport & fitness, wellness





Issues and technologies

healthcare

sport

cost reduction

personal care

wellbeing

human performance

early diagnosis & cure

stimulation

condition monitoring

training coaching

medical

pharma

revalidation

home care

fitness

sport

imaging

personalized medicine

tele care

ict

body function monitoring

implants

targeted drug delivery

lab-on-chip

wireless sensors, rfid

non invasive surgery

robotics

tissue wound skin treatment

nutraceuticals

Issues in Healthcare and Sport

Healthcare and sport share many technologies in view of repair and improving human performance. Technologies for both areas are very human centric and the technologies have to deal with the human biosystem in many aspects such as:

- biomechanics (physical performance, training)
- physiology (food, energy balance, temperature/climate, clothing)
- systems biology (health condition, disease management, treatment, cure)
- neurological system (brain function, alertness, awareness, memory)
- mental and social behavior (decision making)
- genetic predisposition (physical, mental, biological etc)

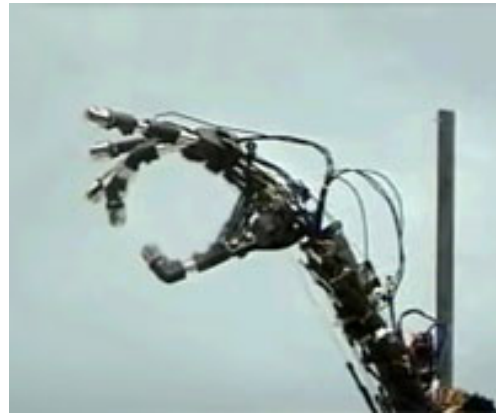
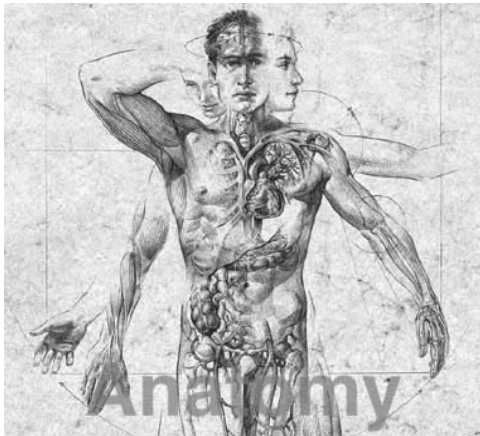
It also implies that technologies developed in one area, can be transferred and adapted to the area in many cases. However the conditions in healthcare and sport are quite different.

Healthcare

- cost reduction is major goal
- acceptable level of healthcare is to be maintained
- separate treatment of mental and physical diseases

Sport

- maximizing human performance
- focus on body performance in combination with equipment and accomadation
- mental condition very important enabler
- creating performance stimulating environment



Growing markets

Health IT: ICT is offering major opportunities in terms of efficiency, cost reduction and quality improvement in healthcare. Current developments cover:

- electronic patient and medical dossiers for having the right information on the right time and place, improving speed, costs and quality of healthcare
- patient empowerment: for better informed and motivated patients
- telemonitoring both in homecare and professional care
- telemedicine and telesurgery
- bio-informatics, genotyping of people for early screening, diagnosis and gene-specific medical treatment

Nanomedicine: discovery of new drugs is slowing down (less new molecules are found, approval costs sky high), pharma companies seek new, more effective drug release systems for their existing drugs and integrate more and more with equipment and devices manufacturers. Most promising and growing area is nanomedicine:

- nano-diagnostics >> € 250 million by 2006
- nanoscale targeted drug delivery >> € 70 billion by 2007
- regenerative medicine >> € 80-100 billion by 2010
- molecular imaging >> € 22 billion by 2015

Homecare: 70% of homecare is on elderly (>65 yr) with heart/vascular disease, diabetes, osteoarthritis, fractures. There are two reasons for expected high growth of homecare:

- demographic reasons: the elderly population rapidly increases for next coming years (in Europe from 17% to 25% in 2025)
- cost reduction in hospitalisation: reduced hospitalisation times will shift care from the hospital to the homecare situation

It is unclear how and when this emerging homemarket will drive innovations in terms of homecare diagnostics (lab-on-chip, dipstick), telemonitoring, robotics etc.

Body repair

Although high expectations exist for the future market in tissue engineering for body, skin and organ repair (tissue replacement or insitu repair), the main markets with considerable growth (5-10%) for the next coming years are in:

- Dental € 100 billion
- Cosmetic/plastic surgery € 35 billion (surgery € 25 billion, non surgery € 10 billion)
- Other implants € 30 billion (pacemakers € 10 billion, stents € 10 billion, other e.g. hips+knee+cochlear € 10 billion)

Current technology issues health companies in NL



Biocompatible coatings

Targeted drug release

Biocompatible coatings

Micro X-ray for brachytherapy

Micro ultrasound transducers

Focused ultrasound

Targeted drug release, release on demand

Alternative drug release systems

Anti counterfeit

Nanodispersion, solubility, drug delivery

Molecular medicine, focused ultrasound

Babycare, skincare, fitness, homecare

High performance materials, coatings for medical

Rapid manufacturing

Intelligent textile, sensor integration

Contamination control, coatings, 3D scanning

biomechanical modelling, packaging

Industrial playing field in the Netherlands: Health

Major health companies involved in health(care) in the Netherlands:

Philips

Philips Medical Systems (9 billion €): monitoring & imaging: ECG, MRI, CT, PET, X-ray, US - defibrillators
-health IT: medical lab IT, clinical IT, telemonitoring
Philips DAP (2 billion €): devices for consumer health & wellness (starting up)

Medtronic (10 billion \$): pacemakers, cardiac surgery, vascular therapy (stents, catheters) -lifelong solutions for chronic diseases - surgery: cardiac/neurological/spinal/oncology/ENT surgery -diabetes, insulin pumps, glucose monitoring

Solvay Pharmaceuticals Group (2,5 billion €): hormone therapies, digestives/enzymes, influenza, antispasmodics, vertigo, alzheimer

Organon (2 billion €)

-pharmaceuticals: contraception, hormone therapy, fertility, mental health, and anaesthesia.

Janssen Pharmaca (2 billion €)

-pharmaceuticals for mental illness, neurological disorders, anaesthesia and analgesia, gastrointestinal disorders, fungal infection, allergies and cancer.

DSM: performance materials (2 billion €), Dyneema for medical, Solutech for sport clothing

Cordis (1 billion \$): vascular disease management, stents, catheters

Ten Cate (600 million €): textile and fabrics for advanced clothing and sport (playing fields)

Delft instruments

Nucletron (100 million €)	Oldelft (12 million €)	Delft diagnostic imaging (18 million €)
-radiotherapy, brachytherapy	-ultrasound	-Xray diagnostics

Mentor Medical (500 million \$)

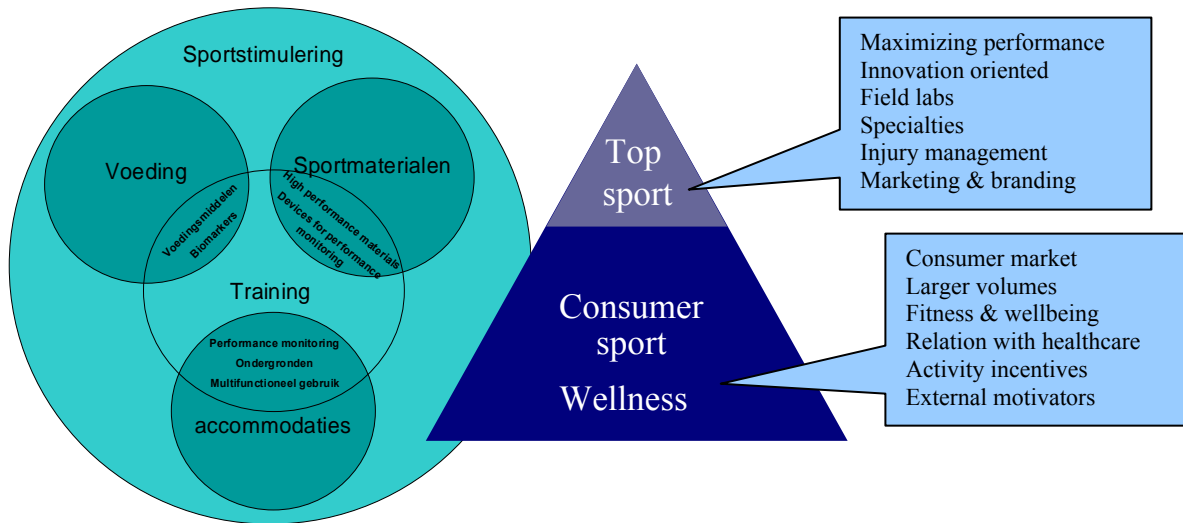
-cosmetic implants, tissue expanders, aesthetic medicine, brachytherapy, personal care

Current technology issues in Sport in NL

Focus areas:

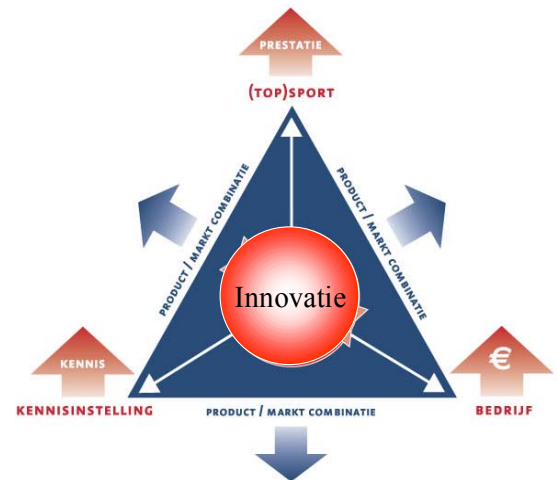
1. Training
2. Equipment, footwear & apparel
3. Accommodations
4. Food
5. Sport stimulation
6. Human factors

devices and systems for performance monitoring and enhancement
 high performance equipment and clothing
 performance stimulating environment
 food engineering
 innovative approaches for sport stimulation
 technology integration with a high level of human acceptance



