BORGES

Sept 17, 2020

Hi, We're BORGES!

We know about Biosensing with ORGanic ElectronicS. In fact, we wrote the blog on it.

by Shubham & Sara *(with inputs from other ESRs)*

A team of 15 **E**arly **S**tage **R**esearchers from 11 different nationalities are recruited by leading institutions and companies in Europe to work towards the common goal, i.e. **B**iosensing with **ORG**anic Electronic**S**.

The **M**arie **S**kłodowska-**C**urie **A**ction (MSCA) funded BORGES collaboration aims to form the next generation of R & D innovators in organic bioelectronics, covering the full spectrum from fundamentals to technological developments. Organic bioelectronics being a highly interdisciplinary field demands a multidisciplinary mindset that spans the whole range of the spectrum to make significant scientific advances. The requirement asserts familiarity with different aspects of the biosensing, but BORGES also trains them in making connections necessary to lead innovations.

Five different elements that BORGES addresses which take the knowledge from labs to the society answer the following *5H* questions:

How the molecular events manifest itself as an electrical response in organic electronic biosensors?

The physical understanding of the transduction mechanism leading to the biosensor response is crucial to improve their performance. The study of these nanoscale events requires the development of characterization tools which could probe them at the nanoscale. That's what *Shubham* and *Mohamed* will achieve within the BORGES project. It will be supported by *Larissa*, who will develop theoretical models and

simulations. The same would be explored by *Roger* via a multifaceted approach combining optical and electrical schemes in novel biosensors' architectures.

How does the selection of active materials and fabrication routes affect the biosensor's performance?

The ability of a biosensor to operate in physiological conditions is highly dependent on the morphology and composition of the active material. It is further influenced by the type of fabrication and functionalization protocols implemented. Towards this end, *Tommaso*, *Pietro* and *Marina* will work on developing biofunctionalized films and interfaces having controlled properties utilizing structure-function relations.

How to make biosensors operatable with complex biological samples?

Sensing analytes or biomarkers of different sizes require fabricating novel biosensor architectures. It generally involves designing a microfluidics-based cartridge for pre-treatment of complex biological samples and then integrating individual sensors in the multiplex platform. Towards this end, *Roger* will fabricate biosensors for small analytes such as food toxins or odorants molecules. *Bernhard* will fabricate and optimize OECT-based (Organic Electrochemical Transistor) biosensors for the detection of chemokines in cerebrospinal fluid samples. *Pamela* and *Kateryna* will develop EGOT-based (Electrolyte Gated Organic Transistor) biosensors for detection and quantification of different proteins in plasma samples. *Deniz* will design microfluidic devices for label-free separation of biomarkers, integrable with devices fabricated above.
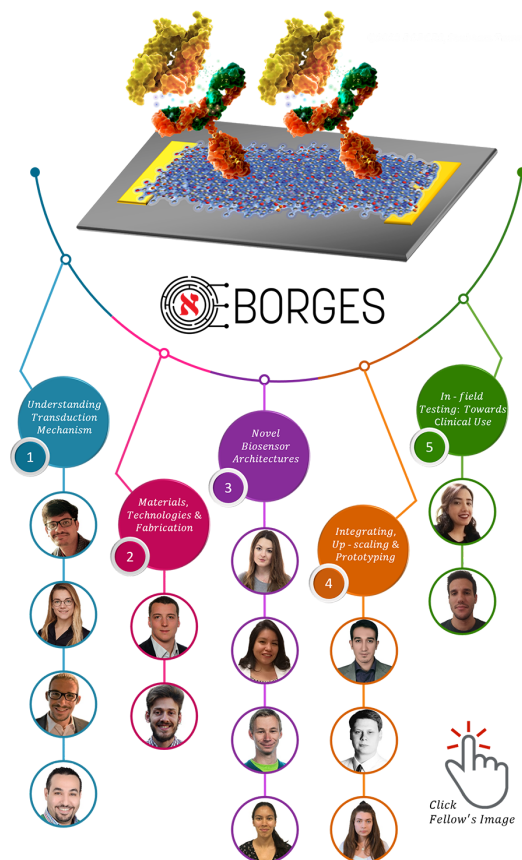
How to take these devices from labs to the market?

