Understanding Biosensors

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Course of Biosensors
for the course of Molecular and Industrial Biotechnologies

Bologna, December 17th 2009

Practical infoes

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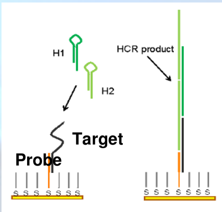
Office hours: by appointment

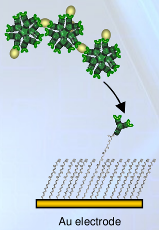
Class slides are given in class..
(bring your USB-keys or computers)
More material is available under request

Group presentation

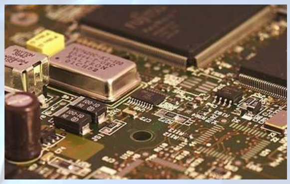
Nanobiotech - Prof. B. Samorì
Biochemistry dept.
http://www.biocfarm.unibo.it/samori/

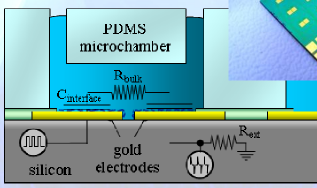
Micrel - Prof. L. Benini
Electrical Engin. dept.
http://www-micrel.deis.unibo.it/

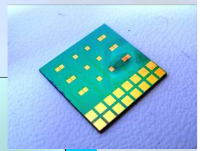




A joint effort towards the development of labelfree point-of-care analysis tools







Collaborators

Academic collaborators:

- Univ. of Pisa
- Area science park - Trieste
- Lausanne EPFL
- University of Tech. - Budapest
- Univ. of Cranfield

Industrial collaborations:

- Olivetti - Arnaud
- Xeptagen - Mestre
- IDEA – Bologna
- Lionix – Netherlands
- Lambda GmbH – Linz
- Hemosoft – Turkey

Evaluation

1. Knowledge of the main concepts:
   - Definitions: biosensor, transducer
   - Immobilization techniques
   - Classification with examples
2. A general idea of the field
3. Participation and creativity

Points of View

Try to imagine
a biosensor

Vision and History Outline

1. Technological background

2. Vision, Market and Expectations

3. Fields of application and social impact

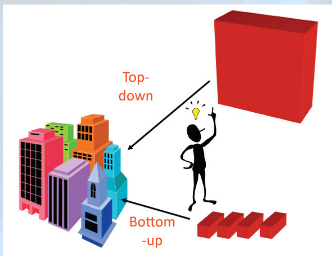
4. Class work

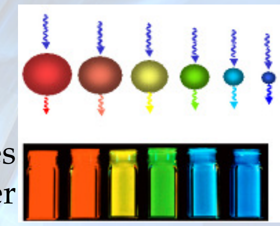
Tech bg 1

Nanobiotechnology:

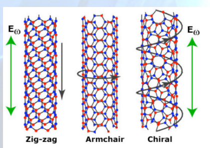
- biotechnology and nanotechnology
- scale effects
- examples of nanoconstructs

You already approached:

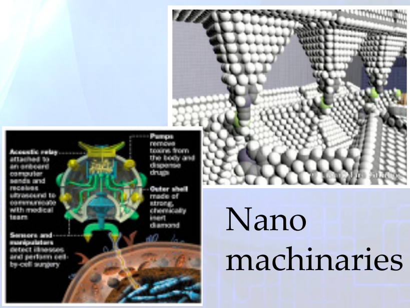




size does matter



Carbon nanotubes

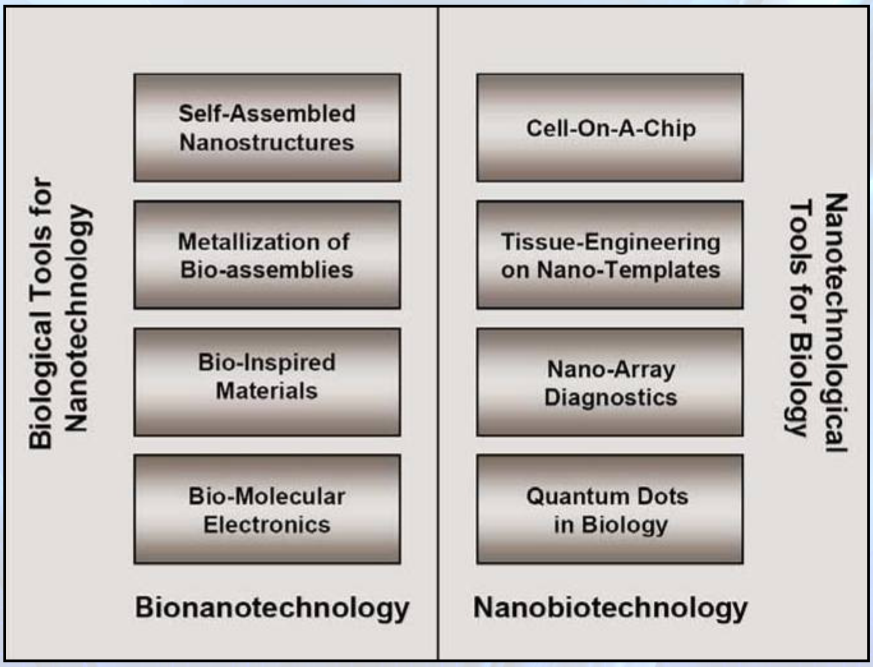


Nano machinaries

Tech bg 2

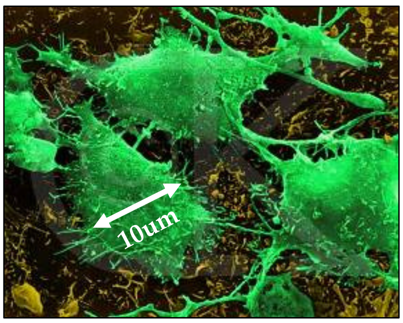
You already approached:

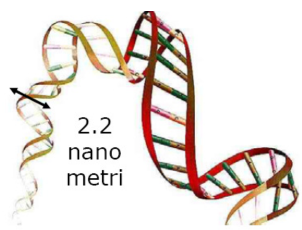
Biology in Nano-technology and Nano-sciences in Biotechnology