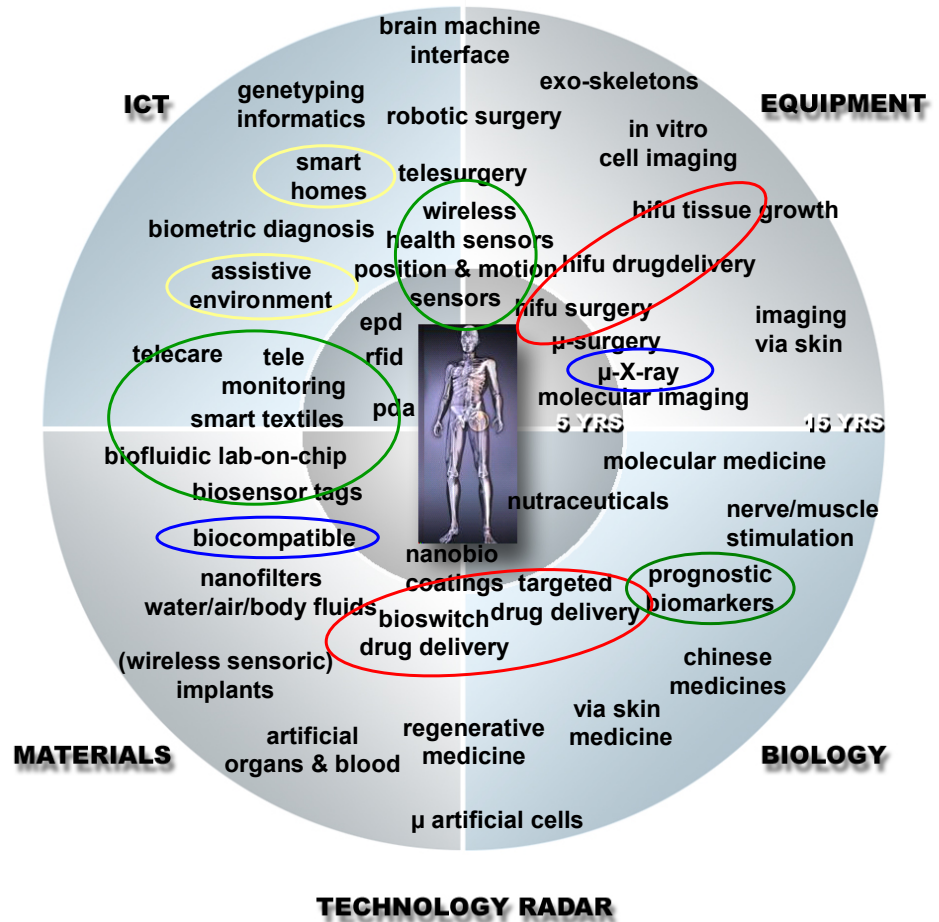
Industrial playing field in the Netherlands: Sport

Organisation	Focus area
Philips	Performance monitoring, electronics in clothing
Ten Cate	Textiles, accomodations (floor), equipment
DSM materials	Equipment and clothing, accomodations
DSM food specialties & ingredients	Food engineering
Decathlon	Performance monitoring, equipment and clothing
Media (NOB, Talpa, Versatel,...)	Monitoring, more information to the consumer
Reebok, Adidas, Asics or Nike	Monitoring, equipment, clothing, footwear
CVZ, Achmea, DSW etc	Sport stimulation



HEALTH CARE

- Less hospitalisation
- Homecare
- Elderly population
- Health IT
- Telemedicine
- Early diagnosis
- Drugs on target
- Minimal invasive
- Body repair & beauty
- Nanobio fusion



Nano for human health and wellbeing

Human centric systems are in development in order to secure and optimize human performance and well-being. The systems provide monitoring and feedback functions of the human being in its environment plus protection and support tools. This approach is seen in top sport, medical care, revalidation, first responders, firefighters, police and the military. In practice such systems result in the ability to participate in a mobile information network, use of more comfortable, protective and functional suits, wearable intelligence such as sensors and displays for situational awareness and body condition monitoring. Nanotechnology is here crucial. Without miniaturization such functionalities can not be adapted to lightweight, wearable systems.

Materials: nanotechnology enables high strength, durable, sensoric and active materials. Nanostructures and nanocomposites are in development for the following functionalities:

- lightweight protective clothes: against heavy, injuries, supportive
- adaptive suit: switchable fabric for improved thermal control, switchable functionality
- microsensors for body & brain sensing, environmental and situational awareness
- wearable and/or flexible displays for visual feedback
- auxiliary supports: flexible/rigid textiles for additional strength, exoskeletons and robotics to assist tasks

Information: in order to operate in a safe and secure wireless network, the human will be equipped with:

- miniaturized hardware: sensors, readers, displays and radio transmitters, some of this already present in pda's and mobile phones
- personal secured access to equipment (biometric id) and information (digital id)

Energy: with the increase in wearable functionalities and electronics, the need for lightweight wearable electric power is very critical. The following developments are present:

- flexible solar cells to recharge batteries
- μ -fuel cell, preferentially to be operated by diesel or biofuel (e.g. sugar)
- μ -nuclear battery for long endurance
- energy scavengers, e.g. electricity from vibrations, for low power applications

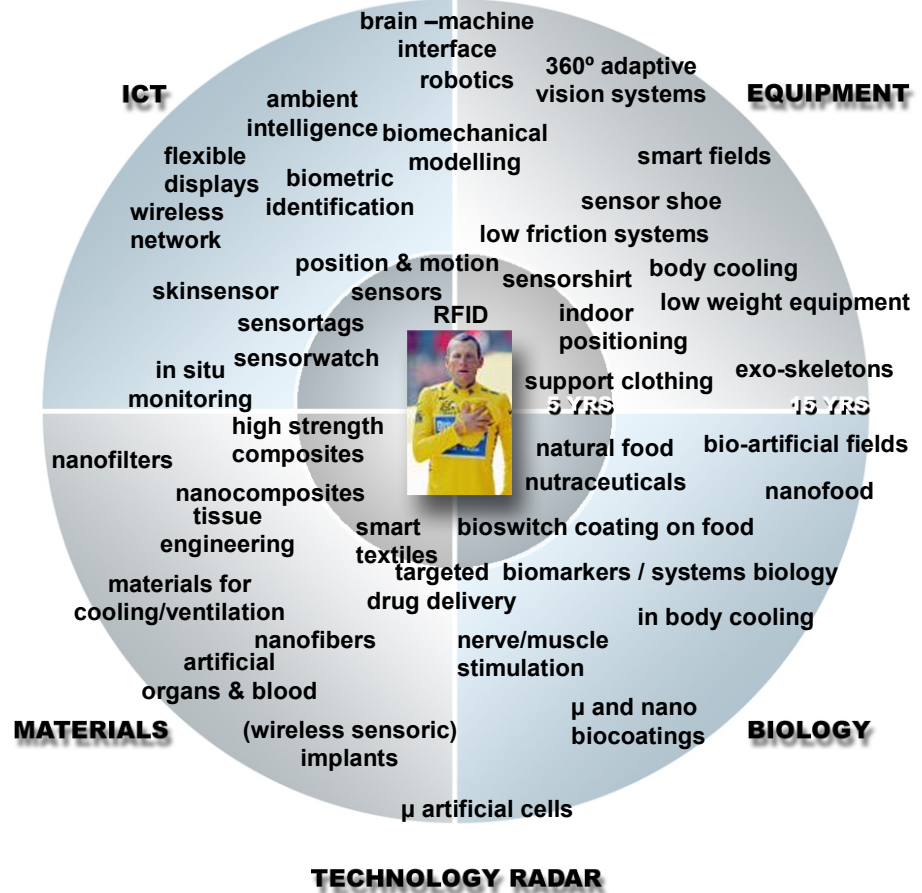
Bio: the nano-bio fusion is a booming area with high expectations that major steps in health treatment, body repair and body improvement can be made. It is regarded as the most innovative domain of this moment.

Developments are in the field of:

- nanomedicine: targeted drug delivery by medically functionalized nanoparticles, for rapid cure without side effects or human stimulation
- regenerative medicine: DNA programmed tissue engineering for quick and efficient wound healing, rebuilt of organs and other body parts
- smart implants: biocompatible implants that can sense and actuate in order to repair or enhance a body function

SPORT WELLNESS

- Body control
- High tech gear
- Smart fields
- Positioning & posture
- Future training
- Fight obesitas



EU 7th Framework 2007-2013

Health is second largest cooperative research theme in the EU 7th FW (after ICT)

1. Information and Communication Technologies	12670 million €
2. Health	8317
3. Transport (including Aeronautics)	5940
4. Nanotech, Materials and new Production Technologies	4832
5. Security and Space	3960
6. Energy	2931
7. Environment (including Climate Change)	2535
8. Food, Agriculture and Biotechnology	2455
9. Socio-economic Sciences and the Humanities	792

Main overall issues in FW 7 are:

- translational research (translation of basic discoveries in clinical applications)
 - data integration, systems biology
 - research on the brain and related diseases (alzheimer), aging, dna-genomics
 - infectious diseases: microbial, hiv/aids, malaria, tbc, sars, pathogenic
 - major diseases: cancer, cardiovascular, diabetes/obesity; other chronic diseases (e.g. osteoarthritis)
- the development and validation of new therapies and diagnostic tools
 - high throughput research
 - detection, prevention and monitoring: non-invasive or minimal invasive
 - new biomarkers, models/simulation, pharmacogenomics, targeting approaches, testing
 - innovative therapeutic approaches
 - innovative medicines (European Technology Platforms)
- optimizing delivery of health care to European citizens
 - two strategic issues: child health and the health of the ageing population
 - quality, efficiency and solidarity of health systems
 - enhanced disease prevention and better use of medicines
 - appropriate use of new health therapies and technologies
- methods for health promotion and prevention

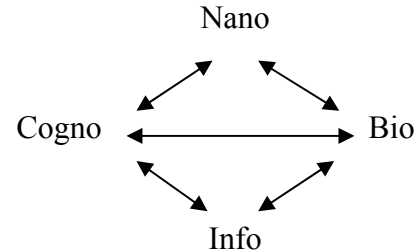
Emerging health technologies: convergence of nano and biotechnology

Technology in life science is rapidly emerging. Thanks to the convergence of nanotechnology, biotechnology, ICT and cognitive sciences, many new technologies are in progress with a high potential impact on future health and health care system. A short list of the technologies of the future:

- Early diagnosis
- Healthcare IT
- Nanomedicine
- Smart implants
- Non invasive surgery
- System biology, chinese medicine

Convergence is also happening in areas such as:

- scientific instruments (nanosensors for biomarkers)
- analytical methodologies (quantum dot fluorescence, dna/proteomic arrays)
- new material systems (biomimic materials, self assembling materials)
- new pharma systems (nanomedicine, nanoparticle labeled drugs, theranostics)



Improving human performance and wellbeing

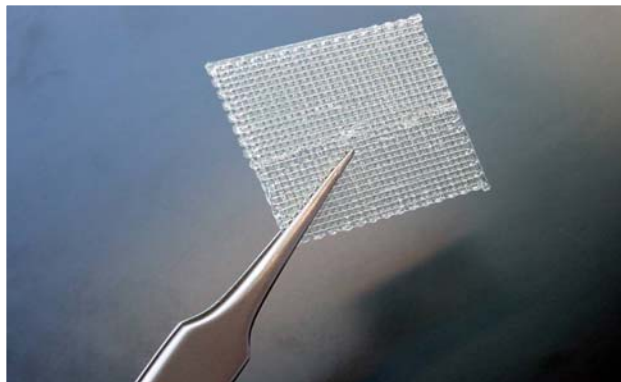
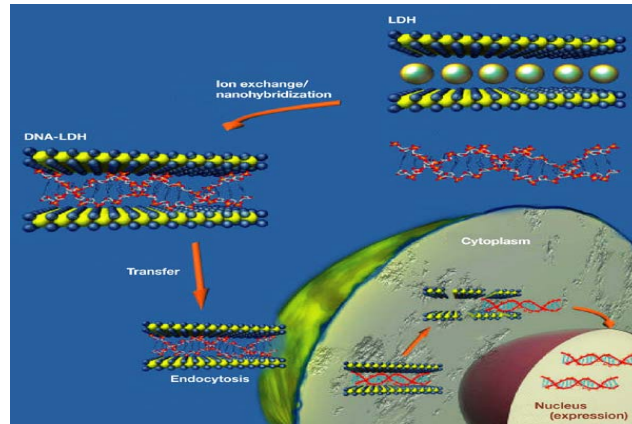
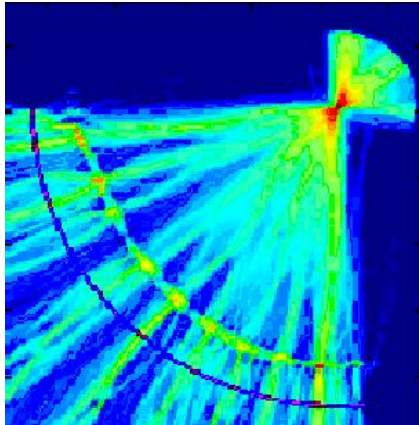
NBIC convergence can give us the means to deal successfully with the challenges to enhance human mental, physical, and social abilities. Better understanding of the human body and development of tools for direct human-machine interaction have opened completely new opportunities. Long term implications of converging technologies are in the key areas of human activity:

