European Network of Fourier-Transform Ion-Cyclotron-Resonance Mass Spectrometry Centers

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Deliverable D1.5 Annual activity report of the EU_FT-ICR_MS network

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Document Abstract

The deliverable D1.5 “Annual activity report of the EU_FT-ICR_MS network” is part of WP1, dedicated to the trans-national access activities of the Consortium. This deliverable reports the networking activities of the Consortium during the whole project duration, including trans-national accesses, staff-exchange, round-robin tests, short courses and end-user and advanced user schools.

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Abbreviations

AUS	Advanced Users School
EUS	End-Users School
TNA	Trans-national access

1. Introduction

Networking activities are a fundamental pillar of the EU_FT-ICR_MS Consortium. These are centered on trans-national access to the FT-ICR-MS technology by academic, SME and industrial communities, staff exchange between the Consortium Centers, joint research activities between the Consortium Centers and advanced training through the organization of short courses as well as end-users and advanced-user schools.

2. Trans-national access

TNA is a key point of the EU FT-ICR MS network and is part of the Objective 1 of the Consortium: “Provide the EU academic, SME and industrial communities with access to world-class FT-ICR MS centers”. All Centers agreed to offer the same number of TNA days (100 days for each Center), considering an average of 2.5 days per project. In fact, a TNA project is not limited to sample analysis, also including post-processing data analysis and interpretation, so the number of days per project was actually higher than foreseen, resulting in an average of 7.5 to 10 days per submitted project. The total number of days offered by the consortium was exceeded, with more than 1181 days offered for TNA accesses, resulting in an increase of 18% in comparison to the original proposal of 1000 days. Four Centers exceeded the number of previewed TNA days, Warwick, Roma, Prague, and Lille, three Centers reached exactly the 100 days, Liége, Finland and Lisbon, and two were slightly below the predicted number of days, Orsay and Rostock. The Moscow Center was not able to receive TNAs in the last period (Figure 1). The highest demands were for Prague and Warwick access sites, most likely to be related to the specificity of the research and the analyses provided at both sites, mostly protein mass spectrometry.

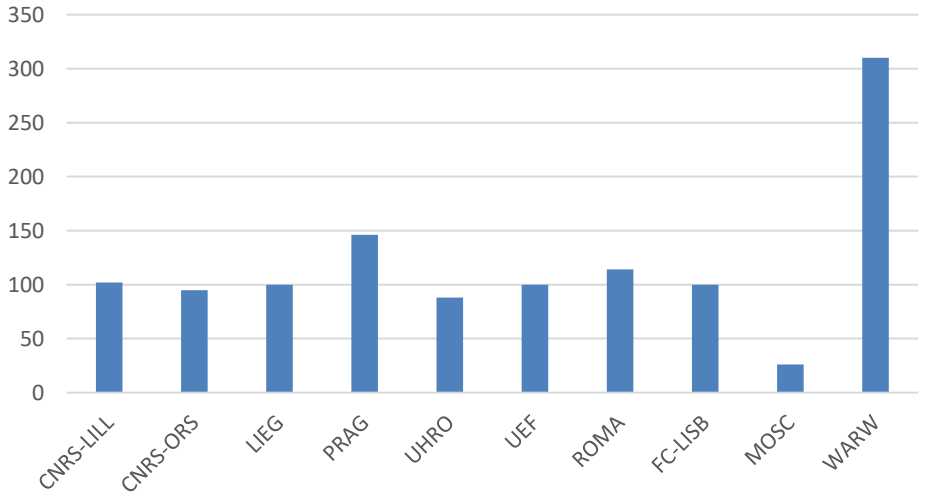

Figure 1. Trans-national accesses during the entire project duration at the different Centers of the EU FT-ICR MS Network.

The duration of the TNAs varied between 3 and 12 days, depending on the number of samples and the need to perform post-processing data analysis and interpretation. Concerning the total number of submitted TNAs, 196 projects were submitted and successfully completed (55 of which being a follow-up of the first submission). This clearly shows the high demand for this advanced mass spectrometry technology, with 28% being a continuation of the first access.

In most of the completed TNAs, the samples were shipped to the Consortium Center, and this was crucial to keep TNAs running during the Covid-19 pandemic. This pandemic was utterly severe and highly disruptive, preventing or reducing the number of accesses during this period, particularly ones that were meant to be presential. Policies varied from country to country with a differentiated impact on each centers. Some labs were able to resume operation before others, even for remote access while some centers only operated in a very limited way with a minimum of staff on-site. As expected, in some TNAs, the researcher(s) or student(s) took the opportunity to visit the site and participate in the analysis. In these cases, TNA users were directly involved in sample preparation, data acquisition and data analysis, gaining training, information, and knowledge on FT-ICR-MS.

During the entire project duration, EU-FT-ICR-MS Centers received TNAs from 30 different countries (Figures 2 and 3). Although most accesses were submitted from European countries, about 12% came from non-European countries.

