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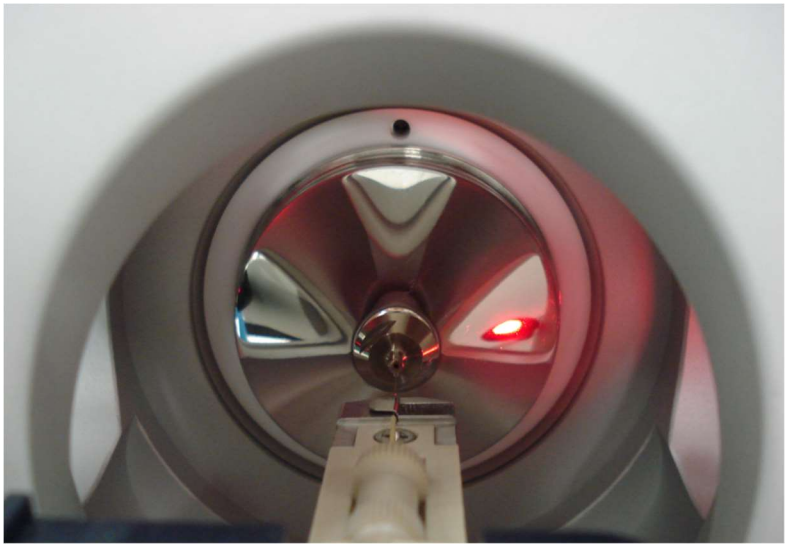
umcg

Annual report 2017

Interfaculty Mass Spectrometry Center



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6 February 2018

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1. Introduction

The annual report of the Interfaculty Mass Spectrometry Center gives an overview of the activities and new developments in the past year, 2017, as well as the current status of the IMSC. The main task of the IMSC is to provide MS services to research groups within the University of Groningen (RUG), and the University Medical Center Groningen (UMCG) as well as to external customers. The IMSC is scientifically oriented and provides not only access to state-of-the-art MS instruments and techniques, but also expertise on analytical aspects including experimental design, sample preparation and data analysis.

A focus point of the IMSC is the support and development of applications in the 'omics' fields, particularly proteomics and metabolomics. The demand for these complex studies is steadily rising, continuing the trend of the last several years. The IMSC has the policy to improve the support for these applications by acquiring appropriate knowledge, hardware and software to address the challenges posed by the complex omics studies. In addition, the IMSC will of course remain a broad MS facility where any project, large or small, will be handled with attention and in a scientifically sound manner. The types of samples we analyze for service, further detailed in section 4, range from proteins to organometal complexes, plant alkaloids to energy metabolites, oligonucleotides to pharmaceutical drugs, synthetic polymers to nanoparticles, and more.

The IMSC, located on the top floor of the ERIBA building in the UMCG complex, is fully established within the research environment of both RUG and UMCG. Contacts with other research facilities, particularly in UMCG, will hopefully lead to an increased service level and streamlining of the operation of the IMSC. In line with this, in 2017 efforts for more outreach to potential customers of the IMSC have started. Although our facility is readily accessed by current customers, and new groups often find us by word-of-mouth, we believe there are still more groups interested in MS or omics analyses that are not yet familiar with, or even aware of, our facility.

The instrumentation in the IMSC has remained constant in 2017. The capacity and capabilities of our current high-end MS systems for omics analyses are a point of concern, however. Efforts for acquiring a new high-end, high-resolution instrument were not successful in 2017, but will be repeated in 2018. Section 2 describes the current status of the instrumentation in the IMSC as well as details on data handling, which has become an ever more important part of the operation of the facility. In section 3 the organizational structure is highlighted, including an update of the access policy of the facility. The overview of projects handled by the IMSC in 2017 is presented in section 4. The scientific output of the IMSC in 2017, both our own research and publications with a direct contribution from IMSC staff, are listed in section 5. Our contributions to the education of (PhD) students and others, in the form of courses and seminars are also detailed in section 5.

ERIBA building

2. Equipment & facilities

The equipment in the IMSC comprises 15 (LC)-MS systems, detailed in the tables below. In addition to these 15 systems, the IMSC since mid-2015 temporarily houses two LC-MS instruments from the UMCG Pharmacy, a Q Exactive Orbitrap and a TSQ Quantum triple quadrupole MS. These instruments are scheduled for relocation to the new Pharmacy lab in mid 2018. From the beginning of 2017 we also house an ABSciex TripleTOF system which is on loan from ABSciex to PRA Health Sciences. PRA closely collaborates with the Analytical Biochemistry department and the IMSC on biopharmaceuticals characterization (see section 4).

Maintenance and repair of LC-MS instruments is a crucial and costly part of running an MS facility. While we remain committed to perform maintenance as much as possible in-house, we have partially outsourced certain tasks; we now make full use of the Medical Technical service of UMCG for vacuum pump maintenance, and have a contract with an independent MS service company, MS Vision, for on-demand service of a range of MS instruments. Our goal is to find the right balance between cost of maintenance and down-time of instruments, to prevent both excessive user fees and waiting times.