- societal productivity
- security from natural and human-generated disasters
- individual and group performance and communication
- life-long learning, graceful aging and a healthy life
- coherent technological developments and their integration with human activities
- human evolution, including individual and cultural evolution

Future scenarios of what converging technologies can bring cover many aspects such as:

- fast, broadband interfaces that enable human brain and machine interaction
- comfortable, wearable sensors for health monitoring and potential hazards
- robots and software agents with human like behavior and interaction
- more durable, healthier, more energetic body, and easier to repair
- adaptive machines and structures
- compensation for mental and physical disabilities
- superior intelligence-gathering systems, information anywhere
- intelligent environments leading to high efficient production and services
- vastly improved awareness of cognitive, social and biological human forces

(Converging technologies for Improving Human Performance, NSF/DOC-sponsored report, June 2002)



TNO S&I technology base

Design & Manufacturing (Jan Smits)

- rapid manufacturing of human related products (wearables, implants)
- scanning and measurement systems for customfit products
- monitoring, analysis and advisory systems for (human) motion and sport
- biomechanical modeling
- ambition: 100% focus on human systems

Materials Technology (Dick Koster)

- nanomaterials for bio-applications e.g. bioswitch, drug encapsulation, nanocarriers for pharma
- ambition: bioactive materials

Industrial Modeling & Control (Henri Werij)

- microfluidics, lab-on-chip, for bio/health applications
- ambition: microfluidic systems, in near future also process-on-chip

Testing & Certification (Odile Steijger)

- testing of (protective) clothing and devices for personal care, on functionality and comfort
- ambition: testing of personal care devices (teeth, hair, skin etc)

Automotive (Leo Kusters)

- biomechanical modeling (sport) based on Madymo
- links: human centric sensors in cars, human comfort in cars
- ambition: biomechanical modeling for rehabilitation (health), protective suits (defence)

Microsystems (Hans Sirks)

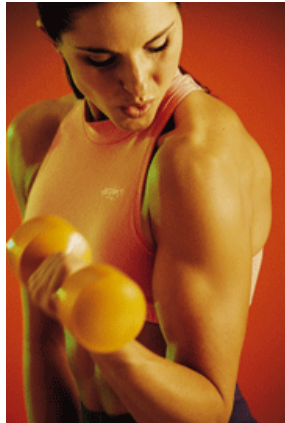
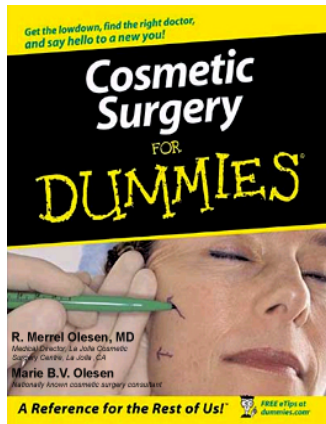
- assembly by wire, micro-assembling by human via telemachining
- antenna's, sensenna as wearable/implantable sensor for human diagnostics
- ambition: telemachining for human, spin-off to medical (telesurgery)

Opto Mechanical Instrumentation (Wart Mandersloot)

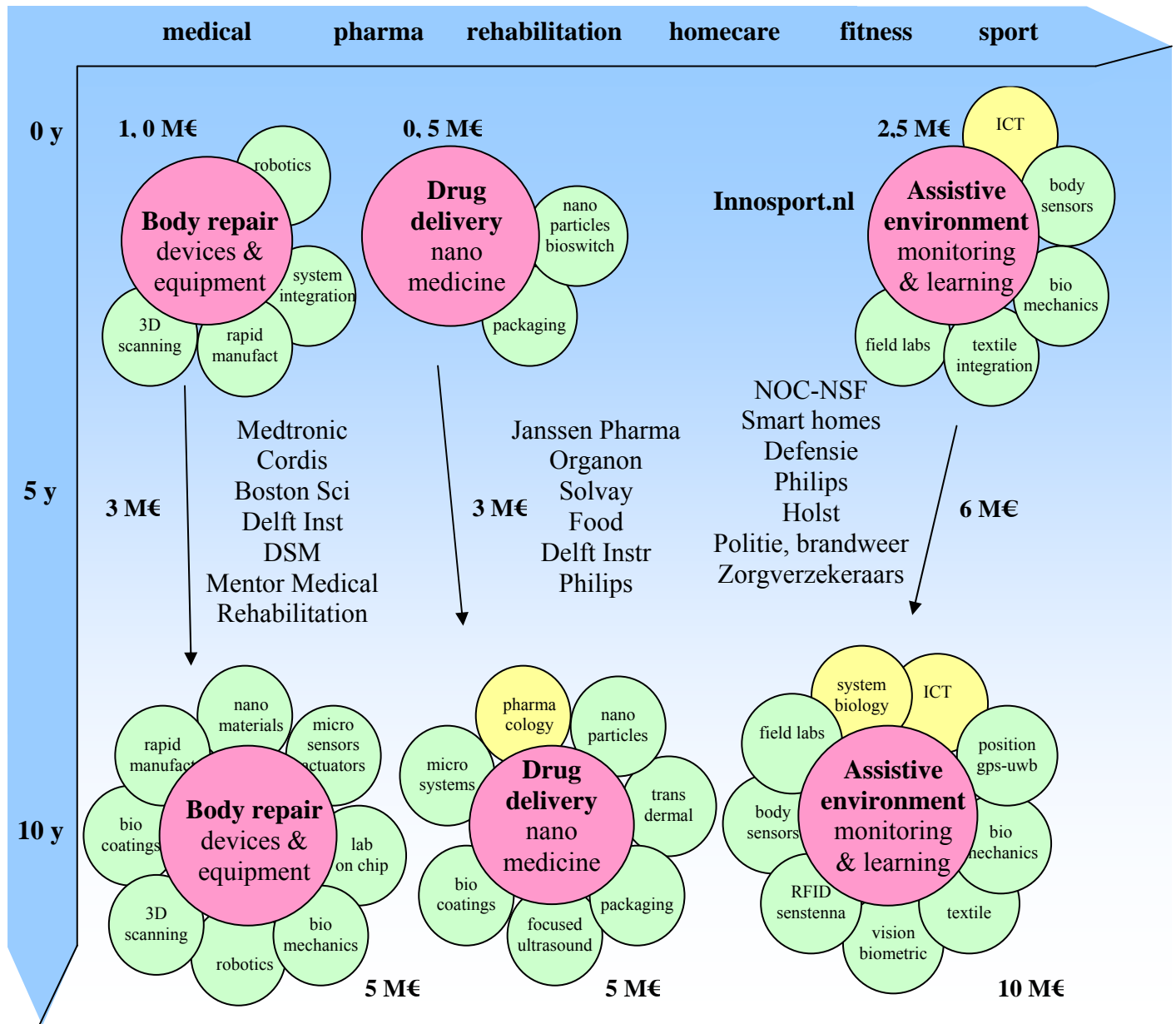
- micro precision surgery, plasma cleaning for medical applications
- links: optics for the eye
- ambition: molecular imaging, biomolecular optical detection on chip, biosensors via nano-imprint

Imaging Systems (Hugo Vos)

- high intensity focused ultrasound for non-invasive surgery
- biometric detection op basis van vision
- robotics for hospital and revalidation
- dataretrieval & handling
- ambition: instrumentation and advisory measurement systems for medical & care



TNO Technology roadmap Healthcare & Sport



Technology selection

The required technologies for the three selected market functions body repair, drug delivery and assistive environment have been ranked against the following criteria: IP position, technical feasibility, development costs, time to market, market size, core business TNO, competition, generic applicability and ease of validation.

High ranked technologies are:

- nanomaterials/bioswitch and nano additives
- focused ultrasound
- biomechanical (human) modeling
- sensor tags, sensstenna

