Biom'@x

Sciences et technologies:
towards a technological translational medicine

femto-st
SCIENCES &
TECHNOLOGIES

FEMTO-ST is a public research institute located in the Bourgogne Franche-Comté region, east of France, next to Switzerland and Germany.

The general aim of the FEMTO-ST institute is to master micro and nanotechnologies, develop new devices and systems, optimise thie performances, find new functions for them ans make them «smart».

It is organized in 7 scientific departments (robotics & automation, digital information science, energy, applied mechanics, micro-nano-sciences and systems, optics, RF and microwave metrology), with an average number of collaborators of about 750 members (PhD students, postdocs, technicians, engineers, administrative staff, researchers and professors).

FEMTO-ST members are essentially employed by four different French public research and higher education institutions: National Center for Scientific Research (CNRS), University of Franche-Comté, CNRS, National Engineering Institute of Mechanics and Microtechnology, University of Technology Belfort-Montbéliard, the three latter being now gathered under the common banner of a unique federal regional university, University Bourgogne Franche-Comté (UBFC).

Our activities cover obviously many different themes within the broad discipline of engineering sciences, from fundamentals to applications. Each scientific department dedicates intense efforts to obtain world class level scientific results in its own area. Beyond these internationally recognized focused expertise, we also have a strong dedication to cross-disciplinary interactions whenever it appears both relevant and with high innovative scientific and technological breakthrough potentials.

FEMTO-ST is a joint Research Institute from:

membres de

Biom'@x

SCIENCES ET TECHNOLOGIES:
TOWARDS A TECHNOLOGICAL TRANSLATIONAL MEDICINE

Biom'@x is a pluri-science research axis aiming at developing smart devices able to understand (as fully as possible) a living system under study. This understanding should lead to the determination of behavior laws that, through prognostic approaches, allows anticipating the evolution of these systems with the ulterior motive of personalizing the therapeutic strategies.

This program is fueled by the wide disciplinary spectrum of the FEMTO-ST Institute, in particular in micro and nano-technologies, robotics, informatics, automation, optics, biomechanics, proteomics and e-health. The goal is to solve scientific and technological biomedical obstacles as well as to develop new paradigm in order to tend to a trans-disciplinary vision of research in health domain.

Biom'@x researchers are not only already recognized at the national and international level through their disciplinary work, they also benefit from a strong interaction with Besançon's University Hospital (in particular the Clinical Investigation Center CIC1431), the biology and medicine research local centers, higher education units, especially in the biomedical and micro techniques fields, and the industry, in a privileged "Research-Translation-Transfer" environment in Franche-Comté.

The next pages summarize projects conducted in the frame of Biom'@x.

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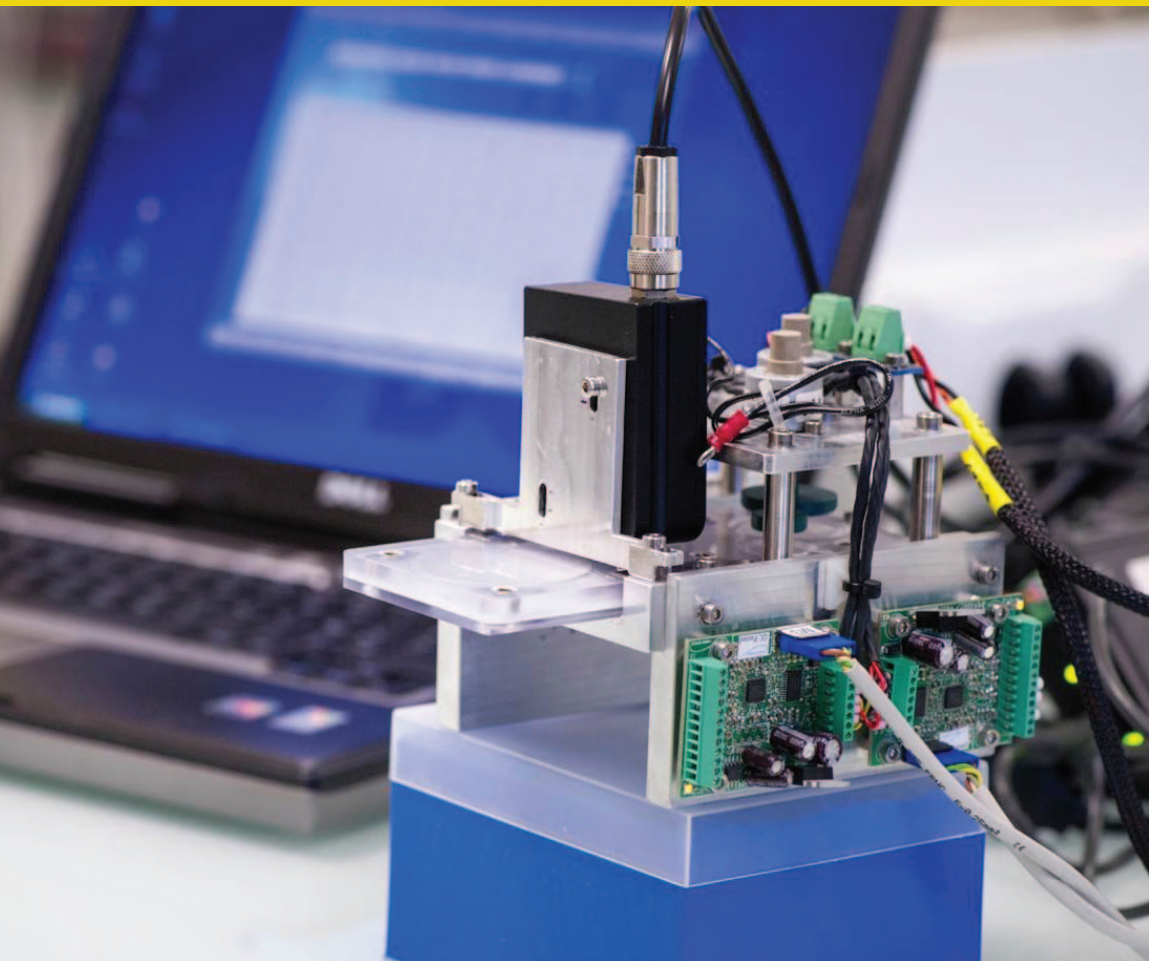
WATCH THE VIDEO
http://bit.ly/2ExpLjM

Décembre 2017

femto-st SCIENCES & TECHNOLOGIES

Biom'@x

PAST PROJECTS

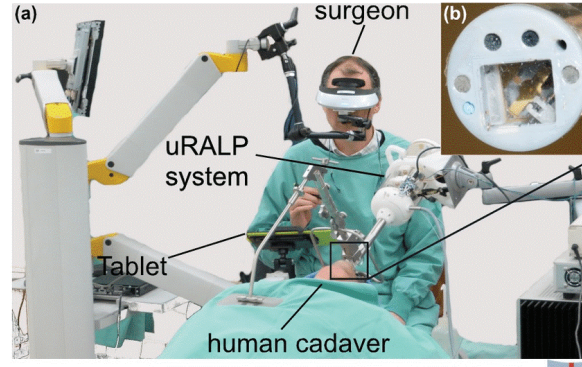


µRALP

MICRO-TECHNOLOGIES AND SYSTEMS FOR ROBOT-ASSISTED LASER PHONOMICROSURGERY

Lasers form an increasingly common tool for precision treatment of pathological conditions on delicate and vital human organs such as the vocal folds. However, laser aiming control still relies completely on the dexterity of surgeons who must operate through a microscope and deals with its associated poor ergonomics. This can have a strong impact on the quality of the procedures. Additionally, in laser phonomicrosurgery, the laser beam is directed from a comparatively large range (400mm), resulting in accuracy and consistency problems that require extensive surgeon training.

In this project a redesign of the surgical setup is proposed to create an advanced micro-surgical system that will allow unprecedented levels of accessibility, controllability, precision and safety during these procedures, resulting in enhanced surgical and patient outcomes. The new technologies developed herein will pave the way towards new and safer minimally invasive laser microsurgeries, leading to a significantly enhanced capacity for cancer treatment in general.



DURATION

2012 - 2015

FUNDING

FP7 European project: 2.6 M€
Internal Project Call at Besançon University Hospital: 60k€

CONTACT

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ABORDAGE

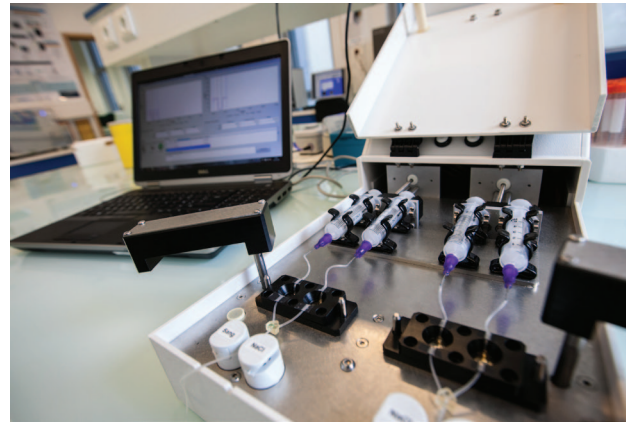
OPTICAL DETECTION OF RED BLOOD CELLS CAPTURED ON BIOCHIPS FOR RH1 COMPATIBILITY CONTROL AT THE PATIENT'S BEDSIDE

Rhesus antigen are very immunogenic and can lead to a rhesus incompatibility (RH1 also known as D antigen). Rhesus incompatibility is the result of 2 main mechanisms. The first concerns RH-1 pregnant women in contact with RH1 red cells of her fetus. In this case RH incompatibility results in an anemia (moderate to severe) or leads to the *in utero* death of the fetus. The second results from a RH1 incompatible transfusion.