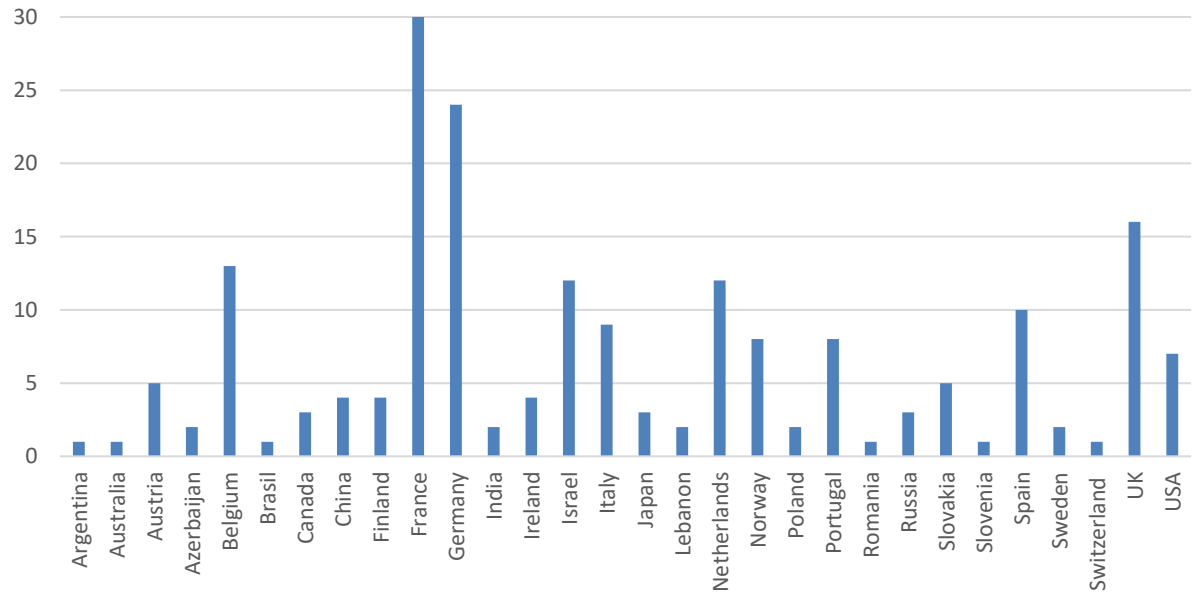

Figure 2. Completed TNAs by country during the whole duration of the EU-FT-ICR-MS project.

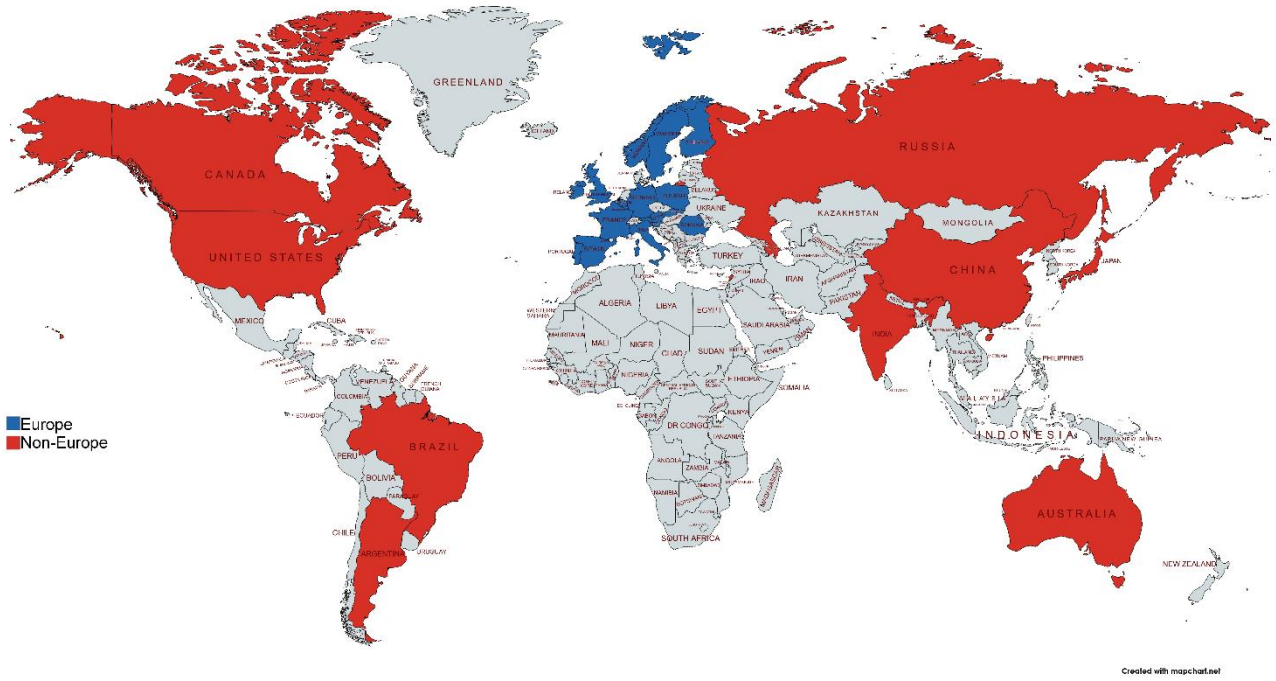

Figure 3. Coloured world map for total TNAs (European countries are labelled in blue and non-European in red).

The submission of a follow-up project by the same researcher is an indicator of the high level of satisfaction of the TNA. Several researchers submitted a second (and sometimes a third) project to the same FT-ICR-MS Center, in a total of 55 follow-ups among the 196 TNAs (28% of total accesses) during the whole duration of the project. These researchers clearly expressed an intention to pursue a collaboration with the selected Centers.

A total of 36 published papers and 2 posters or conference proceedings resulted from these TNAs and collaborations with members of the network, with many others in preparation (members of the EU FT-ICR MS network are highlighted in bold, TNA users are underlined):

Scientific articles:

1. Claudia Hackenberg, Johanna Hakanpää, Fei Cai, Svetlana Antonyuk, Caroline Eigner, Sven Meissner, Mikko Laitaoja, **Janne Jänis**, Cheryl A. Kerfeld, Elke Dittmann, Victor S. Lamzin (2018) Structural and functional insights into the unique CBS-CP12 fusion protein family in cyanobacteria. *PNAS* 115(27), 7141-7146. DOI: 10.1073/pnas.1806668115

2. **Davide Corinti**, **Maria Elisa Crestoni**, **Simonetta Fornarini**, Maren Pieper, Karsten Niehaus, Marco Giampà (2019) An integrated approach to study novel properties of a MALDI matrix (4-maleicanhydridoproton sponge) for MS imaging analyses. *Analytical and Bioanalytical Chemistry* 411, 953-964. DOI: 10.1007/s00216-018-1531-7

3. Frederik Lermyte, Piotr Dittwald, Jürgen Claesen, Geert Baggerman, Frank Sobott, **Peter B. O'Connor**, Kris Laukens, Jef Hooyberghs, Anna Gambin, Dirk Valkenborg (2019) MIND: A Double-Linear Model To Accurately Determine Monoisotopic Precursor Mass in High-Resolution Top-Down Proteomics. *Analytical Chemistry* 91(15), 10310-10319. DOI: 10.1021/acs.analchem.9b02682