Healthcare selection table

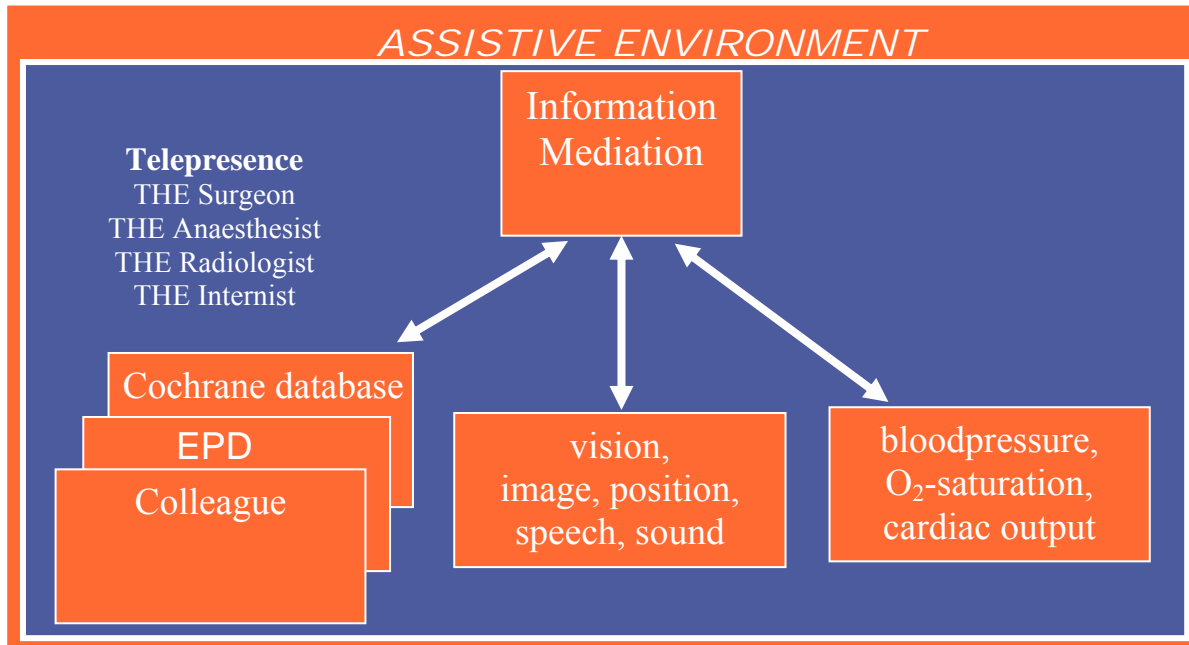
basic function	technology	application	IP position	technical feasibility	development costs	time to market	market size	core business TNO	competition	generic applicability	ease validation	TOTAL SCORE
Drug delivery nano medicine	nanoparticles bioswitch	release on target	2	1	2	1	2	2	1	2	1	30
	focused ultrasound	external triggering	1	2	2	2	1	2	1	1	2	29
	bio coatings	bio compatible	2	1	2	1	1	2	1	0	1	22
	packaging	anti counterfeit	0	2	2	2	0	1	0	1	2	22
	microsystems	injector, sensor	1	1	1	0	2	2	0	2	0	19
	transdermal	skin/wound treatment	1	1	2	1	1	0	2	0	1	18
Assistive environment monitoring & learning	biomechanical modelling	diagnosis system	0	2	2	2	1	2	1	2	2	29
	sensor tags (sensstenna)	powerless sensing	2	1	1	1	2	2	2	2	1	29
	gps/uwb	positioning	0	2	1	2	2	2	0	2	2	28
	vision/biometric	diagnosis	2	0	2	1	2	2	1	2	1	28
	textile	smart suit	0	2	2	2	2	2	1	1	1	26
	microsensors	body performance	1	1	1	1	2	2	0	2	0	22
Body repair medical devices implants	nano additives	drug release, durability	2	1	2	1	2	2	1	2	1	30
	biomechanics	body acceptance	0	2	2	2	1	2	1	2	2	29
	3D scanning	custom fit	0	2	2	2	1	1	0	2	2	27
	rapid manufacturing	custom fit	0	1	1	2	1	2	0	2	2	24
	lab-in-foil / lab-on-chip	body fluid analysis	2	1	1	0	2	2	1	2	0	23
	biocoatings	bio compatible/friction	2	1	2	1	1	2	1	0	1	22
	microsystems	actuation, sensing	1	1	1	0	2	2	0	2	0	19

TNO profile in Health

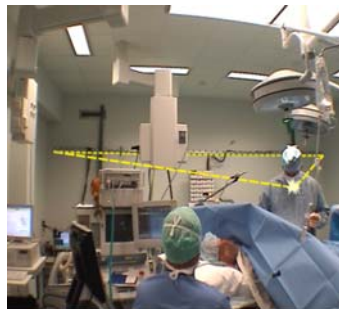
Quality of care	effectivity care system, evaluation technology/devices, security medical ict
Physical activity and health	children, life-style determinants, heritable, perinatology
Biomedical research	diabetes, cardiovascular, inflammatory/autoimmune, tissue repair
ICT in healthcare	wireline, user centric innovations
Pharma	screening, clinical studies, cell based in-vitro, animal, human translational
Toxicology	necropsy, histological processing, histopathological evaluation
Microbiology	microbial genomics, DNA, RNA and metabolites
Biomedicine, systems biology	metabolics, transcriptomics, prognostic biomarkers, chinese medicine
Nanomedicine	nanoparticle encapsulation, (ultrasound) release on demand, lab-on-chip
Medical devices	customized body repair, minimal invasive surgery, micro X-ray
Homecare & Sport	assistive environment, telemonitoring, biomechanical modeling

Surgery room of the near future: assistive environment & telepresence

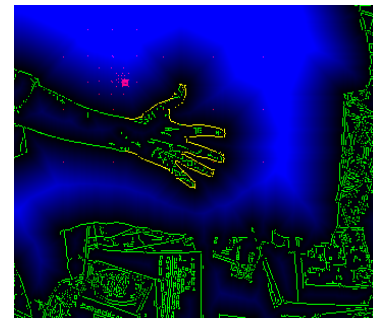
autonomous, pro-active information and consultancy system



photo's, scans
protocols, lab reports
decursions, surgery reports
literature, internet data,
images, video, sound



acoustic arrays for
directional speech recognition



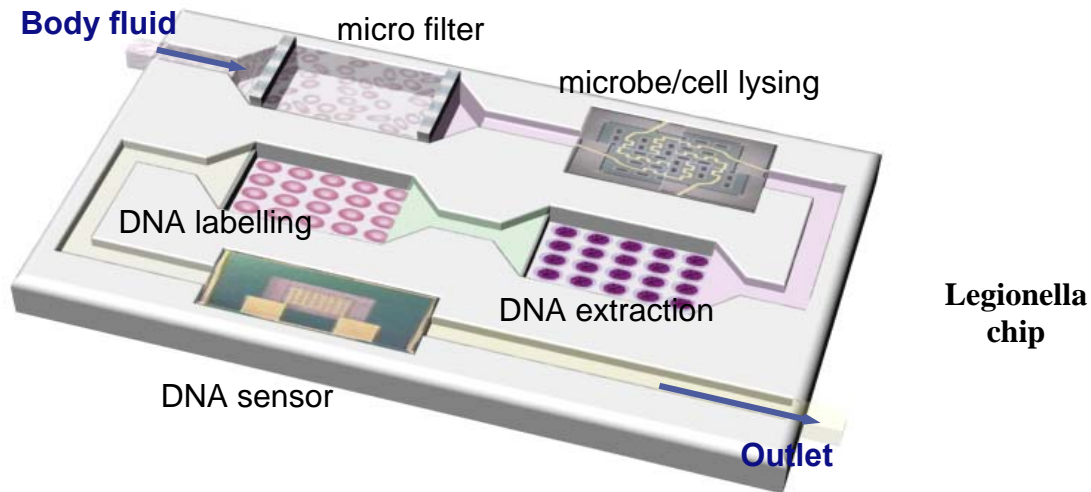
automated recognition of
scene, movements and gestures

Healthcare ICT

- Patient logistics (MEDCON)
 - patient tracking & planning, tracking & tracing consumables (RFID)
 - optimization clinical & care paths, GDMS concepts
- Knowledge management (IZIT cluster)
 - document and information retrieval, security
 - adaptive interfaces for EDP, adaptive multimodal interfaces
 - experimental EPD platform as testbed for new technologies
- Broadband applications (Teleokto, Okto, Freeband PNP / NBL)
 - integrate information, expertise and specialisms
 - separate use for diagnosis, consultation, information and treatment
 - business models, investments models
- Smart health (Freeband B@Home, FRUX, UAS, TUMCAT testbed / VitaValley)
 - ambient serviceplatform at home, monitoring and diagnostic systems
 - testbed services and systems
 - demand and user characteristics, personalized interfaces
- Telecare (ID-lab / VitaValley, IZIT, EZ, KPN)
 - body area network, condition and health monitoring (system level)
 - development new services for telemonitoring, diagnosis, treatment, rehabilitation
 - fieldlab's

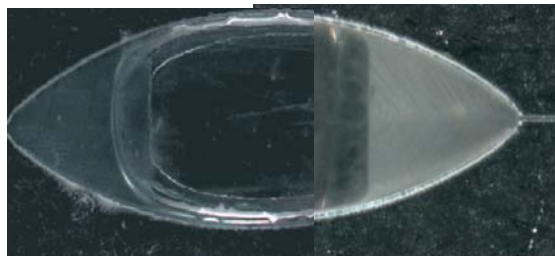
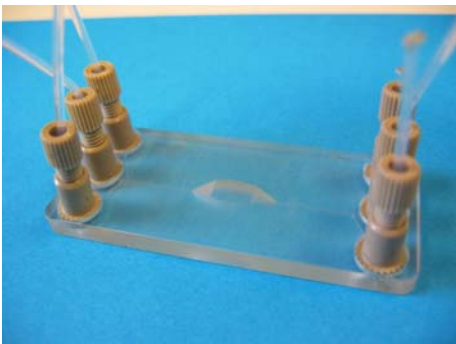
Sample preparation on chip for DNA extraction

Sample preparation on chip for fully automated extraction of early diagnostic biomarkers (dna, proteomics, metabolites from (bio)fluids) and subsequent detection on biochips.



One reaction chamber system

- external fluid controls
- ultrasound for lysing & mixing
- magnetic bead extraction

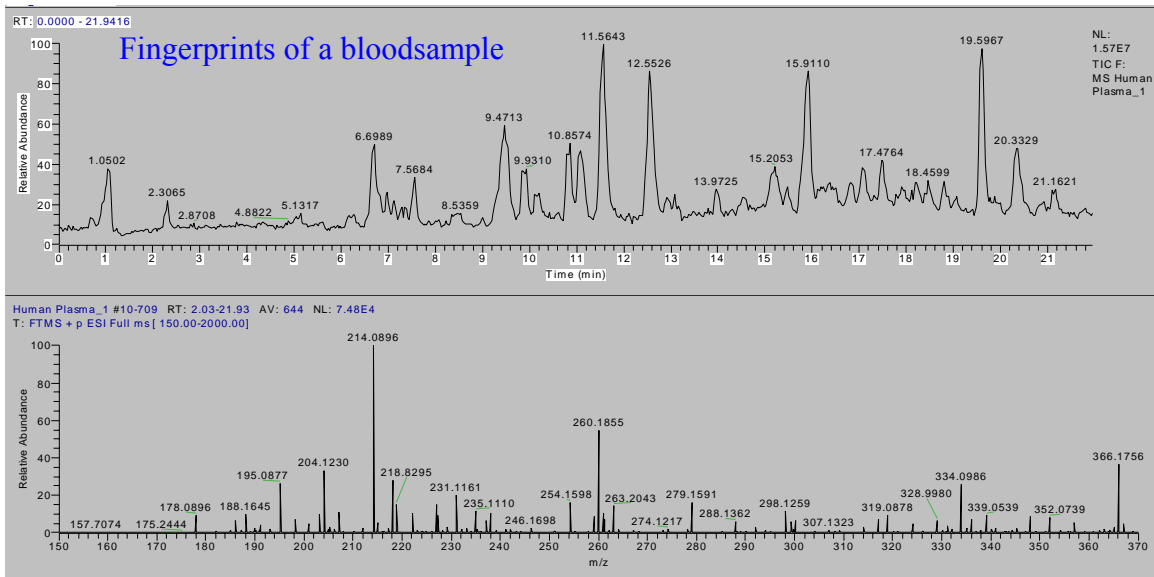
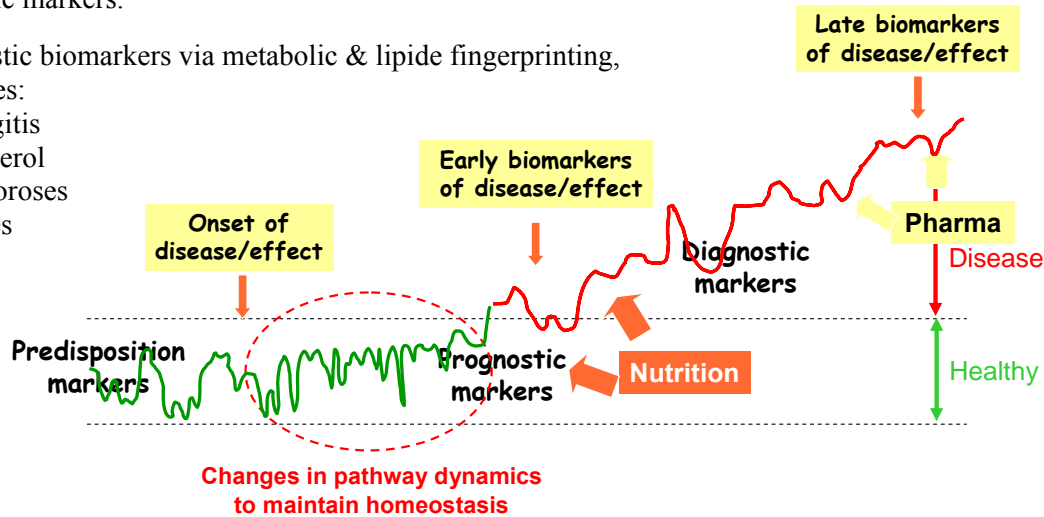


Systems biology: from diagnostic markers to prognostic markers

The goal is to eliminate diagnostic markers and to use prognostic markers. Prognostic markers indicate the early development of a disease and therefore enable early treatment. This can be done with systems biology tools, looking at early changes in the metabolism. It requires sophisticated analytical tools and heavy statistics to detect changes in the wide variety of metabolic markers.

