

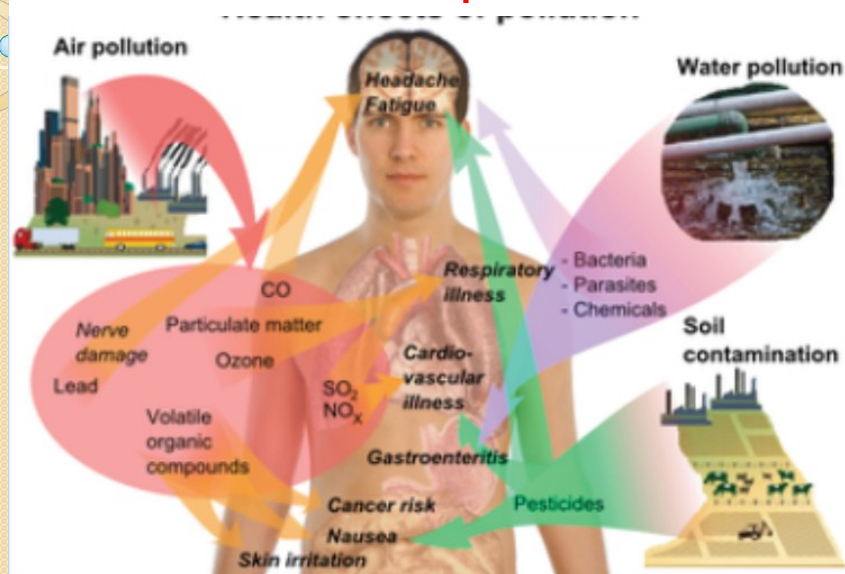
Telemonitoring tools for toxic compounds detection

**Mihaela Badea (1), Carmen Buzea (1), Marius Moga(1),
Arianna Sonia Scollo (2), Patrizia Restani (2)**

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Health effects of pollution



http://www.enotes.com/topic/Pollution#cite_note-26



Monitoring

- Legislation
- Maximum admitted limits

Survey – baseline data

Operational monitoring

Investigative monitoring



Traditional Analytical Techniques

- Time consuming
- Expensive
- Laboratory monitoring
- Trained laboratory personnel
- High tech equipment
- Extensive sample preparation
- Organic solvent consumption
- + Multianalyte detection
- + Commercial availability
- + Standardized
- + Sensitive
- + Specific
- + Reusable

Examples of biomarkers and their applications

From P. Vasseur, C. Cossu-Leguille, Environ. Int. 28 (2003) 711.

Biomarkers	Pollutants
• Biomarkers of exposure	
• HSP	Thermal shock, metals/heavy metals,
• Cytochrome P450	PAHs, PCBs, dioxin
• Metallothionein	Metals
• Biomarkers of effect	
• Lysosomes	Stress
• Antioxidant	PAHs, PCBs, organochlorine pesticides
• Vitellogenin	Endocrine disruptors
• Biomarkers of susceptibility	
• Paraoxonase	Organophosphates
• Aryl human	Receptor PAHs

Emerging Contaminants (ECs)

Can be defined as

- ★ any synthetic or
- ★ any naturally occurring chemical or
- ★ any microorganism

That is not commonly monitored in the environment and has the potential to cause ecological and/or human health effect.

Concentration varies from $\mu\text{g/l}$ to ng/L

Emerging contaminants - classes

- Pharmaceuticals and Personal Care Products (PCPs)
- Industrials and Volatile priority pollutants
- Pesticides
- Biotoxines
- Nanomaterials

Pharmaceuticals and Personal Care Products (PCPs)

- | | |
|---------------------|----------------------------|
| • Antipyretic | * Acetaminophen |
| • Antibiotics | * Gemfibrozil |
| | * Erythromycin... |
| • Fragrance | * AHTN and HHCb |
| • Anti-inflammatory | * Diclofenac |
| | * Ibuprofen |
| • Hormones | * Estrone |
| | * 17 estradiol |
| • Insect repellent | * N,N-diethyl-metatolamide |

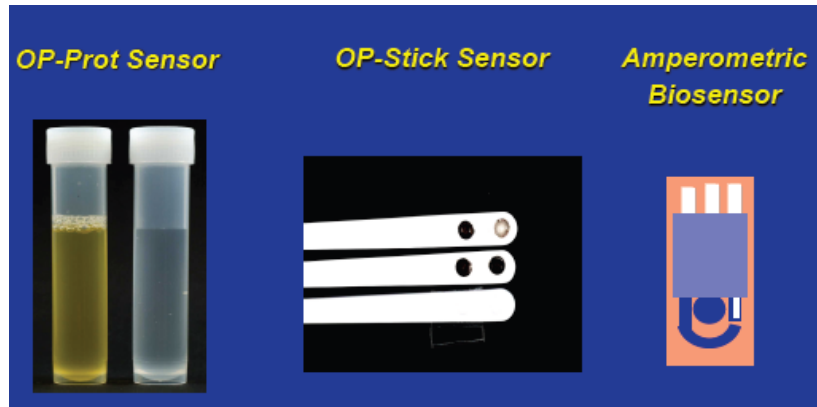
Industrials and Volatile Priority Pollutants

- Plasticiser
 - * Various phthalates
- Flame retardant
 - * Polybrominated diphenylethers
- Corrosion inhibitors
 - * Triazoles
- Surfactants
 - * Nonylphenol
 - * Tert-octylphenol)
- Protective coatings
 - *perfluorates
- Food additive
 - *BHA
 - *BHT