4. Roberto Palos, Timo Kekäläinen, Frank Duodu, Alazne Gutiérrez, José M. Arandes, **Janne Jänis**, Pedro Castaño (2019) Screening hydrotreating catalysts for the valorization of a light cycle oil/scrap tires oil blend based on a detailed product analysis. *Applied Catalysis B: Environmental* 256, 117863. DOI: 10.1016/j.apcatb.2019.117863

5. Pavla Vankova, Eduardo Salido, David J. Timson, **Petr Man**, Angel L. Pey (2019) A Dynamic Core in Human NQO1 Controls the Functional and Stability Effects of Ligand Binding and Their Communication across the Enzyme Dimer. *Biomolecules* 9, 728. DOI: 10.3390/biom9110728

6. Veronica Macaluso, Debora Scuderi, **Maria Elisa Crestoni**, **Simonetta Fornarini**, **Davide Corinti**, Enzo Dalloz, Emilio Martinez-Nunez, William L. Hase, Riccardo Spezia (2019) L-Cysteine Modified by S-Sulfation: Consequence on Fragmentation Processes Elucidated by Tandem Mass Spectrometry and Chemical Dynamics Simulations. *J. Phys. Chem. A* 2019, 123, 17, 3685-3696. DOI: 10.1021/acs.jpca.9b01779

7. **Davide Corinti**, Alessandro Maccelli, **Maria Elisa Crestoni**, Stefania Cesa, Deborah Quaglio, Bruno Botta, Cinzia Ingallina, Luisa Mannina, Aura Tintaru, Barbara Chiavarino, **Simonetta Fornarini** (2019) IR ion spectroscopy in a combined approach with MS/MS and IM-MS to discriminate epimeric anthocyanin glycosides (cyanidin 3-O-glucoside and -galactoside). *International Journal of Mass Spectrometry* 444, 116179. DOI: 10.1016/j.ijms.2019.116179

8. Martina Petrenčáková, František Filandr, Andrej Hovan, Ghazaleh Yassaghi, **Petr Man**, Tibor Kožár, Marc-Simon Schwer, Daniel Jancura, Andreas Plückthun, **Petr Novák**, Pavol Miškovský, Gregor Bánó, Erik Sedlák (2020) Photoinduced damage of AsLOV2 domain is accompanied by increased singlet oxygen production due to flavin dissociation. *Scientific Reports* 10, 4119. DOI: 10.1038/s41598-020-60861-2

9. Michal Lisnyansky Bar-El, Pavla Vaňková, Adva Yeheskel, Luba Simhaev, Hamutal Engel, **Petr Man**, Yoni Haitin, Moshe Giladi (2020) Structural basis of heterotetrameric assembly and disease mutations in the human cis-prenyltransferase complex. *Nature Communications* 11, 5273. DOI: 10.1038/s41467-020-18970-z

10. Giel Stalmans, Anastasia V. Lilina, Pieter-Jan Vermeire, Jan Fiala, **Petr Novák**, Sergei V. Strelkov (2020) Addressing the Molecular Mechanism of Longitudinal Lamin Assembly Using Chimeric Fusions. *Cells* 9(7), 1633. DOI: 10.3390/cells9071633

11. Alisa Ferofontov, Pavla Vankova, **Petr Man**, Moshe Giladi, Yoni Haitin (2020) Conserved cysteine dioxidation enhances membrane interaction of human Cl^- intracellular channel 5. *The FASEB Journal* 34, 9925-9940. DOI: 10.1096/fj.202000399R

12. Barbara Chiavarino, Rajeev K. Sinha, **Maria Elisa Crestoni**, **Davide Corinti**, Antonello Filippi, Caterina Fraschetti, Debora Scuderi, **Philippe Maitre**, **Simonetta Fornarini** (2020) Binding Motifs in the Naked Complexes of Target Amino Acids with an Excerpt of Antitumor Active Biomolecule: An Ion Vibrational Spectroscopy Assay. *Chem. Eur. J.* 27, 2348. DOI: 10.1002/chem.202003555

13. Asma Dhahak, Christoph Grimmer, Anika Neumann, **Christopher Rüger**, **Martin Sklorz**, Thorsten Streibel, **Ralf Zimmermann**, Guillain Mauviel, Valérie Burkle-Vitzthum (2020) Real time monitoring of slow pyrolysis of polyethylene terephthalate (PET) by different mass spectrometric techniques. *Waste Management* 106, 226-239. DOI: 10.1016/j.wasman.2020.03.028

14. Idoia Hita, Tomás Cordero-Lanzac, Timo Kekäläinen, Ogechukwu Okafor, José Rodríguez-Mirasol, Tomás Cordero, Javier Bilbao, **Janne Jänis**, Pedro Castano (2020) In-Depth Analysis of Raw Bio-Oil and Its Hydrodeoxygenated Products for a Comprehensive Catalyst Performance Evaluation. *ACS Sustainable Chem. Eng.* 8, 50, 18433-18445. DOI: 10.1021/acssuschemeng.0c05533

15. Anika Neumann, Uwe Käfer, Thomas Gröger, Thomas Wilharm, **Ralf Zimmermann**, **Christopher P. Rüger** (2020) Investigation of Aging Processes in Bitumen at the Molecular Level with High-Resolution Fourier-Transform Ion Cyclotron Mass Spectrometry and Two-Dimensional Gas Chromatography Mass Spectrometry. *Energy & Fuels* 34 (9), 10641-10654. DOI: 10.1021/acs.energyfuels.0c01242

16. Elisa Millana Fañanás, Sofia Todesca, Alessandro Sicorello, Laura Masino, **Petr Pompach**, Francesca Magnani, Annalisa Pastore, Andrea Mattevi (2020) On the mechanism of calcium-dependent activation of NADPH oxidase 5 (NOX5). *FEBS J* 287, 2486-2503. DOI: 10.1111/febs.15160