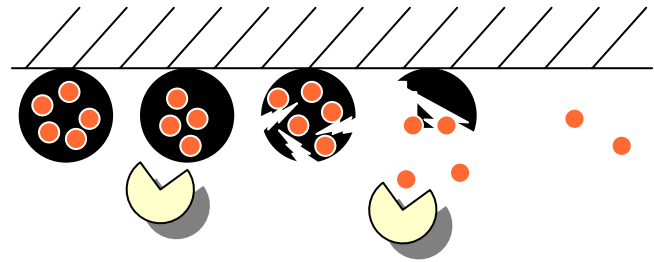
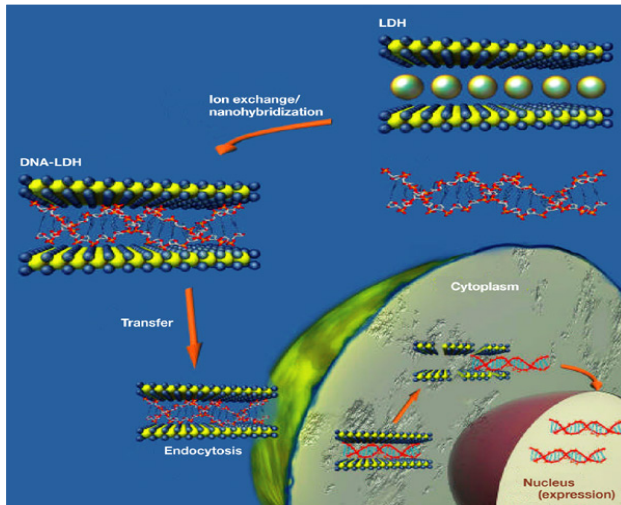
Prognostic biomarkers via metabolic & lipid fingerprinting, examples:

- meningitis
- cholesterol
- osteoporoses
- diabetes



Targeted drug delivery (release on demand)

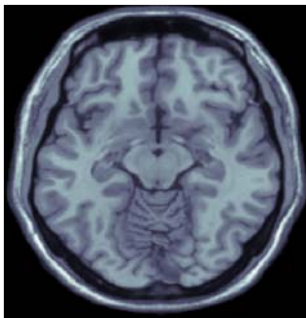
Nanomedicine: nano encapsulation of drugs, release via bioswitch or ultrasound



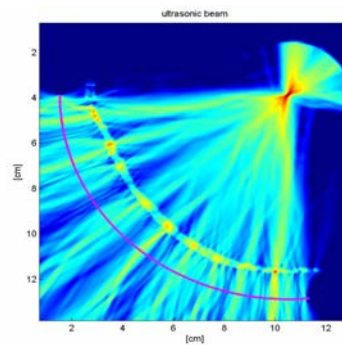
bioswitch

encapsulation

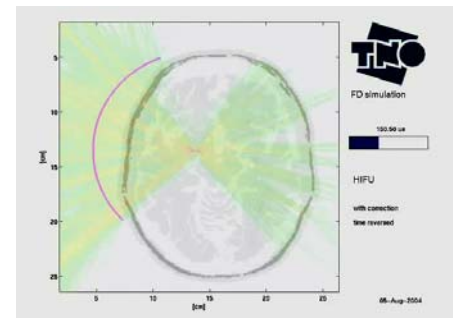
Focused ultrasound: non invasive surgery and local drug delivery



mri brain

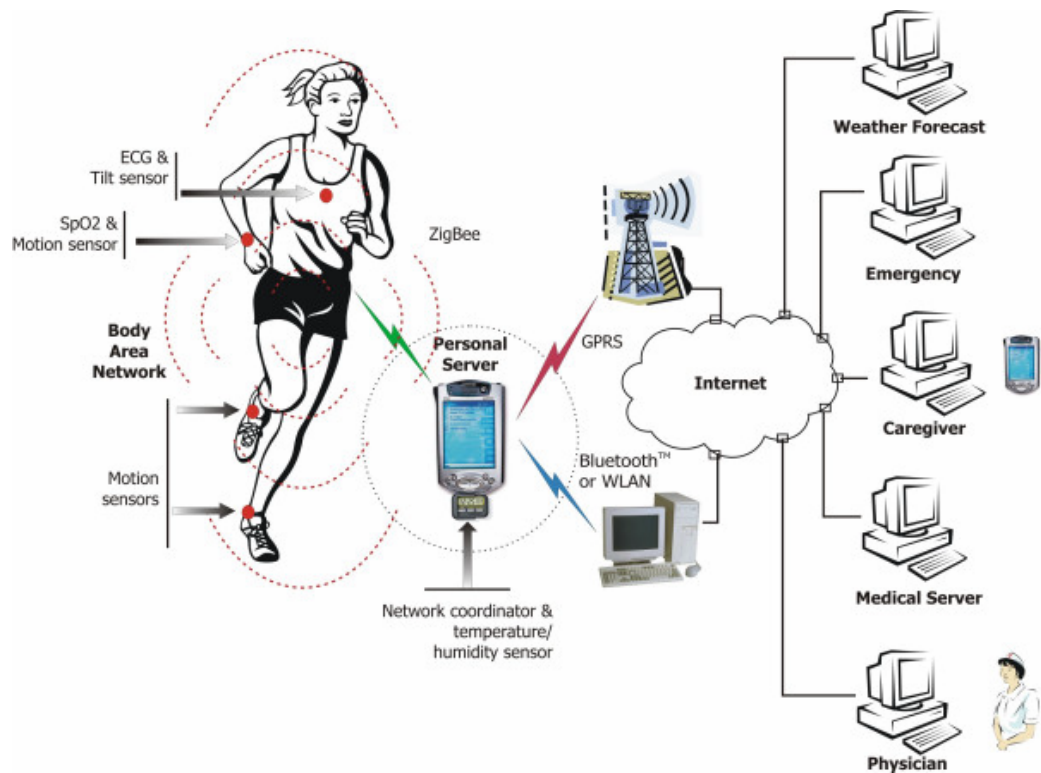
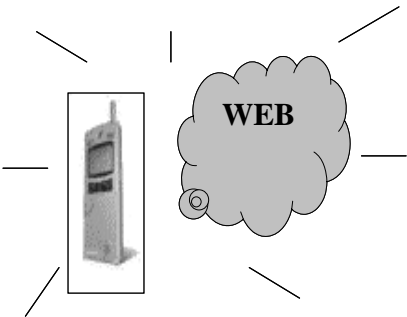


us energy distribution



phased array ultrasound

Body monitoring & sensors



Non invasive treatment

high intensity focussed ultrasound (HIFU)

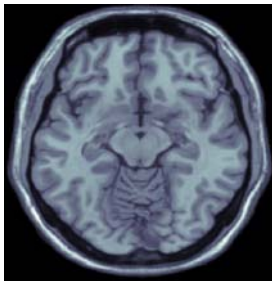
- thermal surgery, tumors and vascular (esp. brain tissue)
- localized drugdelivery

therapeutic ultrasound

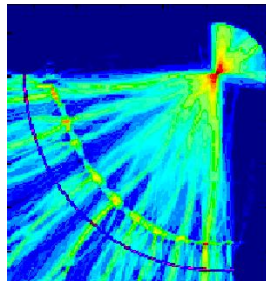
- tissue activation, woundhealing, skin therapy
- transdermal drugdelivery

Non Invasive Brain Surgery with HIFU

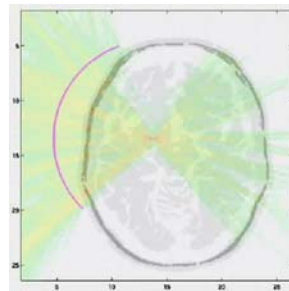
High intensity focused ultrasound is new and promising technology for non invasive surgery. Especially of interest for brain surgery but also applicable for tissue treatment and repair at other locations. It uses a focused array of ultrasound to generate a localized (1-3 mm) energy spot resulting in either cell lysis (high energy, tumors), tissue activation or local drug delivery (low energy). It is a 100% non invasive technique under MRI thermal imaging for guidance.



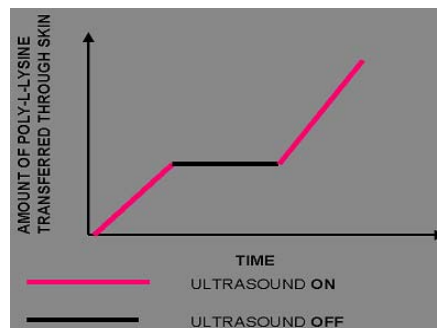
MRI scan brain



HIFU energy distribution



HIFU array pulse (movie)



Transdermal drug delivery assisted by ultrasound

Micro invasive surgery

MIS robot: waferstepper technology in future surgery

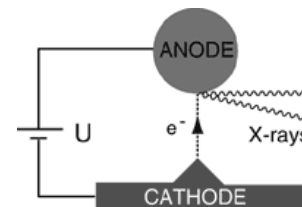
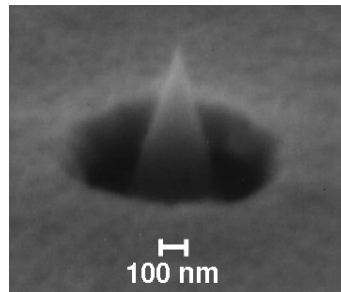
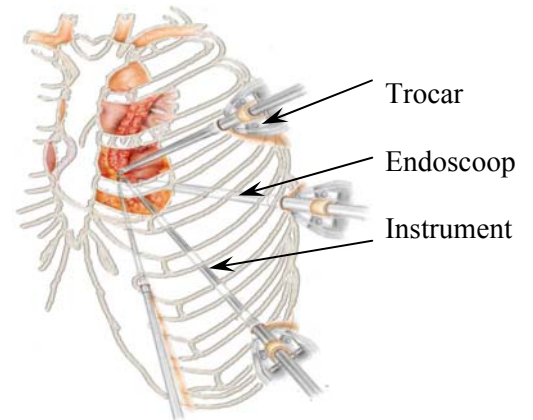
New generation “Da Vinci” robot