Sample preparation has become a larger part of the services we provide in recent years and associated with this is a need for the acquisition and maintenance of sample prep equipment. A significant investment in equipment for Solid Phase Extraction (SPE) was made in 2017, with financial contributions from several large users. In 2016 and 2017 notable investments were also made in data storage hardware and data analysis software.

2.1 Mass spectrometry equipment

All equipment housed and supported by the IMSC is intended to be accessible to researchers from RUG and UMCG, as well as to external customers. Instrument use is charged based on hourly usage or with lump sum payments for larger projects (see section 3).

The list of MS equipment below is organized by instrument type and for each instrument information on the most commonly associated HPLC systems and ion sources is shown. HPLCs are often interchangeable, but ion sources only for instruments from the same vendor and series. Triple quadrupole MS systems are mostly used for targeted quantification, while high-resolution MS systems and ion traps are most useful for identification and characterization of compounds. High-resolution MS systems are becoming increasingly important for quantification purposes as well. Different ionization methods are used for specific compound classes, but the bulk of the analyses are performed with electrospray ionization (ESI). NanoLC and nanoESI are recommended for small sample amounts, primarily for proteomics applications. MALDI-TOF is suitable for fast analysis of single compounds and simple mixtures, particularly of intact biomacromolecules and polymers. All instruments are available for versatile use, but in order to streamline the analysis of samples, some instruments are used primarily or exclusively for specific applications (e.g. untargeted proteomics, energy metabolites).

Table 1a. High resolution MS equipment

	MS instrument	MS Manufac-turer	MS type	Ionization source	LC instrument	LC Manufacturer
1	**LTQ-Orbitrap XL**	Thermo	linear trap-orbitrap	ESI, nanoESI	Ultimate 3000 nanoHPLC Prominence UFLC	Dionex Shimadzu
2	**Synapt G2-Si**	Waters	quadrupole-time of flight	ESI	Acquity UPLC	Waters
3	**MaXis plus**	Bruker	quadrupole-time of flight	ESI, nanoESI	Ultimate 3000 nanoHPLC	Dionex/Thermo
4	**Q Exactive plus**	Thermo	quadrupole-orbitrap	ESI, nanoESI	Ultimate 3000 nanoHPLC	Dionex/Thermo

Table 1b. Triple quadrupole MS equipment

	MS instrument	MS Manufacturer	Ionization source	LC instrument	LC Manufacturer
5	**Xevo TQ-S**	Waters	ESI, IonKey chip-based ESI	Acquity UPLC	Waters
				nanoAcquity	Waters
6	**TSQ Vantage**	Thermo	ESI, nanoESI	Ultimate 3000 nanoHPLC	Dionex/Thermo
7	**TSQ Vantage**	Thermo	ESI, nanoESI, APCI	Accela UPLC Ultimate 3000 nanoHPLC	Thermo Dionex/Thermo
8	**TSQ Quantum AM**	Thermo	ESI, APCI, APPI	Surveyor HPLC LC Packings Ultimate nanoLC	Thermo Dionex
9	**API 3000**	PE Sciex	ESI, nanoESI, APCI, APPI	Prominence UFLC	Shimadzu
10	**API 365, upgraded EP10+**	PE Sciex, Ionics	ESI	Ultimate 3000 HPLC	Dionex
11	**API 365, upgraded EP10+**	PE Sciex, Ionics	ESI	LC Packings Ultimate nanoLC	Dionex
12	**6410**	Agilent	ESI, nanoChipCubeESI	1200 series nanoHPLC	Agilent

Table 1c. Ion trap MS equipment

	MS instrument	MS Manufacturer	Ionization source	LC instrument	LC Manufacturer
13	**HCTultra ETDII**	Bruker	nanoChipCubeESI	1100/1200 series HPLC	Agilent

Table 1d. MALDI-TOF MS equipment

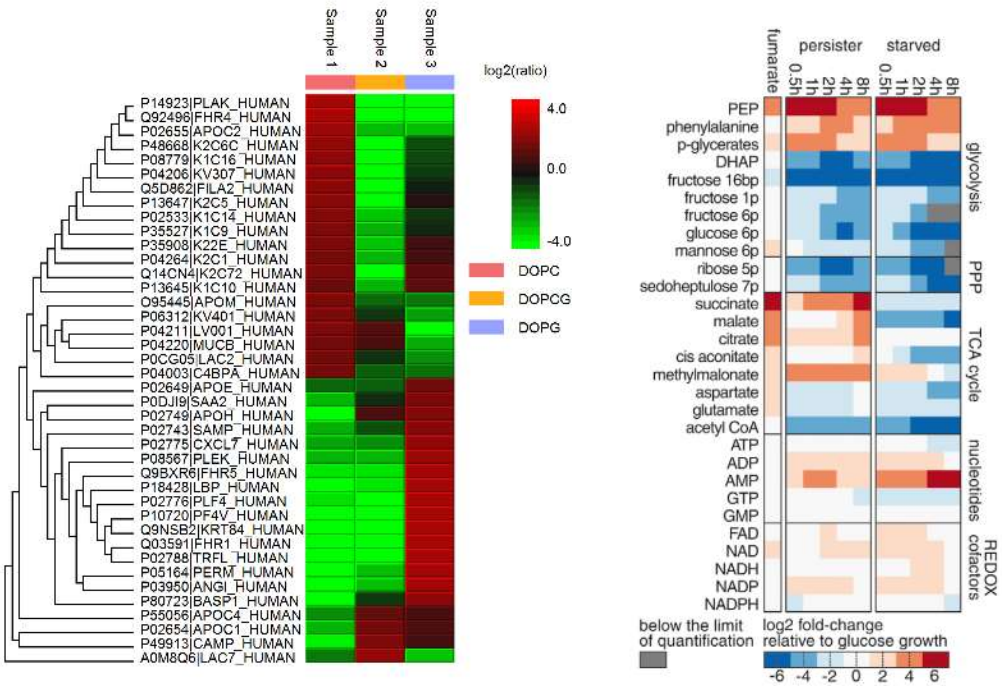
	MS instrument	MS Manufacturer	MS type
14	**Voyager DE-Pro**	Applied Biosystems	MALDI-TOF
15	**UltrafleXtreme**	Bruker	MALDI-TOF/TOF