In France, an ABO compatibility test is performed before each red cells concentrate transfusion at the patient's bed side. However, RH compatibility is not checked.

During the SmarTTransfuser project, we developed both biochips and an optical medical device used to automatically perform an ABO compatibility test at the patient's bed. Based on this project, ABORDAGE aims at developing an immuno-biochip able to specifically capture red cells according to their rhesus status. Again, the device is automated and can be used at the patient's bed.

ABORDAGE project is led by the Clinical Investigation Center at Besançon University Hospital in collaboration with FEMTO-ST and the Etablissement Français du Sang Bourgogne Franche-Comté.



DURATION

2013-2015

FUNDING

Internal Project Call at Besançon University Hospital: 60k€

CONTACT

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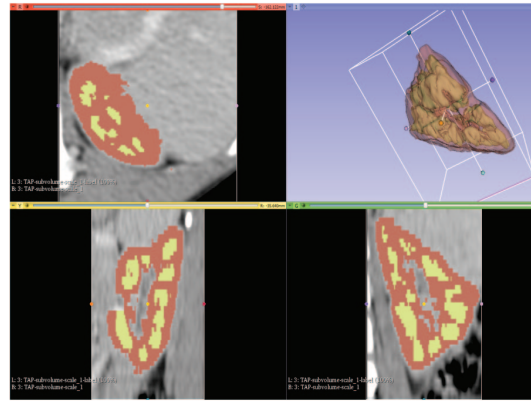
ASKid

AUTOMATIC SEGMENTATION TUMOURS IN CHILDREN USING ARTIFICIAL INTELLIGENCE OF KIDNEY

Nephroblastoma is a cancer disease for which diagnosis, surgery decision and planification are based on imagery exclusively. 3D reconstructions allow surgeons obtaining a representation of the volumes of the different structures around the kidneys, the kidneys themselves and the tumour. This 3D reconstruction requires segmentations of all the scans of the patient abdomen (more or less 250 images). The problem is that the actual segmentation tools require the help and the expertise of surgeons in order to be accurate enough. Thus, this semi-automatic step is time-consuming (11 hours for one patient) and, as a consequence, surgeons usually do not take the time to create 3D representations and base their diagnosis, interpretation and planification using only 2D scans.

The difficulty and imprecision of the automatisation of this segmentation step increases with children which do not have fat that clearly separates tumours and muscles.

The main objective of this project is to explore the possibility to enhance a segmentation method (growing region) with Case-Based Reasoning which is an Artificial Intelligence tool. We hope this tool will be able to introduce knowledge and experience to the actual segmentation process in order to build 3D representations without any human intervention.



DURATION

2016 - 2017

FUNDING

Cancéropôle Grand-Est: 14k€

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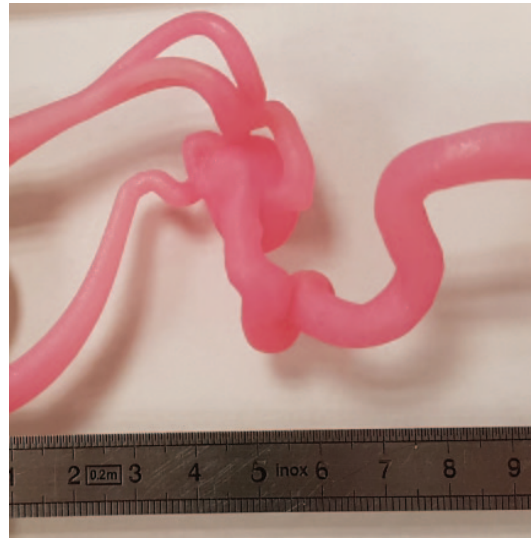
CAPTANEV

DEVELOPMENT OF AN INSTRUMENTED INTRACRANIAL ANEURYSM DEMONSTRATOR

The exponential evolution of minimally invasive treatments for neurovascular diseases, in particular intracranial aneurysms, has allowed the development of several types of endovascular devices which are convenient in case of this pathology for a personalized surgical approach. The hemodynamic phenomena observed following the implantation of the medical devices are still poorly known and nevertheless necessary to facilitate the informed choice of the implanting device adapted to the medical context of each patient.

The project involves developing an experimental test bench for the characterization of various surgical materials. It is a collaboration between the University Bourgogne Franche-comté, the Franche-Comté biomedical engineering school of the University of Franche-Comté and FEMTO-ST (department of applied mechanics – AEH team)



DURATION

2017

FUNDING

INTERREG European Project: 1.5k€

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CARMEO

DEVELOPMENT OF A DEVICE TO STUDY THE MECHANICAL PROPERTIES OF HUMAN OOCYTES

This project is in line with the development of smart systems meant to help evaluation of biological systems at the cellular level. CARMEO is focused on *in vitro* qualification of navigating cells like human oocytes. Mainly two research axes are studied.

- Study and modeling of the mechanical behavior of human oocytes using a nanoforce measurement platform previously developed at the AS2M department of FEMTO-ST.

- Development of a new characterization platform being single use, which can be integrated in a micromanupulation equipment used for intracytoplasmic sperm injection and which obeys constraints imposed by the Biomedicine Agency concerning medically assisted procreation.

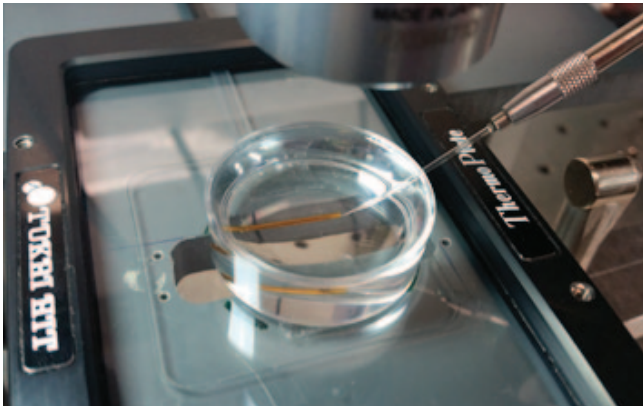
This new platform is based on an innovative magnetic force sensor. The sensor has been experimented and is now patented. Industrial transfer is ongoing in collaboration with the Clinical Investigation Center (CIC 1431) at Besançon University Hospital and is supported by the SATT Grand Est.

DURATION

2013 - 2016

FUNDING

Franche-Comté Council: 46k€
+PhD Grant



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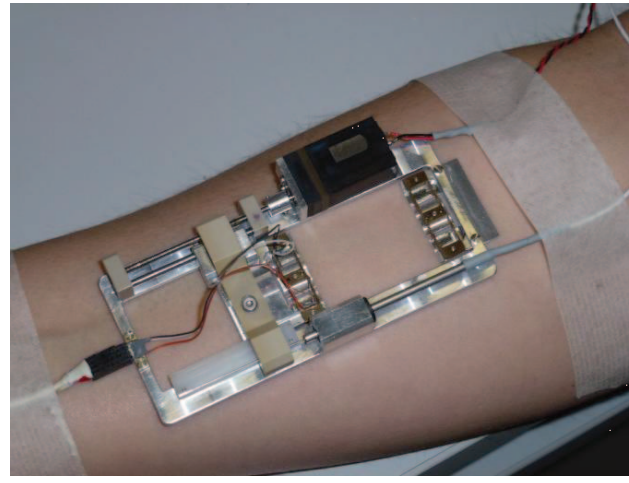
Derm'@x

SKIN PROPERTIES, MULTI-SCALE ANALYSES

The first objective of Derm'@x consists in studying the properties of the skin under a multi-modal approach « biomechanics-biophotonics ».

This multi-modal approach also benefits from computing sciences and image stitching.

The second objective consists in going furhter in the understanding the skin properties by starting studies involving functionalized local optical probes which allow simultaneously recording topology and ionic concentrations at the surface and between cells in culture. The ulterior motive concerns how mechnical sollicitations influences the skin at a cellular level.



DURATION

2014-2015

FUNDING

FEDER European Project: 617k€

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DICODERM

COLLABORATIVE DIAGNOSIS OF TUMORAL DERMATOSIS

The project consists in designing an optical probe for the detection of skin cancers. This probe is linked to sets of dedicated images and a secured and collaborative analysis. The objective is to propose a reliable tool of collaborative surveillance of the evolution of a tumoral dermatosis. The probe exploits one of the characteristics of tumoral cells: the important concentration of protoporphyn. The auto-fluorescence of the cells for which the protoporphyn rate is high allows early detecting tumours.

The probe allows a double acquisistion of white light and auto-fluorescence. The combination of both principles gives the opportunity to match the fonctional image onto the anatomic one. After the acquisitions, it is necessary to compute the positioning of each pair of images (the one in white light and the one in fluorescence). The extraction of characteristic points is performed over white light images since it is easier and more efficient than over fuorescent images. The positioning parameters describe the transformation (rotation, translation, scale, etc.) and they are used to create the final panoramic image (fluorescence).