- force feedback
- haptic feedback
- UMC, AZM, TU/e, TNO (IOP PE)
- long term: MRI & CT compatible system for surgery under real time vision

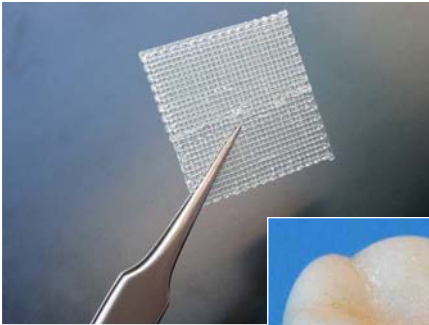
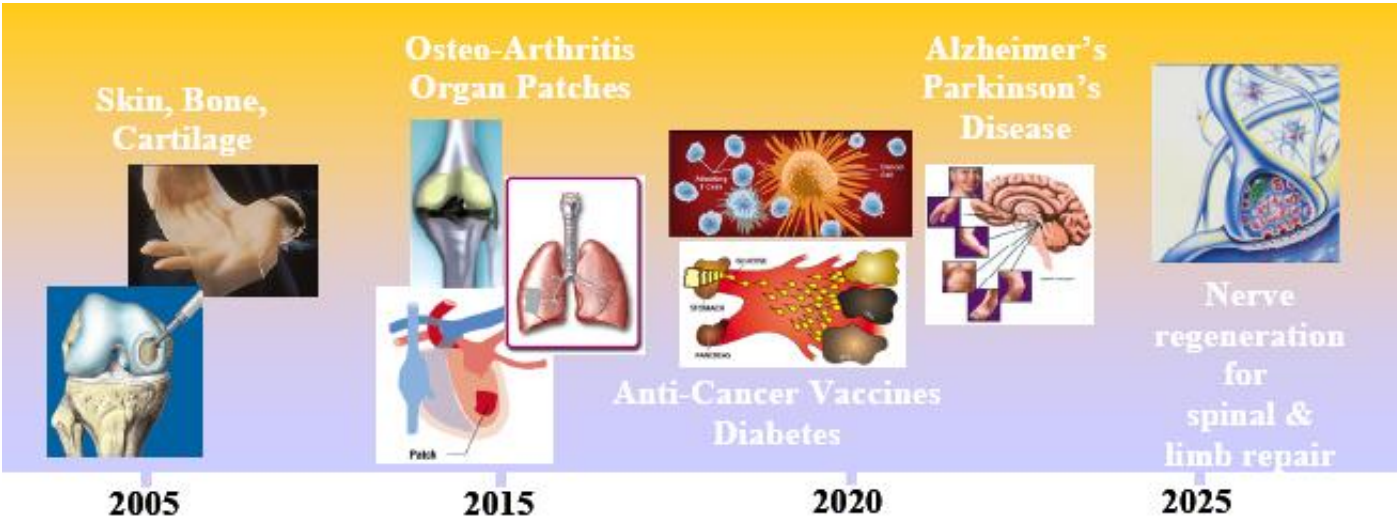


Miniature invasive X-ray source

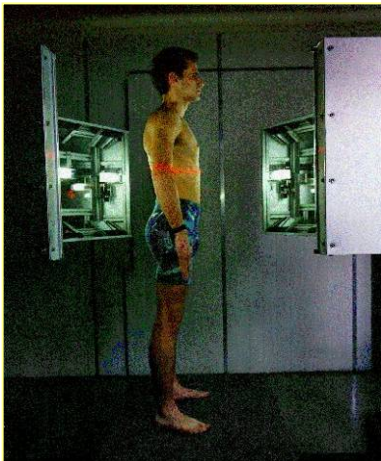
- brachytherapy



Regenerative medicine, tissue engineering



Custom fit, 3D scanning



3D Body scanning



HAL 3

Robotic assistance for elderly or infirm people, or those with disabilities

Backpack

Contains a computer with a wireless network connection

Battery

Actuators

Electric motors provide powered-assisted movement to the limbs

Angular sensor

Detects the angle of the hip, knee and ankle joints

Bioelectric sensors

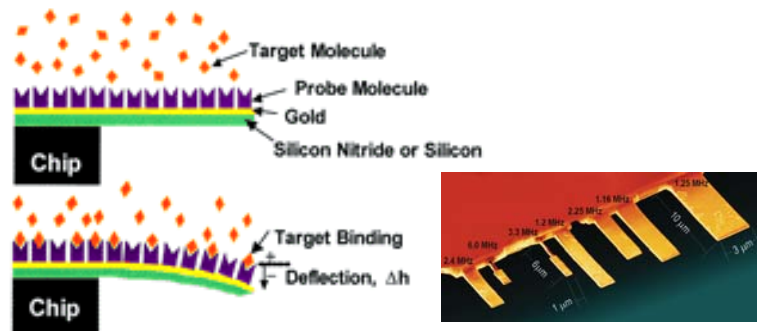
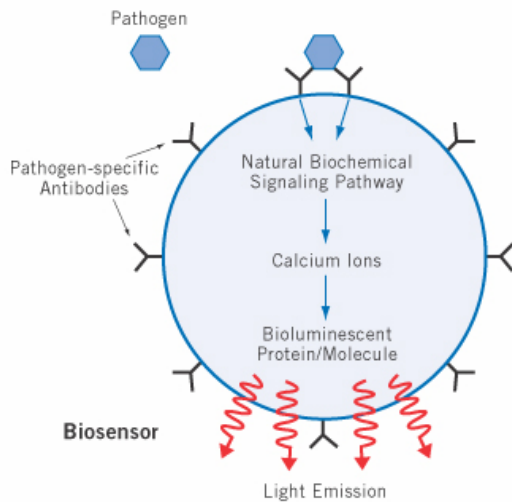
Sensors attached to the skin monitor nerve impulses from the brain to the muscles indicating that a movement like standing or walking is about to take place. The signal is relayed to the computer, where it is analysed and used to launch the actuators even before the suit's wearer moves

Floor reaction force sensor

Detects the user's centre of gravity



SOURCE: UNIVERSITY OF TSUKUBA, JAPAN 2010



Cantilever Sensor; Thundat ORNL

μ Biodiagnostic System

Electrokinetic Microsystems

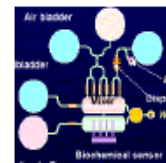


Courtesy of Adara Bioscience



Courtesy of I-STAT Corp.

Biomedicine Chip



Courtesy of Univ. of Cincinnati

Microfluidic Lab Card

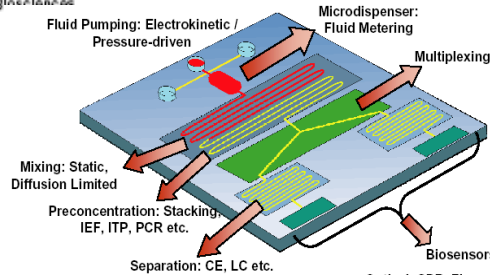


Courtesy of Micronics, Inc.



www.motorola.com/life/sciences/

Motorola Biosciences'
eSensor™ DNA Biochip



Physics-based component-level
representation of a typical biochip



Nanogen's NanoChip™
Microelectronic Array Cartridge¹



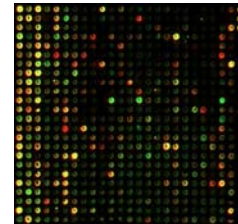
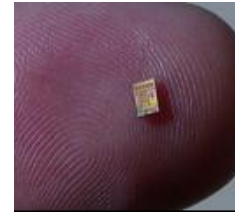
Caliper Technologies' LabChip¹

¹Mitchell, P., *Nature Biotechnology*,
vol. 19, Aug 2001, pp. 717-721

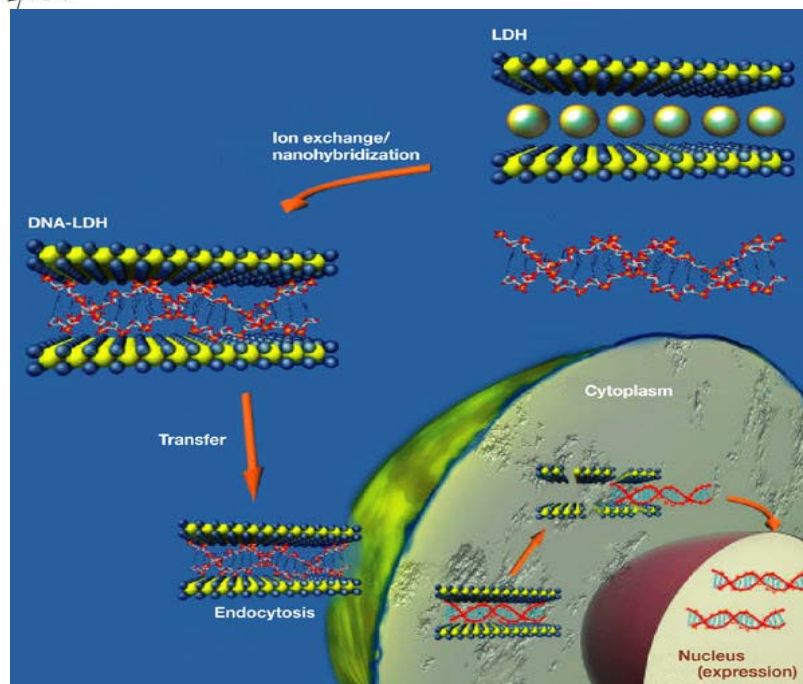
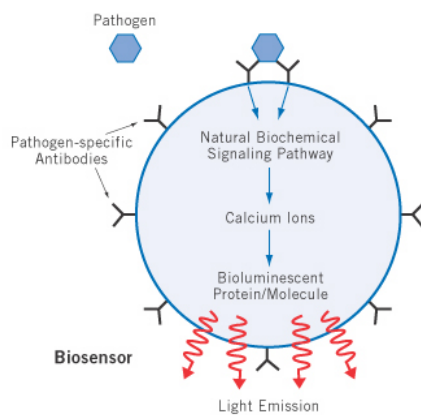
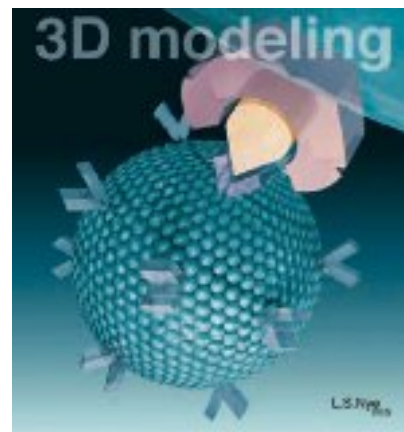
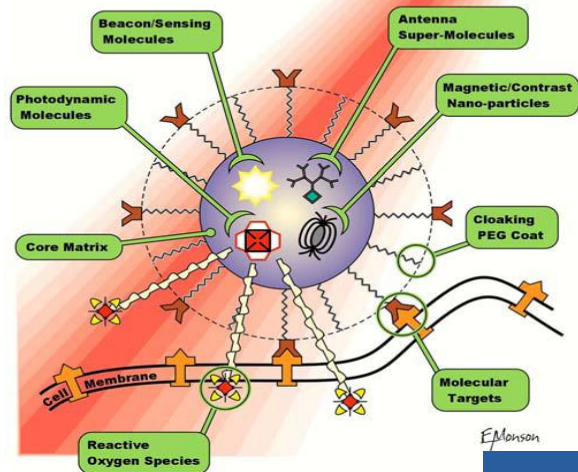
Bio sensors

