

Innovations in ambient mass spectrometry imaging

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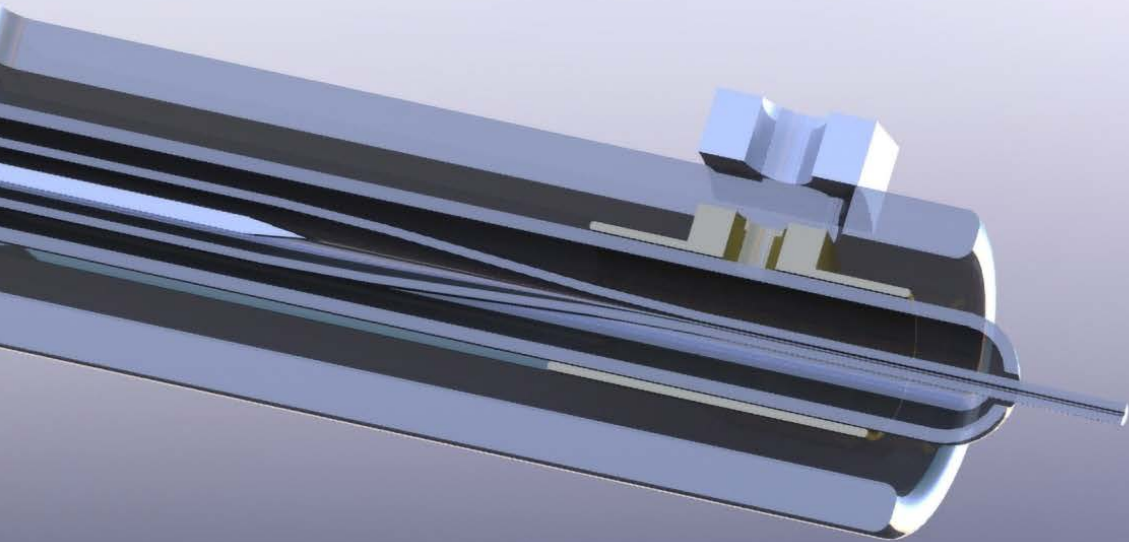
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CHAPTER 6



IMPACT

6.1. OBJECTIVE

The objective of this thesis research was to advance mass spectrometry imaging techniques for challenging real-world samples and analytes. The motivation stems from the belief that better tools enable better research, consequently an increased understanding of the world around us. We have focussed on ambient mass spectrometry because, in comparison to vacuum-based MSI, it is more flexible in terms of sample size, sample material and analyte properties. Infrared laser-based techniques are especially suitable for the analysis of water-containing samples such as biological tissues, foodstuffs, and novel synthetic materials such as hydrogels.

6.2. MASS SPECTROMETRY IMAGING OF BIOMATERIALS

In **Chapter 2** we present the current possibilities in molecular imaging of biomaterials, to lay the foundation upon which the research in this thesis builds. This published review forms a solid knowledge base for anyone who wants to familiarize themselves with the topic. At the same time, the writing and data gathering process has increased the depth knowledge of the authors in this topic, which enabled them to direct their research efforts more effectively.

6.3. AMBIENT PLASMA IONIZATION: NOVEL PROBE DESIGN AND APPLICATIONS

Chapter 3 shows for the first time that atmospheric pressure chemical ionization (i.e. “plasma”) can successfully be incorporated in an MSI setup, and demonstrates clear benefits over the - more common - electrospray ionization alternative. In this project we collaborated with Bayer Crop Science, who are very keen to investigate new analysis techniques to gain more knowledge about their products. In this chapter we investigated how one of their antifungal agents spreads and converts inside a plant. Such information is highly valuable for the creation of more effective antifungal products.

The new combined LAESI/LA-APCI platform has high potential for the analysis of natural materials, such as organic versus non-organic agriculture. Comparisons of agricultural products on a localized, molecular level can produce new insights on their nutritional value and the underlying biological processes. This, in turn, has the potential to influence the public debate on this matter. To spread the knowledge about this novel instrumentation as broadly as possible we published the scientific results from **Chapter 3** in an open access journal and presented it at multiple academic meetings. We designed the two latest prototypes (one at Maastricht University and one at Wageningen University) to a high standard for reliability and safety. Therefore, we feel this design is ready to be commercialised, for which we are seeking an industry partner. The design will be very difficult to copy without direct



access to our prototypes and the raw data, which should protect it from being copied by competitors.

