L2: Laboratory for Microsystems in biomedical and environmental applications

- Mission
- Main expertise
- International Networks
- National Networks
- Research Team

• The **Mission** of the laboratory for microsystems in bio-medical and environmental applications is research, focused on the development of microsensors (chemo resistive and resonant gas sensors), electrodes for biological sensors, micro-probes for recording of electrical activity of cells and tissues, education in the field of micro chemo and biosensors (in cooperation with University "Politehnica" of Bucharest), and services in design, simulation and technology for bio- and chemo-applications.

• **Main expertise:** development of a large area of microsensors (chemoresistive, resonant gas sensors, accelerometers, microarrays, ISFET (Ion Sensitive Field Effect Transistors) sensors, electrodes for biological sensors, microprobes for recording of electrical activity of cells and tissues), in terms of software simulations / modelling, using MEMS–specific CAD software (CoventorWare, CADENCE), technological development and electrical characterisation. Our team was working in 20 national projects during the last 5 years, and is currently involved in 10 FP6 projects (Networks of Excellence, Integrated Projects, Concerted Actions and Specific Support Actions).

The laboratory is involved in several **national** and **FP6 projects and networks**.

• **International projects:** INTEGRAMplus ("Integrated MNT platforms and services – Service Action") – FP6 IP, IST, 2006 – 2008, TOXICHIP ("Development of a toxin screening multi-parameter on-line biochip system") – FP6 STREP, IST, 2006 – 2009; networks: PATENT-DfMM ("Design for Micro and Nano Manufacture") – FP6 IST NoE, 2004 – 2007, 4M ("Multi-Material Micro Manufacture: Technologies and Applications") – FP6 NMP NoE, 2004 – 2008.

• **National projects:** RO-NANOMED ("Integrated Research Network Devoted to Nanobiotechnology for Health – Romanian Nanomedicine Network); RTN-NANOEL ("Romanian Technological Network for integration in the European Platform for NANOELectronics ENIAC") – both are CEEX complex projects – technological networks.

• **Research team:**
The Laboratory **team** includes 12 people, seniors and young researchers with multidisciplinary expertise (microelectronics, physics, chemistry, biology).

Team from left to right: Cladia Roman; Carmen Moldovan; Boagdan Firtat; Rodica Iosub; Cristina Pachiu; Marian Ion;

Laboratory Head - Dr. Carmen Moldovan (cmoldovan@imt.ro)

Dr. Carmen MOLDOVAN, the head of the laboratory, is also the Head of the Microtechnology Department within the National Institute for R&D in Microtechnologies and Associated Professor at the Faculty of Electronics and Telecommunications, University "Politehnica" of Bucharest.

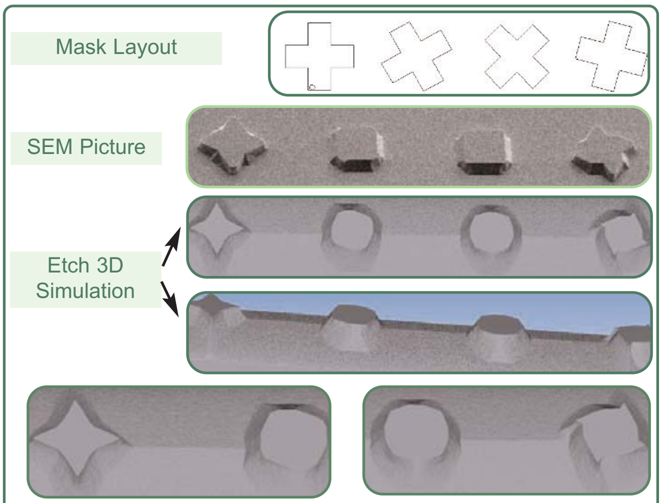
She graduated on Electronics and Telecommunications and she owns a PhD in Microsensors.

