Position Description

1. General Information

Name of the position	**Hybrid nanozymes for biomedical applications**
Foreseen date of enrolment	1 October 2023
Position is funded by	• COFUND, Marie Skłodowska-Curie Actions (MSCA), Horizon Europe, European Union • École Centrale de Lyon (EC Lyon) • Royal Melbourne Institute of Technology (RMIT)
Research Host	École Centrale de Lyon
PhD awarding institutions	École Centrale de Lyon & Royal Melbourne Institute of Technology
Locations	Primary: Écully, France Secondary: Melbourne, Australia
Supervisors	Dr. Virginie MONNIER & Dr. Yann CHEVOLOT (EC Lyon, INL) Pr. Vipul BANSAL & Dr. Rajesh RAMANATHAN (RMIT)
Group of discipline	Chemistry, Biochemistry, Nanotechnologies

2. Research topics (only one of these projects will be funded)

Project 1: *Hybrid nanozymes with synergetic catalytic activity as antimicrobial agents*
Nanozymes are nanoparticles with catalytic properties that can mimic the behaviour of natural enzymes [Walther 2018]. Reactive oxygen species (ROS) can be generated by different nanozymes. These ROS can be used for photodynamic therapy as they can trigger the death of pathogens such as bacteria or cancer cells [Maddheshiya 2022]. The reactive surface of metal nanoparticles associated to their large specific surface area make them interesting candidates for these therapeutic applications [Liu 2021]. In addition, iron oxide nanoparticles can be also considered as nanozymes [Gao 2007], as well as hyperthermic agent. Furthermore, they can be actuated with an external magnetic field. The objectives of the thesis will be to design new nanoparticles composed of an iron oxide core and a metal seeds shell and to use them for the capture and elimination of bacteria from complex media. We recently demonstrated that the resulting vicinity of the two nanomaterials (noble metal seeds/oxide nanoparticles) in the nanozymes give rise to new catalytic activities or synergies by mimicking the colocalization of enzymatic activities as cells do. To capture bacteria and amplify the antimicrobial effect, peptides such as magainin, will be immobilized onto nanoparticles surface.

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The PhD student will work in a first step on the chemical modification of iron oxide nanoparticles surfaces to graft noble metal nanocatalyzers. The structural and surface properties of nanoparticles will be characterized at INL by Transmission Electron Microscopy (TEM), zetammetry, infrared spectroscopy and photoelectron spectroscopy. Then, the catalytic activity of nanozymes will be evaluated through the oxidation of a coloured substrate (TMB) or a fluorescent substrate. Finally, the candidate will study the antimicrobial activity of nanozymes at RMIT Melbourne. Two non-academic partners based in France will be involved in this project. The first is Beaujon Hospital (AP-HP, Paris) and in particular the Endoscopy service. Indeed, one application that will be investigated in this project will be the design of antibacterial surfaces for endoscopes using nanozymes. The second is SON SAS, a company specialized in the conception and production of metal-modified iron oxide nanoparticles.

References:

[Gao 2007] L. Gao et al, Nature Nanotech., 2007, 2, 577.

[Liu 2021] Q. Liu et al, Nano Micro Lett., 2021, 13, 154.

[Maddheshiya 2022] S. Maddheshiya et al, Frontiers in Bioeng. Biotechnol. 2022, 10, 880214.

[Walther 2018] R. Walther et al, Angew. Chem. Int. Ed. 2018, 57, 1.