DURATION

2009 - 2015

FUNDING

Franche-Comté Council: 50k€

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EPOMCET

STUDY OF INNOVATIVE DEVICES FOR THE MEASUREMENT OF OPTO-MECHANICAL PROPERTIES IN TISSUE AND CELLULAR BIOLOGY

Objective discriminations between healthy cells / pathological cells and healthy tissues. Innovative methods have been developed in the following areas:

1. Absorption and fluorescence spectrometry
2. OCT optical coherence tomography
3. Multispectral Imaging
4. Tissue mechanics

The overall study was structured into two main research axes, evaluation of the physical and mechanical properties of cells and tissues, in order to define biological parameters characteristics of living organisms. The analysis of optical properties of the cells has been carried out, starting from the observation that certain specific proteins (porphyrins, Cd137, ...) are stored in greater quantities in cancer cells and are possibly capable of autofluorescing. A spectroscopic optical system and a Scan Free OCT reference OCT system were developed as well as two polarization optical characterization benches to identify pathological dyphasic tissues. The mechanical properties of cutaneous tissues were evaluated experimentally on the basis of uniaxial and biaxial harmonic stress tests.

Into FEMTO-ST Institute, the departments DISC, DO et DMA have collaborated in this project.

DURATION

2010 - 2014

FUNDING

Franche-Comté Council: 107k€
Ministry of Research: PhD Grant

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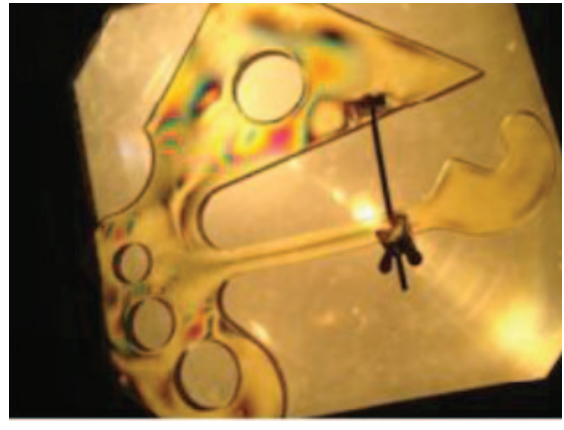


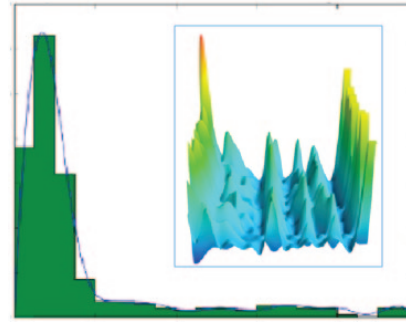
ET

MODELING OF TRANSPOSABLE ELEMENTS

The ET project (transposable elements) is a multidisciplinary study aiming at investigating the mathematical and computer modelling of the movement of transposable elements in genomes. These transposable elements have been studied for more than 60 years but have never, or almost never, been modeled. Describing their dynamics, changes in the number of copies, places of insertion, and the degradation of ETs could, however, be important in the fight against diseases more or less directly related to these ETs: Duchenne muscular dystrophy, hemophilia, cancers of the oesophagus, breast or reproductive organs.

It is therefore becoming clear that understanding the evolution of genomes and pathologies cannot be achieved without taking an interest in the dynamics of ET. A collaboration between mathematicians, computer scientists and biologists has been set up to describe and predict the evolution of transposable elements, based on sequencing data from past and present organizations. These models are intended to describe the transposition of the ETs at transposon level (cut and paste type movement). They involve discrete dynamic systems, Markov chains (hidden on trees), Bayesian inference, and partial differential equations.

The project is a collaboration between the Chrono-environnement laboratory, the Besançon Mathematics Laboratory and FEMTO-ST.



DURATION

2013 -2015

FUNDING

Internal Project Call at Besançon University Hospital: 60k€

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FluoroCorde

FLUORESCENCE SPECTROSCOPY FOR THE DIAGNOSIS OF VOCAL FOLDS CANCERS

Non-invasive methods to descriminate healthy from pathologic tissues is a key issue, especially in cancerology. Fluorescence imaging based on tissue autofluorescence is an advanced and non-invasive imaging technique and allows visualizing zones considered as pathologic.

Given the main proteins present in healthy or pathological tissues (prophyrin, collagen, flavin, NADH, elastine...) the goal of FluoroCorde is to study the autofluorescence properties of these tissues when they are excited with wavelengths which correspond to these proteins as it was shown in other tissues than vocal folds.

Fluorescence spectra obtained on biopsies are analyzed using statistical classification methods in order to discriminate the various benign or pathologic nature of the biopsies.

DURATION

2015 - 2017

FUNDING

Clinical Trial of the µRALP Project

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MECAPELVIS

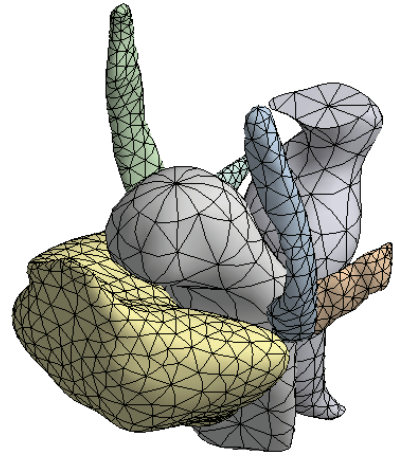
BIOMECHANICAL STUDY OF STRATEGIES FOR SURGICAL CORRECTION OF PELVIS PROLAPSE

Prolapse (a loosening of the organ) is a disease that affects one woman in three, and more than 60% of patients over 60 years. However, its causes and origins are poorly known. The project consisted of the development of a personalized numerical model representative of the pelvic region including the uterus, bladder, colon, ligaments. The geometry was obtained from images of patients with disorders requiring surgery. The mechanical properties of the tissues, stresses and boundary conditions were chosen from bibliographic data.

Numerical simulations of the response of the pelvic region to the conditions of an abdominal cough made possible quantifying the finite element model sensitivity to the mechanical parameters. A reference configuration was chosen from a simplified model (linear elastic, localized loading and contact management).

The objective was to evaluate the incidence of hysterectomy in the treatment of prolapse pathology. The development of a personalized model can be a decision-making tool for the obstetrician surgeon.

The project is a collaboration in the University Bourgogne Franche-comté, between the FEMTO-ST Institute (department of applied mechanics – AEH team), the Obstetric Surgery and Anatomy Laboratory of the university hospital (CHRU) and the Mecanique and Microtechniques National Engineering School (ENSMM) and the Master of Mechanical Engineering of the University of Franche-Comté.



DURATION

2014 - 2015

FUNDING

Besançon University Hospital and FEDER: 6k€

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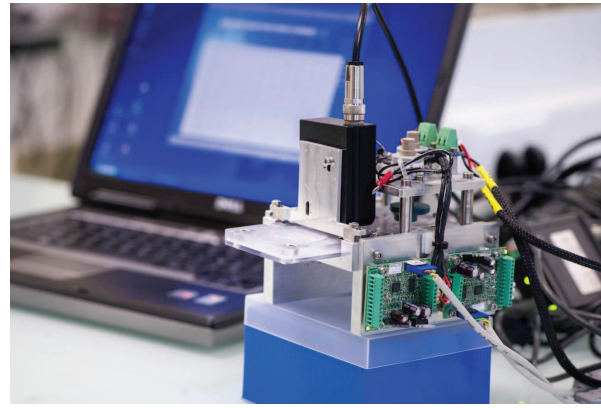
MEDICALIP

SCREENING THE CYTOMEGALOVIRUS AT BIRTH

Cytomegalovirus infection of newborns can lead to late clinical consequences and severe neurologic effects. An early detection of infected newborns would allow medical staff to follow infants and to manage them as soon as possible. Therefore, a rapid diagnostic tool which can be used at the newborn's bed is required and would constitute a major advance compared to current techniques. Nowadays and when it is performed, diagnosis is based on cell culture or PCR. These techniques require sampling urine or saliva from newborns, conserving samples and sending them to specialized biology laboratories. Furthermore, a large amount of biological samples must be obtained to perform tests.

In MEDICALIP project, we developed an automated microsystem used to detect cytomegalovirus by means of a specifically designed biochip.



DURATION

2007 - 2009

FUNDING

French National Research Agency: 511k€

CONTACT

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MELpH

FIBER OPTIC pH SENSOR USING FLUORESCENCE PROPERTIES OF SNARF AND FLUORESCEIN

(JOINT PhD WORK WITH THE CHIANG MAI UNIVERSITY, THAILAND)

Organic functions of the human body are linked to biological constants. Variations of these constants induce pathological troubles. Among these constants, the pH is the central subject of this PhD work. In living beings, biological functions are related to either acid or alkaline constants. Indeed, the action of a protein depends on the surrounding pH. An inadequate value of the pH makes the proteins non active which is deleterious for the organism. There exists a need for pH sensors which can be used in the human body for clinical applications (macroscopic scale), on cells in culture for biology researches (mesoscopic scale) or at a cell membrane level for more fundamental studies (microscopic scale). Among the wide range of technologies potentially useful for these applications, fiber optic fluorescence pH sensing offers the possibility to be adapted to the three above mentioned dimensional scales. This PhD dissertation addresses these constraints by studying fluorescence fiber optics pH sensors using two kind of pH indicators: SNARF and fluorescein. Together with these experimental studies, mathematical descriptions of the fluorescence properties of these indicators are proposed. They allow progressing towards calibration free pH sensing.