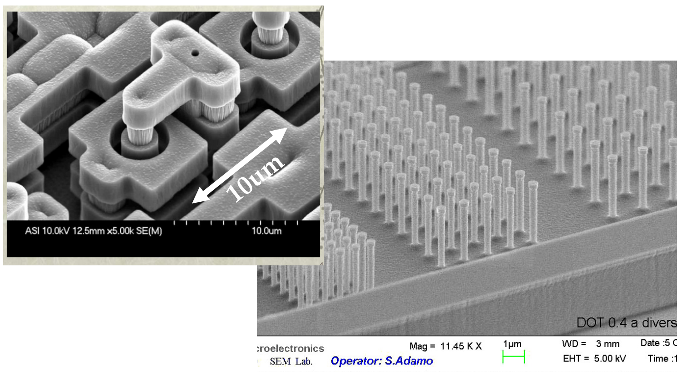


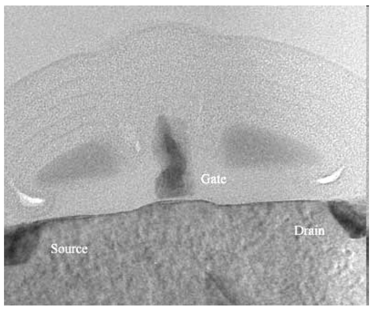
Tech bg 3

Try to imagine a biosensor



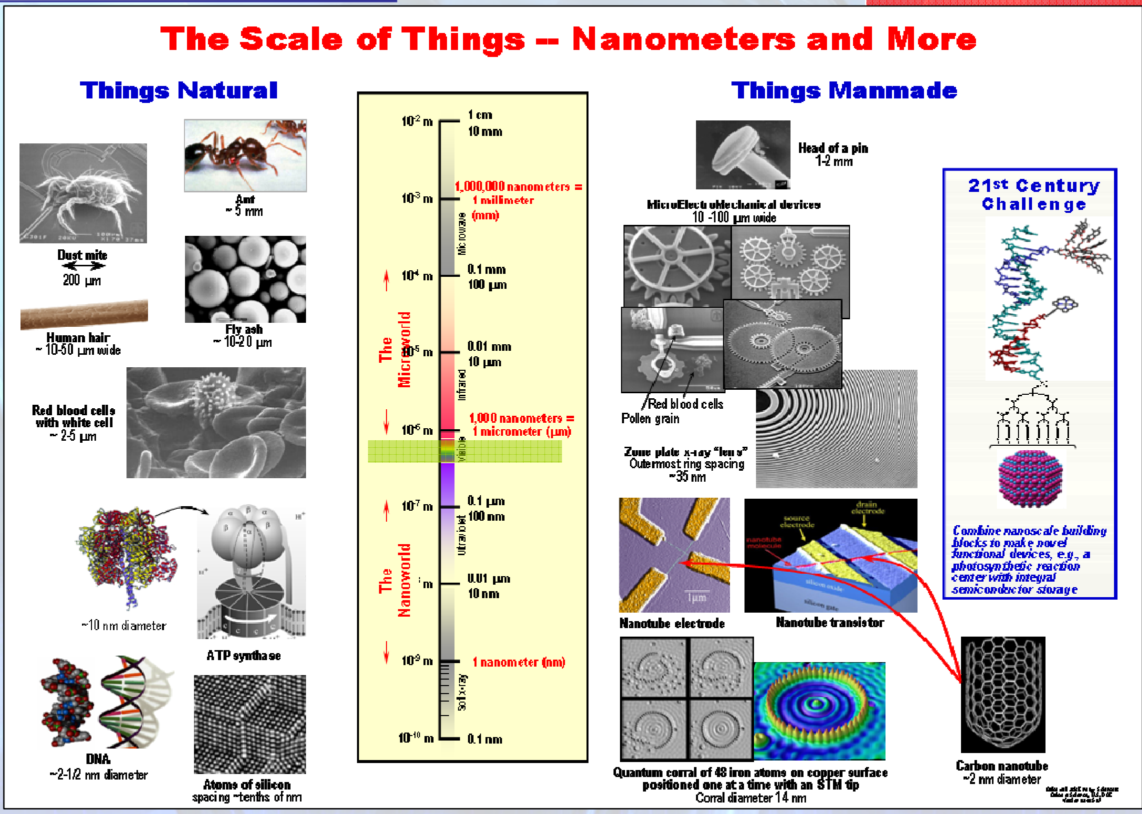






Tech bg 4

Try to imagine a biosensor



Tech bg 5

Try to imagine a biosensor

Vision and History Outline

1. Technological background
2. Vision, Market
3. Fields of application and social impact
4. Class work

Vision and market 1

The "biomedical revolution"

Situation in the late '90, beginning 2000:

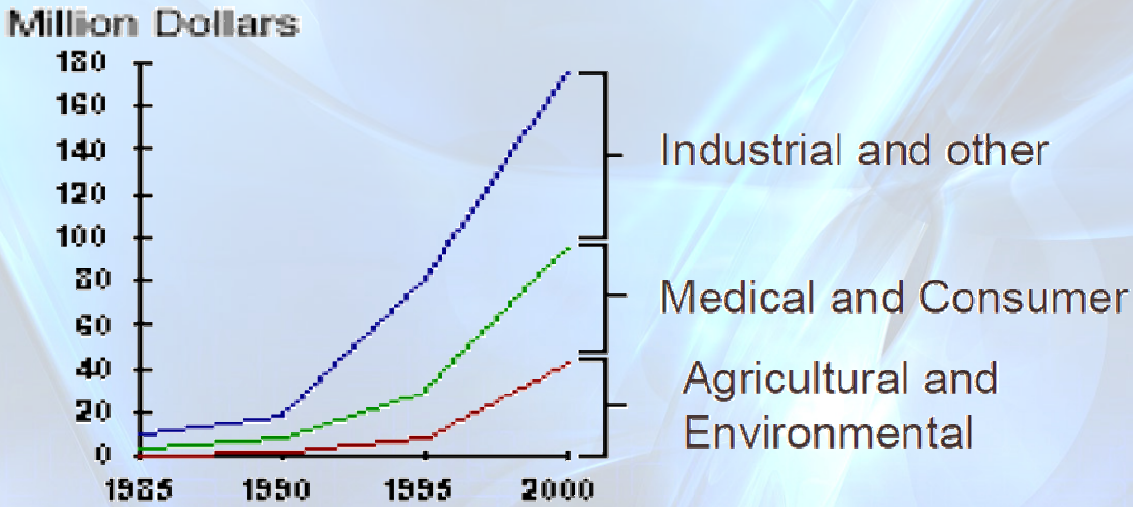
Money injection for the "biomedical revolution"
Lab-On-a-Chip (LOC or LOaC)
Micro Total Analysis Systems (uTAS)