She is contact person for IMT in INTEGRAMplus (FP6 project) within EUROPRACTICE. Dr. Moldovan is the vice-coordinator of the FP 6 SSA "Micro and Nanotechnologies going to Eastern Europe through Networking (MINAEAST-NET)" and "ROManian Inventory and NETworking for Integration in ERA (ROMNET-ERA)". She is involved in the **4M** NoE (NMP), working on demonstrators, in Ceramic cluster, having the goal to integrate a non-standard micromachining processes to a ceramic substrate and in the Sensors and Actuators cluster, in the **PATENT-DfMM** NoE (IST), in **INTEGRAMplus** IP (IST), dealing with technology convergence and integration and virtual design and manufacturing and **TOXICHIP** STREP (IST), as responsible for the development of temperature and pH sensors.

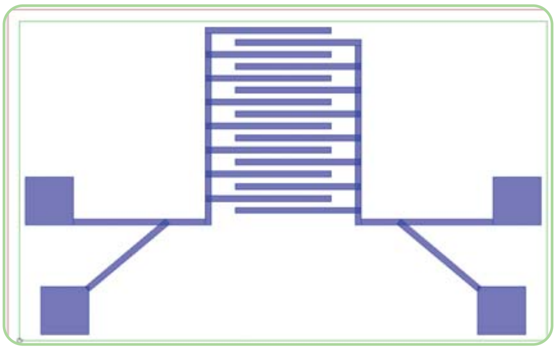
She is a **member of: IEEE and Science and Technology Commission of the Romanian Academy** and **NEXUS-PLUS** and **BRIDGE** subcontractor (and also a *member of the NEXUSPLUS Steering Committee*). The scientific activity is published in more than 55 papers in journals, books and communications in Proceedings.

E-mail: cmoldovan@imt.ro

The simulations were performed by modifying the internal program parameters in such a way to tune them for the maximum precision compared to the real silicon wet etchings performed in the lab. The simulations were performed using both KOH and TMAH as etchants.
Examples of simulations vs. real etchings, for KOH, 80ºC, 40% concentration:



Etch 3D Simulation (details)


Interdigital electrodes for biomaterials deposition

Also, IMT was responsible for the interdigital electrodes design and fabrication, for biomaterials deposition. Corresponding masks were fabricated and the wafers were processed. The chip will have bio-materials deposited on the inter-digital electrodes area and it will be integrated in a microfluidics module, for the biomaterials characterization. Two dimensions are available for the microelectrodes: 4.6 mm x 2.8 mm and 2.7mm x 1.7 mm. The microfluidic channels are covering the interdigitated microelectrodes, leaving the pads for electrical connections outside the channels.

Development of a toxin screening multi-parameter on-line biochip system

Acronym: **ToxiChip**, **STREP**, Priority 2 -**IST**, Contract Number: 027900, 2006-2009,
Coordinator: PhD. Eric Moore, e-maileric.moore@tyndall.ie; Univ College Cork - National University of Ireland.
http://www.toxichip.org

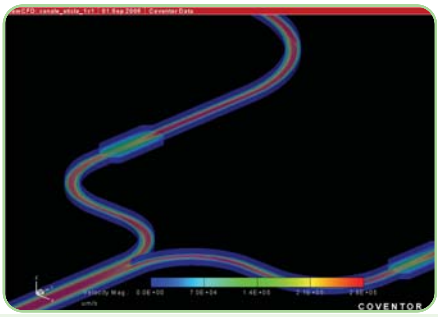
Within TOXICHIP, IMT is responsible for the **development of a temperature sensor, as well as a pH sensor, that will be integrated with the micro-fluidic platforms.** This objective will be carried out within WP4 (Development of Sensor Platforms), led by IMT. It will also include the development of the data acquisition system to be used with these platforms.