Supervisors:

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Pr. Frédéric PRAT (Beaujon Hospital AP-HP, Paris)

Dr. J. Paris (SON SAS, Dijon)

Research Fields: Chemistry, Nanotechnologies, Therapy

Project 2: *Hybrid nanozyme biosensors with synergetic catalytic activity for the detection of agricultural analytes*

The sensitive on-field detection of deleterious biological or chemical entities for the management of crop is of key importance for the preservation of the environment. Therefore, we aimed at the development of a colorimetric assays based on the catalytic activity of multimaterial nanoparticles for the detection of entities involved in crop protection. Indeed, many colorimetric biossays (for example ELISA) are based on the oxidation of a dye mediated by an enzyme leading to a change of colour. Herein, we aimed at replacing the catalytic activity of natural enzymes by the so-called nanozymes. Nanozymes are nanoparticles with catalytic properties that can mimic the behaviour of natural enzymes [Walther 2018]. Herein, the combination of, metal nanocatalyzers on oxide nanoparticles will allow increasing their oxidative activity, because oxidation reactions are preferentially achieved onto oxygen vacancies [Song 2013 & Qin 2019].

The specificity of the assay can be addressed using aptamers which can interact selectively with given entities. Indeed, the presence of aptamers onto nanoparticles surface blocks the catalytic properties of the nanozyme. When the biological targets interact with the aptamers, the aptamers leave the surface and the oxidation activity is restored. Using the specificity of aptamers, any kind of biological target (oligonucleotides, proteins, cells, bacteria) could be detected. For example, it was recently shown that nanozymes can be used as ultrasensitive and ultrafast biosensors able to detect target molecules with a concentration as low as 0.1 ppm and in few minutes, using aptamers as bioreceptors [Sharma 2014].

The objectives of the thesis will be to design new nanoparticles composed of an oxide core with nanometric noble metal seeds deposited on its surface and to use them as nanozymes for the detection of several targets of agricultural and environmental importance, such as pesticides, per- and poly-fluoroalkyl substances (PFAS) and plant viruses.

The PhD student will work in a first step on the chemical modification of oxide nanoparticles surfaces to graft noble metal nanocatalyzers. To achieve this, he(she) will use different polyelectrolytes to monitor metal seeds surface density. In a second step, he(she) will select specific aptamers and adsorb them onto hybrid nanoparticles surface. At each step, the structural and surface properties of nanoparticles will be characterized at INL by Transmission Electron Microscopy (TEM), zetammetry, infrared spectroscopy and photoelectron spectroscopy. Then, the catalytic activity of nanozymes

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will be evaluated through the oxidation of colour- or fluorescence-generating substrates. Finally, the candidate will perform the detection of several agricultural analytes at RMIT Melbourne and will evaluate biosensor performances (detection threshold, sensitivity, selectivity) depending on the hybrid nanoparticles structural and surface properties. Two non-academic partners based in Melbourne, Universal Biosensors, a nanosensor manufacturing company, and DAFF, the Australian Government's Department of Agriculture, Fisheries and Forestry will be integrally involved as the potential end-users to facilitate technology adoption towards the end of the project.

References:

[Qin 2019] L. Qin et al, Sci. Total Environ. 2019, 652, 93.
[Sharma 2014] T. K. Sharma et al, Chem. Commun. 2014, 50, 15856.
[Song 2013] W. Song et al, J. Phys. Chem. C 2013, 2, 7721.
[Walther 2018] R. Walther et al, Angew. Chem. Int. Ed. 2018, 57, 1.

Supervisors:

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Pr. Vipul BANSAL, Dr. Rajesh RAMANATHAN (RMIT)
Dr. Daniel LANGLEY (Universal Biosensors Inc, Australia)
Dr. Adrian DINSDALE (DAFF, Department of Agriculture, Fisheries and Forestry, Australia)

Research Fields: Chemistry, Nanotechnologies, Biosensing

Project 3: *Anti-oxidative properties of nanohybrids*

The generation of reactive oxygen species (ROS) and more generally of free radicals, is at the origin of many health issues such as liver diseases (hepatitis for instance) or cancers. They can also be produced as a consequence of poisoning by environmental pollutants (heavy metals, acid, base, halogen,…) or radiations (such as X-Ray used in radiation therapy). The resulting oxidative stress can cause damage or even apoptosis of cells.

It was shown that nanoparticles can eliminate the excess of cellular ROS and be used as free radicals scavengers [Huang 2016].