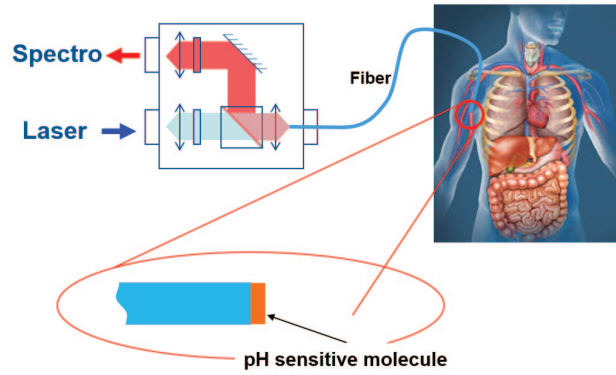
DURATION

2013-2017

FUNDING

Optics and Photonics Network: 5k€

Government of Thailand
PhD Grant



CONTACT

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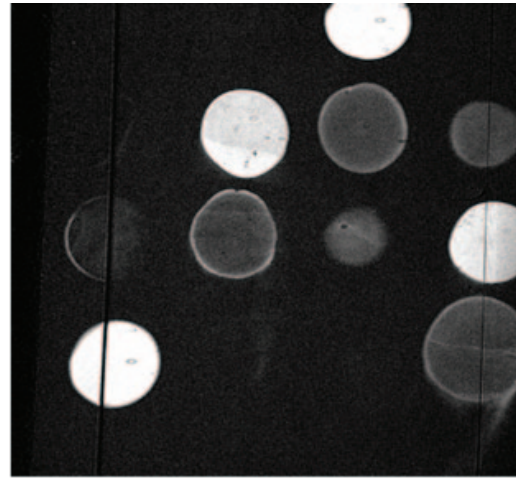
NEOTAG

AUTOMATED DOSAGE FOR 3 PATHOLOGIES OF THE FRENCH PROGRAM OF NEONATAL SCREENING

Co-certified by the Pole of Microtechnics and the Nutrition Health Longevity's Pole, the Neotag project has for objective to create a solution of an automated dosage for three pathologies which are in the French program of neonatal screening using the Mass-Plex Technonology of the Imabiotech company (Lille).

The development of theses dosage kits will allow an improving screening and investigation of metabolic dysfonctions by decreasing the time of analysis, reducing the number of samples while allowing a better reliability of theses analysis.



DURATION
2014 - 2017

FUNDING
FUI Project: 2M€

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P'AIR

SURFACE ACOUSTIC WAVES SENSORS FOR THE MEASUREMENT OF FINE PARTICLES CONCENTRATION IN THE AIR

Nowadays, atmospheric pollution is becoming a health issue. Among different pollutants, particles matter (PM) are considered as the most threatening for human health. More specifically, particles called PM10 and PM2.5, corresponding respectively to those exhibiting an aerodynamic diameter smaller than 10 and 2.5 µm, can deeply penetrate the human lungs. More than 2 million premature deaths are caused by air pollution according to the World Health Organization (WHO).

This project aims at developing a tool to perform PM2.5 and PM10 concentration measurements based on acoustic waves sensors.

This research was funded by an industrial scholarship (CIFRE) within a partnership between FEMTO-ST and the company Ecologicsense. It was undertaken in the framework of the P'AIR (Particle Atmospheric Intelligent Research) project, which aims at developing a network of new innovative low cost sensors in order to create a pollution map of a city.

To achieve this, a device based on Surface Acoustic Waves (SAW) sensors combined with a cascade impactor was developed. A prototype, operating at 3~Lpm, was built during this research and its ability to separate and measure PM2.5 and PM10 particles in real time was demonstrated. This innovative combination SAW/impactor led to a patent in April 2016.

DURATION

2013-2017

FUNDING

FUI Project: 220k€

CONTACT

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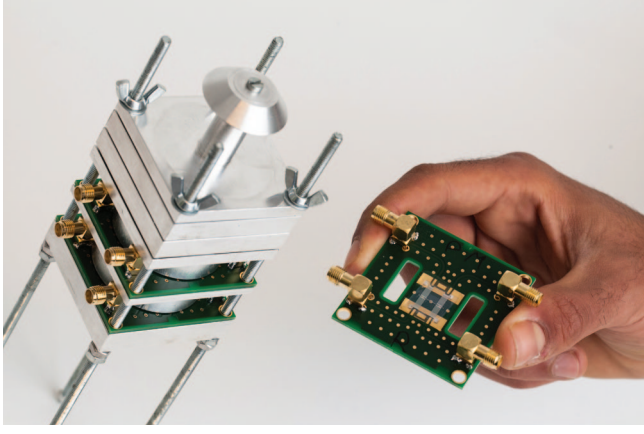


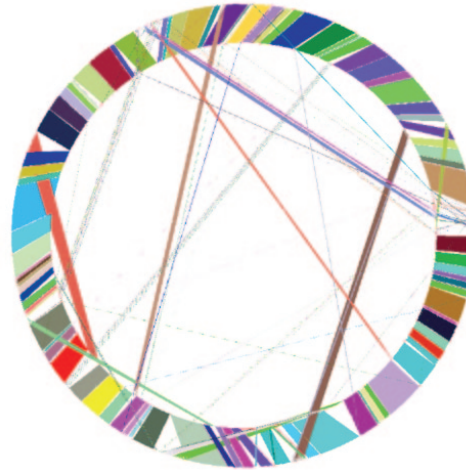
PEG

PREDICTION OF GENOME EVOLUTION

The PEG (Prediction of Genome Evolution) project is a multidisciplinary project aiming at modeling the evolution mechanisms of DNA sequences. This project is based on skills and themes that have been developed over many years (work on predictive models for protein evolution), and others more recently installed at the University of Franche-Comté within the framework of CRNS/UFC scientific excellence chairs.

The project is divided in two parts. The first fundamental part consists of the acquisition of genetic data resulting from the study of ancient parasites (paleoparasitology). The second component and core of the project is the development of mathematical and statistical models of genome evolution. These models are intended to describe nucleotide mutations and genomic rearrangements. These two aspects of the project are closely linked in the sense that the reality of the established models can only be achieved through the study of ancient archaeological sequences.

The project is a collaboration between the Chrono-environnement laboratory, the Besançon Mathematics Laboratory and FEMTO-ST.



DURATION

2012 - 2015

FUNDING

Franche-Comté Council: 130k€

CONTACT

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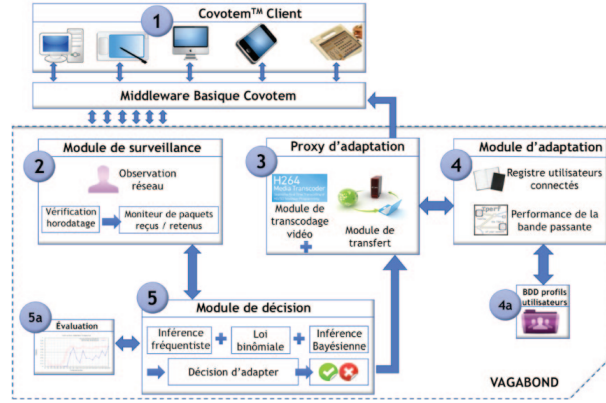
PhD with COVALIA

MULTIMEDIA FLOW ADAPTATION APPLIED TO MEDICAL TELEDIAGNOSIS

In the context of collaborative software dedicated to telemedicine, quality and reliability are of primary importance. Hence, when a doctor must establish a telediagnosis by means of audio and/or video flows, the consistency, quality and reliability of received data must be guaranteed during the entire communication session. It is also important to guarantee the continuity and the quality of service during the entire data transport.

Consequently, it is necessary to implement tools which garantee that the multimedia flow has arrived without alteration and with a quality which allow end-users to operate them.

The use of adaptation mechanisms should allow creating flows adapted to the context, to the constraints of the environment and to the requirements and preferences of the users. It is also important to be able to test these adaptation choices in real conditions.



DURATION

2014 - 2017

FUNDING

CIFRE PhD with COVALIA: 30k€

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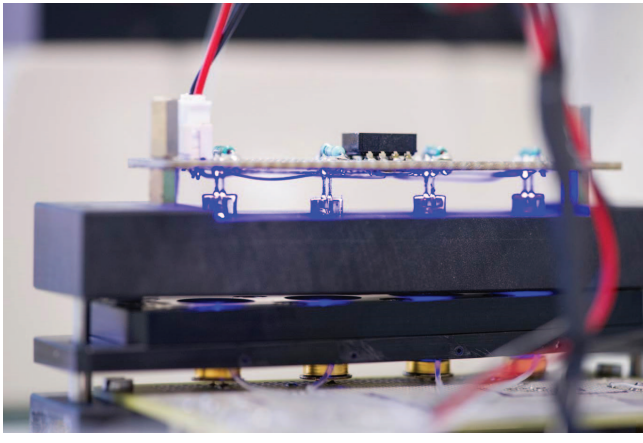
SmarT Transfuser

A SMART DEVICE FOR ABO ULTIMATE CONTROL PRIOR TO BLOOD TRANSFUSIONS

The SmarTTransfuser project is led by the Clinical Investigation Center at Besançon University Hospital and is conducted in collaboration with FEMTO-ST and the Etablissement Français du sang Bourgogne Franche-Comté. SmarTTransfuser aimed at developping an automated and mobile device used to control the ABO compatibility between a red cells concentrate and a patient.