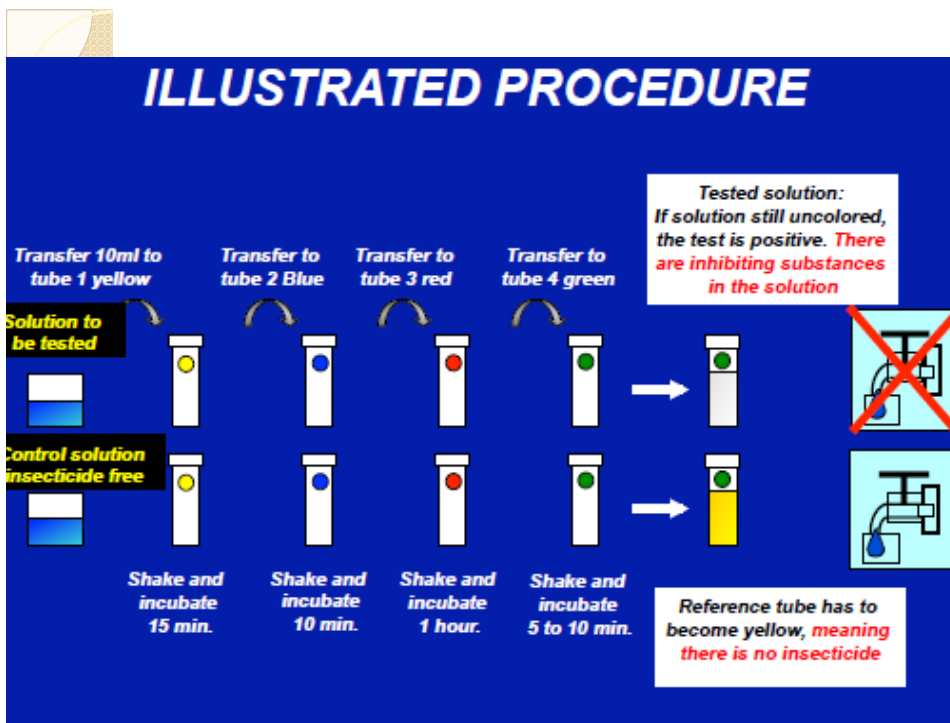
Pesticides

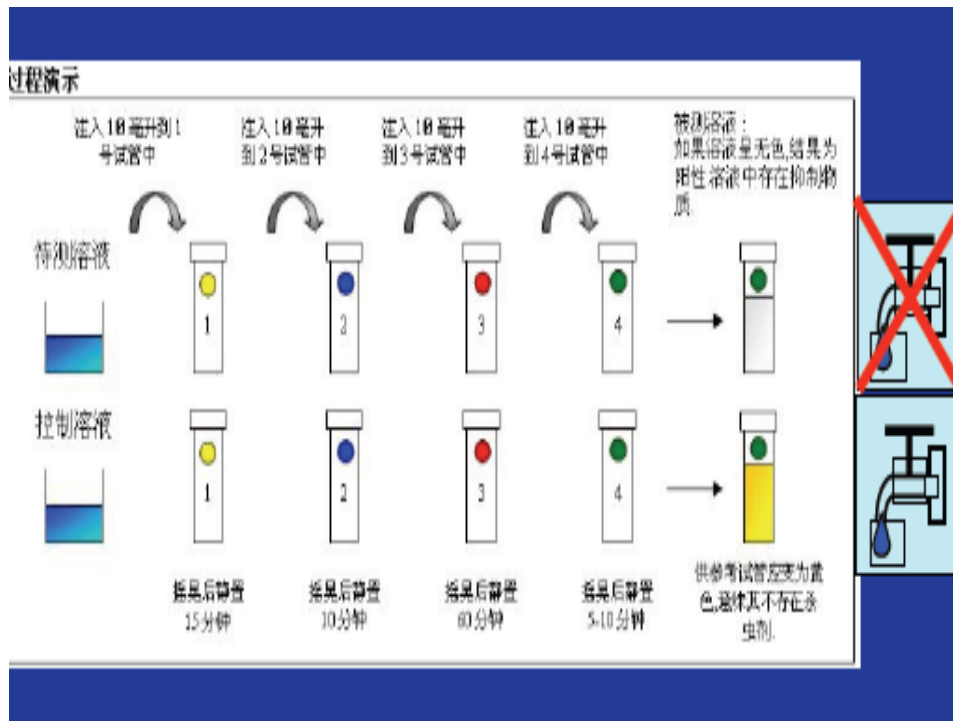
- Fungicides
 - * Benomyl
 - * Carbendazim
- Herbicides
 - * Chlorophenoxy acids
 - * Chloroacetalinides
 - * Triazines
- Insecticides
 - * Organochlorines
 - * Organophosphates
 - * Pyrethroids

Organophosphorus pesticide – colorimetric sensors



(Semi)quantitative data





Toulouse (FRANCE)

OP-Prot sensor

O Biocaptor para detecção de insecticidas na água
Domínios de aplicação:

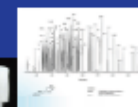
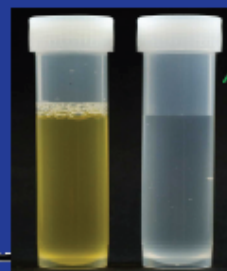
Água de superfície, água potável e água residual
Baseado numa acetilcolinesterase optimizada para engenharia de proteínas.