Holy Grail keyword for grants acceptance
=
NANO-BIO..
and afterwards MICRO-BIO

now it is a field at risk. Why?
(the *UNIVERSAL SENSOR??*)

Vision and market 2

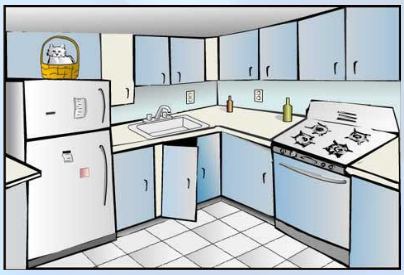
Biochips Market



Vision and market 3

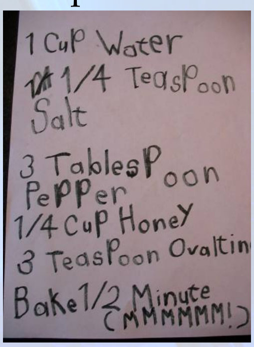
The "biomedical revolution":
Lab-on-a-Chip (LoC or LoaC)
Micro Total Analysis Systems (uTAS)

A kitchen



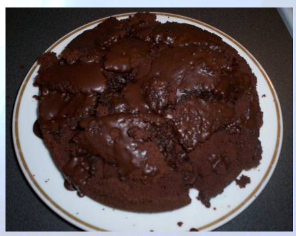
Any bio- lab

A protocol



Mom's cake

My cake



Vision and market 4

The "biomedical revolution":
Lab-on-a-Chip (LoC or LoaC)
Micro Total Analysis Systems (uTAS)

A kitchen

Vision and market 5

The "biomedical revolution":
Lab-on-a-Chip (LoC or LoaC)
Micro Total Analysis Systems (uTAS)

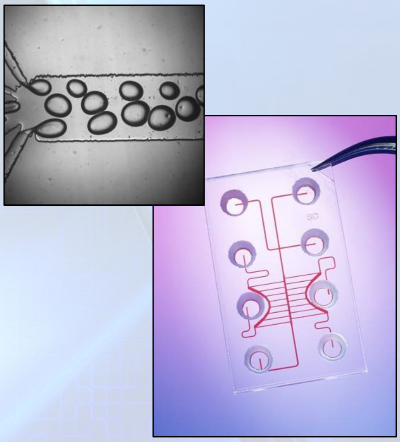
medicine
biology
biotechnology
chemistry
physics
computational science

microfluidics
electrical engineering
Microtechnology (MEMS)
nanotechnology
micro-Total Analysis Systems (µTAS)
Lab-on-a-chip (LoaC)

Vision and market 6

The "biomedical revolution":
Lab-on-a-Chip (LOC or LOaC)
Micro Total Analysis Systems (uTAS)

Electrical Engineering for the bio-sciences:
- from developing devices for lab-analysis,
- towards automatization (PCR).

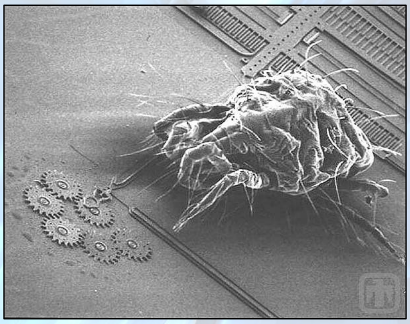


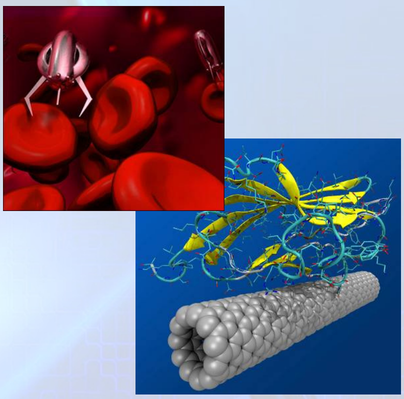
Microfluidics deals with the behavior, precise control and manipulation of fluids that are geometrically constrained to a small, typically sub-millimeter, scale. .