Mass spectrometry systems installed at the IMSC. The numbers refer to table 1.

2.2 Data storage and analysis

All the data that is produced at the IMSC is stored in two locations: locally on off-line hard drives, and on a data storage server in the server room in the basement of the ERIBA building. The data server was installed in 2016 and has a capacity of about 45 Tb. The amount of data generated in 2017 is approximately 5 Tb. Large, high-resolution LC-MS/MS experiments will produce several 100s Gb of data each. Storage is not yet a major bottleneck, but data transfer and data processing are particularly challenging. Users are encouraged to store a copy of their data themselves, but raw data can always be requested and retrieved from IMSC storage.

Simple data processing for characterization and quantitation of compounds is typically performed with software packages provided by the MS instrument vendors. In some cases, depending on licensing options, software can be made available to users. For more complex omics-targeted data processing we have installed several dedicated computers running data analysis software packages, some commercially licensed and some open-source. These include **PEAKS** (protein identification and untargeted quantitation), **MaxQuant** (protein quantitation), **Skyline** (targeted proteomics), **Progenesis QI** (untargeted metabolomics, lipidomics), **mMass** (general MS analysis). Some packages can also be installed on user computers in 'viewer mode', allowing data visualization and limited data processing at the user's convenience. Licensed or server versions of the commercial software packages can be accessed in the dedicated data analysis lab at the IMSC. In addition, the Computational Mass Spectrometry group of Prof. Peter Horvatovich in the Analytical Biochemistry department is developing new tools for quantitative proteomics and biomarker discovery, and has extensive knowledge on statistical interpretation of omics data and on experimental design.



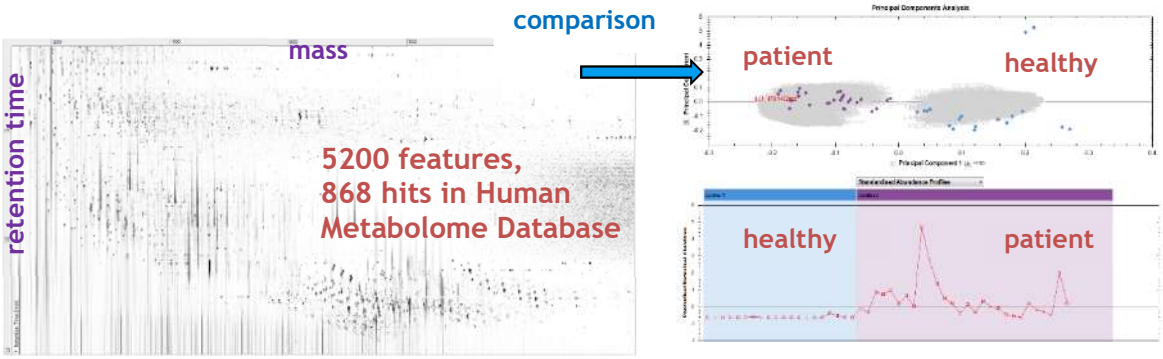
Relative quantification of proteins (left, Yang 2017) and energy metabolites (right, Radzikowski 2016)

2.3 Sample preparation equipment

Sample preparation is becoming increasingly important for producing consistent and scientifically valid data, and the IMSC has invested in upgrading the appropriate equipment to facilitate this part of the workflow. The sample preparation equipment, which is shared and maintained together with the Analytical Biochemistry department, is available to IMSC customers both indirectly and directly. Customers are encouraged to participate in sample preparation steps for LC-MS analysis under the (initial) guidance of IMSC staff.

Sample preparation equipment includes solid phase extraction, sample drying, centrifugation, gel electrophoresis and imaging, pipetting, heating, mixing and so on. Automated equipment, capable of multiplexed sample processing, are preferred for standardization purposes. Further investments in high-throughput sample preparation equipment is expected to become necessary in the coming years.