Deploying the variety of "proof-of-concept" biosensors developed by research labs needs reliable and cost-effective scaleable fabrication strategies. Towards this end, *Anatolii* will evaluate the different printing and dispensing techniques for fabricating OECTs and EGOFETs. *Pooya* will create a simulation model for optimizing the design of 3D-printed microfluidics, validated and implemented via additive manufacturing techniques. And *Marina* will investigate cost-effective manufacturing methods and integrating solutions for the development of a wearable multimodal health platform suitable for clinical validation.

How to validate the usability of the developed biosensors in clinical practice?

Biosensors response correlated with the stages in a disease progression or the efficacy of a particular treatment would render them as an essential tool in clinical practices. That's what *Sara* will try to understand by discovering novel biomarkers in body fluids such as cerebrospinal fluid (CSF) and plasma. But transferring such knowledge about biosensors from peoples working in one domain into another requires establishing a bidirectional communication interface accessible to both parties, taking into account the non-bioinformatics medical end-user. Here comes the work of *Panagiotis*, who will develop graphical user interface visualizing outcomes of a sensing experiment from a molecular modelling perspective.

The ESRs tackles each aspect via collaborations and secondments at various nodes within the BORGES network. Their individual roles can be explored in more detail through the interactive image below (*click on the fellow's picture*).

Stay tuned for more updates!

Pamela Allison Manco Urbina

Università degli studi di Modena e Reggio Emilia (UNIMORE)

UNIMORE
UNIVERSITÀ DEGLI STUDI DI
MODENA E REGGIO EMILIA

Within the BORGES network, the main goal of my project is the demonstration of biosensors based on electrolyte-gated organic transistors (EGOT) to monitor healthy aging biomarkers. To achieve that goal, I will first fabricate and test individual biosensors for detecting such biomarkers in test solutions and, at a later stage, in biological fluids like plasma.
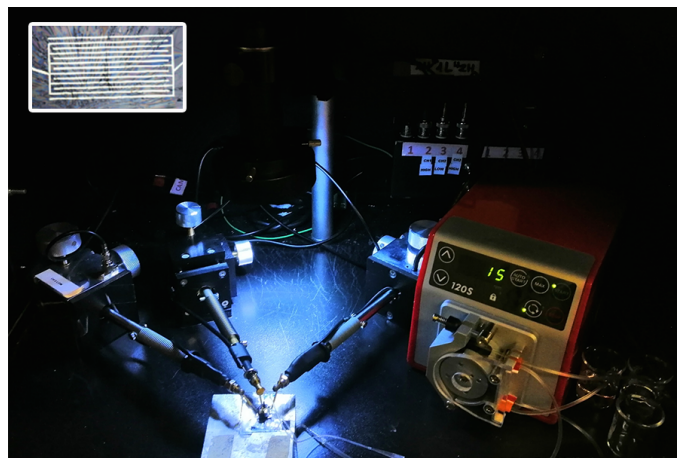

Fig : Electrical Characterization Setup (inset: TIPS-Pentacene on Quartz Substrate)

The figure above shows the electrical characterization setup for an organic transistor alongside a peristaltic pump and a microfluidic system. To this end, protocols for functionalizing the device interfaces with specific recognition elements (e.g. antibodies, aptamers against those biomarkers) will be developed. Moreover, the operability and stability of the EGOTs in biological fluids will be assessed and optimized in a microfluidic system. In the second part of my project, it is envisioned that the individual biosensors will be merged into a single sensing Multiplex platform; in which, with one small sample of plasma, we will be able to detect four different biomarkers at the same time.