The concept constitutes a breakthrough with current techniques as it integrates a biochip directly in the transfusion line. This method allows performing an ABO compatibility test without any risk of blood exposure, in an automated way at the patient's bed side.



DURATION

2007 - 2011

FUNDING

Grant from the Etablissement Français du sang, Translational research program INSERM/ DGOS, OSEO/Innovative Project Maturation: 350k€

CONTACT

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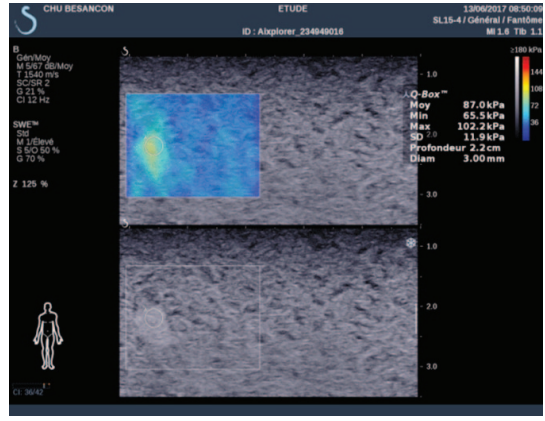
SWEP

ELASTOGRAPHY IN SOFT TISSUES

SWE elastography is a medical imaging technique that maps the elastic properties of soft tissues and allows non-invasive analysis of internal tissues. The use of this technique is progressing in the medical field to serve as a diagnostic tool in the case of some pathologies.

However, the technique is based on several assumptions which are not always relevant in the case of living tissues. In particular, living tissues generally have nonlinear (hyperelastic) viscoelastic behavior. Similarly, the supposed homogeneity of the tissues to identify a defect with abnormal mechanical behavior is not always valid.

The project consists in identifying, from a mechanical point of view, the domain of validity of the quantitative elastography technique (SWE). It is a collaboration between the University Bourgogne Franche-Comté, the gynecology-obstetric department of Besançon University Hospital (CHU), the Franche-Comté biomedical engineering school of the University of Franche-Comté and FEMTO-ST (department of applied mechanics – AEH team).



DURATION

2017

FUNDING

Auto-funding

CONTACT

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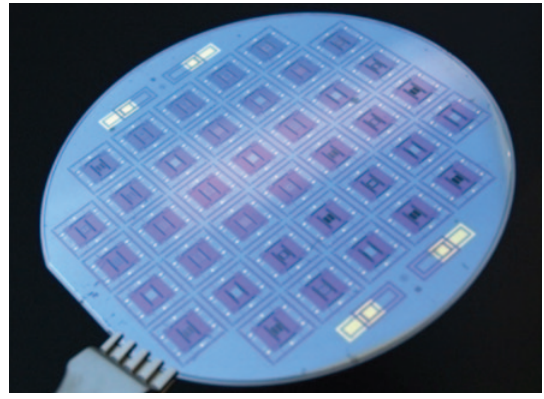
VIAMOS

VERTICALLY INTEGRATED ARRAY-TYPE MIRAU-BASED OCT SYSTEM FOR EARLY DETECTION OF SKIN PATHOLOGIES

Today, histopathology examination is the gold standard for various cutaneous pathologies. However, a large number of unnecessary surgical procedures are still performed. Consequently, new non-invasive methods such as ultrasounds, MRI or optical coherence tomography (OCT) are employed in order to perform optical biopsies of skin, improving patient's quality of life. Nevertheless, the existing bulk systems are expensive, only affordable at the hospital and thus, not sufficiently used by physicians or dermatologists as an early diagnosis tool.

The goal of VIAMOS is to benefit from advanced MOEMS technologies, enabling a new generation of miniature instruments. The challenge is to provide handheld, low-cost, fully parallel spectral domain miniature OCT devices, adapted for early diagnosis of cutaneous pathologies. For this purpose, the system is based on a matrix of Mirau interferometers fabricated by MOEMS technologies associated to electrically-pumped MEMS-VCSEL light-sources operating at 850 nm and taking advantage of polymers and semiconductors-based collective micro-nanotechnologies. Thanks to this combination, a miniature and low-cost SS-OCT imager providing cross-sectional tomograms with a depth greater than 0.5 mm, axial and transverse resolutions of 6 µm and imaging field of 8x8 mm2, is developped.



DURATION

2012 - 2015

FUNDING

FP7 European Project: 760k€

CONTACT

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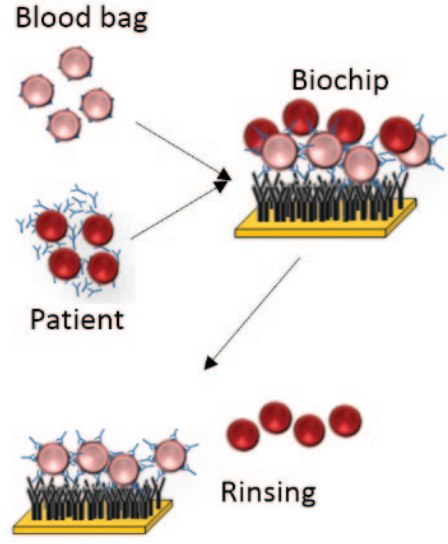
X-ult

HUMAN IMMUNOGLOBULIN COATED BIOCHIPS AND SENSITIZED RED BLOOD CELLS: TOWARDS AN INTEGRATED CROSSMATCH AT THE PATIENT'S BED SIDE

In line with SmarTTransfuser and ABORDAGE projects (ABO and RH1 compatibility), X-ult aims at developing biochips able to capture red cells sensitized by irregular antibodies. The ulterior motive is to improve transfusion safety by developing a mobile and automated device able to realize a crossmatch test at the patient's bed side. Currently, biochips technology is investigated in order to mix red cells form the blood bag and patient's blood. Specifically designed antibodies coated onto the biochip ensure specific immuno-capture of the sensitized blood bag's red cells. Proof of concept is studied using Surface Plasmon Resonance (SPR) technology. Translational research is then conducted in order to transfer SPR technology in a device where the detection of captured red cells is based on optical absorption. The device is also developed so that identito-vigilence is re-inforced and it should ideally be wirelessly connected to the hospital informatics system.

This project is led by the Etablissement Français du Sang in collaboration with FEMTO-ST and the Clinical Investigation Center (CIC 1431) at Besançon University Hospital.



DURATION
2014 - 2017

FUNDING
French Blood Agency: 129k€

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femto-st SCIENCES & TECHNOLOGIES

Biom'@x

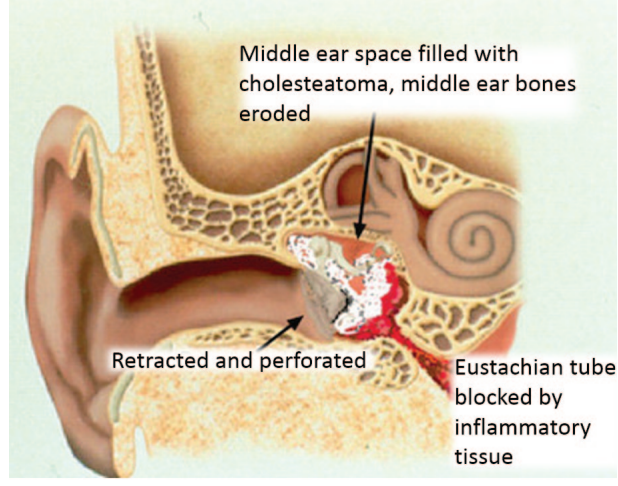
CURRENT PROJECTS

µRoCS

MICROROBOT-ASSISTED CHOLESTEATOMA SURGERY

Cholesteatoma is a skin growth that occurs in an abnormal location in the middle ear. It is usually due to repeated infections. It was estimated that one new case per 10,000 citizens occurs each year. Over time, cholesteatoma expands in the middle ear, filling in the empty cavity around the ossicles and then eroding the bones themselves (ossicles, mastoid). Cholesteatoma is often infected and results in chronically draining ears. It also results in hearing losses and may even spread through the base of the skull into the brain. Nowadays, the most effective treatment of cholesteatoma is to surgically remove the infected tissues through an invasive procedure. Therefore, there is a real need for a minimally invasive robotic system able to access the epitympanum cavity, with high accuracy and dexterity.

This project is part of the Challenge 4 – Life, Health and Well-being of the ANR call. It will focus in a surgical protocol breakthrough for the middle ear diseases through basic research in robotics, microrobotics, differential diagnosis methods, and image-guided interventions, following a cross-disciplinary approach.