17. Asma Dhahak, Christoph Grimmer, Anika Neumann, **Christopher Rüger**, Martin Sklorz, Thorsten Streibel, **Ralf Zimmermann**, Guillain Mauviel, Valérie Burkle-Vitzthum (2020) Real time monitoring of slow pyrolysis of polyethylene terephthalate (PET) by different mass spectrometric techniques. *Waste Management* 106, 226-239. DOI: 10.1016/j.wasman.2020.03.028

18. Michal Lisnyansky Bar-El, **Pavla Vaňková**, Adva Yeheskel, Luba Simhaev, Hamutal Engel, **Petr Man**, Yoni Haitin, Moshe Giladi (2020) Structural basis of heterotetrameric assembly and disease mutations in the human cis-prenyltransferase complex. *Nature Communications* 11, 5273. DOI: 10.1038/s41467-020-18970-z~

19. Federica Rinaldi, Linda Maurizi, Antonietta Lucia Conte, Massimiliano Marazzato, Alessandro Maccelli, **Maria Elisa Crestoni**, Patrizia Nadia Hanieh, Jacopo Forte, Maria Pia Conte, Carlo Zagaglia, Catia Longhi, Carlotta Marianecci, Maria Grazia Ammendolia, Maria Carafa (2021) Nanoemulsions of Satureja montana Essential Oil: Antimicrobial and Antibiofilm Activity against Avian *Escherichia coli* Strains. *Pharmaceutics* 13(2), 134. DOI: 10.3390/pharmaceutics13020134

20. Nataša Tomášková, **Petr Novák**, Tibor Kožár, Martina Petrenčáková, Daniel Jancura, Ghazaleh Yassaghi, **Petr Man**, Erik Sedlák (2021) Early modification of cytochrome c by hydrogen peroxide triggers its fast degradation. *International Journal of Biological Macromolecules* 174, 413-423. DOI: 10.1016/j.ijbiomac.2021.01.189

21. Roberto Palos, Timo Kekäläinen, Frank Duodu, Alazne Gutiérrez, José M. Arandes, **Janne Jänis**, Pedro Castaño (2021) Detailed nature of tire pyrolysis oil blended with light cycle oil and its hydroprocessed products using a NiW/HY catalyst. *Waste Management* 128, 36-44. DOI: 10.1016/j.wasman.2021.04.041

22. Helene J. Bustad, Juha P. Kallio, **Mikko Laitaoja**, Karen Toska, Inari Kursula, Aurora Martinez, **Janne Jänis** (2021) Characterization of porphobilinogen deaminase mutants reveals that arginine-173 is crucial for polypyrrole elongation mechanism. *iScience* 24 (3), 102152. DOI: 10.1016/j.isci.2021.102152

23. **Davide Corinti**, Barbara Chiavarino, Mattia Spano, Aura Tintaru, **Simonetta Fornarini**, **Maria Elisa Crestoni** (2021) Molecular Basis for the Remarkably Different Gas-Phase Behavior of Deprotonated Thyroid Hormones Triiodothyronine (T3) and Reverse Triiodothyronine (rT3): A Clue for Their Discrimination? *Analytical Chemistry* 93(44), 14869-14877. DOI: 10.1021/acs.analchem.1c03892

24. Andrés F. Cruz-Ortiz, Rafael A. Jara-Toro, Matias Berdakin, **Estelle Loire**, Gustavo A. Pino (2021) Gas phase structure and fragmentation of [Cytosine-Guanine]Ag+ complex studied by mass-resolved IRMPD spectroscopy. *The European Physical Journal D* 75, 119. DOI: 10.1140/epjd/s10053-021-00129-0

25. Andrés F. Cruz-Ortiz, Franco L. Molina, **Philippe Maitre**, Gustavo A. Pino (2021) Guanine Tautomerism in Ionic Complexes with Ag+ Investigated by IRMPD Spectroscopy and Mass Spectrometry. *J. Phys. Chem. B* 125, 26, 7137–7146. DOI: 10.1021/acs.jpcb.1c03796

26. Kevin Jeanne Dit Fouque, Valeriu Scutelnic, Julian D. Hegemann, Sylvie Rebuffat, **Philippe Maître**, Thomas R. Rizzo, Francisco Fernandez-Lima (2021) Structural Insights from Tandem Mass Spectrometry, Ion Mobility-Mass Spectrometry, and Infrared/Ultraviolet Spectroscopy on Sphingonodin I: Lasso vs Branched-Cyclic Topoisomers. *J. Am. Soc. Mass Spectrom.* 32, 4, 1096–1104. DOI: 10.1021/jasms.1c00041

27. Walter E. Olmedo, Liliana B. Jimenez, Andrés F. Cruz-Ortiz, **Philippe Maitre**, Gustavo A. Pino, Maximiliano Rossa (2021) Infrared Multiple Photon Dissociation Spectroscopy of Protonated Cyameluric Acid. *J. Phys. Chem. A* 125, 2, 607–614. DOI: 10.1021/acs.jpca.0c09394

28. Pieter-Jan Vermeire, Giel Stalmans, Anastasia V. Lilina, Jan Fiala, **Petr Novak**, Harald Herrmann, Sergei V. Strelkov (2021) Molecular Interactions Driving Intermediate Filament Assembly. *Cells* 10(9), 2457. DOI: 10.3390/cells10092457

29. Juan Luis Pacheco-Garcia, Ernesto Anoz-Carbonell, **Pavla Vankova**, Adithi Kannan, Rogelio Palomino-Morales, Noel Mesa-Torres, Eduardo Salido, **Petr Man**, Milagros Medina, Athi N. Naganathan, *Angel L. Pey* (2021) Structural basis of the pleiotropic and specific phenotypic consequences of missense mutations in the multifunctional NAD(P)H:quinone oxidoreductase 1 and their pharmacological rescue. *Redox Biology* 46, 102112. DOI: 10.1016/j.redox.2021.102112

30. Aleš Hnízda, Petr Tesina, Thanh-Binh Nguyen, **Zdeněk Kukačka**, Lukas Kater, Amanda K. Chaplin, Roland Beckmann, David B. Ascher, **Petr Novák**, Tom L. Blundell (2021) SAP domain forms a flexible part of DNA aperture in Ku70/80. *FEBS J* 288, 4382-4393. DOI: 10.1111/febs.15732