The objectives of the thesis will be to design new nanoparticles composed of an oxide core and a metal seeds shell and to test their anti-oxidative properties onto bacteria and cancer cells. Indeed, we recently demonstrated that the resulting vicinity of the two nanomaterials (noble metal seeds/oxide nanoparticles) in the nanozymes give rise to new catalytic activities or synergies by mimicking the colocalization of enzymatic activities as cells do.

The PhD student will work in a first step on the chemical modification of oxide nanoparticles surfaces to graft noble metal nanocatalyzers. The structural and surface properties of nanoparticles will be characterized at INL by Transmission Electron Microscopy (TEM), zetammetry, infrared spectroscopy and photoelectron spectroscopy. Then, the catalytic activity of nanozymes will be evaluated through the oxidation of a coloured substrate, TMB. Finally, the candidate will study the anti-oxidative activity of nanozymes at RMIT Melbourne. A non-academic partner based in Melbourne, DAFF, the Australian Government's Department of Agriculture, Fisheries and Forestry will be integrally involved as a potential end-user to facilitate technology adoption towards the end of the project.

References:

[Huang 2016] Y. Huang et al, Angew. Chem. Int. Ed. 2016, 55, 6646.
[Walther 2018] R. Walther et al, Angew. Chem. Int. Ed. 2018, 57, 1.

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3. Employment Benefits and Conditions

École Centrale de Lyon offers a 36-months full-time work contract (with the option to extend up to a maximum of 42 months). The employment contract includes a probation period of one month, which may be renewed once for a period not exceeding the initial duration. The total working hours per week is 35h.

The remuneration, in line with the European Commission's rules for Marie Skłodowska-Curie fellows, will consist of a gross monthly salary of EUR 2,044 in 2023. Of this amount, the estimated net salary to be received by the researcher is EUR 1,640 per month. However, the final amount to be received by the Researcher is subject to national tax legislation (approximately EUR 100 / month). This salary will increase during the thesis and should reach, on average, EUR 2,340 gross (i.e. EUR 1,870 net) per month.

Benefits include

- Access to all the necessary facilities and laboratories at EC Lyon (INL) and RMIT University.
- Tuition fees exemption at both PhD awarding institutions.
- Yearly travel allowance to cover flights and accommodation for participating in AUFRANDE events.
- 10,000 EUR allowance to cover flights and living expenses for up to 12 months in Australia.
- 27 days paid holiday leave.
- Sick leave.
- Parental leave.

4. PhD enrolment

Successful candidates for this position will be enrolled by the following institutions and must comply with their specific entry requirements, in addition to AUFRANDE's conditions.

EC Lyon

To be admitted in a Doctorate program, Applicants must hold a Master's degree (foreign degrees are examined by the doctoral schools to determine whether they are equivalent to a Master's).

More information: https://www.ec-lyon.fr/en/research/doctorate/admission-enrolment-doctorate

Important: the authorisation of the Defence Security Officer may be required before admission. In case of denial, the enrolment will not be carried out.

RMIT University

The minimum requirements for admission to a PhD program at RMIT University are:

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- a Bachelor's degree requiring at least four years of full-time study in a relevant discipline awarded with honours. The degree should include a research component comprised of a thesis, other research projects or research methodology courses that constitute at least 25% of a full-time academic year (or part-time equivalent). The applicant must have achieved a high distinction average in the final year; or
- a Master's degree that includes a research component comprised of at least 25% of a full-time academic year (or part-time equivalent) with an overall high distinction or a master degree without a research component with at least a high distinction average; or
- evidence of appropriate academic qualifications and/or experience that satisfies the Associate Deputy Vice-Chancellor, Research Training and Development or nominee that the applicant has developed knowledge of the field of study or cognate field and the potential for research sufficient to undertake the proposed program.

Applicants will also need to meet English proficiency requirements: https://www.rmit.edu.au/study-with-us/international-students/apply-to-rmit-international-students/entry-requirements/english-requirements

More information: https://www.rmit.edu.au/research/research-degrees/how-to-apply

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