Sample preparation in the open lab space of IMSC and Analytical Biochemistry, ERIBA building



Metabolite #8 abundance profiles

Untargeted metabolomics of extracts from patients and healthy subjects (Seerangaiyan 2017)

3. Personnel & organization

3.1 Personnel

The core IMSC staff members are Hjalmar Permentier, head of the IMSC, and the technicians Margot Jeronimus-Stratingh and Annie van Dam. The head of the scientific board of the IMSC is Prof. Rainer Bischoff (Analytical Biochemistry). Marcel de Vries is seconded to the IMSC as an MS technician from Paediatrics, UMCG. MS technician Jos Hermans of Analytical Biochemistry is responsible for several LC-MS instruments which are used both for AB projects and within the IMSC. Data analysis and bioinformatics support is also provided as part of the IMSC, with support from Prof. Peter Horvatovich (Computational Mass Spectrometry).

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  Room 3226.0613; tel +31-50-3633170/8081; a.van.dam@rug.nl
- Rainer Bischoff, scientific head of IMSC, and dept. of Analytical Biochemistry 1.0 fte (RUG)
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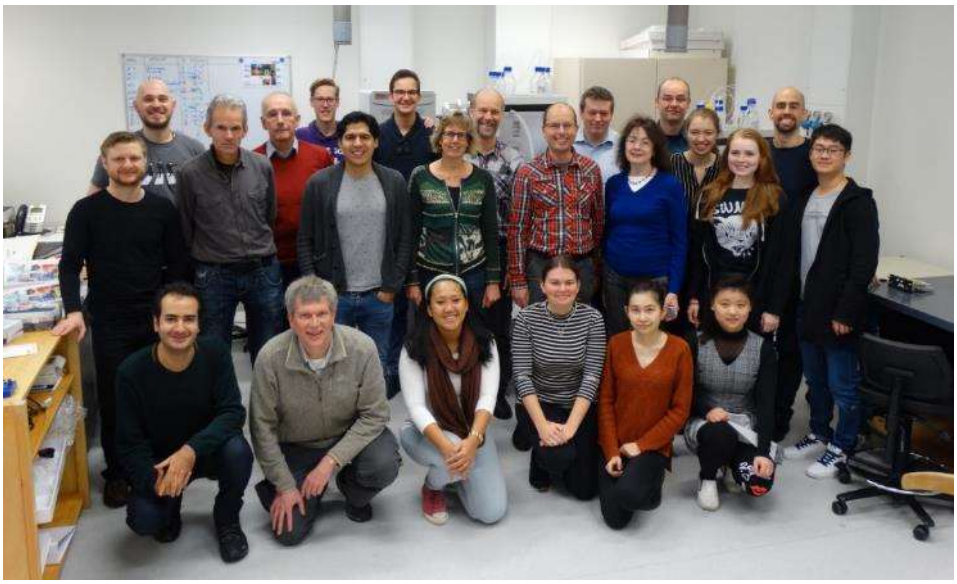


Group photo of IMSC and Analytical Biochemistry department, December 2017

From left to right and from back to front: Back row: Marcel Kwiatkowski, Dirk-Jan Reijngoud, Frank Klont, Marc Joosten, Jan Willem Meints, Peter Horvatovich, Hjalmar Permentier, Victor Bernal; Middle row: Andrei Barcaru, Jos Hermans, Andres Gil, Jolanda Meindertsma, Nico van de Merbel, Natalia Govorukhina, Alienke van Pijkeren, Karolin Sommer, Xiaobo Tian; Front row: Ali Alipour, Rainer Bischoff, Robin Soemopawiro, Naomi Sanders, Wenxuan Zhang, Yang Zhang. Not on photo: Margot Jeronimus-Stratingh, Annie van Dam, Karin Wolters, Marrit Hadderingh, Marcel de Vries, Jiaying Han, Hedwich Meindertsma, Peter Bults.

3.2 Organization and policy

All MS instruments and associated equipment listed in the previous section are operated, supported and/or supervised by one or more IMSC technicians. The technicians all have a long experience with a broad range of MS and LC-MS methods, and often have in-depth knowledge on specific subjects or methods, such as specific compound classes (e.g. proteins, lipids, drug metabolites), data analysis software and instruments. The general policy of the IMSC is to provide high-level service to every scientist and research group from the RUG and UMCG to the best of our abilities. However, since many research groups make use of the facilities, and resources are sometimes limited (both instrument availability and personnel time), access to the IMSC has to be granted and regulated. The facility head together with its director are responsible for making optimal use of equipment and personnel. There are different levels of users depending on their initial commitment to the IMSC, their involvement in acquisition of instrumentation and in providing personnel:

1. Regular customers: scientists that wish to have samples analyzed on an occasional basis, with questions that do not require extensive methods development, will usually interact directly with the technical staff of the IMSC and have their analyses done for the hourly user fee, which is currently 30 euros irrespective of which MS instrument is used. Long analyses which run for more than a day consecutively and require limited or no extra work from the technicians are charged at half the hourly rate for the hours in excess of 10 h. These high-throughput measurements pose a smaller burden on the IMSC resources, and for even larger projects a lump sum may be negotiated as discussed in the next category.
2. Project customers: scientists that have research questions which require extensive method development discuss first with the IMSC head and, if necessary, the scientific head, to define the approach and workload. Users will have to contribute financially to the methods development work at least on a partial basis, by paying the regular hourly user fee. In the case of long-term developments (e.g. 3 months or more), which will also enhance the overall competence of the IMSC, an agreement can be made for a fixed fee (lump sum) according to agreed-upon criteria which will be lower than just adding the hourly user fee. Users foreseeing such a use of the IMSC are encouraged to apply for funding to include the significant MS costs in their regular project budget. Lump sums of 5000 euros per year per project/group are deemed reasonable to cover in the order of 300-400 MS hours.
3. Collaborators: scientists that have research questions where the use of cutting-edge biological mass spectrometry and related techniques is required on a structural basis (e.g. biomarker discovery projects, systems biology projects) collaborate with the IMSC on a scientific level. This implies, in general, that the IMSC is already involved at the stage of the grant application and that cost for the use of instrumentation, personnel and consumables are part of the project budget. Such projects may also request dedicated instrumentation in their grants, which will be housed in the IMSC and operated with priority for these users.
4. External customers: scientists and commercial parties from outside the RUG or UMCG will be classified in the same way as internal academic users, but the user fees include salary cost and instrument depreciation or agreed-upon contract criteria as mentioned above.

The services of the IMSC are discussed and reviewed on an annual basis with a committee composed of committed users and other stakeholders.

4. Overview of projects

The IMSC performs MS service for numerous groups using a variety of instrumental techniques and on a wide range of sample types. This section lists the service work categorized by research institute and department with a brief description of the type of analyses and techniques. For project background information please refer to the respective research groups or their websites. The size of the service projects varies greatly, from a few hours to hundreds of hours a year, but the list gives a good indication of the variety of samples and techniques that the IMSC handles. In parentheses after the group name the number of different researchers with service requests is indicated. In 2017 more than 130 researchers of 40 groups or clusters were assisted with MS analyses.
The work is performed primarily by the IMSC technicians, in most cases not only the MS analysis itself but also a significant amount of sample preparation and data analysis. Most of the listed work involving the MALDI-TOF is performed by RUG or UMCG researchers independently, after initial training on the instrument, but continuously supported by the IMSC.
We also are involved in a number of scientific collaborations, listed in section 4.2, where a researcher is working for extended periods, or permanently, in the IMSC, and in the case of PhD students and postdocs usually supervised by our staff. The distinction between service work and collaboration is sometimes small, and we support proposals to upgrade service work into collaborative projects.

4.1 Service work and projects

University of Groningen

Engineering and Technology Institute Groningen

- **Products and Processes for Biotechnology (1)**
  LC-MS of proteins
- **Product Technology (1)**
  MALDI-TOF

GBB (Groningen Biomolecular Sciences and Biotechnology Institute)

- **Chemical Biology 1 (1)**
  LC-MS
- **Enzymology (1)**
  LC-MS of proteins
- **Molecular Genetics (13)**
  MALDI-TOF and LC-MS, of peptides and proteins
- **Molecular Microbiology (1)**
  LC-MS of proteins
- **X-ray Crystallography (1)**
  LC-MS and MALDI-TOF of proteins and peptides

GRIP (Groningen Research Institute of Pharmacy)

- **Analytical Biochemistry (10)**
  MALDI-TOF and LC-MS/MS (un)targeted proteomics, biopharmaceuticals, bioconjugates
- **Chemical and Pharmaceutical Biology (25)**
  (LC-)MS of enzyme substrates, metabolomics of bacteria
  MALDI-TOF and (LC-)MS of proteins and peptides

- **Drug Design (13)**
  (LC)-MS of organic synthesis products, protein ligands
- **Molecular Pharmacology (1)**
  LC-MS proteomics and protein oxidation analysis
- **Pharmaceutical Analysis (1)**
  LC-MS proteomics
- **Pharmacokinetics, Toxicology and Targeting (4)**
  MALDI-TOF of proteins
  LC-MS proteomics and drugs analysis

Stratingh Institute for Chemistry

- **Biomolecular Chemistry & Catalysis (5)**
  MALDI-TOF and LC-MS of proteins and nucleic acids
- **Chemical Biology 2 (1)**
  (LC)-MS of synthetic organic compounds
- **Chemistry of (Bio)organic Materials and Devices (1)**
  MALDI-TOF
- **Molecular Inorganic Chemistry (3)**
  ESI-MS of organometallic complexes
- **Synthetic Organic Chemistry (6)**
  ESI-MS of organometallic complexes
  (LC)-MS of synthetic organic compounds
  MALDI-TOF and LC-MS of modified peptides & proteins

ZIAM (Zernike Institute for Advanced Materials)

- **Macromolecular Chemistry & New Polymeric Materials (4)**
  MALDI-TOF and LC-MS of polymers
- **Polymer Chemistry and Bioengineering (9)**
  MALDI-TOF of polymers, modified peptides and proteins, and nucleic acids