31. Muhammed Fatih Sert, Helge Niemann, Eoghan P. Reeves, Mats A. Granskog, Kevin P. Hand, **Timo Kekäläinen**, **Janne Jänis**, Pamela E. Rossel, Bénédicte Ferré, Anna Silyakova, Friederike Gründger (2022) Compositions of dissolved organic matter in the ice-covered waters above the Aurora hydrothermal vent system, Gakkel Ridge, Arctic Ocean. *Biogeosciences* 19, 2101–2120. DOI: 10.5194/bg-19-2101-2022

32. **Davide Corinti**, Alessandro Maccelli, Barbara Chiavarino, Markus Schütz, Aude Bouchet, Otto Dopfer, **Maria Elisa Crestoni**, **Simonetta Fornarini** (2022) Cation-π Interactions between a Noble Metal and a Polyfunctional Aromatic Ligand: Ag+(benzylamine) *Chem. Eur. J.* 28, e202200300. DOI: 10.1002/chem.202200300

33. Alba Lasalvia, Francesco Cairone, Stefania Cesa, Alessandro Maccelli, **Maria Elisa Crestoni**, Luigi Menghini, Simone Carradori, Beatrice Marinacci, Marialucia Gallorini, Osama Elsallabi, Mirko Pesce, Antonia Patruno (2022) Characterization and Valorization of 'Sulmona Red Garlic' Peels and Small Bulbs. *Antioxidants* 11, 2088. DOI: 10.3390/antiox11112088

34. **Davide Corinti**, Roberto Paciotti, Cecilia Coletti, Nazzareno Re, Barbara Chiavarino, **Maria Elisa Crestoni**, **Simonetta Fornarini** (2022) Elusive intermediates in cisplatin reaction with target amino acids: Platinum(II)-cysteine complexes assayed by IR ion spectroscopy and DFT calculations. *J Inorg Biochem* 237, 112017. DOI: 1016/j.jinorgbio.2022.112017

35. Eric Schneider, Barbara Giocastro, **Christopher P. Rüger**, Thomas W. Adam, **Ralf Zimmermann** (2022) Detection of Polycyclic Aromatic Hydrocarbons in High Organic Carbon Ultrafine Particle Extracts by Electrospray Ionization Ultrahigh-Resolution Mass Spectrometry. *J. Am. Soc. Mass Spectrom.* 33, 11, 2019–2023. DOI: 10.1021/jasms.2c00163

36. Lukas Friederici, Sara-Maaria Meščeriakovė, Anika Neumann, Ekaterina Sermyagina, Arūnas Meščeriakovas, Anna Lähde, Christoph Grimmer, Thorsten Streibel, **Christopher P. Rüger**, **Ralf Zimmermann** (2022) Effect of hydrothermal carbonization and eutectic salt mixture (KCl/LiCl) on the pyrolysis of Kraft lignin as revealed by thermal analysis coupled to advanced high-resolution mass spectrometry. *Journal of Analytical and Applied Pyrolysis* 166, 105604. DOI: 10.1016/j.jaap.2022.105604

37. Isabel Nogues, Laura Passatore, M. A. Bustamante, E. Pallozzi, João Luz, Francisco Traquete, **António E.N. Ferreira**, **Marta Sousa Silva**, **Carlos Cordeiro** (2023) Cultivation of *Melilotus officinalis* as a source of bioactive compounds in association with soil recovery practices. *In preparation*

Posters in conferences and conference proceedings:

1. Marisa Maia, Rebecca Höfle, Ana R. Cavaco, Alessandro Maccelli, Gonçalo Laureano, Joana Figueiredo, **António Ferreira**, **Maria Elisa Crestoni**, **Carlos Cordeiro**, Reinhard Töpfer, Anna Kicherer, Andreia Figueiredo, **Marta Sousa Silva** (2018) Grapevine resistance to *Plasmopara viticola*: the search for metabolic biomarkers. *XII International Conference on Grapevine Breeding and Genetics*, Bordeaux (France) - Poster

2. **Janne Jänis**, Helene J. Bustad, Juha Kallio, Mikko Laitaoja, Karen Toska, Inari Kursula, Aurora Martinez (2018) Characterization of hydroxymethylbilane synthase and its acute intermittent porphyria associated mutants by Fourier transform ion cyclotron resonance mass spectrometry - Conference proceeding

3. Training, education and networking activities

3.1. Staff-exchange

Staff exchange between the different Centers of the network promoted sharing of specific skills and competences. This network activity was particularly valuable for young students and young members of each team, and one week of staff exchange per partner per year was predicted.
The Covid-19 pandemic situation reduced the number of staff exchange visits, due to Institutional and travelling restrictions. Nevertheless, collaborative work was maintained by sending samples and discussions through zoom meetings.

During the whole project duration, 12 staff exchanges occurred between the different Centers. Some of the resulting joint publications are listed below:

1. ROMA – LISBON:
   Ingallina, C., Maccelli, A., Spano, M., Di Matteo, G., Di Sotto, A., Giusti, A.M., Vinci, G., Di Giacomo, S., Rapa, M., Ciano, S., Fraschetti, C., Filippi, A., Simonetti, G., **Cordeiro, C**., **Sousa Silva, M.**, **Crestoni, M.E**., Sobolev, A.P., **Fornarini, S**., Mannina, L. (2020) Chemico-biological characterization of Torpedino di Fondi® tomato fruits: a comparison with San Marzano cultivar at two ripeness stages. *Antioxidants* (Section: Natural and Synthetic Antioxidants; Special Issue: "The Potential of Dietary Antioxidants") 9(10), 1027. DOI: 10.3390/antiox9101027

2. ROMA – LISBON:
   Maia, M., Maccelli, A., Nascimento, R., Ferreira, A.E.N., **Crestoni, M.E**., **Cordeiro, C**., Figueiredo, A., **Sousa Silva, M.** (2019) Early detection of *Plasmopara viticola* infected leaves through FT-ICR-MS metabolic profiling. *Acta Horticulturae* 1248, 575-580. DOI: 10.17660/ActaHortic.2019.1248.77

