PhD description in English

PhD thesis position available at the research team 'Physical Chemistry of Surfaces and Interfaces', Interdisciplinary Laboratory of Continental Environments (LIEC, UMR 7360 CNRS-Université de Lorraine, Vandœuvre-lès-Nancy, France)

PhD project title.

Bacterial biosensors for trace metal detection: measurement and rationale of metal species speciation and toxicity via bacterial bioluminescence.

PhD project summary.

Brief context. For several decades, the scientific community has been trying to develop reliable methods for fine-monitoring concentration of metals in natural aquatic samples and for adequately assessing their toxicity. In this context, the use of so-called whole-cell microbial biosensors (bacteria that emit light after internalizing target metal elements) was considered as a promising solution that could meet the two objectives above, namely: measure the concentration of metal species (from nM to µM) in aqueous solutions of complex compositions, and estimate their toxic effects in the more or less long term. Despite the efforts made, the number of commercial biosensor-based solutions remains limited and tests in natural environments are rare. This is mainly explained by the complexity of the different intra- and extra-cellular biological and physico-chemical processes (and their coupling) that ultimately determine the time dependence of the signal produced by a biosensor. This complexity makes it difficult to obtain quantitative and predictive physical laws explaining how the signal of a given biosensor varies over time according to the concentration and speciation of metallic species in solution. Sound rationale of biosensors signal cannot be derived by current calibration-based correlative approaches.

Description of the PhD doctoral project. The general objective of the doctoral project is to understand mechanistically and quantitatively the time dependence of the bioluminescence signal emitted by a whole-cell bacterial biosensor in the presence of a given metal element, depending on the extracellular speciation conditions of the metal, modulated here by the introduction of model (nano)colloidal complexants. Particular attention will also be paid to the analysis of competitive effects between the metallic element to be detected and other metallic elements that can be internalised via similar bioaccumulation processes, as well as to the detection of the biosensor's 'exhaustion' conditions following toxicity effects. The two main questions this project will attempt to answer are: **1**. How does the temporal response of a biosensor sensitive to a given target metal element quantitatively reflect the speciation and bioavailability of that element and the lability of metal-(nano)colloid complexes in solution? **2**. Can toxicity effects be identified and quantified from a biosensor signal, and if so, how? In order to answer these generic questions, we will consider the case of cadmium-sensitive luminescent biosensors *Escherichia coli*, the team's model system for several years. Following recent results obtained by the team with which the doctoral student will closely interact (Pagnout et al. *Sensors and Actuators B: Chemical* **2018**, *270*, 482 & Duval et al. *ACS Sensors* **2019**, *4*, 1373), the project will include a theoretical component that will attempt to rationalize the dependence of bacterial bioluminescence on the dynamics of extracellular, bio-interfacial and intracellular processes involving the target metal element and leading to the measured signal (modelling of reactive transfers and luciferase production). In order to verify the validity of the physical formalisms developed, the project will also include an experimental component, where the time signatures of different model *E. coli* biosensors will be

measured under various incubation conditions allowing modulation of the speciation of the metal species to be detected (competition and vectorization of the metal elements by model (nano)particulate complexants). Finally, the toxicity effects of metals on biosensors will be assessed by combined cytometric, confocal microscopy, fluorescence lifetime imaging (FLIM) and atomic force microscopy (AFM) analyses.

Required knowledge and skills.

It is expected that the doctoral student has a background in physical-chemistry of surfaces, interfaces and/or bio-interfaces, with skills in modelling (reactive transfers, chemical kinetics, mathematical methods for physicists/physical-chemists), that he/she will actively lead/participate in experiments related to the acquisition of biosensor luminescence signals, to AFM, confocal and FLIM microscopy studies, and that he/she will bridge experimental and theoretical aspects. To carry out the project successfully, it is not necessary for the doctoral student to have extensive training in microbiology. The doctoral student will be supervised, accompanied and trained by an interdisciplinary team with recognized expertise in microbiology and physical-chemistry/chemical-physics of bio-interfaces.

Other prerequisites: good communication skills in English, ability to work in a team and to adapt, intellectually curious, good writing and synthesis skills, good skills for presenting scientific results orally, autonomous.

Contacts and application.

The thesis will be supervised by: Jérôme F.L. Duval (CNRS Research Director), physical-chemist (https://duvaljfl.webnode.fr/), and Christophe Pagnout (Associate Professor, Lorraine University), microbiologist (http://bddc.liec.univ-lorraine.fr/cv/PAGNOUT%20C.htm).
Students wishing to apply are invited to send by email (jerome.duval@univ-lorraine.fr and christophe.pagnout@univ-lorraine.fr)
- A curriculum vitae,
- A recommendation letter,
- A copy of the results obtained in the Master's degree and/or Engineering School,
- A copy of their last internship report (if applicable).