Adapted from: http://drpaulose.com/wp-content/uploads/cholesteatoma.jpg

DURATION

2018 - 2023

FUNDING

French National Research Agency: 687k€

CONTACT

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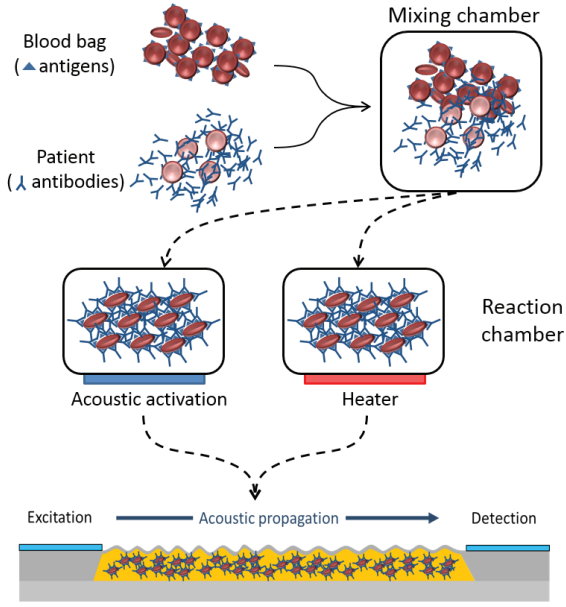
Acousto Blood

ACOUSTO-FLUIDIC DETECTION OF THE COMPATIBILITY BETWEEN RED CELL CONCENTRATES AND PATIENTS DURING BLOOD TRANSFUSIONS

During transfusions, blood incompatibilities may lead to severe or lethal consequences. Today, there exists no technique able to account for all incompatibility situations. To summarize, whatever the situation is, when incompatibility occurs, patient's antibodies destroy the red cells concentrate being transfused. In all cases, mechanical properties of red cells are modified when an incompatibility occurs. The goal of AcoustoBlood is to mix red cells to be transfused and patient's blood in an acousto-fluidic microsystem. A possible modification of the mechanical properties of red cells (due to incompatibility) leads to variations of the rheological properties of the mixture. These variations are detected by means of an acoustic sensor. All cases of incompatibility should then be addressed.



DURATION
2017 - 2018

FUNDING
CNRS PEPS Projects: 12k€

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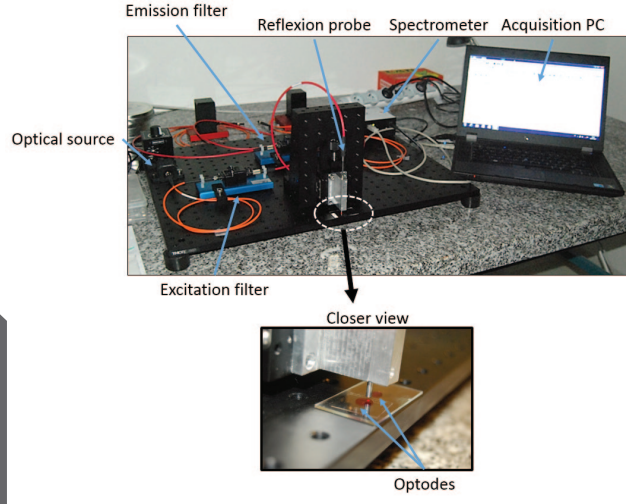
ALiBi

FLUORESCENCE AND COLORIMETRIC DETECTION Li^+ USING OPTODES TECHNOLOGIES

Bipolar disorders are a major cause of suicide in youg adults. 1/3 of patients under lithium treatment show impressive improvements of their mental health. 1/3 show no response to the treatment. For others the poor adherence to treatment may be the cause of an apparent non-response to lithium therapy.

ALiBi aims at improving the adherence to treatment by proposing a self-monitoring device to patients. Lithium levels will be measured in saliva. Optical methods based on optodes and using either fluorescence or colorimetry can potentially be used to this end.

Here, we study the physical-chemical characteristics of different optodes configurations. At the end of the project, the most promising technology which can be translated for use at home will be identified.



DURATION

2017 - 2018

FUNDING

CNRS PEPS Projects: 14k€

CONTACT

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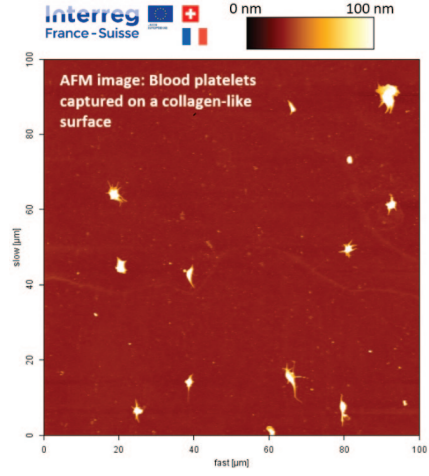
BlooDe

INVESTIGATION OF PRIMARY HAEMOSTASIS IN FLOWING BLOOD

Primary haemostasis is the physiological process by which a bleeding is stopped: the vascular breach is occluded with platelets plug. The main players are platelets, collagen, a fibrillar protein present in the vessel wall and exposed to the blood in case of vessel injury, and von Willebrand factor (vWF), an adhesive protein, which can bind collagen and recruit platelets. Haemostasis disorders lead to varying degrees of bleeding tendency or excessive blood clotting. Global and realistic investigation of the platelets activity do not address well enough the medical needs in terms of (i) metrology, (ii) diagnosis and (iii) prognosis.

The BlooDe project (Blood Device) aims at reproducing the platelets adherence and aggregation process on a collagen-like recombinant protein coated surface, within a microfluidic device. It will enable to better understand and quantify platelets and von Willebrand factor activities, and to study the interactions involved.

Each team provides its competences: microsystem, sensor and microfluidic at FEMTO-ST (Besançon), proteins engineering in NVH Medicinal (Dijon), haemostasis in UNIGE & HUG (Geneva), EFS Bourgogne Franche-Comté (Besançon), CHU of Dijon, consulting in *in vitro* diagnosis test: Diagnoswiss (Monthey). The gathering and interactions between those teams will enable the development of a new haemostasis test, usefull for personalized care of patients, on whole blood sample, analysed in flow conditions, with precise and medically pertinent rheological parameters.



DURATION

2014 - 2020

FUNDING

INTERREG FEDER European Project: 445k€

CONTACT

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CAVEOTANK

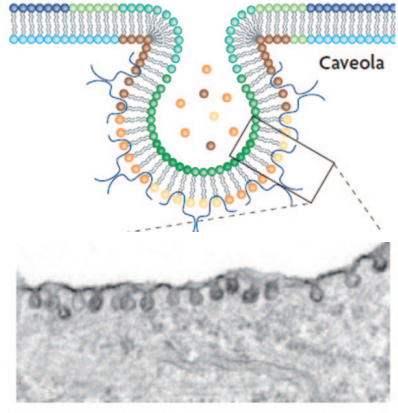
PRODUCTION OF RECOMBINANT MEMBRANE PROTEINS EMBEDDED IN HETEROLOGOUS CAVEOLAE

Caveolae to evaluate whether sub-microvesicles can improve the production and characterization of membrane proteins (MPs).

MPs encoded by 25 % of human genome play crucial functions in a wide variety of cellular processes. They are involved in numerous pathologies and therefore represent important drug targets. Nevertheless, their overexpression in heterologous systems, required for detailed structural and functional analysis, encounters numerous obstacles (toxicity towards hosts, quality of the MP produced).

The original approach is to produce MP-enriched sub-microvesicles using the ability of a small MP to generate vesicles within the cytoplasm in various hosts. The final objective is to facilitate MP functional and structural characterization. The production, already observed in Escherichia coli bacteria and Sf21 insect cells, will be tested into two other organisms: the bacteria Lactococcus lactis and the parasite Leishmania tarentolae, for 3 human MPs of high pharmaceutical interest.

This project, supported by the I2BC Institute (Saclay), is based on the close collaboration of 3 laboratories (I2BC/LPSM (Saclay), IBCP/MMSB (Lyon) and FEMTO-ST (Besançon) with complementary knowledge and know-how in the different institutions (in particular the BMD group at FEMTO-ST for its unique expertise in MP characterization in L. lactis) as well as in the functional and structural analysis of the 3 MPs.



DURATION

2017 - 2020

FUNDING

French National Research Agency: 346k€

CONTACT

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PhD with MAINCARE

SECURED LAYER FOR INTEROPERABILITY, COLLABORATION AND USER PROFILE MANAGEMENT FOR MOBILE APPLICATION DEDICATED TO MEDICAL TELEDIAGNOSIS

The mobility becomes a more and more frequently asked requirement for telediagnosis. In order to address this requirement, we propose a secured layer for interoperability, collaboration and user profile management for mobile medical telediagnosis. Two aspects are studied in this thesis:

- Material and equipment: considering the evolution of new terminals (smartphones for example), mobile telediagnosis becomes a reality and flows must be adapted in order to suit to terminals and networks,

- User profile: it is important to dynamically adapt the users profile to the type of terminal used and also to their real-time situation. For example, a dermatologist will need skin images (scars, tumoural dermatosis, etc.) of high quality in terms of graphical resolution and colorimetry, a neurologist will need a fluent video (24 frames/second) without resolution constraint in order to evaluate the seriousness and consequencies of a cerebrovascular accident. In addition to video streaming constraints, patient case file must be download cleverly, depending on users and use.

DURATION

2017 - 2020

FUNDING

CIFRE PhD with MAINCARE: 30k€

CONTACT

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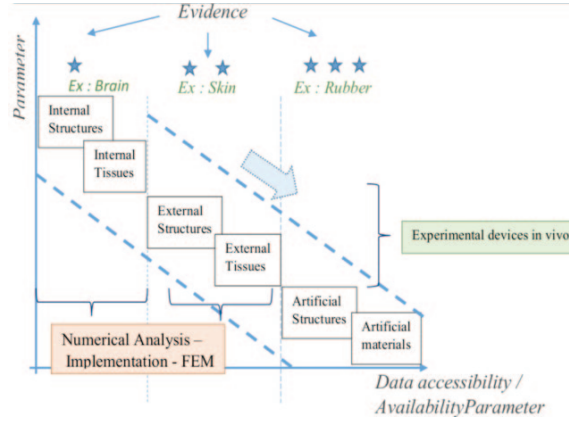
CLUE

CLINICAL UNCERTAINTY QUANTIFICATION IN SOFT TISSUE BIOMECHANICS

The project will deliver error-controlled algorithms enabling the biomechanics community to select the most suitable constitutive model for soft tissues or phantoms, identify their parameters, assess the uncertainty of this model on the parameters and give clues on optimal experimental design to minimize uncertainty. *In vitro* tests and clinical trials in dermatology will be planned. The project involves implementing models and validation based on experiments with high-variability of parameters and unknown boundary conditions. Open-source algorithms will be implemented in widely distributed software (FEniCS). The medical, practical and societal impact will come from quantitative tools for diagnostic and medical examination planning designed collaboratively with end-users such as surgeons or biomedical designers.