University Medical Center Groningen

- **Aging Biology (5)**
  LC-MS proteomics
- **Biomedical Engineering (1)**
  LC-MS proteomics
- **Cardiology and Thorax Surgery (1)**
  LC-MS proteomics
- **Cell Biology-Autophagy (1)**
  LC-MS proteomics
- **Cell Biology-General (1)**
  LC-MS proteomics
- **Hematology (2)**
  LC-MS proteomics
- **Lung Diseases (1)**
  LC-MS proteomics

- **Medical Microbiology (1)**
  LC-MS proteomics
- **Medical Microbiology-Molecular Virology (1)**
  LC-MS proteomics
- **Medical Oncology (5)**
  LC-MS proteomics
- **Neuroscience-Medical Physiology (1)**
  LC-MS proteomics
- **Ophthalmology (1)**
  LC-MS proteomics
- **Paediatrics (6)**
  LC-MS metabolomics and proteomics
- **Pathology & Medical Biology (3)**
  LC-MS proteomics
- **Plastic Surgery (1)**
  LC-MS proteomics

External

- **Lanthio Pharma, Groningen**
  MALDI-TOF and LC-MS of peptides
- **IQ products, Groningen**
  LC-MS proteomics of serum & plasma
- **Biocatalysis Group, Delft University of Technology**
  HR-MS of reagents
- **ImmuCell Corp, Portland, ME, USA**
  LC-MS of peptides
- **InGell Labs, Groningen**
  MALDI-TOF of polymers

4.2 Scientific projects and collaborations

The IMSC is closely involved in several larger scientific projects, where equipment and/or PhDs and postdocs are placed in the IMSC and make use of our infrastructure, expertise and scientific input.

Electrochemistry-mass spectrometry
A research project that has been running in the Analytical Biochemistry group and the IMSC for more than 15 years involves the coupling of electrochemistry (EC) with mass spectrometry, for drug and protein oxidation research. A new TTW project started in 2017 with Dr. Mathieu Odijk of the BIOS group at the University of Twente and several industrial partners. One PhD student started in our group and one in Twente; a third PhD student with a Chinese Scholarship Council grant has started at the same time in our group, under the supervision of Hjalmar Permentier and Rainer Bischoff. The projects make extensive use of the older triple quadrupole LC-MS systems, as well as dedicated EC equipment acquired as part of earlier EC-MS projects. The new research focuses on developing combined EC/spectroscopic devices both to elucidate reaction mechanisms and to improve reaction yields of (1) specific drug metabolites and (2) the specific digestion of proteins by EC. Product formation will be

analyzed spectroscopically (SERS, UV/Vis) and by LC-MS. Miniaturized devices are developed and fabricated in Twente, and we will focus on developing nanoporous gold surfaces which have both catalytic and electrochemical reactivity towards drug molecules, and electrochemical protein cleavage on boron-doped diamond electrodes followed by new enrichment strategies for the electrochemically cleaved peptides.
In 2018, a RUG-funded PhD student will start on a project combining liquid chromatography-electrochemical detection with mass spectroscopy for characterization of novel neuroactive gut bacterial metabolites with potential antimicrobial activity. This project is a collaboration between Hjalmar Permentier and Dr. Sahar El Aidy, from the Microbial Physiology group (RUG). In the project we will set up an integrated LC-EC-MS system for the concurrent electrochemical measurement and partial conversion of electroactive metabolites (e.g. neurotransmitters) with high-resolution mass spectrometric detection. The aim is to sensitively and selectively detect previously undetected neuroactive metabolites of gut microbiota, and subsequently test these for antimicrobial activity in vitro.

Targeted proteomics and metabolomics of ageing
New LC-MS/MS methods based on SRM analysis have been developed for large-scale, high-throughput quantitative analyses of complex proteome and metabolome samples of yeast and mouse model systems, as part of the Systems Biology Centre for Energy Metabolism and Ageing (SBC-EMA). The expertise and methods developed in this project have proven to be very useful for many other groups and these analyses are now also part of the service of the IMSC. The quantitative energy metabolite LC-MS/MS methods were taken over by the IMSC technicians. There are plans to extend the metabolite analyses to enable flux measurements using ^{13}C labeling experiments
Dr. Karin Wolters has been employed by UMCG since 2015 and continues to develop and perform targeted proteomics analyses for a host of UMCG research groups, which she performs at the IMSC facilities in close collaboration with IMSC staff. Her methods employ isotopically labeled peptide standards or synthetic proteins (QConCAT technology) for absolute quantification of dozens of proteins in a single experiment. This method has become a core technology in the Paediatrics department (UMCG) and additional personnel is seconded to Karin to process the large volume of samples submitted by a variety of collaborators. Bioinformatics support for these projects is also indispensable and efforts to improve the required infrastructure are in progress.