Link: Academic Background ⧉

Pietro Antonio Livio

Université de Strasbourg (UNISTRA)

Université

de Strasbourg

Electrolyte-Gated Transistors (EGTs) have gathered the attention of the scientific community in the last decades for their promising applications towards sensing and bio-sensing. Since the first reports, many works have been published highlighting the advantages of these devices, such as the low limit of detection, low operational voltages and direct exposure of the active material to water. Apart from the extensive use of organic semiconductors in EGTs, graphene and its derivatives, Graphene Oxide (GO) and reduced Graphene Oxide (rGO), have shown the same versatility (e.g. flexibility, high transparency, unique conduction properties).
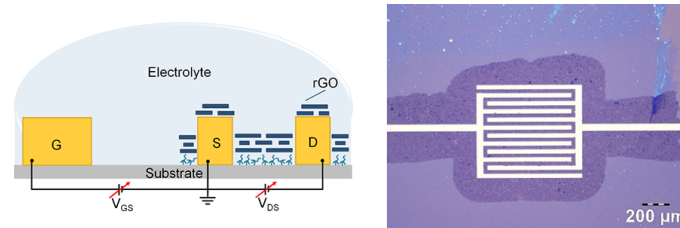

Fig : rGO-EGT Architecture & Optical Image of the Active Material

My activity within BORGES is mainly focused on the fabrication and characterization of Graphene-based EGTs, optimization of the deposition parameters and the electrical and morphological characterization of these devices. My main goal is to produce easy to use and cost-effective platforms that could be chemically modified with specific receptors (e.g. proteins, antibodies, DNA) to function as highly sensitive biosensors.

Link: Academic Background

Roger Hasler

Austrian Institute of Technology (AIT)

My research activity focuses on developing novel biosensor architectures based on graphene field-effect transistors (gFET) and surface plasmon resonance (SPR) spectroscopic devices. The surface of these devices will be functionalized with different biomolecular receptors (aptamers or odorant binding proteins) which are able to recognize and bind to small analytes. This can be detected as electrical signal in the gFET or as optical signal in case of SPR. The combined use of these two detection techniques will allow a better understanding of molecular events underlying the signal transduction mechanism in such organic electronics biosensors.

Link: Academic Background 🗗

Shubham Tanwar

Institute for Bioengineering of Catalonia (IBEC)

Biosensing using organic electronics is an active area of research in both academia and industry. The synergy between the two has resulted in a variety of 'proof-of-concept' biosensors. However, the lack of understanding in their transduction mechanism has hindered the progress. In BORGES project, I am trying to elucidate the chemistry and physics behind their operation mechanism in-situ through the development of novel experimental techniques, correlating the molecular events at the nanoscale with the observable parameters at the macroscale in a bottom-up fashion.
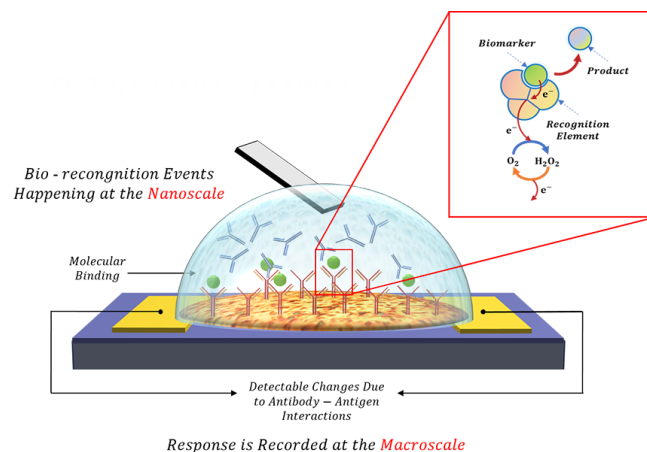

Fig : Nanoscale Events & Marcoscale Response

Specifically, the work includes designing and fabricating a setup to carry out Electrostatic Force Microscopy (EFM) measurements on functional organic devices operating in-liquid and developing specific imaging and spectroscopic measuring modes. The development is stemmed firstly through characterizing the static, transient and frequency-dependent behaviour of the electrolyte-gated transistors and then fabricating a transistor having specific characteristics. In the end, characterizing the transistor using in-liquid EFM in different scenarios, for example, during analyte recognition or while recording extracellular potentials in excitable cells.