Thanks to miniaturisation down to micron & nano level:

- | | |
|--|--|
| <ul style="list-style-type: none">• small dimensions
(mm, μm, nm) | <ul style="list-style-type: none">function integration possible (dsp, rf-wireless)efficient thermal and material transportcheap, easy for mass productionportable, point of analysisdisposable |
| <ul style="list-style-type: none">• small sample volume
(μL, nL, pL) | <ul style="list-style-type: none">fast responsehigh throughputmulti parallel analysis, matrix arraysingle cell/molecule detectionless chemical waste |
| <ul style="list-style-type: none">• high sensor-sample ratio | <ul style="list-style-type: none">high sensitivityhigh signal to noise |



DYNAMIC NANO-PLATFORM



Nanomedicine

The ageing population, the high expectations for better quality of life and the changing lifestyle of the society lead to the need for improved, more efficient, and affordable healthcare. Nanomedicine is defined as the application of nanotechnology in medicine. It exploits the improved and often novel physical, chemical, and biological properties of materials at the nanometric scale. Nanomedicine has the potential impact on the prevention, early and reliable diagnosis and treatment of diseases.

In nanomedicine, three areas are of special interest:

Nano-diagnostics, including medical imaging, for identification and diagnosis at earliest stage possible

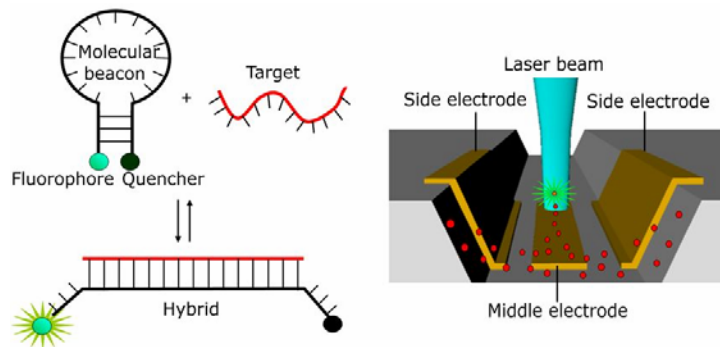
- high sensitive, preferentially single molecule, detection of (early) biomarkers
- high resolution microscopic and spectroscopic techniques, both in-vitro as well as in-vivo
- high resolution in-vivo imaging techniques such as MRI, CT, PET and Ultrasound
- target specific contrast nanostructures for imaging
- theranostics: combination of diagnostic (targeted contrast agents) with therapeutic molecules (e.g. radio isotopes)

Targeted drug delivery and controlled release

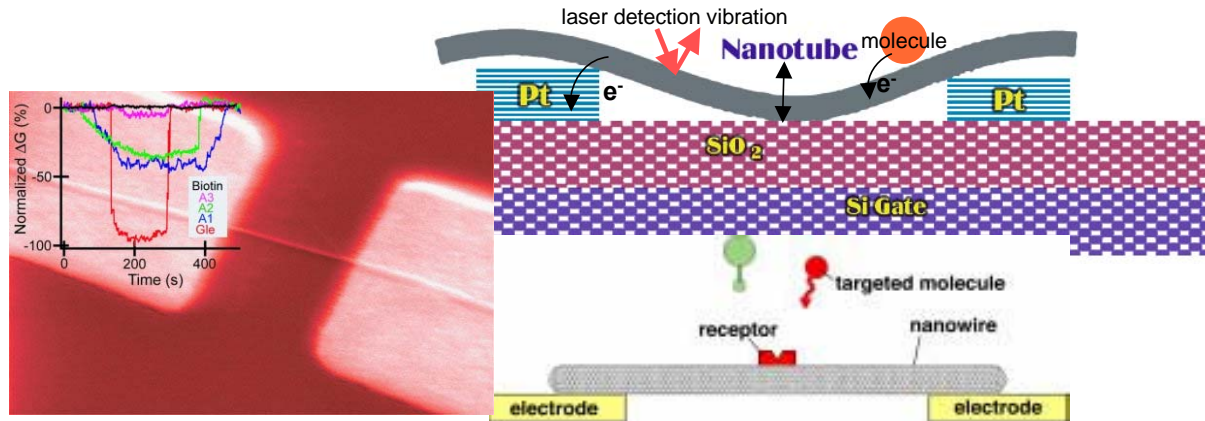
- drug delivery microchip technology, implantable (e.g. automated glucose delivery)
- nanoparticles that can release on demand pharmaceuticals, triggered by bioreaction or by external forces
- dna loaded nanoparticles that can be transfected into cells to repair malfunctioning of cells

Regenerative medicine, tissue engineering

- in-situ tissue regeneration and repair with bioactive (DNA carrying) particles that induce specific cell growth
- biomimic nanostructures to be used in scaffolds for optimal tissue uptake and regeneration

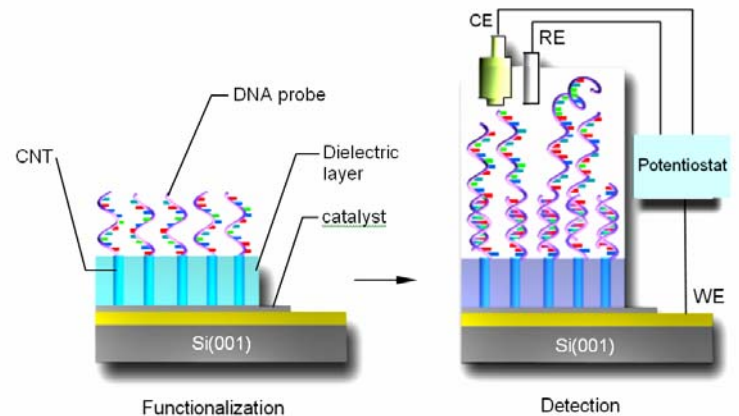
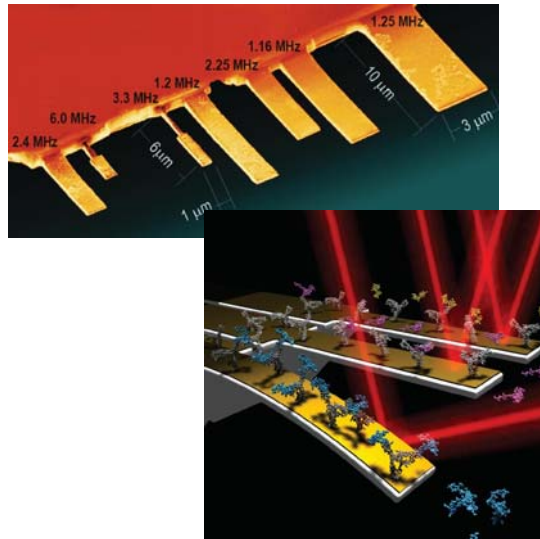


Single molecule detection (DNA, proteomics) by Jeff Wang, Johns Hopkins Univ, USA



Nanowire molecular sensor concept, NASA Ames:

- electrochemical detection by electrical current
- weight: change in mechanical resonance indicates molecular weight



DNA array: DNA probes on nanotubes

- electrochemical detection
- and/or fluorescence

Electronic nose on chip, ppb/ppt gas/vapor detection

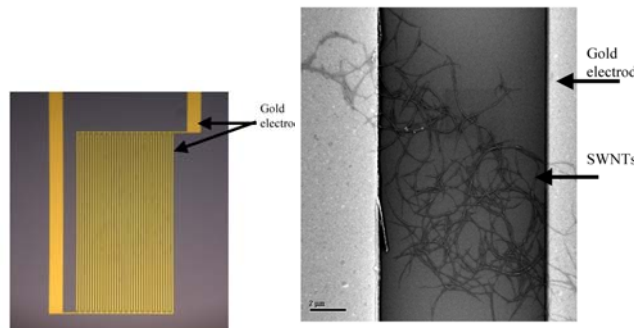
- change in mechanical resonance by molecule absorption
- detection via laser readout

Nanosensors

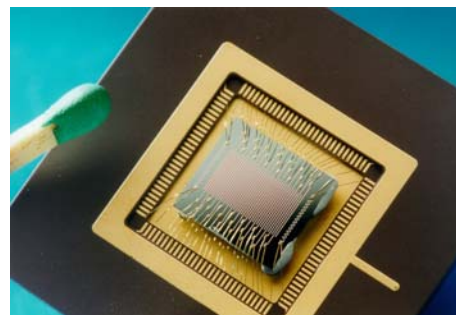
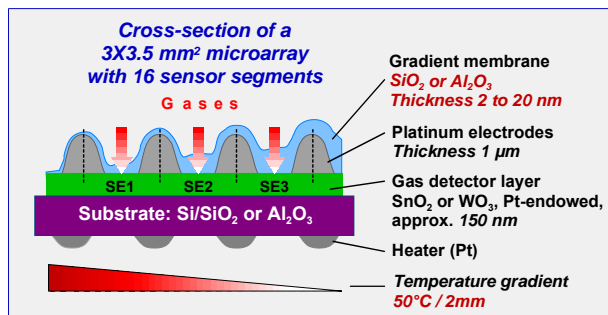
Nanotechnology has great potential for sensing devices since the nanoscale enables a high surface area coupled to a very low mass, featuring a high sensitivity and a high signal to noise ratio at a level that can not be obtained on the macro scale. Also the high functional density and the ability to produce matrix-array sensors have many advantages.