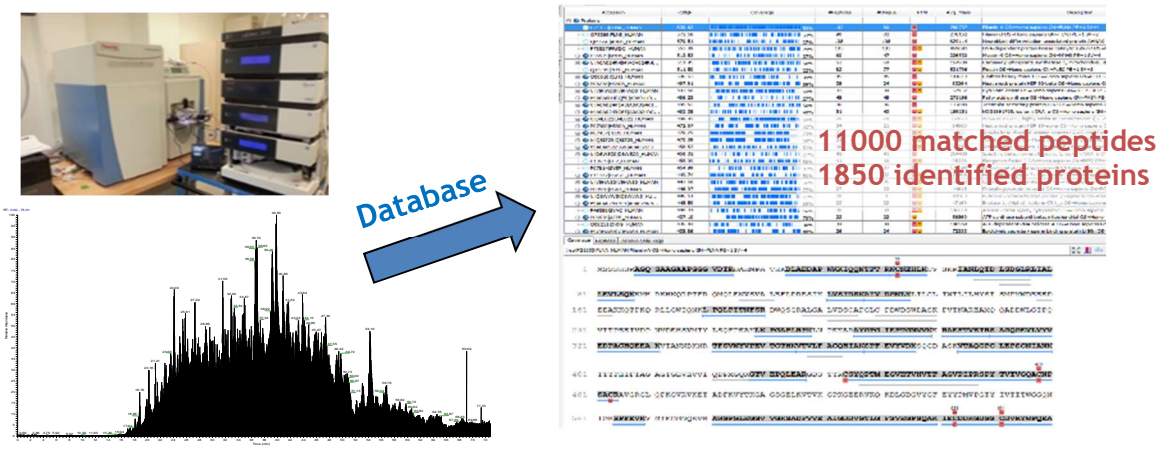
Lipidomics in metabolic disorders
Prof. Dirk-Jan Reijngoud (Laboratory Medicine department, UMCG) supervises a project on lipid-related metabolic disorders of genetic origin. Since 2013 the IMSC houses a high-resolution Q-TOF LC-MS instrument with ion mobility capability for this project. From 2016 a PhD from the Analytical Biochemistry group together with a PhD student of Prof. Reijngoud starting with implementing high-resolution screening of lipids in complex samples, using methods developed in close collaboration with the IMSC. In 2017 this method has been used for screening patient and control groups with metabolic disorders, where the relative abundance of more than 700 lipids can be compared. The lipidomics method is expected to become a robust tool for lipid screening in the IMSC.

Metallocages for drug targeting and imaging of proteins
This collaboration project, started in 2014 with a Chinese Scholarship PhD student, supervised by Prof. Angela Casini (Cardiff University, formerly RUG) and Prof. Peter Horvatovich, and with daily supervision of Hjalmar Permentier, aimed at the synthesis of photocleavable organometal complexes which can be employed in MALDI imaging of proteins. The current focus has shifted towards the synthesis and characterization of metallocages bioconjugated with peptides. Cage and conjugate formation are performed with MS and LC-MS and toxicological studies are performed on organ slices at the Pharmacokinetics, Toxicology and Targeting group (RUG).

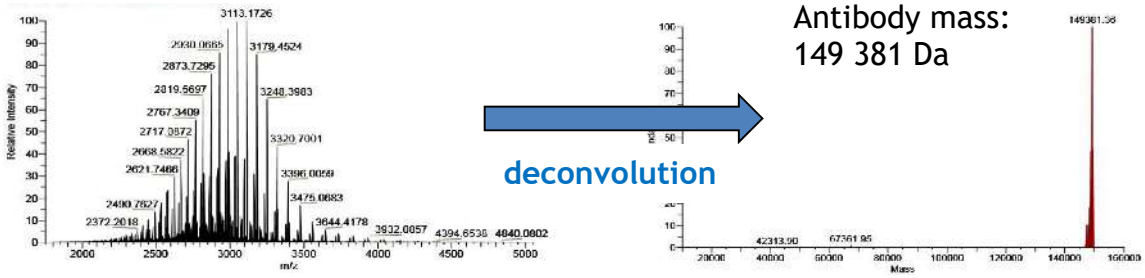
Analysis of biopharmaceuticals

There is a growing interest in accurate and validated analytical methods for therapeutic peptide and proteins, both from industry and medical professionals. Within the Analytical Biochemistry group there is a close collaboration with PRA Health Sciences, and the team of Prof. Nico van de Merbel (PRA and RUG) on the development of these methods using improved sample preparation and sensitive SRM approaches. The IMSC houses a TripleTOF quadrupole-time of flight mass spectrometer on loan to PRA since spring 2017, used for further optimization of the methods by a PhD student in our group.

The IMSC also houses a Q Exactive quadrupole-orbitrap spectrometer of the UMCG Pharmacy (Prof. Daan Touw) which is used to develop better analysis method for therapeutic antibodies such as trastuzumab. Close interaction between the groups, facilitated by the IMSC, has helped to drive the methodological developments forward in 2017.



Shotgun proteomics with nanoLC-MS/MS, 0.2 µg HeLa cell tryptic digest on-column, 1.5 h analysis



Antibody analysis with high-resolution ESI-MS to determine accurate mass and purity

5. Publications & education

In this section papers and activities are included of IMSC-employed personnel (Hjalmar Permentier, Annie van Dam, and Margot Jeronimus-Stratingh), as well as Marcel de Vries (seconded to IMSC from UMCG). Papers with explicit mention of IMSC personnel in the acknowledgements are separately listed. For other (unpublished) contributions refer to section 4. Teaching comprises both lectures and practical courses and demonstrations. The two-day mass spectrometry course is organized yearly to inform, educate, and interest students and researchers on the practical and theoretical aspects of MS and how they can make use of the IMSC.