6.4. AMBIENT COLLECTION AND IONIZATION OF INTACT PROTEIN COMPLEXES WITH LAESI

Native MS could be used in high-throughput diagnostic screening approaches by use of infrared laser ablation, as described in **Chapter 4**. Native MS holds great promise for the analysis of dysfunctional enzymes, which are the root cause of many illnesses. Native MS is not quite ready for such approaches, yet. With this, the social impact of our research is still very much undecided. However, our method has only recently been published in an open-access journal, and we expect swift adoption by the scientific community once diagnostic native MS applications have been developed. The impact on the diagnosis and treatment of metabolic diseases with such a screening methodology cannot be overstated.

Interestingly, a few months after the publication of our results the group of Bunch published results of non-covalent protein complex analysis by DESI-MS.³²⁵

6.5. EXTENDING THE DETECTION LIMITS IN AMBIENT MASS SPECTROMETRY IMAGING

The methods and approaches presented and described in **Chapter 5** are expected to be incorporated in new (commercial) analytical equipment and software, for enhanced performance without time or hardware requirements. In fact, our high mass resolution MSI platform was developed in collaboration with Spectroswiss, an industry partner which specialises in advanced add-on data acquisition systems and data processing tools. The platform is commercially available and has already been implemented in other investigations.³²⁶⁻³²⁸ The data processing and analysis software was recently launched by Spectroswiss as software product "Mozaic", which is used at the M4i institute in novel academic research. Currently, there are ongoing

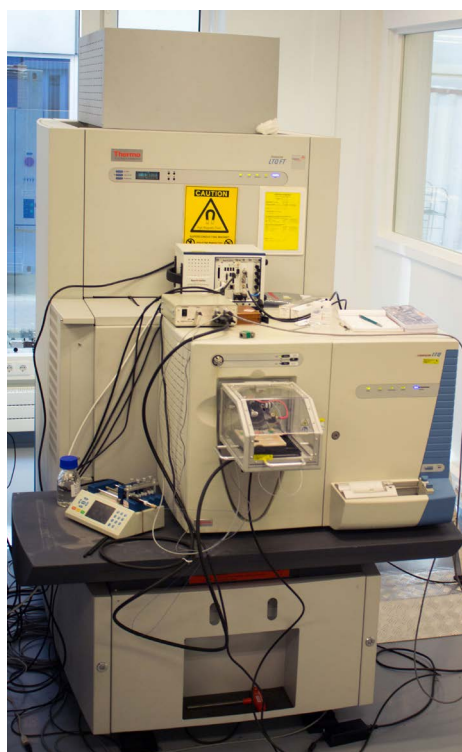


Figure 6.1: The ultra-high mass resolving power MSI platform as present at Maastricht University

collaborations with Spectroswiss for further improvements in high resolution and high throughput MSI at the M4i institute. This research project is a good example of a complete technological development cycle: academic research leads to a product, which in turn leads to improved academic research.

In addition, the published results should help to raise awareness on the potential interferences observed with (low-resolution) mass spectrometry. Any researcher should be vigilant that their results might be compounded by other ion species, potentially affecting their interpretation. We ensured quick dissemination of our results by publishing in an open-access journal (Scientific Reports) and making the experimental data available in a public database (Metaspace). The effective dissemination of this publication is confirmed by a citation rate of 28, at the time of writing.

6.6. ADDITIONAL IMPACT

In addition to the published works upon which this thesis is based, the research project at Maastricht University yielded other significant results. Two examples are the multi-purpose ambient imaging setup, and the low-temperature plasma (LTP) probe which were developed in collaboration with IDEE from Maastricht University (see Figure 6.2). The multi-purpose imaging setup has been developed and used to optimize novel ambient ionization probes accurately and fast.

The LTP probe has been developed to provide accurate (approx. 100 μm) spatial resolution plasma desorption and ionization. Though the spatial resolution and ionization were achieved, the desorption capabilities of the low-temperature plasma probe are too weak for practical applications. Only volatile compounds (e.g. capsaicin from peppers) could be successfully imaged, which we judged to be insufficiently novel for publication. However, the knowledge obtained in this project did lay the foundation for the combined LAESI/LA-APCI probe from **Chapter 3**. The LTP probe itself can be used in future LA-APCI imaging instruments. The dense and narrow plasma stream would be ideal for a miniaturized LA-APCI imaging source, which could surpass the sensitivity and spatial resolution of the current LAESI/LA-APCI MSI instrument. In this role the LTP probe can be of great value for an industry partner during commercialisation of LA-APCI.