The University of Luxembourg (LEGATO team) and the University Bourgogne Franche-Comté (Laboratoire de Mathématiques de Besançon and FEMTO-ST/Department of Applied Mechanics, AEH team) collaborate around three axes: error quantification to choose the best approximation, numerical methods to optimize the way to simulate reality and experimental approach to compare reality and virtual results.



DURATION

2018

FUNDING

Bourgogne-Franche-Comté Council: 48k€

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CO3SENS

SMARTY

ENVIRONMENT TOXIC GASES MONITORING: CARBON MONOXIDE (CO) DETECTION (CO3SENS) AND FORMALDEHYDE (SMARTY)

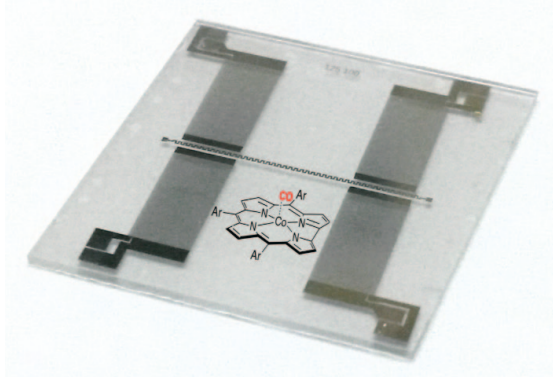
Our environment is composed of numerous nano particles suspended in the air. Carbon monoxide is a colorless, scentless and toxic gas which can be produced by the combustion of any organic matter, in particular when oxygenation is not sufficient. Aldehydes are also considered hazardous gases. Therefore, there is a need for sensors able to detect the presence of these molecules in the air at low concentrations.

In these projects, specific functionalizations based on cobalt metallocorroles and sol-gel are developed to selectively coordinate carbon monoxide and capture formaldehyde in ambient air.

These sensitive layers, combined with a device based on surface acoustic waves, allow a very high sensitivity to these toxic gases.

Indeed, by capturing these molecules, the mass of the sensitive layer increases. This mass variation can be measured by the sensor and therefore be related the targeted gas concentration with a great sensitivity up to a few ppb.

This research consists of the development of a device able to perform precise detection of low variations of gas molecules present in the air, in particular carbon monoxide and formaldehyde.



DURATION

2015 - 2018

FUNDING

French National Research Agency: 250k€

CONTACT

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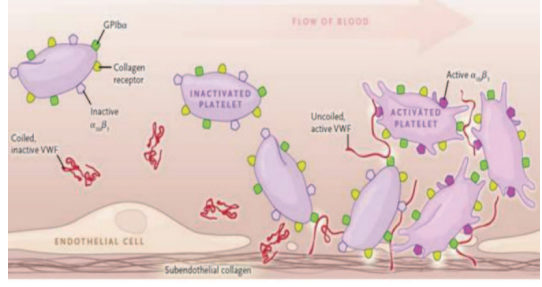
GHOST

STUDY OF THE PRIMARY HEMOSTASIS

Primary hemostasis is the initial step, which culminates in a platelets plug and precedes the formation of the blood clot. Defects may predispose to hemorrhage whereas platelets deposits within the lumen may culminate in thrombosis. The key factors are, in addition to circulating platelets, plasma, von Willebrand factor and the vessel wall and more specifically collagen of the matrix exposed in cases of vascular damage or of rupture of an atherosclerotic plaque.

Most of the currently available devices are for research use only and those for clinical use have serious limitations. The objective of this project is to develop a totally innovative microfluidic device system to explore, in clinical practice primary haemostasis as a whole with smallest blood volumes and immobilized recombinant collagenlike proteins, in flowing whole blood under the appropriate rheological conditions. A multiparameter acoustic biosensor will be integrated to perform real time measurements.



DURATION

2017 - 2021

FUNDING

French National Research Agency: 450k€

CONTACT

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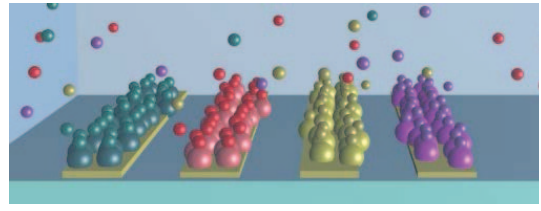
MADNESS

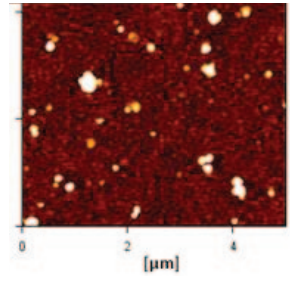
A GENERIC MICROFLUIDIC APPROACH FOR DECIPHERING NANOSCALE BIOVESICLES PROPERTIES

The overall objective of MADNESS project is to develop a miniaturized conceptual platform allowing the isolation, fractionation and classification of Extracellular Vesicles. We propose a microfluidic approach coupling a hydrodynamic separation module with analysis and reaction chambers. The microfluidic module will perform size fractionation within the 100-500 nm range where flow cytometers cannot operate. In front of each collecting chambers, we envision to interconnect miniaturized immuno (and ligands)-µarray in microchannels in order to perform specific captures in a multiplex format followed by nanometrological investigation of trapped species with an AFM instrumentation.

Then, each fractionated sample will be collected in order to be quantified and qualified with multi-omics approaches by coupling mass spectrometers available in our instrumental park.

Although this project focusses on instrumental issues, we propose to make the proof of concept on the representative case of platelet microvesicles (PMVs). Depending on the stimulus responsible for their production, PMVs exert different biological functions (*i.e.*, capacity to stimulate or not endothelial cells, dendritic cells). This will be used as a functional read-out to analysed fractioned PMV samples. This multiparametric and multifunctional approach will pave the way to a generic instrumentation for bio-nanoparticles qualification enabling new diagnostic/ prognostic assays.





DURATION

2017 - 2020

FUNDING

French National Research Agency: 358k€

CONTACT

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MiMédi

MICROTECHNIQUES FOR INNOVATIVE MEDICINES

Innovative medicines (MedI=ATMP advanced therapy medicinal products (eg cells)) have recently been developed to offer new treatment solutions for patients with therapeutic impasses. The fabrication of these MEDI requires the implementation of complex technologies in a controlled environment. Like industrial products, their range of production represents a significant cost for a large part because of the complex infrastructure required as well as the complexity of the production line to be developped.

It is at this level that the MiMédI project comes, by combining microtechnology skills with the production of these drugs of the future.

Associating 10 partners (6 private companies, 3 academic partners and a transfer organization), the contributions of this project will be:

- the possibility to review and simplify the production range thanks to numerous technological and conceptual contributions in microfluidics, acoustics, vision, automation, nano and micro-technology.

- the optimization of the fabrication of MEDI by the contribution of microtechnology to reduce manufacturing costs and increase the number and access of these therapeutic strategies to the evaluation phases for humans.

Source: https://geneticliteracyproject.org

DURATION
2017 - 2021

FUNDING
FEDER RIS3: 13,6M€

CONTACT
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NBA-QuaVEs

A NANOBIOANALYTICAL PLATFORM FOR THE QUALIFICATION OF EXTRACELLULAR VESICLES

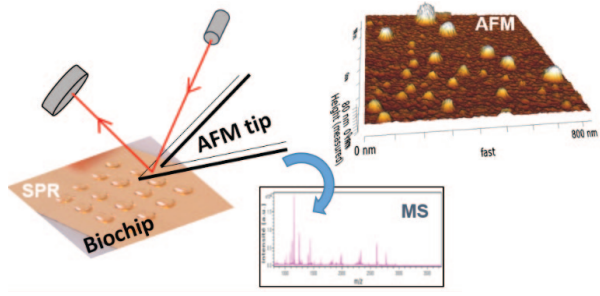
Extracellular vesicles (EVs) are produced by the majority of cell types. They are released into the extracellular space and found in the various physiological fluids of the human body (plasma, saliva, urine, cerebrospinal fluid, etc ...) following activation or apoptosis of these cells. These vesicles are currently recognized to participate in various (patho-) physiological processes but also as biomarkers of different pathologies. Although the study of these vesicles has become increasingly interesting in recent years, it has been hampered by limitations in isolation, purification, and fine characterization techniques that allow accessing to their concentration, phenotyping, and size.

In this EVs context, we propose the development of a NanoBioAnalytic platform (NBA), the fruit of a combination of several technologies, to access this triptych concentration / phenotyping / size of EVs (Obeid S. et al , Biosens, Bioelec, 2017 Jul 15, 93: 250-259).

Today, developments are focused on the evolution of this NBA platform, in particular:

- in the development of a microfluidic sorting module according to size (collaboration with LAAS, Toulouse, Dr AM Gué),

- on-line monitoring of the production of EVs in bioreactors by cancer cells in contact with blood cells (collaboration with Tapei Medical University, Taiwan, Pr T. Burnouf).