IMT's SPECIFIC ACTIVITIES in TOXICHIP:

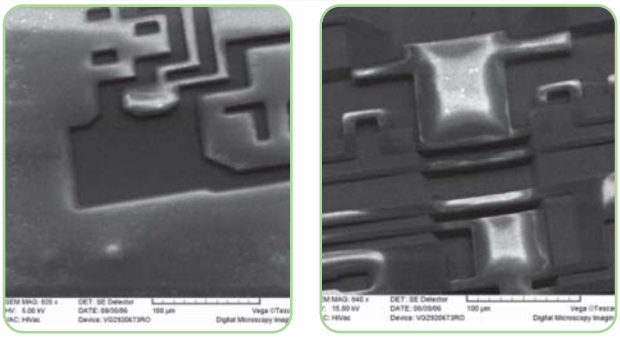
- ***Development of temperature sensor integrated with the microfluidic platform:***
  - Simulation and design of the temperature sensor together with the microfluidic part where the sensor is integrated;
  - Study of the compatibility of the sensor with the chemical aggressive working environment;
  - Biocompatibility of the microsensor materials with the biological media;
  - Experiments, manufacturing design and testing;
- Development of pH sensors integrated with the microfluidic platform:
  - Simulation and design of the pH sensor together with the microfluidic part where the sensor is positioned;
  - Development of materials, manufacturing steps, experiments and testing;
- ***Development of the data acquisition system:***
  - Methodology on the data acquisition system;
  - Design and implementation of the data acquisition system

RESULTS in TOXICHIP:

IMT has provided microfluidics simulations (using CoventorWare), in order to analyse the designed microchannels behaviour at specific fluid flow rates. Also, IMT has developed the initial layout of the microchannels platform and worked on partial experiments for the technological implementation of the sensors platform.



Microchannels simulations (fluid flow detail)


SEM pictures: integrated sensors experiments

L2: Participation to NoE's, IP's, STREP's in FP6

MULTI-MATERIAL MICRO MANUFACTURE: Technologies and Applications

Acronym: **4M**; Priority: 3- **NMP**; Instrument: Network of excellence **NoE**; 2004-2008

Coordinator: Dr. Stefan Dimov; Cardiff University; **e-mail: dimov@cardiff.ak.uk**; **http://www.4m-net.org/**

Within **4M**, IMT has an important role in several 4M clusters: *Polymers, Ceramics, Micro-Optics, Micro-Sensors and Actuators*, and also in integrating activities (assembling a critical mass in different research domains).

IMT's SPECIFIC ACTIVITIES in 4M:

• polymer and ceramics processing
• micro-fluidics – micro-manufacture platforms for high pressure & high temperature applications; micro-fluidic manufacturing operations: compatible tooling and machining processes
• micro-optics – manufacturing of micro-moulds with free form surfaces in different kind of materials; assembly and testing of micro-optical systems
• micro-sensors and actuators – simulation and design (COVENTOR, IE 3D Fidelity, ANSYS, OptiFDTD), micromachining, thin layers deposition, photo-lithography, masks fabrication, SEM, AFM, electrical characterization, packaging
• micro-components produced in different materials including IC-compatible ones

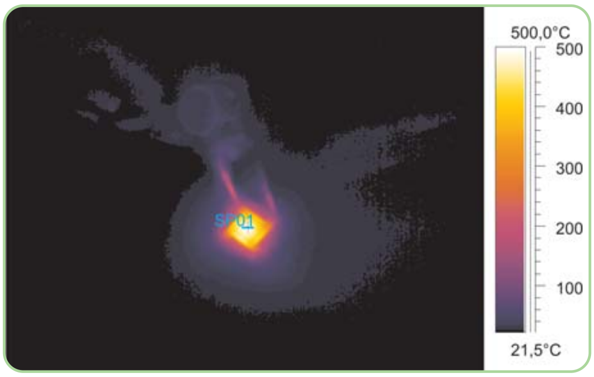
RESULTS in 4M:

Mixed technologies for gas sensors microfabrication

The main goal was developing a novel class of chemoresistive gas sensors, miniaturized, low cost and with low power consumption, by using mixed techniques such as: laser milling techniques, conductive ceramic technology, thin film technology, bulk micromachining techniques.

The sensor's operating principle is change in conductivity due to the chemisorption of gas molecules at the sensitive layer surface. Small quantities of gas can be detected by measuring the resistance of an interdigitated capacitor with a sensitive film deposited on top.