3. ROMA – ORSAY:
   Roberto Paciotti, Davide Corinti, **Philippe Maitre**, Cecilia Coletti, Nazzareno Re, Barbara Chiavarino, **Maria Elisa Crestoni**, **Simonetta Fornarini** (2021) From Preassociation to Chelation: A Survey of Cisplatin Interaction with Methionine at Molecular Level by IR Ion Spectroscopy and Computations. *J. Am. Soc. Mass Spectrom*. 32, 8, 2206–2217. DOI: 10.1021/jasms.1c00152

4. LISBON – LIÉGE:
   Marisa Maia, Andrea McCann, C. Malherbe, **Johan Far**, Jorge Cunha, José Eiras-Dias, **Carlos Cordeiro**, G. Eppe, Loid Quinton, Andreia Figueiredo, **Edwin De Pauw**, **Marta Sousa Silva** (2022) Grapevine leaf MALDI-MS imaging reveals the localisation of a putatively identified sucrose metabolite associated to *Plasmopara viticola* development. *Frontiers in Plant Science - Sec. Technical Advances in Plant Science* 13, 1012636. DOI: 10.3389/fpls.2022.1012636

3.2. Courses and schools

During this project, 10 short courses, 2 end-user schools and 2 advanced-user schools were organized (Table 1).

Date	Short Course / School	Location
12 - 16 December 2022	**EU_FT-ICR_MS - End-User School #2 - Final**	Lille - France
21 - 26 November 2022	**EU FT ICR MS - Short Courses #8 and #10**	Liège - Belgium & Lille - France
19 - 22 April 2022	**EU FT ICR MS - Short Course #9**	Joensuu - Finland
17 - 20 October 2021	**EU FT ICR MS - Short Course #6**	Lisbon - Portugal
26 - 30 September 2021	**EU FT-ICR MS - Advanced-User School #2**	Prague - Czech Republic
16 - 19 August 2020	**EU FT-ICR MS - Short Course #7**	Prague - Czech Republic
10 - 12 October 2019	**EU FT-ICR MS - Short Course #5**	Moscow - Russia
21 - 23 August 2019	**EU FT-ICR MS - Short Course #4**	Warwick - UK
25 - 27 June 2019	**EU FT-ICR MS - Short Course #3**	Roma - Italy
14 - 18 April 2019	**EU FT-ICR MS - Advanced-User School #1**	Lisbon - Portugal
05 - 07 November 2018	**EU FT-ICR MS - Short Course #2**	Orsay - France
20 - 24 August 2018	**EU FT-ICR MS - End-User School #1**	Joensuu - Finland
05 - 07 March 2018	**EU FT-ICR MS - Short Course #1**	Rostock - Germany

Table 1. Short courses and Schools organized by the EU-FT-ICR-MS consortium.

End-User and Advanced-User Schools had an average duration of 5 days per school, while the short courses had a duration of 2-3 days, as proposed. Due to the pandemic situation, some schools were postponed and rescheduled. All these training events reached the maximum number of students allowed and after the pandemic situation, some included a virtual attendance of the theoretical talks by zoom.

3.3. The proposal for the organization of the European Fourier Transform Mass Spectrometry Conference

An important contribution for networking was the organization of the European Fourier Transform Mass Spectrometry conference (EFTMS). This conference had been already organized or co-organized in the past by members of this Consortium (E. Nikolaev: Moscow, 2008; P. O'Connor: Warwick, 2012; G. van der Rest: Paris, 2014), and the 14th EFTMS was organized on behalf of the EU FT-ICR-MS Consortium in Lisbon.
The proposal for the organization of the 14th EFTMS conference was announced during the 13th EFTMS in Freising by FC-LISB (on behalf of the EU FT-ICR MS Consortium) and was successful. Lisbon was supposed to organize the 14th EFTMS in 2020, but the pandemic situation worldwide forced a postponing to 2022.

The 14th EFTMS workshop and the 3rd EFTMS School took place at the Thalia Theatre in Lisbon, from 11 to 14 July 2022, (http://eftms2022.campus.ciencias.ulisboa.pt/). All PIs of the Consortium were invited as speakers and the program had also the participation of Alexander Makarov, Roman Zubarev and Yuri Tsybin, among others. The scientific program was the following (consortium PIs are highlighted in bold). There was also ample opportunity for your researchers to present their work, as a poster but also as oral presentation. This combination of experienced researchers and speakers presenting their work together with young and aspiring researchers is fundamental to keep these field alive, evolving and to maintain a vital intergenerational bond.