Throughout this PhD research we have been keen to apply our technological advances to (commercial) challenges. Academic collaborators, as well as industry partners such as DSM and Bayer Crop Science provided samples for which they sought suitable analytical techniques. Examples include fungal colonies on agar, plant seeds and roots, cheese, contact lenses, human hair and lung mucus of a patient. The experiments allowed our project partners to make informed decisions on which technologies are able to answer their research questions.



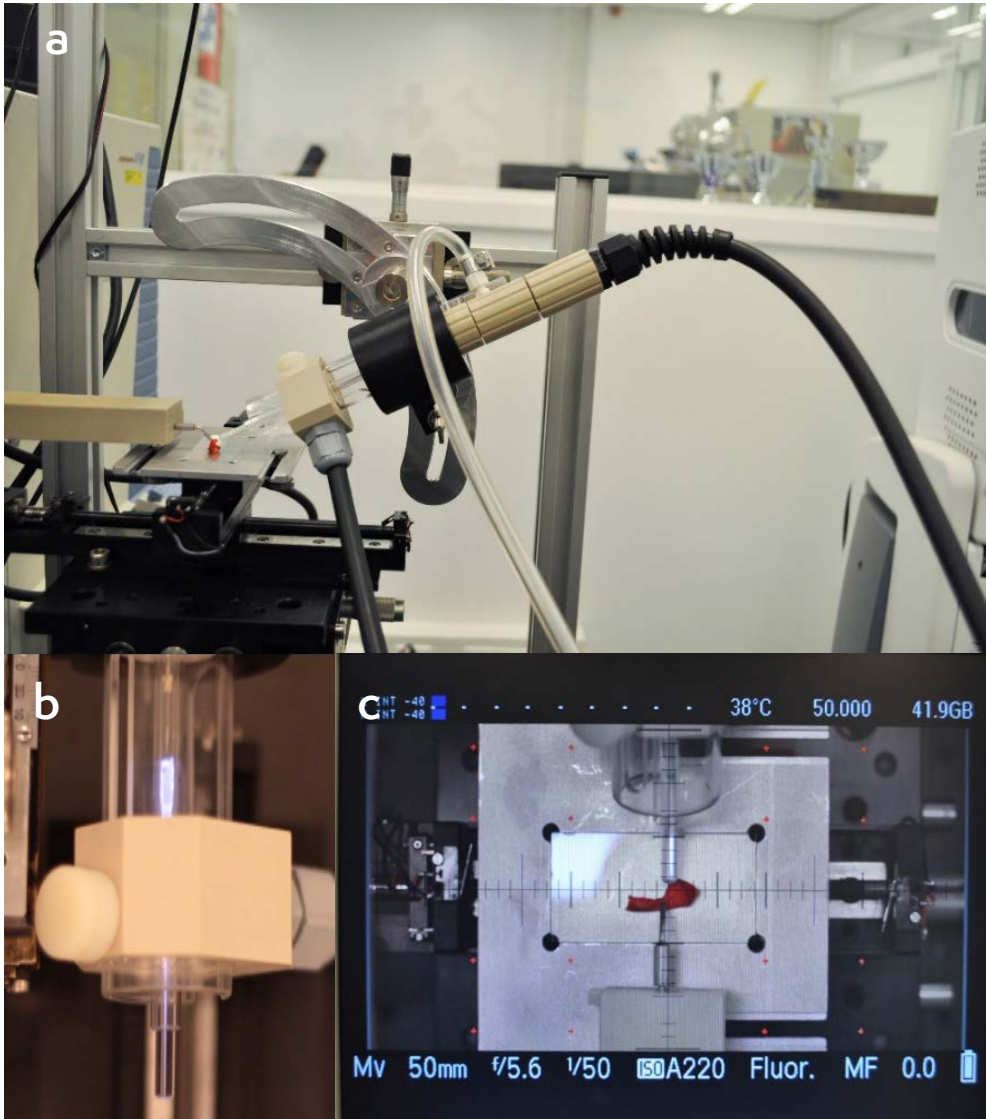


Figure 6.2: The Maastricht University low-temperature plasma (LTP) probe in the multi-purpose ambient imaging setup (a). The probe produces a tight (approx. 100 μm) stream of charged gas (b), to be directed onto a surface. The ambient imaging setup (c) can be accurately tuned to the optimal geometry of any probe.