OP-Prot sensor permite a detecção de insecticidas organofosforados e carbamatos

Protótipo / Preliminar

OP-Prot sensor é:

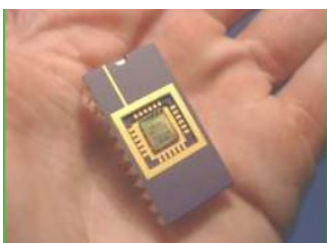
- Análise simples e rápida (75 minutos)
- Sensibilidade: cerca de 1ppb (µg/litro) a OP
- Nem extração nem equipamento necessário
- Análise transportável
- Baixo custo de análise
- Bioensaio tradicional: largo espectro



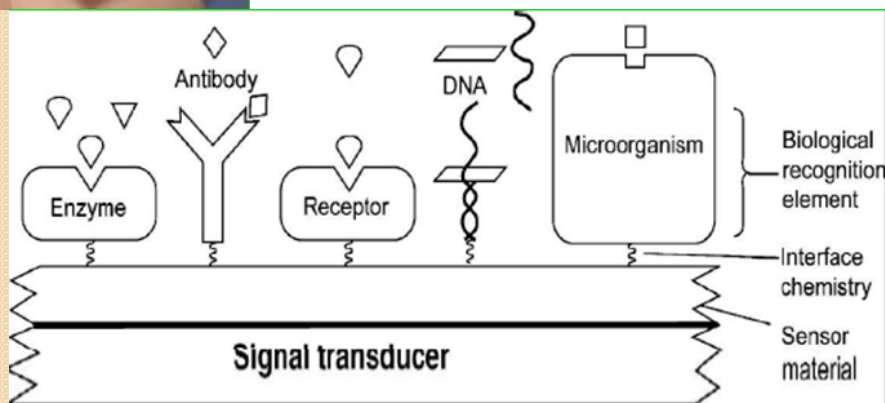
Análise físico-química GC/MS

Teste terreno específico

Protein BioSensOr - Incubateur Midi-Pyrénées, 29 rue Jeanne Marvig - 31400 TOULOUSE, France
Tél : +33 (0) 561 47 00 07 Fax : +33 (0) 561 47 00 04 email : protein.recherche@toulouse.fr



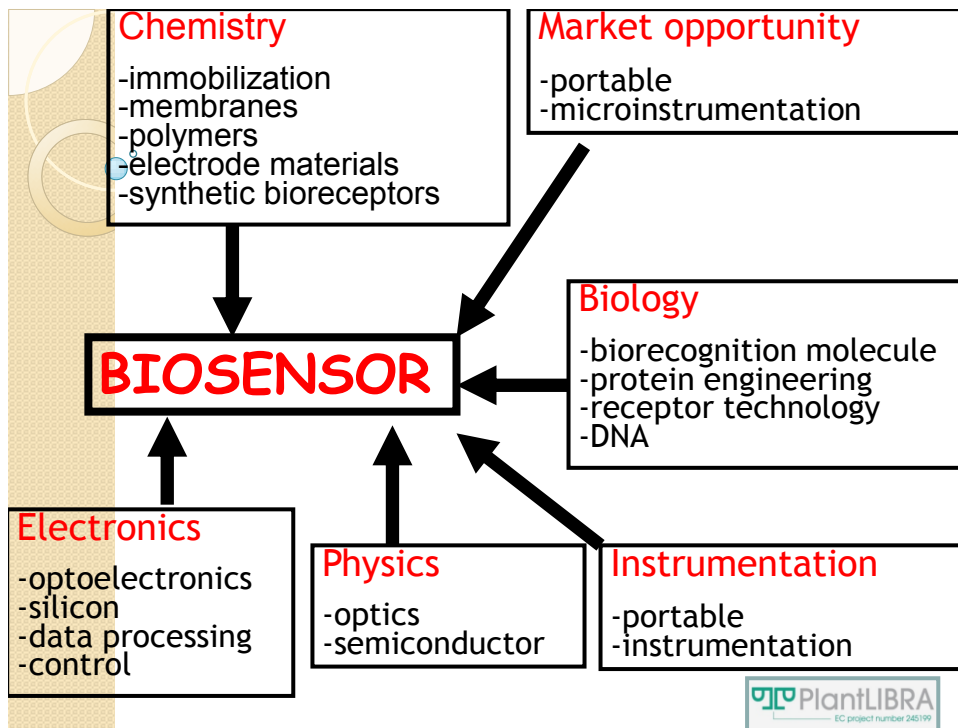
Biosensor



The Open Electrochemistry Journal, 2010, Volume 2

History of biosensors

- Concept - Lyons and Clark (1956)
- Urea Sensor - Guibault & Montalvo (1969)
- Glucose Analyser - Yellow Springs Instr. Co. (1973)
- Enzyme Thermistor – Mosbach (1974)
- Microbial Electrodes – Divis (1975)
- Fibre-Optic Oxygen Sensor – Lubbers & Opitz (1975)
- Biostator – Clemens et al. (1976)
- Immunosensor – Liedberg et al. (1982)
- Enzyme Electrode – MediSense Inc. (1987)
- BIAcore – Pharmacia, Sweden (1990)
- NanoSensor – Vo-Dinh (2000)



Biosensors in Clinical chemistry

Transducer	Mode	Applications
Ion selective electrode	Potentiometric	Ions in biological media, enzyme electrodes
Gas sensing electrode	Potentiometric	Gases, enzymes, organelles, cell or tissue electrodes
Field effect transistors	Potentiometric	Ions, gases, substrates and immunological analytes
Optoelectronic and fibre-optic devices	Optical	Hydrogen ion concentration, enzymes, immunological analytes
Thermistors	Calorimetric	Subcellular organelles, enzymes, vitamins, antibiotics
Enzyme electrodes	Amperometric	Enzymes, immunological systems
Conductimeter	Conductance	Enzyme substrates
Piezoelectric crystals	Acoustic mass	Volatile gases and vapors, antibodies