Vision and market 7

The "biomedical revolution":
Lab-on-a-Chip (LOC or LOaC)
Micro Total Analysis Systems (uTAS)

Microtechnology The term MEMS, for Micro Electro Mechanical Systems, was coined in the 1980's to describe new, sophisticated mechanical systems on a chip, such as micro electric motors, resonators, gears, and so on. .





Nanotechnology is very diverse, ranging from extensions of conventional device physics to completely new approaches based upon molecular self-assembly, from developing new materials with dimensions on the nanoscale to investigating whether we can directly control matter on the atomic scale.

Vision and market 8

The "biomedical revolution":
Lab-on-a-Chip (LOC or LOaC)
Micro Total Analysis Systems (uTAS)

A **lab-on-a-chip** (LOC) is a device that integrates one or several laboratory functions on a single chip of only millimeters to a few square centimeters in size.

A **micro-Total Analysis System** (μTAS) is a device dedicated to the integration of the total sequence of lab processes to perform chemical analysis (but not only chemical and not only analysis).

Vision and market 9

The "biomedical revolution":
Lab-on-a-Chip (LOC or LOaC)
Micro Total Analysis Systems (uTAS)

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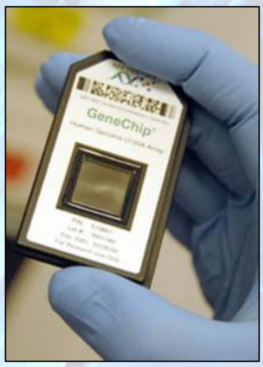
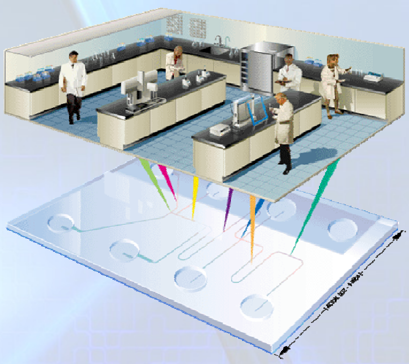