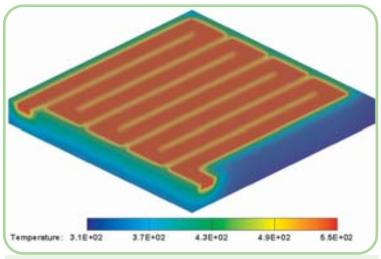
• **Ceramic Micro Heater Technology for Gas Sensors**



Heat distribution from the released heating element

The micro heaters are designed and fabricated by combining laser milling techniques and conductive ceramic technology. Trenches are created in the ceramic substrate in order to define the geometry of the heater using laser processing of the substrate. The heater is completed by filling the trenches with conductive ceramic paste and then baking to remove the solvent from the paste.

The temperature of the heater element was measured with a heat camera from FLIR 40 system comparing the case of the heater positioned on top of a released membrane and that of the non-released membrane. The heater reaches about 490° C in 5 seconds.


Thermal distribution after 0.02s at 550°C

The results indicated a very uniform thermal distribution in the sensor substrate to be used in gas sensors microfabrication.

Results obtained in cooperation with 4M Ceramic Cluster.

Multi-domain platforms for integrated micro-nano technology systems – *Service Action*

Acronym: **INTERGRAMplus**, **IP**, Priority 2 -**IST**, Contract no.: 027540; 2005-2007

Coordinator: Chris Pickering; **e-mail:** cpickerig@qinetiq.com; **QinetiQ Ltd**, UK.; **http://www.integramplus.com**

Within INTEGRAMplus, IMT is involved in different ACTIVITIES, corresponding to different project tasks:

Related to Design and virtual manufacture, IMT deals with modelling and simulation for MEMS, optical and microfluidic devices as well as Silicon-Polymer hybrid simulation. Different tools will be used and analysed in order to provide complete and comparative modelling for multi-domain design and simulation.

IMT is involved also in the Technology convergence and integration activities, acting in microfluidic simulation (3-D models and fluidic functions), developing methodologies for integration of bio-materials into micro and nanosystems, including new processes for biomaterials deposition, packaging and measurement.

Due to it's previous experience from FP6 SSA projects, IMT has also training and educational activities, developing new training modules for the INTEGRAMplus portfolio, preparing and delivering courses, training visits (presenting and visiting the technological facilities), organizing regional events for Eastern participants to attract industry as potential users of the project services.

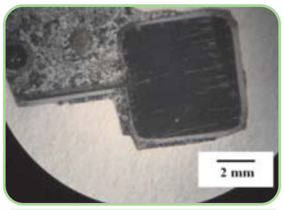
RESULTS in INTEGRAMplus:

IMT worked on calibrating a CAD tool (Etch 3D, from Coventor, Inc.) for simulating the silicon anisotropic etching. This was done by etching silicon wafers with a test mask (containing very "sensible" shapes) and comparing the results with the simulations.

DIAMOND-LIKE CARBON BASED BIOMEDICAL MEMS

An implantable probe for electrical activity monitoring of the living tissues was engineered and fabricated on a silicon chip. In order to improve the mechanical resistance and the biocompatibility of the device, an original technology was used for coating the implantable parts with diamond like (DLC)/carbon zero stress (CS0) films.

The microprobe was packaged using copper wire bonding, in order to allow the electrical signals reading and processing. The electronics accomplish the separation and reduction of the biological noise recording.



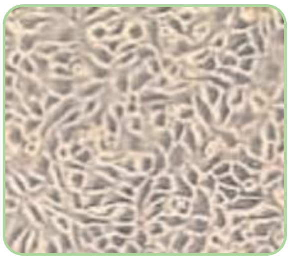
SEM picture of the device

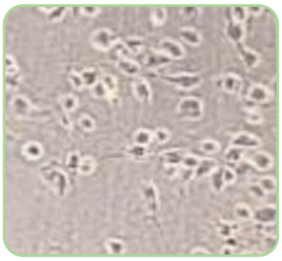

Pen-shape microprobe mounted on an electrical board

Packaging in “pen” shape allows the device handling in biological environments, respectively insertion of small quantities of liquids in tissues and cells.