(Adopted from Malhotra *et al.* 2003)^[15]

Murugaiyan SB, Ramasamy R, Gopal N, Kuzhandaivelu V., Biosensors in clinical chemistry: An overview., Adv Biomed Res. 2014 Jan 27;3:67

Large applications – different matrices



PlantLIBRA Plant Food Supplements: Level of Intake, Benefit and Risk Assessment no. 245199

Seventh Framework Programme

Theme 2

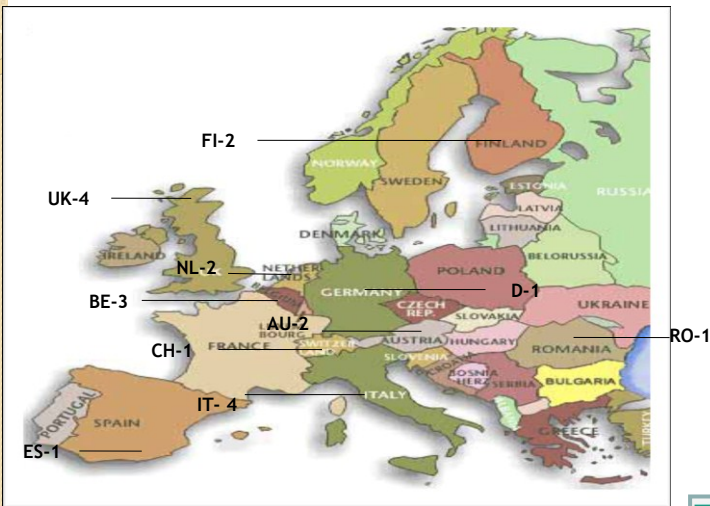
**Food, Agriculture and Fisheries, and
Biotechnology**

**Large-scale integrating project for specific
cooperation actions dedicated to international
cooperation partner countries (SICA)**

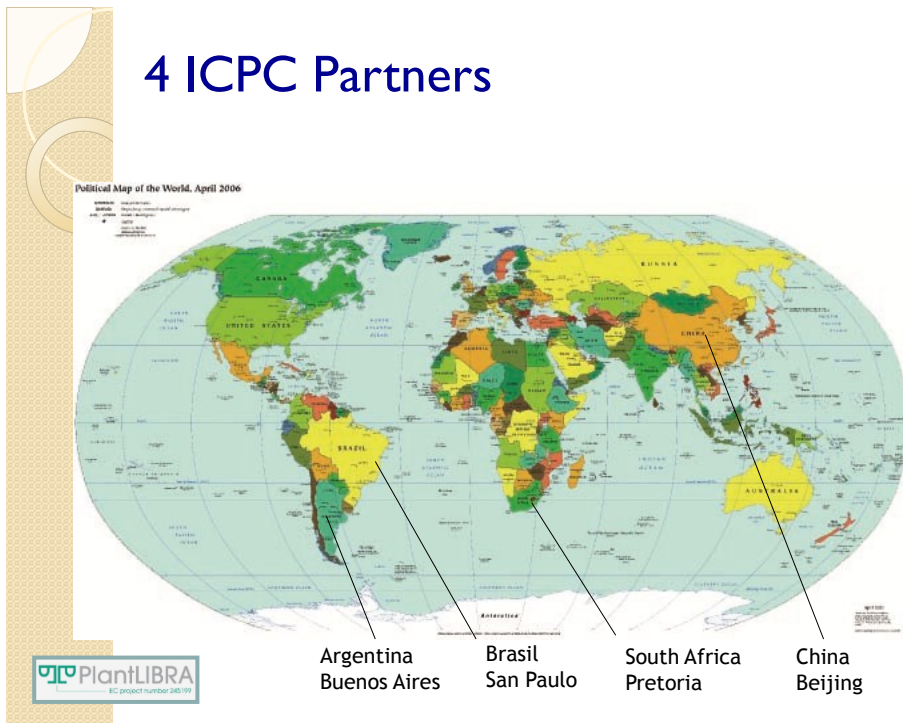


1 (coordinator)	Università degli Studi di Milano	UMIL	Italy
2	BioDetection Systems B.V.	BDS	The Netherlands
3	Council for Scientific and Industrial Research	CSIR	South Africa
4	European Advisory Services	EAS	Belgium
5	European Botanical Forum	EBF	Belgium
6	Evira	Evira	Finland
7	Fundación para la Investigación Nutricional	FIN	Spain
8	Hylobates Consulting Srl	HYLO	Italy
9	International Association for Cereal Science and Technology	ICC	Austria
10	Institute of Food Research	IFR	United Kingdom
11	Institute of Medicinal Plant Development	IMPLAD	China
12	Istituto Superiore di Sanità	ISS	Italy
13	Phytolab GmbH & Co. KG	PLFIN	Germany
14	Società Italiana Scienze e Tecniche Erboristiche	SISTE	Italy
15	Swiss Toxicological Information Center	STIC	Switzerland
16	Kansanterveyslaitos	THL	Finland
17	Hospital de Clinicas "José de San Martín", University of Buenos Aires	UBA	Argentina
18	University of Surrey	UNIS	United Kingdom
19	University of Leeds	UoL	United Kingdom
20	Universidade de São Paulo	USP	Brazil
21	Universitatea Transilvania DIN Brasov	UTBV	Romania
22	Universität Wien	VUW-Bot	Austria
23	Wageningen University	WUR	The Netherlands
24	European Food Information Resource Network AISBL	EuroFIR	Belgium
25	Department for Environment, Food and Rural Affairs	Defra	United Kingdom

