COLLEGE ED BIOLOGIE DOCTORAL SANTE PAYS DE LA LOIRE

Year 20 /20

THESIS TOPIC

Subject N° (to be completed by the ED):	**FUNDING:** ☐ **Requested** **X Acquired**	**Funding origin: EU Commission**
Thesis title: **INTEGRATING IM INTO NTS WORKFLOWS: ADVANCING FOOD SAFETY AND UNDERSTANDING OF EXPOSURE**		3 keywords: Ion Mobility Mass Spectrometry, Risk Assessment, Contaminants of Emerging Concern
Unit / team: **UMR 1329 LABERCA**		
Supervisor's name: **Dr DERVILLY Gaud**		Phone number: 0240687880 Email address: gaud.dervilly@oniris-nantes.fr

Socio-economic and scientific context (approximately 10 lines):

Experimental ion mobility (IM) measurements involve measuring the friction of molecular ions in the presence of a neutral drift gas, e.g., nitrogen. An electric field drags the ions through the drift gas. Ions collide with drift gas molecules to reach a steady state velocity. Larger ions drift slower than compact ones of the same charge and this facilitates the separation and identification of ions having the same mass-to-charge ratios (m/z), but different size or shape. Moreover, the arrival time distribution of an ion allows derivation of a physical quantity termed the collision cross section (CCS). This property captures the influences of the shape, size and conformation of an ion and its mobility. When IM is combined with HRMS, both mass and mobility information can be captured in a single measurement. IM-HRMS thus offers addition of a rapid (millisecond-scale) separation that improves the analysis of complex samples and helps the structural characterization of molecules. IM-HRMS is the rising technology to study structural ensembles across a wide size range, including small molecules, The CCS has emerged across different disciplines in the last 5-10 years as a candidate identification parameter supporting an enormous range of applications. However, critical limitations include a discrepancy between the IUPAC and community-accepted definitions of CCS and the use of different instrument technologies (i.e., DTIMS, TIMS, TWIMS) that have unique design characteristics and use different external calibration approaches. Major gaps in fundamental knowledge of exact ion conformations and the influence of ion generation and measurement conditions also limit progress.

Working hypothesis and aims (approximately 8 lines):

As IM-HRMS technology is increasingly used for a plethora of analytical and molecular characterisation applications, the diversity of instrumentation and the non-uniformity of applied measurement and calibration approaches prevent the establishment of rigorous standardisation and reporting standards. The objective of the project is to deliver harmonisation and allow IM-HRMS to impact tomorrow's applications. In particular in the context of chemical risk assessment, the project aims at providing new tools and datasets enhancing confidence in nontarget screening for accurate assessment of chemical contamination. It will address the emerging challenge of exposure research in chemical food safety to cover through IM-HRMS measurment, the analysis of an extremely broad range of chemical classes.

Main milestones of the thesis (approximately 12 lines):

The PhD student will address major shortcomings in accessible and practicable data processing to allow full use of the IM separation and CCS in a new software tool for IM-HRMS. Data generated will directly contribute to guidelines for creating a new CCS database relevant to the domain with long-term value for compounds of emerging concern (CECs). This covers chemicals not currently regulated, but that may be under scrutiny for future regulation. The database will be open access and will contain different sample types and matrices, measurement conditions, identification level, risk assessment, and chemical class.

Main milestones of the MOBILITRAIN project are as follows :

1) Develop NTS software tool to support chemical risk assessment of the exposome.
2) Create a robust and dynamic approach to deliver a vendor-independent CCS database for NTS using CECs associated with public health concerns (Persistent Organic Pollutants, Endocrine Disruptors),
3) Increase the performance and user-friendliness of high-throughput IM-HRMS nontarget screening (NTS) workflows.

Expected results are :

1) An innovative, rapid and robust tool for the detection of a wide range of chemical compounds of historical and emerging interest using IM-HRMS.
2) A harmonised approach to generate FAIR CCS databases, including QA/QC and reporting criteria.
3) Successful application of new methods and data processing tools to assess consumer exposure to the expanding range chemical hazards.

Scientific and technical skills required by the candidate (2 lines):

Master in Analytical Chemistry, Mass Spectrometry, Ion Mobility, MS Data Processing and Analysis.

3 publications from the team related to the topic (last 5 years):

1. Feuerstein, M.L., Hernández-Mesa, M., Valadbeigi, Y., Le Bizec B., Hann S., Dervilly G., Causon T. Critical evaluation of the role of external calibration strategies for IM-MS. Analytical and Bioanalytical Chemistry 2022;414: 7483–7493. https://doi.org/10.1007/s00216-022-04263-5

2. Carbonell-Rozas, Laura and Hernández-Mesa, Maykel and Righetti, Laura and Monteau, Fabrice and Lara, Francisco J. and Gámiz-Gracia, Laura and Le Bizec, Bruno and Dall'Asta, Chiara and García-Campaña, Ana M. and Dervilly, Gaud, Ion Mobility-Mass Spectrometry to Extend Analytical Performance in the Determination of Ergot Alkaloids in Cereal Samples. Journal of Chromatography A 2022;1682:463502. https://doi.org/10.1016/j.chroma.2022.463502.

3. Hernández-Mesa M, D'Atri V, Barknowitz G, Fanuel M, Pezzatti J, Dreolin N, Ropartz D, Monteau F, Vigneau E, Rudaz S, Stead S, Rogniaux H, Guillarme D, Dervilly G, Le Bizec B. An Inter-Laboratory and Inter-Platform Study of Steroids Collision Cross Section By Traveling Wave Ion Mobility Spectrometry. Analytical Chemistry. 2020;92(7):5013-5022. https://doi.org/10.1021/acs.analchem.9b05247.

National and international collaborations:

This thesis project is part of a Doctoral Network under the European Commission's Marie Curie program. In this sense, the international dimension is intrinsic to the project. The doctoral student will follow an international training program with 10 other international doctoral students, and will also have the opportunity to spend 3 periods of several weeks at universities and companies in Belgium, Germany and the UK.