Link: Academic Background

Bernhard Burtscher

Linköping University (LiU)

In BORGES, I will contribute towards functionalization, optimization and implementation of biosensors, especially Organic Electro-Chemical Transistors (OECT), to help detect and monitor Multiple Sclerosis. The work involves the coupling of a bio-recognition element with transistor and then enhancing its performance. It requires a fundamental understanding of each component and their interplay. This is especially important when it comes to biosensors, where the performance could be improved via different approaches like architectures, materials, biorecognition elements or the functionalization process itself. Furthermore, we would like to operate our sensors in a real biological fluid, like cerebrospinal fluid and ideally with a microfluidic setup to enhance its applicability. The other side is the need for multiple biomarkers to conclusively detect multiple sclerosis and their possible integration into a single detection platform.

Link: Academic Background

Pooya Azizian

Leitat Technological Center

At Leitat, I work on the design, simulation, and fabrication of microfluidic devices for organic biosensors. For fabrication purposes, I mainly use 3D printers using additive manufacturing to build the desired microfluidics from computer-aided designs by successively adding materials layer by layer.
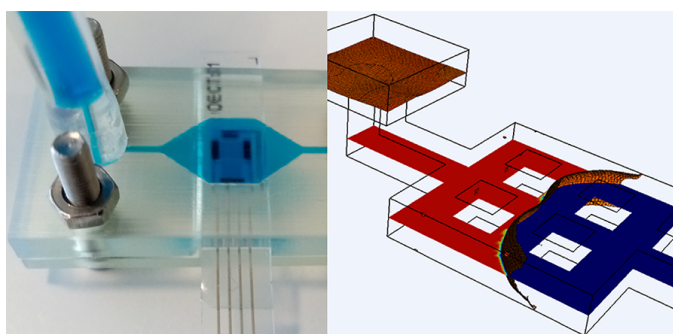

Fig : Microfluidics Design & Simulation

For simulation tasks and to obtaining a deep understanding of the physical phenomena regarding the fluid flow considering biosensing requirements, I mainly utilize computational fluid dynamics open source codes, with some required modifications. The targeted microfluidic devices will consist of micron size channels to optimally drive the fluid samples containing biological components to the physicochemical detectors for biosensing.

Link: Academic Background ⬈

Mohamed Awadein

Keysight Technologies

At Keysight, we are studying the bio-organic interfaces by applying a wide range of impedance spectrum up to 1 GHz with a very sophisticated calibration for optimal accuracy. Electrochemical impedance spectroscopy (EIS) is a highly sensitive and powerful technique for the analysis of the interfacial properties related to biorecognition such as antibodies and antigen, occurring at the modified surface. It allows direct detection of biomolecular recognition, Label-free, cost-effective, fast analytical techniques more easily integrated into multi-array or microprocessor-controlled diagnostic tools.

Link: Academic Background ⌷

Gulseren Deniz Saygin

Scriba Nanotecnologie

My role in BORGES is to design and fabricate microfluidics for the sensing units. The microfluidics will help to achieve separation of biomarkers within the sample and then perfusing to the sensin devices. This microfluidic-based process will replace several pretreatment steps of the samples, thus avoiding waste of reagents and reducing the time to complete the analysis.