DURATION

2017 - 2020

FUNDING

CNRS: 19k€

Franche-Comté Council PhD Grant: 123k€

CONTACT

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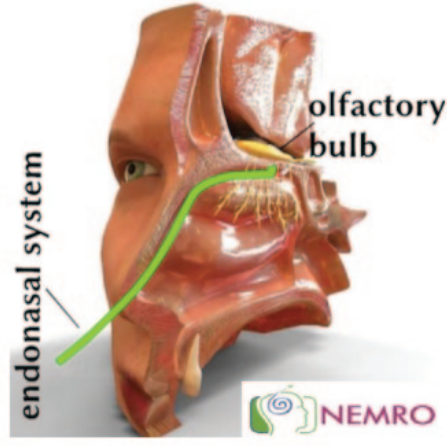
NEMRO

MICROROBOTIC NASAL ENDOSCOPY BY OCT: IMPACT OF SMELL DEFICIENCY ON NEURODEGENERATIVE DISEASES

NEMRO refers to a transdisciplinarity and fundamental research project. It grounds itself in Engineering and Information Science (microrobotics) but with a strong anchor into the medical field (neurosciences). NEMRO addresses a wide research field, with both scientific and technological ambition, as well as a clear clinical application: neurodegenerative diseases (Alzheimer, Parkinson) and other pathologies with similar effects (drug addiction).

Although this field has been widely studied, our approach is in total shift with the state-of-the-art and the state of clinical practice in the field. It relies on the recent finding of a strong correlation between the olfactory system deficiency and the appearance of the first symptoms of neuronal degeneracy. With NEMRO, clinicians will be given unprecedented technical means for *in vivo* investigation, characterization and, hopefully, *in situ* stimulation of olfactory cells, thanks to an Optical Coherence Tomography (OCT) miniature probe, steered and positioned accurately by a microrobotic flexible structure.



DURATION

2015 - 2019

FUNDING

French National Research Agency: 498k€

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R-LiNK

IMPROVING THE ADHERENCE TO LITHIUM TREATMENT FOR BIPOLAR PATIENTS BY MEANS OF A SELF-MONITORING DEVICE

The research developed in this project is part of the H2020 European Project R-LiNK. The consortium consists of 22 European partners including research institutes, hospitals, Clinical Investigation Centers and SMEs.

Bipolar disorder (BD) is a prevalent mental disorder and a leading cause of suicide. Lithium is the key mood stabilizer for prevention of BD relapse and suicide. Whilst many cases become asymptomatic with lithium treatment, the majority show sub-optimal response. Identifying biomarkers for predicting lithium response would enable personalization of treatment define criteria for stratification of BD cases and further refine the clinical response phenotype. In fact, 1/3 of patients under lithium treatment show impressive improvements of the mental health. 1/3 show no response to the treatment. For others the poor adherence to treatment may be the cause of an apparent non-response to lithium therapy.

One of the objectives of the R-LiNK project is to develop a self-monitoring medical device used to enhance adherence to treatment and monitor the Li level in saliva. The idea is that, becoming actors of their treatment, patients will increase their adherence to lithium therapy.

Source: http://www.onhealth.com/content/1/bipolar_disorder

DURATION

2018 - 2023

FUNDING

H2020 European Project: 7,7M€

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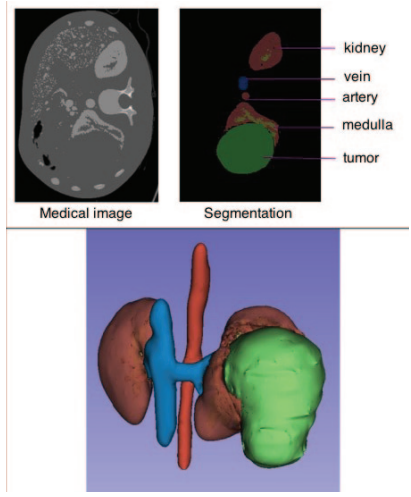
SAIAD

AUTOMATIC SEGMENTATION OF NEPHROBLASTOMA OF CHILDREN USING DISTRIBUTED ARTIFICIAL INTELLIGENCE

Nephroblastoma is the abdominal cancer tumour the most frequently observed in children kidneys. Its diagnosis and the planification of the surgery are exclusively based on imaging. The segmentation is a key-step of the construction of 3D representations of kidneys, tumours and structures around. Such representations would give precious information to surgeons about the tumour itself, as well as the structures infected and the material required for the surgery (quantity of blood, etc.). Nevertheless, nowadays, this segmentation step cannot be performed without any surgeon help since segmentation methods are not capable of accurately separate tumour from other structures like muscles for example. Indeed, the experience and knowledge of the surgeons are required to obtain an accurate representation of the patient abdomen. This is a time-consuming process (11 hours or more per patient) and finally, surgeons usually decide to interprate the 2D scans directly (250 scans per patient).

This european project is financed by Interreg and led by FEMTO-ST with different partners of Switzerland and France: CHU of Besançon, IDO-In, EPFL and CFI. The idea is to to develop a platform based on different artificial intelligence tools that will work together and enhance the existing segmentation programs at our disposal nowadays. Multi-agent systems, Deep learning and Case-based reasoning are some of the more promising tools.



DURATION

2016 - 2019

FUNDING

FEDER / INTERREG European project: 1M€

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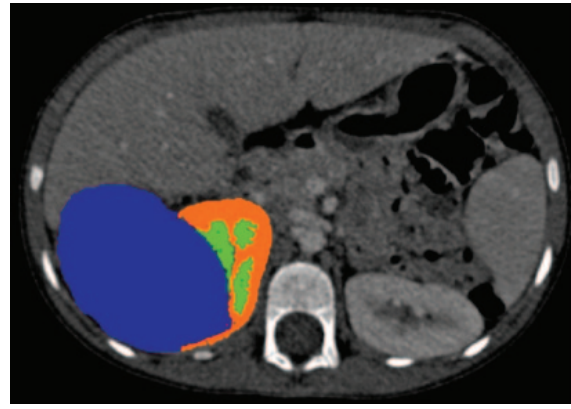
PhD Besançon Conurbation

MANAGEMENT OF CONCURRENT SOLUTIONS OVER A DISTRIBUTED PLATFORM DEDICATED TO IMAGE SEGMENTATION

Segmentation is a key-process of imagery. In the context of cancer disease, surgeons use this process in order to create 3D representations of organs and structures around them. Nevertheless, actuel segmentation algorithms are not always efficient enough, and require the expertise and experience of surgeons in order to create accurate 2D representations. Indeed, in the particular case of children affected by nephroblastoma (cancer disease of kidney), the margin between tumour and muscles are usually not found by the segmentation programs. Thus, if they want to build a 3D model of the children abdomen, surgeons must spend 11 hours or more to verify and correct the results of the segmentation of all the scans (more or less 250 per patient). As a consequence, although important for cancer diagnosis and surgery planification, this segmentation step is never performed and surgons have to interprate more than 200 2D scans directly.

Since we have identified that these segmentation process lack of experience and interpretation knowledge, we propose to enhance these processes with many Artificial intelligence tools like Deep learning and Case-based reasoning. We propose to design and implement a platform of agents that will interact with each other in order to preform in parallel and agregate concurrent segmentations to create 3D representations as accurate and consistent as possible.



DURATION
2016 - 2019

FUNDING
Besançon Conurbation
PhD Grant

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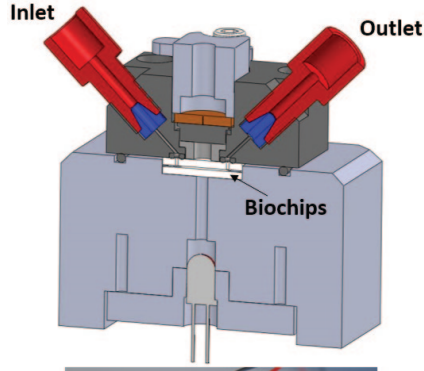
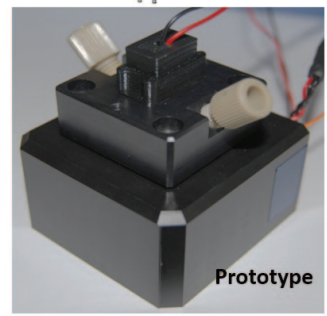
VIRUMILK

DETECTION OF CMV WITH A BIOCHIP FROM WHOLE MILK OF LACTATING MOTHER OF VERY PRETERM INFANTS

Cytomegalovirus (CMV) infaction may result from a mother-fetus transmission during the pregnancy (congenital infection) or from post-natal transmission. Currently, the viral status of the breastmilk is not cheked because of the lack of diagnosis tool which could be used on a routine basis. Clinicans face a dilemna concerning milk feeding. Either they decide to de-activate beastmilk (mainly by freesing) but they loose the interest of mother milk for infant development, or they decide to use native breastmilk with the risk of re-inforcing possible post-natal infections.

In order to help clinicians in their practice, VIRUMILK project aims at developing a rapid diagnostic test (RDT) which could be used at the hospital or at home in a self-evaluation manner. Prior to this, a technico-clinical study is ongoing to develop an integrated ELISA-like device able to detect CMV in native breastmilk.





DURATION

2017 - 2018

FUNDING

Internal Call Besançon University Hospital: 25k€

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