The following sensing techniques at the nanoscale are being employed:

- mechanical resonators such as nano-cantilevers: the shift in resonance is a measure for the absorbed particle/molecule
- optical resonators (optical cavity): resonance shift upon presence of change in optical index due to molecular absorption
- electrical/electrochemical: measuring charge transfer in contact with a nanowire, can be promoted with enzyme or catalyst
- electrical resistance: conductivity over a nano-porous (nanoparticles, nanofibers) substrate
- magnetic detection (GMR) via magnetic nanolabelling of molecules
- specific, targeted detection via DNA functionalized nanoparticles, with subsequent electrical or optical read-out
- single molecule detectors, enabled via quantumdot fluorescent labeling
- lab-on-chip systems for processing, upconversion and detection of DNA and proteomics

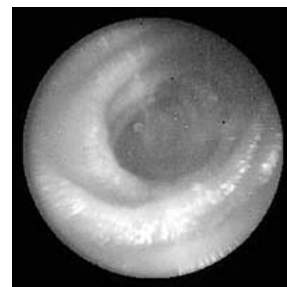
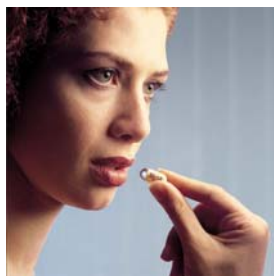
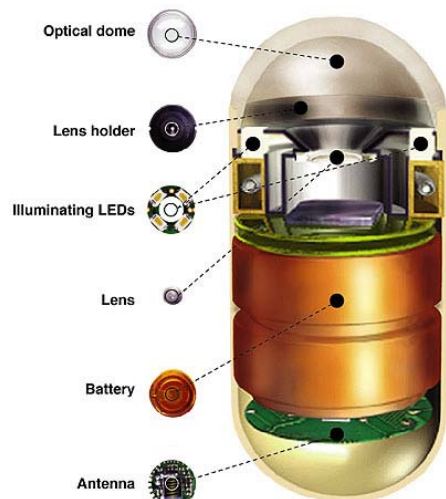


Chemiresistor with cnt's or nanofiber fabric, for gases (NASA Ames)



MOx gradient matrix gas sensor, ppb level, Forschungszentrum Karlsruhe

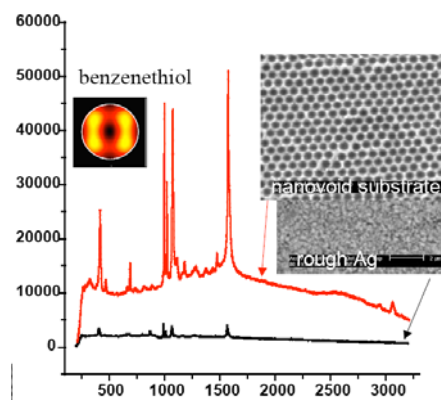
Implantable sensors



Camera in a pill by Given Imaging (Israel), PillCam ESO.
Over 150.000 patients since 2001

Optical sensors

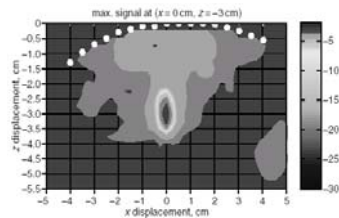
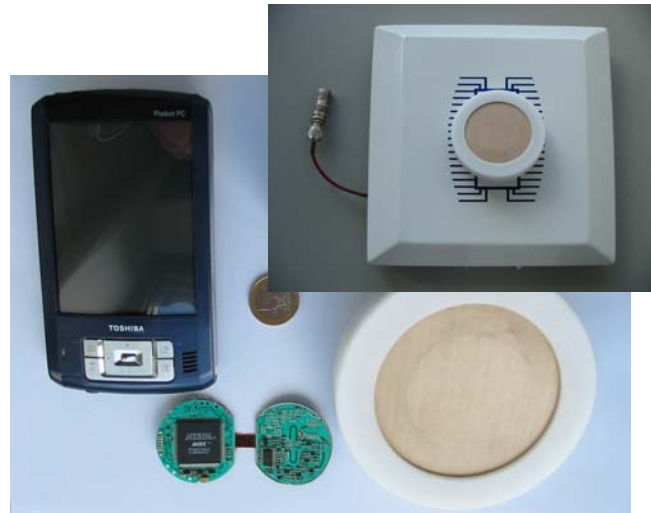
SERS: Surface enhanced Raman scattering



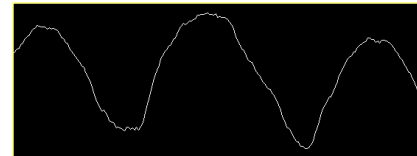
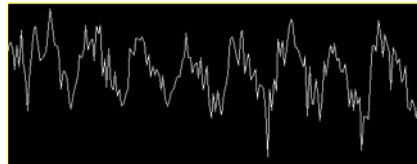
SERS on fiber tip for tissue analysis

FMCW radar (2,4 9,8 76,6 GHz)

- Portable
 - detects motion, distance, direction
 - low power, handheld, low cost
 - antenna array
- Non contact measurement
 - heartbeat (through clothes)
 - respiration rate (through wall)
 - skin cancer detection
- In body imaging
 - breast cancer imaging (1-2 mm)



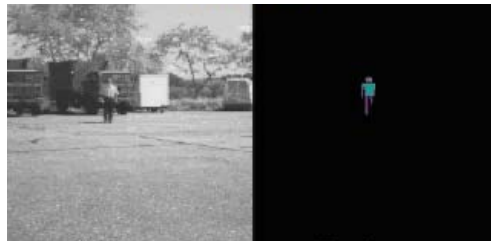
breast cancer



heartbeat and breathing



baby surveillance

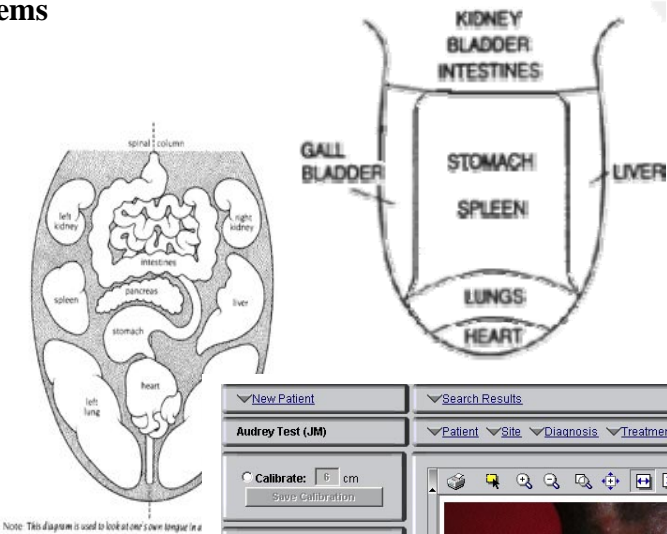


combined video and radar

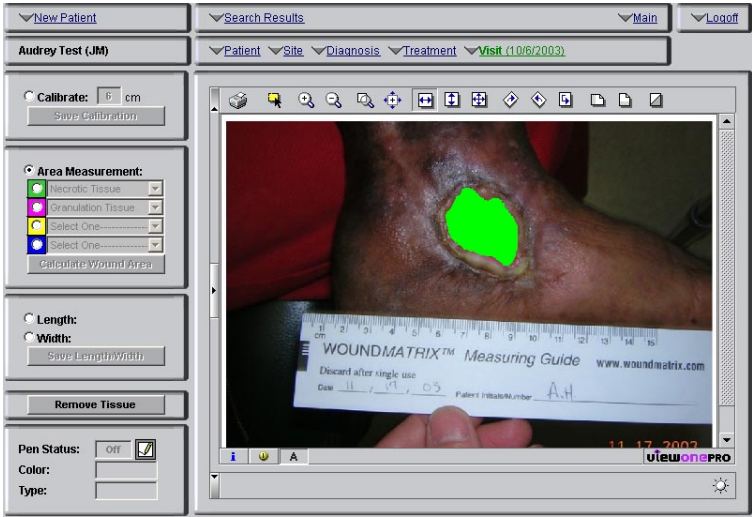


through clothes vision

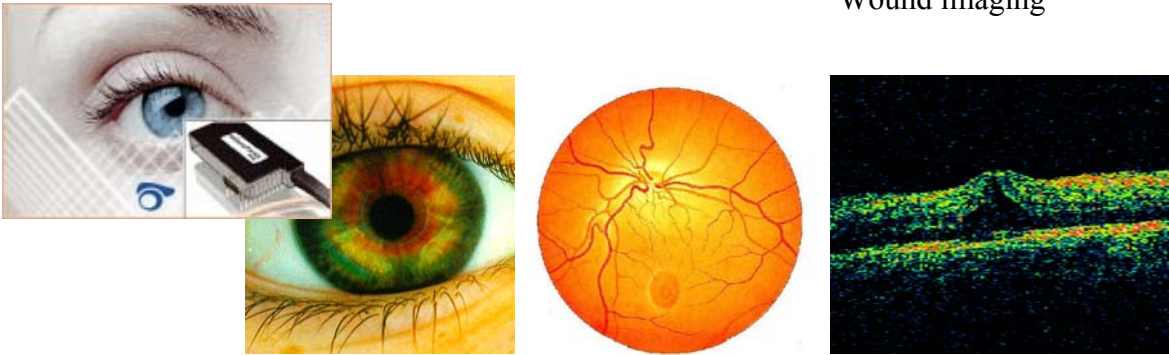
Diagnosis with vision systems



Tongue analysis by vision (Taiwan, USA)



Wound imaging



Retina scan, detection of macular edema (diabetes) with OCT

Evaluation quality of healthcare

QMT

To support hospitals improve their quality TNO developed the 'Quality to Medical Technology' quality system. This system creates a control circle that ensures a shorter response time to errors and lower costs. A smoothly running QMT can save 6 to 10% on the costs of medical technology management. The Medical Centre for Rijnmond South was awarded the first QMT certificate in 2002.



QMIC

The TNO QMIC certificate for website stands for approval of content, information and transactions that are being serviced by the website/

Gezondzoeken.nl

Alle QMIC® gecertificeerde webpagina's op het gebied van gezondheid zijn via, het door TNO opgerichte, internet-portaal "www.gezondzoeken.nl" te vinden.

Gezondzoeken.nl maakt het zorgconsumenten mogelijk te zoeken naar relevante, objectieve en betrouwbare informatie en diensten binnen de volgende gebieden:

- Medische informatie
- Geneesmiddelen
- Medische hulpmiddelen
- Voedingssupplementen





Future sport training

Future sporters and trainers will make use of wireless technology to get access to real time performance data, physical and mental condition. Together with expertise from human modelling for interpretation, an intelligent analysis and decision making system is obtained to for immediate responsive actions or future training scheduling. The necessary tools require the following technologies:

- wireless, real-time body sensors for heart rate, position, motion, acceleration, energy/fatigue
- 3D-visualisation and analysis of posture, movement, performance
- biomechanical modeling for analysis muscle and skeleton loading
- physiological modeling for energy and heat balance (food and clothes)
- optimisation of training schemes
- design of sport equipment, clothes and food
- optimisation of sporting accommodations



TNO zorginnovatie programma 2007 2010

systeeminnovatie

- **Patient empowerment**
Patient veiligheid, patient empowerment:
informatie, kennisoverdracht, gedragsbeïnvloeding
- **Ketenzorg**
Informatie: ICT info & infra structuur, networkdevices & services,
ICT systeemontwikkeling, uitwisselbaarheid, koppelbaarheid
Organisatie: Arbocuratief, Slimmer werken in de zorg, Telemedicine,
nieuwe zorgsystemen, kennismanagement, decision tools
- **Medische technologie**
Technologie voor thuiszorg, transmuraal, eerste lijn
assistive environment & selfcare, targeted drug delivery, medical devices & implants
- **Virtuele proeftuin, fieldlab**
Virtuele testomgeving nieuwe zorgsystemen
- **Transitiemanagement**
Implementatie en pilot trajecten



Participatie van de hele keten:
patienten & artsen verenigingen
zorginstellingen, zorgverzekeraars
overheid,
bedrijven (ICT, medical equipment)