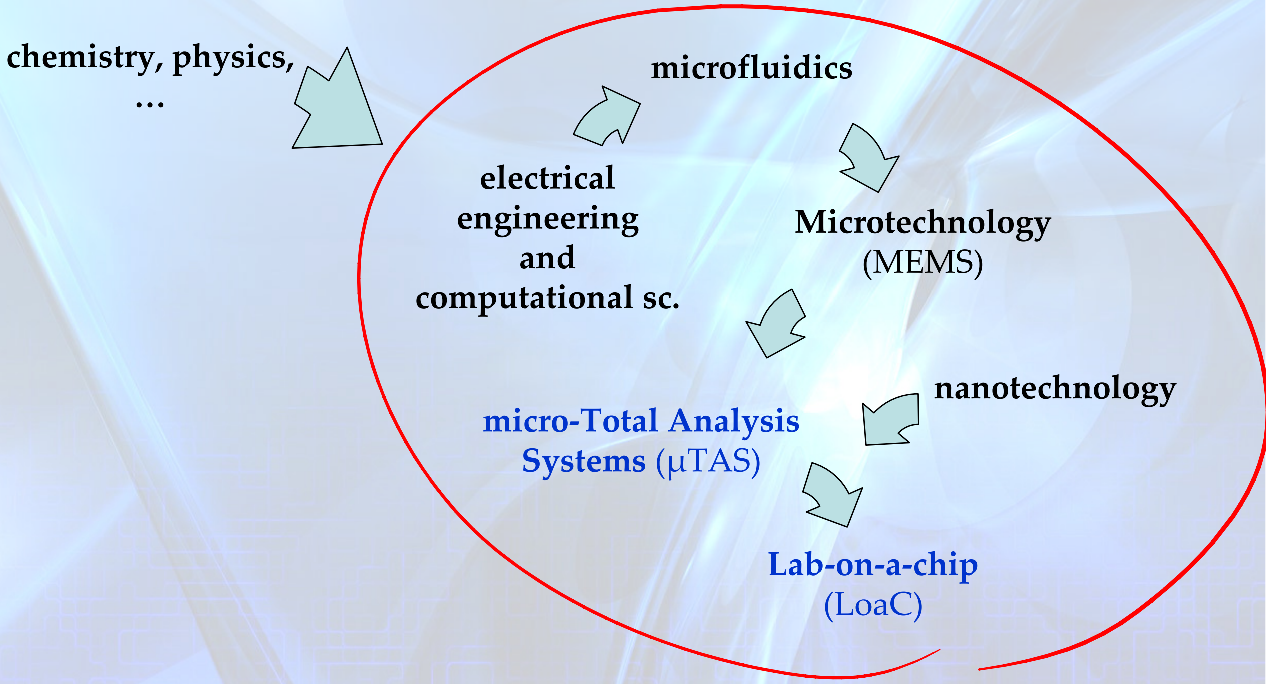


A **micro-Total Analysis System** (μTAS) is a device dedicated to the integration of the total sequence of lab processes to perform chemical analysis (but not only chemical and not only analysis).

Vision and market 10

The "biomedical revolution":
Lab-on-a-Chip (LoC or LoaC)
Micro Total Analysis Systems (uTAS)

fields having an impact on the bio-sciences (biology, biotech, medicine…)



Vision and market 11

Expectations in few decades:
a new vision for the bio-sciences

StarTrek-like medicine

Like in the fifties for computing:

- ✓ Will there be hospitals?
  Point of Care
- ✓ Personalized care
- ✓ Agriculture, food processing/controlling
- ✓ Security

Vision and market 12

The "biomedical revolution":
Lab-on-a-Chip (LoC or LoaC)
Micro Total Analysis Systems (uTAS)

A lab and a doctor inside you

Vision and History Outline

1. Technological background

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3. Fields of application and social impact

4. Class work

Social impact 1

Not only biomedical

Medical system
(point-of-care, diagnosis, implantable sensing and drug delivery, personalized treatment)

Pharma- e bio-chem- research
(high throughput through parallel assays, low time-to-market)

Food industry
(local and real time food quality control, biotechnologically improved quality, improved agriculture)

Industrial processes
(nanoscale process control, bottom-up fabbrication control)

Environmental
(pollution monitoring, waters and security, bioremediation)

Social impact 2

Pharma e bio-chem- research

Molecular Diagnostics

- rapid diagnosis of hemoglobin disorders, many infectious diseases, cancer diseases (expression analysis) [1]
- monitoring of **viral** infections (viral expression analysis) [2]
- parallel protein biomarkers monitoring for cancer diseases [3]
- typing patients for **genetic resistance to drugs** (eg: used in HIV/AIDS treatment) (gene-based test) [1]

In vivo Drug Delivery

- treatments that need a continuous release of drugs (eliminate injection pain and infections) (eg: used in diabetes and pain treatment) [4]
- treatments that need a very precise targeting of drugs (eg: solid tumors) [5]
- treatments that employ expensive drugs (reduce drugs volume) [6].

Drug Discovery

- high-throughput screening platforms for drug lead identification [7]
- pharmacogenomics (biochemistry and physiology of drug action, uptake and metabolism, and how this is affected by genetics; the opportunities for discovery and design of new therapeutic agents)
- personalizing medicine; understanding and managing adverse drug reactions

Genetic Research

- SNP microarrays for genome-wide genotyping [8]
- Comparative genomic hybridization (CGH) microarrays for DNA-copy number variation analysis
- Chromatin immunoprecipitation (ChIP) microarrays for in-vivo protein-DNA interaction analysis
- RNAi cell microarrays for loss-of-function (gene silencing) studies

Social impact 3

Food industry

Environmental and ecological monitoring	Defense/forensic
•Pesicides, fertilizers, oestrogen, CO, CO_2 ▪In the environment, the measurement of biological oxygen demand (BOD) which provides a good indication of pollution, atmospheric acidity, and river water pH, detergent, herbicides, and fertilizers	antrax, cocaine, nerve agents
Industrial Bioprocess monitoring •yeast, ethanol, lactic acid, amino acids •In the food industry biosensors identify species and determine concentrations of multiple pathogens – (E. coli 0157:H7 and Salmonella) •Biosensors to the wine industry. These sensors are being developed to analyze the sugar to alcohol ratio in grapes and in wine	

Vision and History Outline

1. Technological background
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3. Fields of application and social impact
4. Class work

Class work 1

How to approach the design of new biosensors?