5.1 Peer-reviewed publications in 2017

Journal papers, co-authored:

1. Gil A, Siegel D, Bonsing-Vedelaar S, Permentier H, Reijngoud DJ, Dekker F, Bischoff R. **2017**. The degradation of nucleotide triphosphates extracted under boiling ethanol conditions is prevented by the yeast cellular matrix. *Metabolomics* 13(1): 1.
2. Gul T, Bischoff R, Permentier HP. **2017**. Mechanism of aromatic hydroxylation of lidocaine at a Pt electrode under acidic conditions. *Electrochimica Acta* 224: 636-641.
3. Han J, Schmidt A, Zhang T, Permentier H, Groothuis GMM, Bischoff R, Kühn FE, Horvatovich P, Casini A. **2017**. Bioconjugation strategies to couple supramolecular *exo*-functionalized palladium cages to peptides for biomedical applications. *Chemical Communications* 53: 1405-1408.
4. Hemelaar SR, Nagl A, Bigot F, Rodriguez-Garcia MM, de Vries MP, Chipaux M, Schirhagl R. **2017**. The interaction of fluorescent nanodiamond probes with cellular media. *Microchimica Acta* 184: 1001-1009.
5. Kuipers A, de Vries L, de Vries MP, Rink R, Bosma T, Moll GN. **2017**. Semi-microbiological synthesis of an active lysinoalanine-bridged analog of glucagon-like-peptide-1. *Peptides* 91: 33-39.
6. Pantophlet AJ, Roelofsen H, de Vries MP, Gerrits WJJ, van den Borne JJGC, Vonk RJ. **2017**. The use of metabolic profiling to identify insulin resistance in veal calves. *PLOS One* 12: e0179612.
7. Stolle S, Ciapaite J, Reijne AC, Talarovicova A, Wolters JC, Aguirre-Gamboa R, van der Vlies P, de Lange K, Neerincx PB, van der Vries G, Deelen P, Swertz MA, Li Y, Bischoff R, Permentier HP, Horvatovich PL, Groen AK, van Dijk G, Reijngoud DJ, Bakker BM. **2017**. Running-wheel activity delays mitochondrial respiratory flux decline in aging mouse muscle via a post-transcriptional mechanism. *Aging Cell* e12700.
8. Zhang T, de Vries MP, Permentier HP, Bischoff R. **2017**. Specific affinity enrichment of electrochemically cleaved peptides based on Cu(II)-mediated spirolactone tagging. *Analytical Chemistry* 89: 7123−7129.

Journal papers, acknowledged:

1. Padamati SK, Angelone D, Draksharapu A, Primi G, Martin DJ, Tromp M, Swart M, Browne WR. **2017**. Transient formation and reactivity of a high-valent nickel(IV) oxido complex. *Journal of the American Chemical Society* 139: 8718-8724. (van Dam A)
2. Unjaroen D, Chen J, Otten E, Browne WR. **2017**. Switching pathways for reversible ligand photodissociation in Ru(II) polypyridyl complexes with steric effects. *Inorganic Chemistry* 56: 900-907. (van Dam A)

3. Unjaroen D, Swart M, Browne WR. **2017**. Electrochemical polymerization of iron(III) polypyridyl complexes through C–C coupling of redox non-innocent phenolato ligands. *Inorganic Chemistry* 56: 470-479. (van Dam A)
4. Urban JH, Moosmeier MM, Aumüller T, Thein M, Bosma T, Rink R, Groth K, Zulley M, Siegers K, Tissot K, Moll GN, Prassler J. **2017**. Phage display and selection of lanthipeptides on the carboxy-terminus of the gene-3 minor coat protein. *Nature Communications* 8: 1500. (de Vries MP)

Conference proceedings:

1. van den Brink FTG, Zhang T, Ma L, Odijk M, Olthuis W, Permentier HP, Bischoff RPH, van den Berg A. **2017**. Electrochemical protein cleavage in a microfluidic cell for proteomics studies. *Procedia Technology* 27: 62-64.

5.2 Teaching and education in 2017

28 January:	COAST Biomarker Day, Groningen, lecture
10 February:	Quantitative Bioanalysis WMFA14005, lecture
24 February:	FATEM WLFB1210, lab tour
10 March:	Workshop Biomarker Development Center, Experience Groningen
9 & 14 March:	One-day Mass Spectrometry courses, UMCG
March-April:	Proteomics & Genomics course WLB07041, lectures & lab practicum
May:	Medical Genomics & Proteomics course WLB07090, lectures & lab practicum
15 May:	practicum day VWO student project on glyphosate
18 October:	MPDI Masters, lab introduction on protein analysis
30 Nov & 1 Dec:	Two-day course on Mass Spectrometry