21 EUROPEAN PARTNERS FROM 10 COUNTRIES



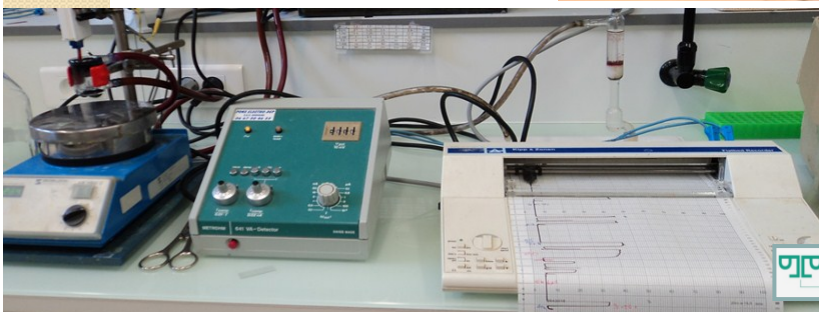
4 ICPC Partners



PlantLIBRA Work Packages

- WP1: Intake estimation of Plant Food Supplements (PFS)
- WP2: Methodology of benefit assessment for PFS, application and validation
- WP3: New concepts for the risk assessment of PFS, application and validation
- WP4: Investigation on adverse effects to botanicals and PFS: methods, biological markers, network of Poison Centres
- WP5: Integration of risk and benefit assessment models, risk benefit assessment and validation
- WP6: Meta-database of composition, biologically active compounds, safety information, residues and contaminants
- **WP7: Investigation on botanical ingredients and PFS: plant identity, methods, new compounds, toxic compounds, network of laboratories**
- WP8: Consumer and stakeholder perceptions of PFS
- WP9: Dissemination, international cooperation and stakeholders
- WP10: Policy implications
- WP11: Management

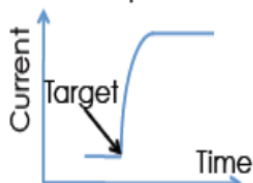
ELECTROCHEMICAL BIOSENSORS



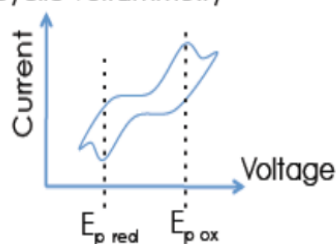
PlantLIBRA
EC project number 245199

Electrochemical Measurements

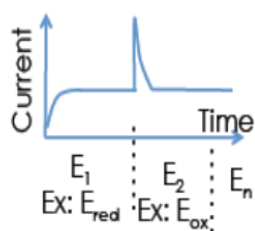
Amperometry
at fixed potential



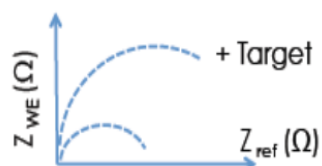
Cyclic voltammetry



Chronoamperometry



Impedance : The opposition of WE to the passage of an **Alternative** current when a voltage $E = (E_{p \text{ red}} + E_{p \text{ ox}})/2$ is applied



Electroanalysis in telemedicine

- Quantification of compounds – **urine, serum, blood**
- Electrochemical detection of **glucose, lactate, uric acid** from biological samples

➔ Badea M., Idomir M., Florescu M., Rogoza L., *Electrochemical Sensing in Telemedicine (A Review)*, in Sensing in Electroanalysis, Vol. 6 (Kalcher K., Metelka R., Švancara I., Vytřas K.; Eds.), pp. 149-156, 2011, University Press Centre, Pardubice, Czech Republic. ISBN 978-80-7395-434-5 (printed); 978-80-7395-435-2 (on-line)

Biological receptor for contaminants detection

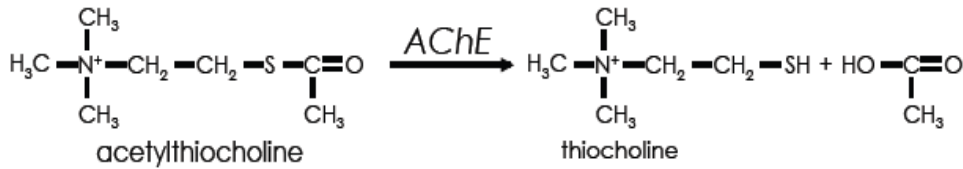
- Antibodies
- Enzymes – commercial and/or mutants
- Aptamers
- Molecular imprinted polymers - MIPs



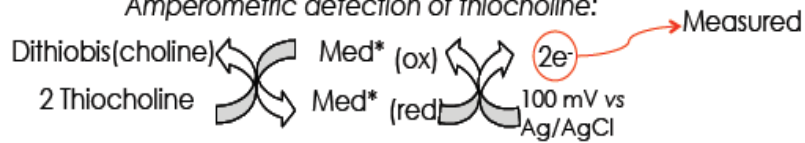
Acetylcholinesterase-based biosensor

Detection Principle

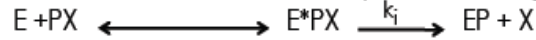
Acetylcholinesterase (AChE) hydrolyzes acetylthiocholine to thiocholine:



Amperometric detection of thiocholine:



OP & Carbamate inhibit the AChE & Block acetylthiocholine degradation:

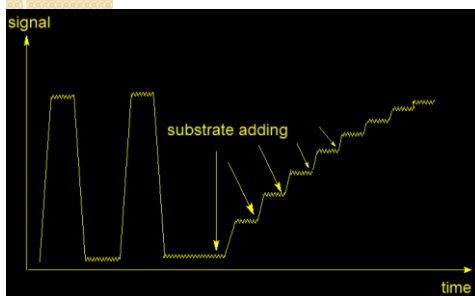


E: AChE, PX: carbamate or OP, X: leaving group, k_i : constant of inhibition

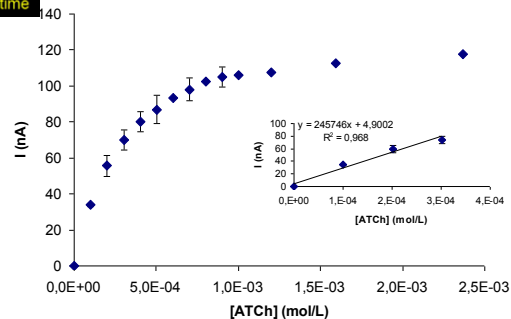
Med = Tetracyanoquinodimethane (TCNQ), Cobalt phthalocyanine (CoPh), or PEDOT:PSS



Calibration of the biosensors



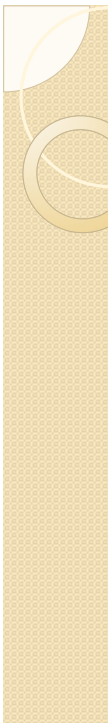
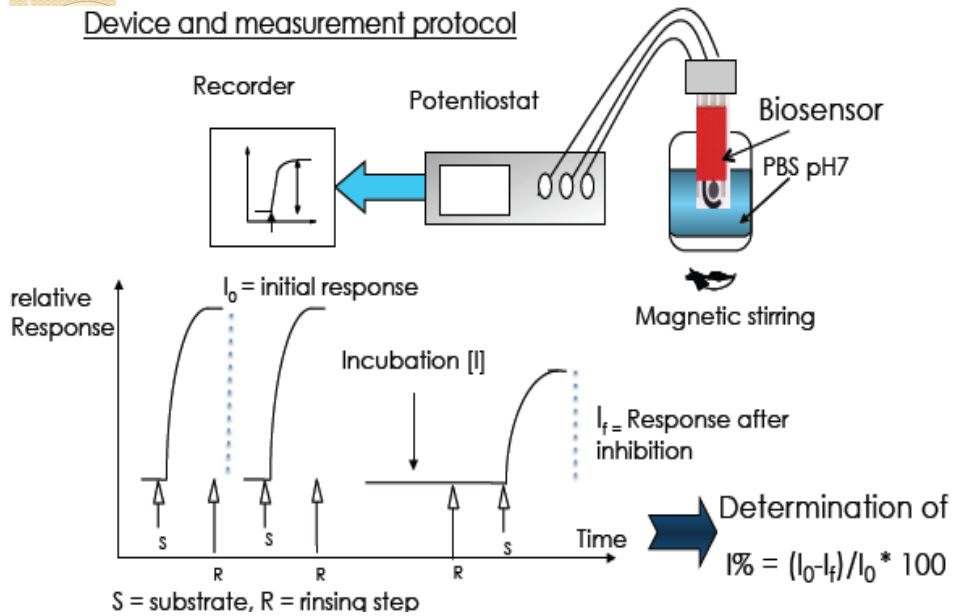
Immobilization of AChE
with sol-gel method ;
Working potential 100mV vs. Ag/AgCl