Link: Academic Background ⬈

Anatolii Makhinia

Research Institutes of Sweden (RISE)

As an Early Stage Researcher at RISE, I intend to evaluate different printing techniques (including inkjet printing, screen printing, gravure printing and aerosol jet printing) for the manufacturing of organic electrochemical transistors (OECTs) and electrolyte-gated organic field-effect transistors (EGOFETs) on different substrates. Printed transistors based on organic materials will be employed in biosensing applications for the detection of various chemical substances, etc.
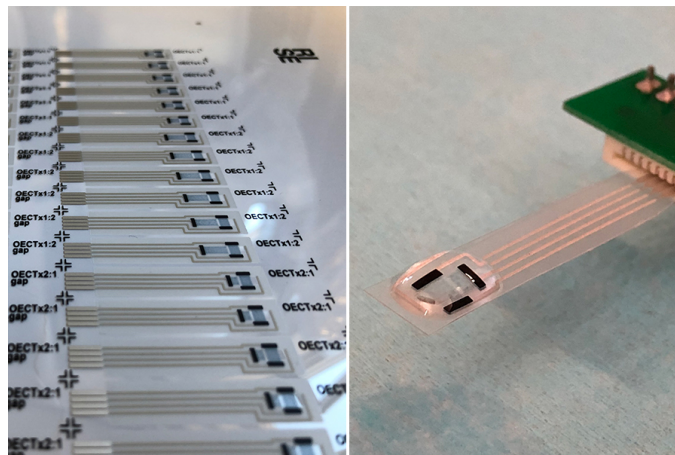

Fig : Screen Printed Lateral OECTs for Sensor Applications

Fabrication of OECTs and EGOFETs, by using various printing techniques, will generate knowledge and requirements of materials, ink formulations and device structures, all aiming at an optimized manufacturing process. A variety of manufacturing methods will give a certain degree of freedom in terms of different device designs and architectures as well as materials with different physical, electrical and chemical properties. The fabricated organic transistors will be characterized in order to understand the impact on the switching behavior when varying e.g. device dimensions and manufacturing processes. Knowledge of key features of each fabrication method will open pathways towards rational manufacturing strategies and integration.

Fabrication and development of OECTs and EGOFETs, exemplified by screen printed OECTs in the figure above, is currently ongoing at the Printed Electronics Arena in

Norrköping, Sweden, an innovation cluster and ecosystem for research and development in printed electronics.
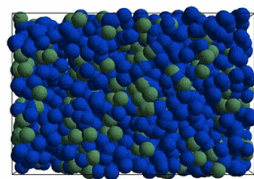
Link: Academic Background ⬈
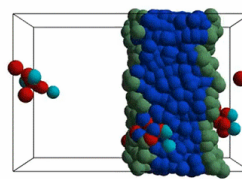
Panagiotis Petris

CULGI

CULGI

As a computational physicist, I investigate phenomena arising in a biosensor from a molecular modelling perspective. Molecular simulations allow for a fast and inexpensive prediction of how mechanisms and systems of interest behave in an organic electronic device. For instance, the study of the affinity of protein/vitamin binding in aqueous media, or a cell's membrane could be rather challenging experimentally.

Self-assembly of a lipid bilayer | Vitamins binding onto bilayer

Fig : Molecular Simulation

As one can easily observe in the above animation, the self-assembly of a lipid bilayer, as well as the study of binding phenomena on it, is a rather straightforward application using molecular simulations. Additionally, I use machine learning and chemical informatics in experimentally extracted data to calibrate existing molecular models.