The microprobe functionality was tested in vivo and in vitro, in specialized laboratories, by recording electrical signals from cells cultures and mice organs. The impedance measurements revealed different values for different tissues and organs, but reproducible at the same tissue/organ level.

Biocompatibility tests were performed at the National Institute for Chemical-Pharmaceutical R&D on implantable microprobes, coated with DLC/CS0, introduced in cells cultures. The standard procedure was based on citotoxicity tests in vitro, using fibroblasts cells L929. The cells viability was estimated by functional tests (evaluation of cells breath, MTT and MTS tests, protein synthesis, DNA quantification) and permeability tests.


Cells culture L929
untreated reference sample

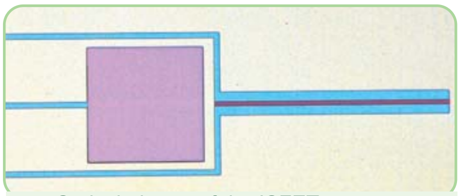

Cells culture L929
citotoxicity control

An improvement of cells adhesion and growth was observed for microprobes coated with DLC films. The extracting and contact methods proved that no significant differences exist between the viability of the treated environment and the control one, therefore no citotoxic products from the tested materials are released into the growing cell environment.

MATNANTECH project “Advanced technologies for MEMS devices with biomedical applications, based on Diamond-Like Carbon layers” – BIOMEMS-DLC.
Project coordinator: Dr. Carmen Moldovan, IMT-Bucharest

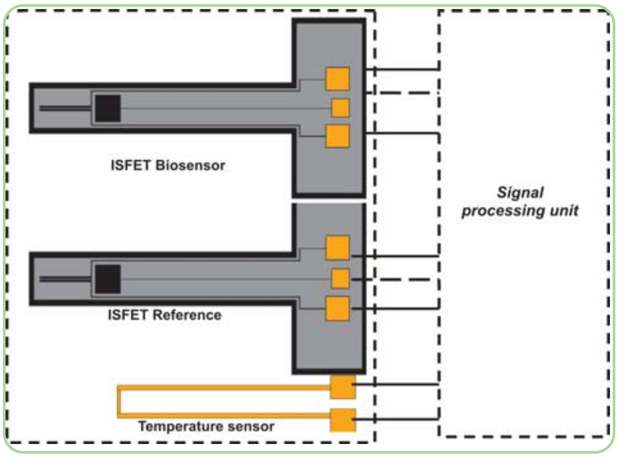
TECHNOLOGY FOR OBTAINING BIOSENSORS FOR BIOTERRORISM TOXINS DETECTION

The project aims to develop the technology for manufacturing a micro-system to monitor and detect toxins from natural environments (water, air, food). The integrated microsystem includes the biosensor that permits electrical measurements of several toxins and electronic circuits for signal processing.


Optical picture of the ISFET structure (source-drain and gate)

Field effect gas sensors are based on metal-insulator-semiconductor structures in which the enzyme deposited on the gate is detecting the toxins presence. ISFET sensors use the field effect transistors to detect very small quantities (10-3 g). Examples are biological and medical applications. The ISFET is essentially an extended gate field effect transistor with the surface of the transistor and the reference electrode.

SECURITY project Technology for obtaining biosensors for bioterrorism toxins detection” – TOXISISTEM.
Project coordinator: Dr. Carmen Moldovan, IMT-Bucharest



BIOSENSORS FOR NEUROTOXIC SUBSTANCES DETECTION

The biosensors for neurotoxic substances will be developed as ISFET-type biosensors. The ISFET structure is represented by a concentration-potential transducer, with a biosensitive layer deposited on the gate (acetyl-cholinesterases, immobilised on chitosane), which generates an interface potential on the gate.

The enzymatic ISFET structure is developed in CMOS technology and the sensor’s response characteristics depend mainly on the AChE enzyme immobilisation mode.