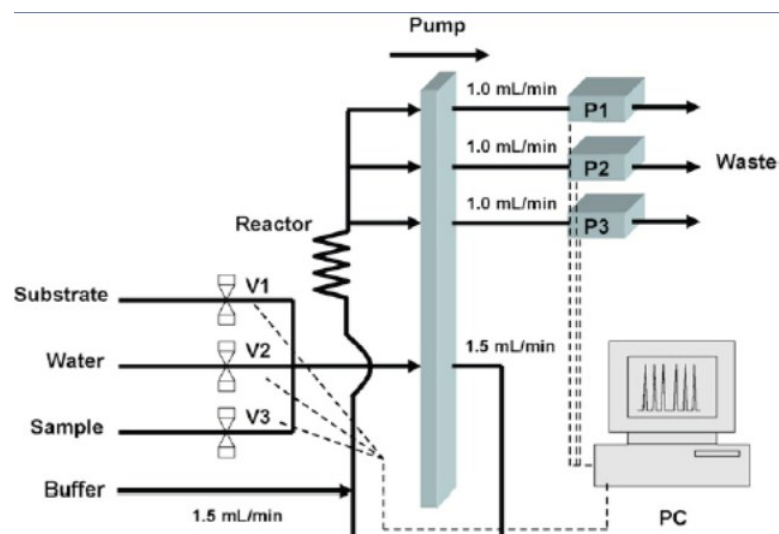


Amperometric measurements

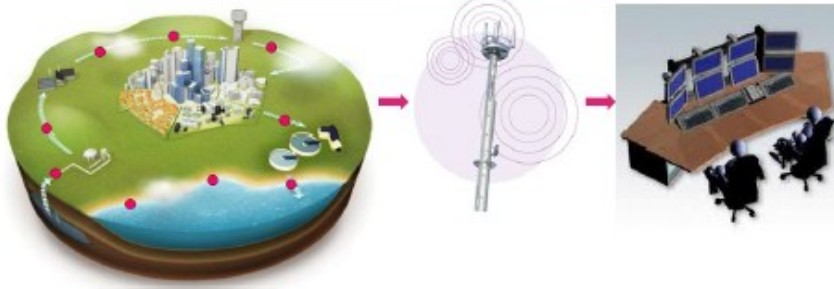
Device and measurement protocol



Multidetetection – flow injection



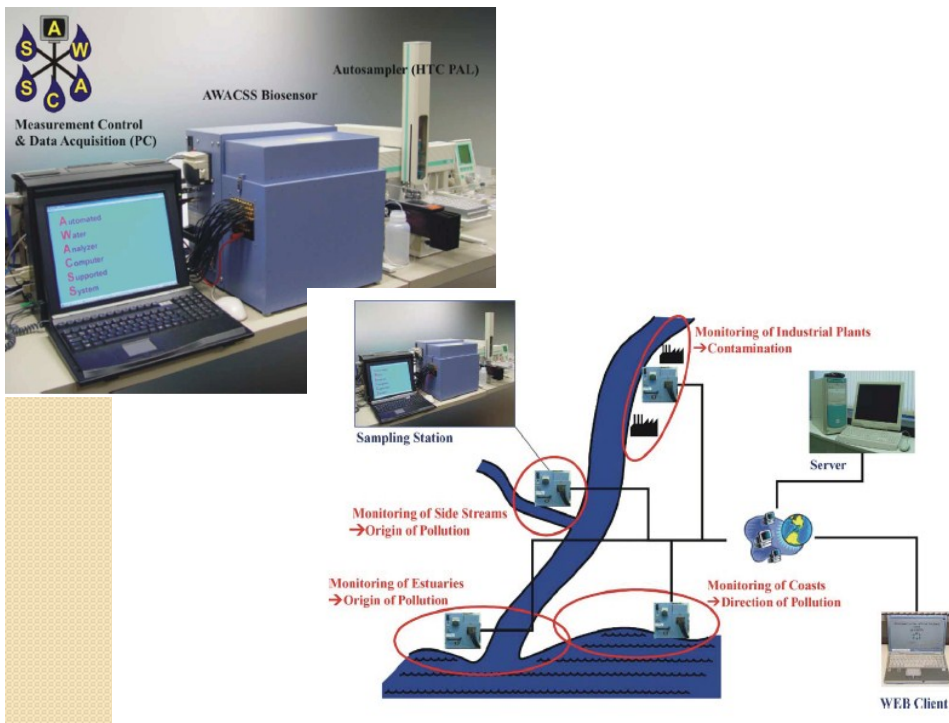
Aim : biosensors network



TODAY

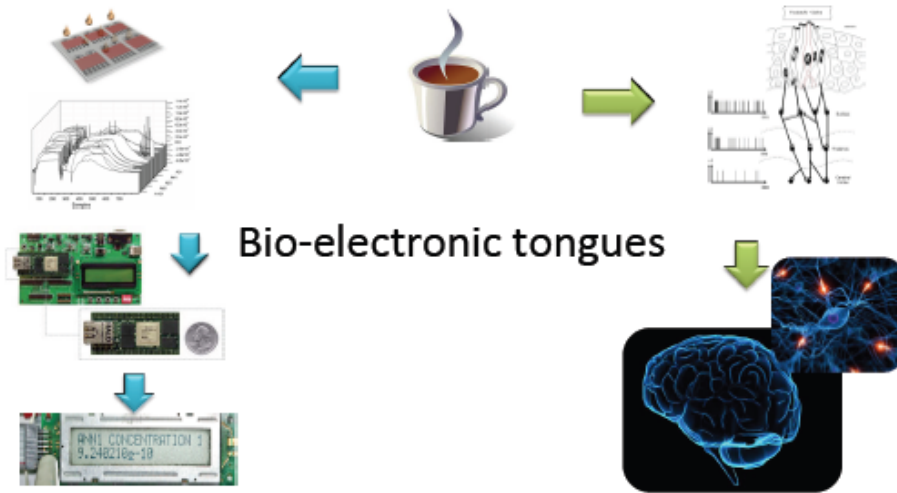


TOMORROW



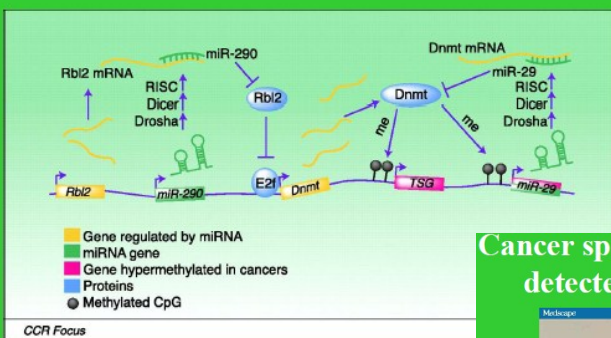


Bioelectronic tongues



8

Cancer diagnostic approaches: specific nucleic acid methylation

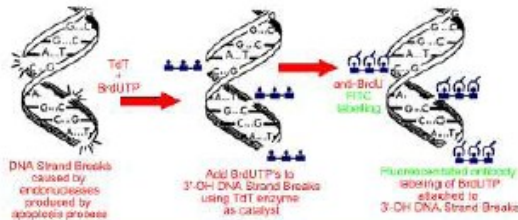


Cancer specific DNA methylation detected by telemonitoring

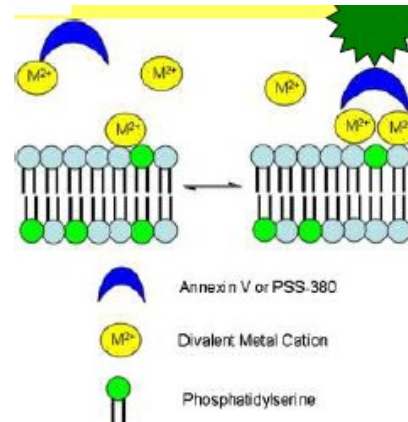
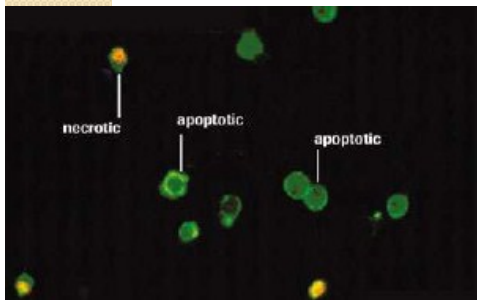