- ✓ Application-based approach:
  Determine market and social needs
  Find a breakthrough solution
- ✓ Analyze social impact and
  Quantify the potential market (money)
- ✓ Determine and quantify R&D efforts
  Money
  Time
  Regolamentation and lobbing
- ✓ Available technology
  State of the art
  Required advancements
- ✓ Get a grasp of the required development
  Interface with the user and packaging
  Industrialization
  Commercialization

Class work 1

How to approach the design of new biosensors?

HOW TO GET TO THE REALIZATION OF A GLUCOSE SENSOR

- ✓ Application-based approach:
  Determine market and social needs
  Find a breakthrough solution
- ✓ Analyze social impact and
  Quantify the potential market (money)
- ✓ Determine and quantify R&D efforts
  Money
  Time
  Regolamentation and lobbing
- ✓ Available technology
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  Required advancements
- ✓ Get a grasp of the required development
  Interface with the user and packaging
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  Commercialization

Class work 2

How to approach the design of new biosensors?

- ✓ **Application-based approach:**
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  Find a breakthrough solution
- ✓ Analyze social impact and
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  Money
  Time
  Regolamentation and lobbing
- ✓ Available technology
  State of the art
  Required advancements
- ✓ Get a grasp of the required development
  Interface with the user and packaging
  Industrialization
  Commercialization

- Easy tratment for chronic diseases and followups. Home treatment
- Point of Care devices

Class work 3

How to approach the design of new biosensors?

- ✓ Application-based approach:
  Determine market and social needs
  Find a breakthrough solution
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  Required advancements
- ✓ Get a grasp of the required development
  Interface with the user and packaging
  Industrialization
  Commercialization

- High variability of requirements for followup treatments↓
- Chronic diseases are not as variable↑
- Large number of dibetic people needing a constant lifelong care. *170 million in the world, increasing*
- It's a 15 billion dollars market

Class work 4

How to approach the design of new biosensors?

- ✓ Application-based approach:
  Determine market and social needs
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- ✓ **Determine and quantify R&D efforts**
  Money
  Time
  Regolamentation and lobbing
- ✓ Available technology
  State of the art
  Required advancements
- ✓ Get a grasp of the required development
  Interface with the user and packaging
  Industrialization
  Commercialization

- Before a scientific concept was demonstrated, it was very difficult to address the required efforts. The concept for a sensor was first developed in the '60s, since then it's mostly develoment and industrialization (~1 million)
- Time for development and industrialization of a mature concept of electrochemistry is 3-5 years (mid term project)
- Lobbying efforts for defining the requirements for commercialization

Class work 5

How to approach the design of new biosensors?

- ✓ Application-based approach:
  Determine market and social needs
  Find a breakthrough solution
- ✓ Analyze social impact and
  Quantify the potential market (money)
- ✓ Determine and quantify R&D efforts
  Money
  Time
  Regolamentation and lobbing
- ✓ **Available technology**
  State of the art
  Required advancements
- ✓ Get a grasp of the required development
  Interface with the user and packaging
  Industrialization
  Commercialization

- Patents!!!!!
  Available techniques and protocols
  Membranes for sample filtering
  Packaging
  Needle-to-chip fluidics
  …
- Required competences
  Stability and repetability of the measurements
  Simplification of existing research setup
  Towards engeneerable materials

Class work 6

How to approach the design of new biosensors?