11th July - School
12:30 - 13:30 Registration + welcome cocktail
13:30 - 13:40 Opening school | **Carlos Cordeiro**
13:45 - 14:30 Fourier Transform Ion Cyclotron Resonance Mass Spectrometry: Fundamental Concepts | **Peter O'Connor**
14:30 - 15:15 2D FT-MS | **Christian Rolando**
15:15 - 16:00 Discussion over coffee
16:00 - 16:45 Fundamental concepts of Orbitrap | Alexander Makarov
16:45 - 17:30 FTMS proteomics methods for post-translational modifications | Roman Zubarev
17:30 - 18:15 MRMS in the new world of metabolomics | **Carlos Cordeiro**
12th July - Workshop
09:30 - 10:00 Registration
10:00 - 10:15 Opening workshop | **Carlos Cordeiro** & Luis Carriço (FCUL Director)
Session 1: FTMS fundamentals and instrumentation, Chair: Alexander Makarov
10:15 - 11:00 Expanding Capabilities of Orbitrap Instrumentation | Alexander Makarov
11:00 - 11:20 Coffee break
11:20 - 12:05 FT Mass Spectrometer Based on Multielectrode Harmonized Kingdon trap | **Evgeny Nikolaev**
12:05 - 12:50 Combining Ultraviolet Photodissociation and 2-Dimensional Mass Spectrometry | Peter O'Connor
12:50 - 14:00 Lunch & posters
14:00 - 14:40 FT Mass spectra simulation: Fundamentals and applications | Yury Tsybin
14:40 - 15:20 FTMS in Cultural Heritage | **Christian Rolando**
15:20 - 15:50 Vacuum Photoionization on an Orbitrap FTMS Platform: Prototype and Perspectives | **Christopher Rüger**
15:50 - 16:30 Differential Ion Mobility Spectroscopy of Metabolites | Chiraz El-Saddik
16:30 - 17:00 Coffee break
Selected oral presentations, Chair: ***Christopher Rüger***
17:00 - 17:15 Investigation of Asphaltenes and Asphaltene-related Materials with Thermal Analysis coupled to Fourier Transform Ion Cyclotron Resonance Mass Spectrometry | Anika Neumann
17:15 - 17:30 Linking Asphaltene characterization by LDI(+) FT-ICR MS with its stability behavior | Boniek Gontijo
17:30 - 17:45 Speciation and semi-quantification of nitrogen-containing species in complex mixtures: application to plastic pyrolysis oil | Charlotte Mase
17:45 - 18:00 Chemical characterization of wildfire particulate matter emissions by ESI/APPI FT-ICR MS | Eric Schneider
18:00 - 18:15 Investigating the insoluble organic matter in primitive chondrites using ultra-high-resolution mass spectrometry | Julien Maillard
18:15 - 18:30 Selective characterization of petroporphyrins in shipping fuels and their corresponding emissions using electron-transfer matrix-assisted laser desorption/ionization Fourier transform ion cyclotron resonance mass spectrometry | Maxime Sueur
20:30 - 22:00 Gala Dinner (supported by Bruker), At Casa do Alentejo (Rua Portas de Santo Antão, 58, 1150-268 Lisboa)
13th July - Workshop
Session 2: Protein analysis and Proteomics, Chair: Francisco Amado
09:30 - 10:15 Fourier Transform Isotopic Ratio Mass Spectrometry | Roman Zubarev
10:15 - 11:00 Utilization of Fast Photo-Oxidation of Proteins and Top down Mass Spectrometry for structural characterization of proteins | **Petr Novak**
11:00 - 11:20 Coffee break

11:20 - 12:05 Structural characterization of major donkey seminal plasma proteins with high-resolution bottom-up/top-down mass spectrometry | **Janne Jan**is
12:05 - 12:50 Current Advances in Deep, Proteome-Wide, MS-based PISA Assay for High Throughput Identification of Drug Targets and Action Mechanisms | Massimiliano Gaetani
12:50 - 14:30 Lunch (supported by Bruker)
Session 3: MRMS, Chair: Mike Easterling
14:30 - 14:50 Comprehensive top-down analysis of proteins using multi-mode fragmentation on ScimaX MRMS | Alina Theisen
14:50 - 15:30 The Paracell: optimisation and MRMS developments | Christopher Wootton
15:30 - 16:10 New insights in bitumens and lubricants characterization by Fourier transform Mass spectrometry | **Carlos Afonso**
16:10 - 16:30 Coffee break (supported by Bruker)
Selected oral presentations, Chair: ***Maria Elisa Crestoni***
16:30 - 16:45 Structural Characterization of Harwood Xylan with Direct-Infusion ESI FT-ICR Mass Spectrometry | Mikko Nikunen
16:45 - 17:00 Noble gas oxide cations in the gas phase - examining Ng+–O energetics (ng = Kr, Xe, Rn) by experiment and theory | Sandrina Oliveira
17:00 - 17:15 Molecular characterization of hydrophobic burned soils by ultra-high resolution mass spectrometry | Nicasio T. Jiménez-Morillo
17:15 - 17:30 FDS – first instrument independent database for natural organic matter | Alexander Zherebker
17:30 - 17:45 PyC2MC: A Python-Based Framework for Processing Multidimensional High-Resolution Mass Spectrometry Data | Carlos M. Celis-Cornejo
17:45 - 18:00 Our metal brain: amyloid protein aggregation and metal binding | Francesca O. Bellingeri
18:00 - 18:15 Glycoproteomics of glycoengineered simples cells for the identification of bladder cancer molecular targets | André M. N. Silva
18:15 - 18:30 Dark Charge | Callan Littlejohn
14th July - Workshop
Session 4: FTMS in real life, Chair: ***Petr Novak***
09:30 - 10:15 From ESI analysis to MALDI imaging – studying lipid oxidation on a 7T MALDI FT-ICR instrument | Martina Marchetti-Deschmann
10:15 - 11:00 Salivary proteome of patients with Autoimmune Hepatitis (AIH) and Primary Biliary Cholangitis (PBC): scratching problems and solutions | Francisco Amado
11:00- 11:30 Coffee break
11:30 - 12:10 LC-HRMS Analysis of Marine Biotoxins in Complex Samples | José Paulo da Silva
12:10 - 12:50 Cation-π Interactions in Ag+(Benzylamine) Complex Unveiled by IRMPD Spectroscopy and Ion-Molecule Reactions | **Maria Elisa Crestoni**
12:50 - 14:00 Awards by Refeyn & Closing | **Carlos Cordeiro** & Margarida Santos-Reis (FCUL Vice-Director)
14:00 - 15:00 Farewell cocktail, (supported by Refeyn)

The European FTMS conference was attended by 83 participants from 10 European countries and 1 non-European country (Brasil). The abstract book can be downloaded here: http://eftms2022.campus.ciencias.ulisboa.pt/assets/files/Abstract-bookEFTMS2022.pdf

This event had several sponsors, Bruker Daltonics at Platinum level, ThermoFisher as Silver Sponsor, Refeyn sponsored the Awards (best short oral presentation and best poster), and had also the support from Faculdade de Ciências da Universidade de Lisboa, Spectroswiss, Instruct, FCiências.ID, and the EU-FT-ICR-MS consortium.

4. Joint Research Actions

4.1. The first round-robin test

The first Round-robin test performed within the EU_FT-ICR_MS network aimed to provide information on the different equipment performance among the network centers, as well as the consistency of data including mass accuracy, sensitivity and MSMS performance. This test was performed in August / September 2018 and the chosen sample was the peptide Leucine-enkephalin (Sigma), shipped from FC-LISB to all EU FT-ICR MS Centers. The minimum requirements for the analysis were the determination of the exact mass of the molecular ion in positive and negative ionization modes, the measurement of the relative intensities of the molecular ion and the two first isotopes in positive and negative ionization modes, and the measurement of the exact mass of the MS/MS spectra also in positive and negative ion modes.