Source: Peter Obein (St. 10) 2012. Centers for Disease Control and Prevention (CDC)

APO-BrdU TUNEL Assay Diagram



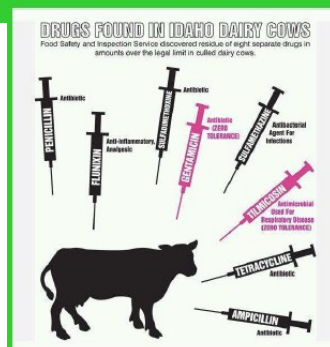
**Apoptosis test
- fluorescence
microscopy**



Biosensors in food quality assessment

- Spectroscopy:
 - Absorbance
 - Fluorescence
 - Chemiluminescence
- SPR
- DNA microarray
- Electrochemical techniques
- Immunological methods

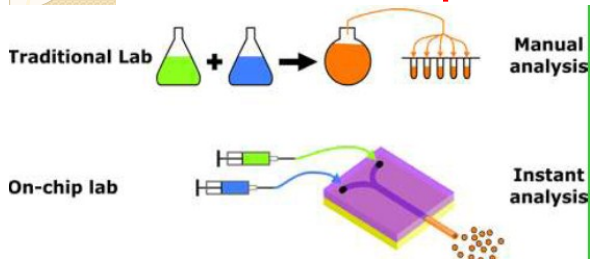
How to detect?



- Microbes
- Mycotoxins
- Heavy metals
- Organic pollutants
- Pesticides



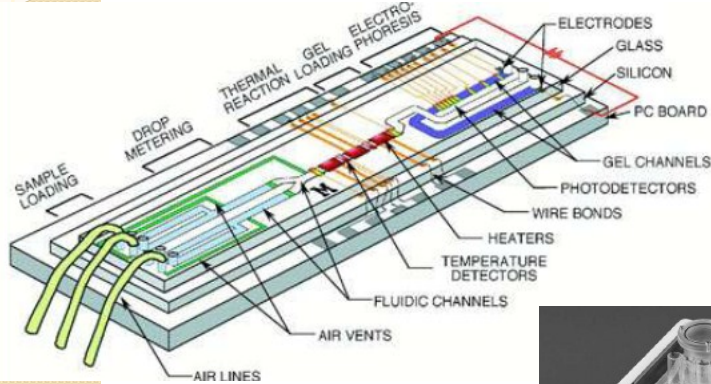
Lab on a chip technology



Redrawn from: Brivio, M., Verboom, W., & Reinhoudt, D. N. (2006). Miniaturized continuous flow reaction vessels: influence on chemical reactions. *Lab on a Chip*, 6, p. 329.



Lab on a chip technology - separation



Lab on a chip
technology
– mycotoxin detection



Biosensors/Analytical Techniques

- | | |
|------------------------------------|--------------------------------|
| + Real time detection | - Time consuming |
| + Cost effective | - Expensive |
| + Portable (Insitu monitoring) | - Laboratory monitoring |
| + Simple use | - Trained laboratory personnel |
| + Simple apparatus | - High tech equipment |
| + Limited sample preparation | - Extensive sample preparation |
| + Less organic solvent consumption | - Organic solvent consumption |
| - Single analyte detection | + Multianalyte detection |
| - Limited commercial availability | + Commercial availability |
| - Non standardized | + Standardized |
| + Sensitive | + Sensitive |
| + Specific | + Specific |
| + Reusable | + Reusable |

Acknowledgements

- *The research leading to these results has received partial funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 245199. It has been carried out within the PlantLIBRA project (website: www.plantlibra.eu). This report does not necessarily reflect the Commission views or its future policy on this area*

Partners

UTBV

- Mihaela Badea, Monica Florescu, Angela Marculescu, Lorena Dima, Laura Floroian, Gheorghe Coman, Liliana Rogozea, Marius Moga, Carmen Buzea

Collaborators

- Simone Romano, Alice Paneratti, Arianna Scollo, Aurora Perini, Patrizia Restani – University of Milan, Italy
- Jean Louis Marty – University of Perpignan Via Domitia, France
- Alina Vasilescu – Research Center of Biodynamics, Bucharest, Romania
- Tamas Koszegi, University of Pecs, Hungary...

International Conference

New Trends on Sensing- Monitoring-Telediagnosis for Life Sciences

July 24-26, 2014, Brasov, Romania - smt.ls.2014@gmail.com

Telediagnosis for Medicine

- Analytical and bioanalytical methods for screening and diagnosis in medicine
- Telemedicine and e-Health
- Personalized medicine
- Improving health information, data exploitation and providing an evidence base for health policies and regulation
- Social innovations to improve the quality of life and well-being of older people
- Active ageing, independent and assisted living
- Improving health promotion & disease prevention
- Assessment of disease susceptibility and diagnosis

Integrative Environmental Sciences

- Environmental pollution and its effects on health
- Environmental pollution -sensing, telemonitoring and modeling of environmental factors
- Environmental toxicology
- Risk assessment of contaminated environments

New Trends in Biomedical Engineering Sciences

- Electronic medical devices
- Data and signal processing
- Medical image processing
- Biomedical computing and simulation
- Personalized electronic tools for effective virtual rehabilitation environment after a stroke.

Thank you for your attention!

For contact concerning the conference

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