Link: Academic Background

Marina Galliani

ARMINES

Within the BORGES project, I will deep dive into the field of wearable technologies to develop organic biosensors for human health monitoring. Flexibility must be a distinctive trait while designing comfortable and prolonged wearing medical devices. Organic conductive materials offer a large set of proprieties allowing their application in flexible electronic devices. Indeed, organic devices are paving the way to portable sensing platforms able to monitor human health parameters.
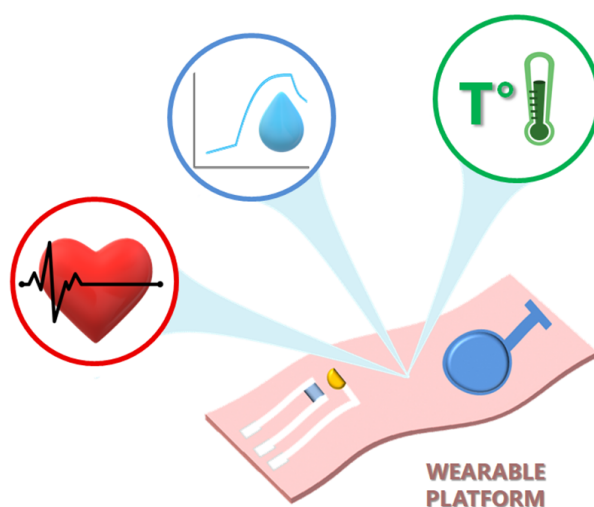

Fig : Multimodal Sensing Platform Overview

During my PhD, I will work with solution-processable organic semiconductors, for OECTs and amperometric devices fabrication. In particular, I will develop cutaneous electrophysiological sensors and wearable chemical sensors for human metabolite monitoring, with the idea of developing a multimodal sensing platform for human health data collection I will focus on various integrating strategies of these devices on wearables. Since the clinical application is the core objective biocompatible, low-cost and reproducible solutions will be key requirements that will have to be balanced.

Link: Academic Background

Tommaso Marchesi D'Alvise

Max Planck Institute for Polymer Research (MPIP-Mainz)

The field of biosensors and bioelectronics poses new challenges to the traditional organic electronics, with consequent development of materials and devices, for translating signals between biology and electronics. Majorly it concerns selectivity, reproducibility and operational lifetime of devices when exposed to real biological fluids like blood or plasma.

Towards this end, I'm designing novel polymeric materials that will be functionalized with different receptors. Surface functionalization protocols will be developed to ensure retention of functionality and control of the receptor orientation. The homogeneous ultrathin film (~10nm) will be prepared by electro-polymerization consisting of mussel-inspired polymer related bio-inspired materials. Model reactions of the ultrathin film with amine or thiol-containing molecules will be performed to study the functionalization capacity. When this is successful, films containing antibodies or specific DNA aptamers attached in a site-specific fashion will be prepared based on bioconjugation chemistry. The ultrathin films will be characterized by a multitude of techniques ranging from physical to chemical and electrochemical. Thereafter, the film will be tested in the integration within a device to develop electronic biosensor to detect for instance tumour markers.

Link: Academic Background ☒

Kateryna Solodka

Università degli studi di Modena e Reggio Emilia (UNIMORE)

Within the BORGES network, my project aims to develop ultrasensitive biosensors based on electrolyte-gated organic field-effect transistor (EGOFET) architecture for the detection of biomarkers of Multiple Sclerosis (MS) in plasma. Since neurofilaments and DAMPs (damage-associated molecular patterns) are directly related to the damage in the pathology of MS, these molecules will be chosen as potential biomarkers to be detected.
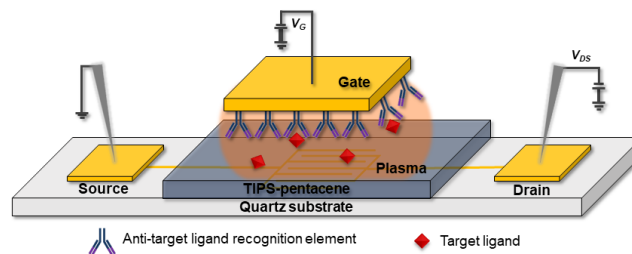

Fig : Electrolyte-Gated Organic Field-Effect Transistor

During my project, I will develop an EGOFET-based biosensor able to identify and quantify neurofilaments and DAMPs; and will test it in plasma samples from patients with progressive forms of MS. The obtained results will be validated with standard, state-of-the-art diagnostic techniques, such as ELISA and flow cytometry. Putting it all together, I will try to establish a correlation between the levels of these molecules and the progression of the disease, to get a better understanding of the mechanism underlying MS progression.