All centers were able to obtain mass spectra in positive and negative ion modes, reporting resolution and mass accuracy. All centers were able to report the isotopic pattern of carbon, but only 50% calculated the relative intensities of the molecular ion and the two first isotopes. Isotopic fine structure was only presented by 50% of the centers. Concerning MSMS, 2 centers did not report it. MSMS was performed by 80% of the centers, using mainly CID. Two centers also fragmented with IRMPD and one used 2D MSMS.

Analysing the effect of magnetic field in maximum reported resolution, it is clear that it increases non-linearly with the magnetic field. Nevertheless, more uniform conditions are needed to compare achieved resolution at a given magnetic field strength. This test achieved at least 80% response in the proposed objectives as is representative of the expected routine performance of all FT-ICR-MS centres.

4.2. The second round-robin test

The purpose of the second Round-robin test was to evaluate each site for instrument performance concerning resolution, mass accuracy and capabilities to detect isotope fine structure. Most importantly, to quantify how close the experimental isotopic distributions are in relation to the theoretical ones. The test sample had to be amenable to analysis on every site, be easily analysed both positive ionisation mode and stable at room temperature for the duration of the measurements. This test was performed in June-July 2021 and the chosen sample was the peptide glutathione, purchased by each EU FT-ICR MS Center. This tripeptide plays a central role in biochemistry and contains sulphur, thus creating an analytical challenge in terms of resolution and dynamic range.

EU_FT-ICR_MS center	CNRS	LIEG	PRAG	UHRO	UEF	ROMA	FC-LISB	MOSC	WARW	ROUEN	ORSAY
Mass spectrometer	SolariX XR	SolariX XR	SolariX XR	SolariX	SolariX XR	BioApex	SolariX XR	Apex Ultra	SolariX XR	SolariX XR	Apex Q
ICR cell tyoe	Paracell	Paracell	Paracell	Infinity	Paracell	Infinity	Paracell	Paracell	Paracell	Paracell	Infinity
FT-ICR magnetic field	9.4T	9.4T	15T	7T	12T	4.7T	7T	7T	15T	12T	7T
Ionization mode	nanoESI+	ESI+	ESI+	ESI+	ESI+	ESI+	ESI+	ESI+	ESI+	ESI+	ESI+
Infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion	Direct infusion
Analysis mode	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude	Magnitude
Accurate mass measured (m/z)	308.09102	308.0909	308.09107	308.09059	308.0909778	308.091245	308.09109	308.09107	308.091084	308.09108	308.091404
Deviation (ppm)	-0.194	-0.594	0.03	1.61	-0.341	0.53	-0.03	0.03	0.0032	0.01	1
Highest resolution achieved (monoisotopic peak), broad band	1 716 285	883 389	870 598	975 071	1 328 618	60 000	695 339	971 978	1 956 550	492 276	918 000
Isotopic distribution of GSH	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
Nr. Isotopologues identified	12	12	9	11	12	5	12	12	12	12	9
Highest deviation (isotopologue number)	59.31% (10th)	67.19% (6th)	2.5% (4th)	58% (8th)	48% (11th)	17% (4th)	27% (11th)	37% (8th)	58% (2nd)	50% (5th)	125% (12th)

Table 1. Analysis of glutathione by the different EU_FT-ICR_MS centers.

The analysis we made with the purpose achieving the best possible coverage of the 12th most abundant isotopologues of GSH while striving for the highest relative intensities match between the observed and predicted intensities for each isotopologue thus pushing the limits of the instruments towards isotope pattern accuracy (table 1). All centres were able to detect carbon isotopologues (100%), 6 were able to detect all 12 (55%), one detected 11 (9%), 2 centres detected 9 (18%) and 1 only detected 5 (9%). Instruments of higher magnetic field, newer generation and equipped with the paracell performed better, although any field strength between 7 and 15 T allows detection of all the 12th isotopologues. Concerning the deviation between observed and estimated isotopologue intensities at the nth worst case, it varied between 2.5% and 125%. For half the centres, the worst deviation was between 37% and 67%. These results were irrespective of instrument generation, field strength or cell type. PRAG achieved a deviation of 2.5% while WARW stood at 58% (most recent instruments, both 15T) while ROMA achieved 17% (oldest generation, lowest field, at 4.7 T).

Concerning mass accuracy, all centres, except one were accurate to 1 ppm or better, 5 were accurate to 0.03 ppm or better and one was accurate to 0.003 ppm. Most of these results were again independent of instrument generation, cell type or magnetic field strength although the best result was achieved at 15 T.

Resolution was above 500000 for all centres, except one that reached 60000. Six centres were close or moderately above one million resolving power, while two centres were close to two million resolution to m/z 308. Achieving the highest possible resolution was not an objective of the test hence the reported data should be interpreted as the resolution required to achieve a certain purpose such as identifying all isotopologues with the best possible intensity accuracy.

Future work will be aimed at understanding the roots of these deviations while investigating a real world scenario where a complex mixture will be analysed to obtain the highest number of possible molecular formulas.

5. Conclusion and perspectives

This project was extremely well successful concerning transnational access (TNA), dissemination and training activities. As an example, all courses and schools had more applicants than available seats, showing the high interest that the project is generating in the European Scientific community, laying the foundation for new generations of FT-ICR-MS scientists and experts. Staff exchanging was also a great opportunity to take advantage of all different skills and instrumentation available in all Centers. Concerning TNAs, the number of foreseen access days were exceeded by 18% in relation to the initially allocated ones, with many projects submitted as a follow-up pf the first ones. Many of these teams showed interest in pursuing research work in cooperation with the Consortium Centers after the completion of the project, that's why the EU-FT-ICR-MS Network decided to continue to provide access to FT-ICR-MS instruments, in a collaboration-type model, following a project submission and approval, to researchers who need this technology for their research. The figures show a high satisfaction upon access and a clear need for an European FT-ICR-MS consortium, granting access to a an analytic technology and know-how that has no alternative, thus solving problems that would otherwise remain without solution.