- ✓ Application-based approach:
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  Money
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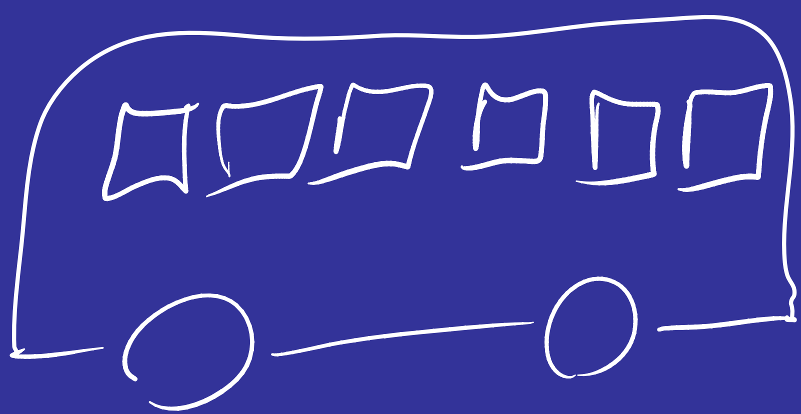
- ✓ Available technology
  State of the art
  Required advancements
- ✓ **Get a grasp of the required development**
  Interface with the user and packaging
  Industrialization
  Commercialization

- -Electronic board: dimension for portability, user interface (control and data output)
  -Towards KISS protocol and device (keep it simple and stupid)
- -Materials and processes for industrialization
  -Subcontracting and dependency on other companies
- Marketing efforts

Class work 7

How to approach the design of new biosensors?

Where does the bus go?



Class work 8

CLASSWORK

Get coupled and design a futurable LoaC, given <u>ANY</u> compence and knowledge:

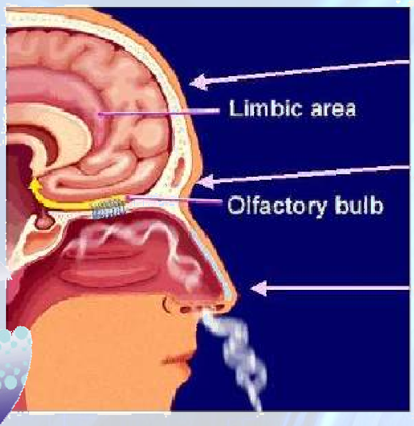
1. Market need
2. Social impact
3. Required R&D competences

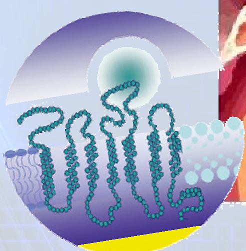
Write a small report in class and give it to me at the end of class

1 h

Next…

What is a biosensor and it's architecture





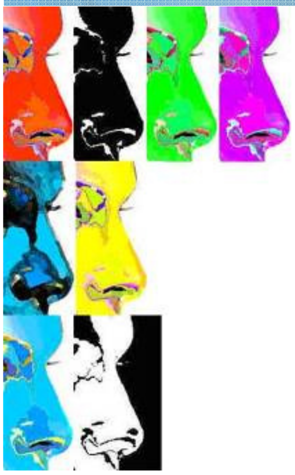
Pattern classifier (*real* neural network)

Sensor array 10^7 cells of ~100 different receptor types

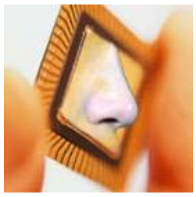
Sampling system (temperature, humidity control, filtering)

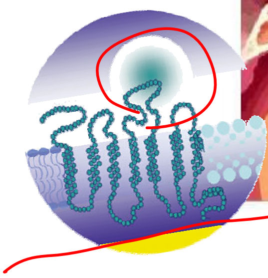
The end…

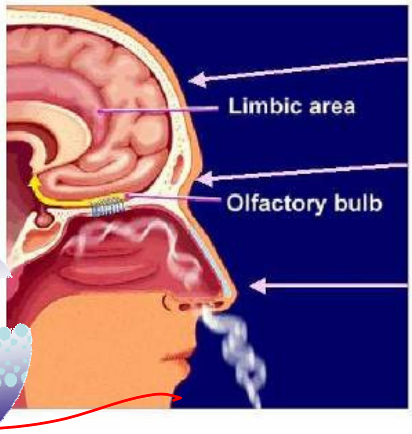
How do you imagine a biosensor?



The nose







Pattern classifier
(*real* neural network)

Sensor array
10^7 cells of ~100 different receptor types

Sampling system
(temperature, humidity control, filtering)