Link: Academic Background ☐

Sara Hojjati

Linköping University (LiU)

In the department of Clinical and Experimental Medicine, at Linköping University, there has been many great studies done to pave the way for diagnosis and prognosis of Multiple Sclerosis (MS) disease. Through BORGES network, I will try to make use of biosensors technology to meet the current need of healthcare providers for dealing with this disease.
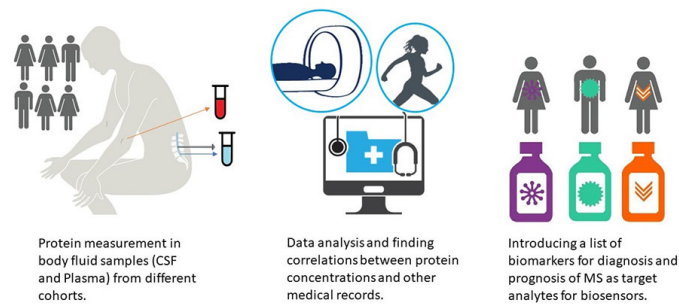

Protein measurement in body fluid samples (CSF and Plasma) from different cohorts.

Data analysis and finding correlations between protein concentrations and other medical records.

Introducing a list of biomarkers for diagnosis and prognosis of MS as target analytes for biosensors.

Fig : Biomarker Discovery & Developing Biosensor for MS Disease

During my project, the main focus will be to discover novel biomarkers in body fluids such as CSF and plasma that show correlations with stage of the disease or efficacy of a certain treatment. These biomarkers will be the target analytes for the OECT biosensors that will be designed to detect trace amounts of them with high sensitivity and selectivity in order to predict the disease behavior in patients and provide them with personalized treatments.

Link: Academic Background ⬚

Larissa Hütter

Institute for Bioengineering of Catalonia (IBEC)

Multiscale understanding of the biosensors, spaning from macroscale to nanoscale, is crucial for their optimization. The nanoscale events giving rise to macroscale properties encode the information about the transduction mechanism. Understanding them will subsequently result in the development of improved designs and better active materials.
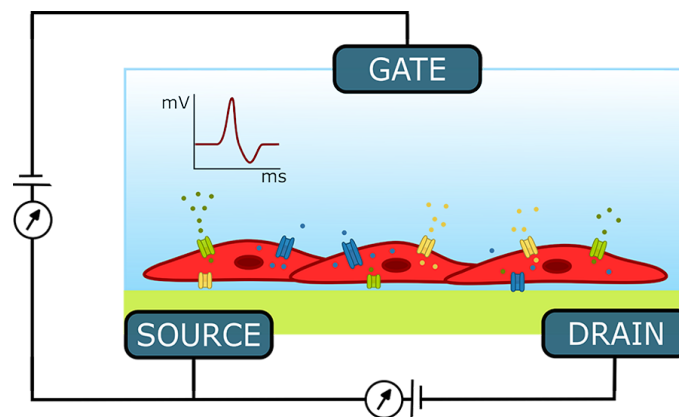

Fig : Electrolyte-gated Transistor Coupled with Electrogenic Cells

Computational models are fast, reproducible, and mostly cheaper than experimental studies. Therefore, in-silico models allow predicting the outcome of empirical studies, that will enable us to try out different configurations and materials. In my thesis, I will develop a computational framework of electrolyte-gated transistors for applications in biosensors and recordings of excitable cells. Specifically, I will focus my study on relating the measured transistor response to the extracellular potentials generated by the cells, which can provide information on the cell's activity.

The project of the thesis is divided into two phases. In the first phase, I will run multiscale simulations of the functional response of an electrolyte-gated transistor under different operational conditions. In the second phase, we will couple the electrolyte gated-transistor with an electrogenic cell model and study the device response in response to the cell's electrical activity.

Link: Academic Background