Thesis start date: **October 1, 2019**.

Presentation of the research team where the PhD project is completed.

The research team ‘Physical-Chemistry and Reactivity of Surfaces and Interfaces (PhySI)’ aims to analyze, through experience and theory, the processes governing the spatial and temporal dynamics of ionic (e.g. metals) and (nano)particulate contaminants in synthetic and natural bio-organo-mineral complex assemblies (e.g. biofilms, sediments or colloidal heterogeneous dispersions). Particular attention is paid to the analysis of the reactive transfers of these contaminants, and their physical, chemical and biological interactions with the components and fluids of the assemblies, upon integration of the dynamics and complexity of the multi-scale transport and reaction kinetic processes. Our mechanistic studies aim to rationalize the relationships between the physico-chemical properties of natural colloids or model analogues (clays, microorganisms, organic or inorganic (nano)particles) and their reactivity in different settings, e.g. bioadhesion, particulate aggregation, bioavailability-speciation-toxicity of contaminants. The methodology adopted involves (i) the coupling between experimental measurements resolved in space and time over a wide range of Deborah numbers (spectroscopic measurements, imaging techniques, interaction force measurements, electrokinetics, electrochemical and textural

analyses, laboratory and field studies), and (ii) the development of conceptual and theoretical frameworks to address (bio)particulate reactivity from the molecular scale to the scale of the interface and macro-assembly. In connection with the doctoral project, the team's recent work on the speciation of metallic pollutants in colloidal suspensions, on the partitioning of ionic pollutants at microbial interphases, or on the nanoscale evaluation of physical proxies reflecting the impact of nanoparticles on living cells, will place the doctoral student in a dynamic scientific context recognized at the national and international levels.

The doctoral student will closely interact with microbiologists (LIEC, EMMA team) and physical-chemists (LIEC, PhySI team) who will contribute to the student's training/coaching in the experimentation and modelling components of the PhD project.

Presentation of the laboratory.

LIEC (https://liec.univ-lorraine.fr/) is a joint research unit (UMR 7360 CNRS-Lorraine University) whose primary objective is to understand the functioning of continental ecosystems that are severely impacted by human activity, and the elaboration of rehabilitation/remediation strategies. To this end, we implement interdisciplinary research combining concepts and methods taken from environmental mineralogy, soil science, microbial ecology, colloidal physical-chemistry, ecotoxicology and functional ecology. The laboratory is organized according to five research teams:

- Biogeochemical cycles in disturbed ecosystems (CyBLE),
- Physical-chemistry and reactivity of surfaces and interfaces (PhySI),
- Microbial Ecology of Disturbed Environments (EMMA),
- Environmental Toxicology (TEv),
- Ecology of Stress (ECoSe).

This structure ensures continuity in LIEC's disciplinary and interdisciplinary themes. The above research teams are positioned on two interdisciplinary and complementary transversal axes whose main objective is to strengthen interdisciplinarity through the emergence of original inter-team projects.

Selections of recent publications by members supervising the PhD project.

- Duval, J.F.L. and Pagnout, C. Decoding the time-dependent response of bioluminescent metal-detecting whole-cell bacterial sensors. *ACS Sensors* **2019***, 4*, 1373-1383.
- Pagnout, C.; Présent, R.M.; Billard, P.; Rotureau, E. and Duval, J.F.L. What do luminescent bacterial metal-sensors probe? Insights from confrontation between experiments and flux-based theory. *Sensors and Actuators B: Chemical* **2018**, *270*, 482-491.
- Duval, J.F.L.; Town, R.M. and van Leeuwen, H.P. Lability of nanoparticulate metal complexes at a macroscopic metal responsive (bio)interface: expression and asymptotic scaling laws. *Journal of Physical Chemistry C* **2018**, *122*, 6052-6065.
- Van Leeuwen, H.P.; Duval, J.F.L.; Pinheiro, J.P.; Blust, R. and Town, R.M. Chemodynamics and bioavailability of metal ion complexes with nanoparticles in aqueous media. *Environmental Science: Nano.* **2017**, *4*, 2108-2133.
- Duval, J.F.L. Chemodynamics of metal ion complexation by charged nanoparticles: a dimensionless rationale for soft, core-shell and hard particle types. *Physical Chemistry Chemical Physics* **2017**, *19*, 11802-11815.
- Présent, R.M.; Rotureau, E.; Billard, P.; Pagnout, C.; Sohm, B.; Flayac, J.; Gley, R.; Pinheiro, J.P. and Duval, J.F.L. Impact of intracellular metallothionein on metal biouptake and partitioning dynamics at bacterial interfaces. *Physical Chemistry Chemical Physics* **2017**, *19*, 29114-29124.