Valorisation at HIMS

Chemistry research that matters

Van ’t Hoff Institute for Molecular Sciences
The Van 't Hoff Institute for Molecular Sciences (HIMS) is one of eight research institutes of the Faculty of Science (FNWI) of the University of Amsterdam. HIMS houses 135 staff members from 34 nationalities. Together they publish over 180 peer reviewed scientific articles, 18 PhD theses and on average 4 patents per year. The institute focuses on top-quality chemistry research and at the same time has an open eye to technological applications and innovations. HIMS is organized in four strong research themes: Sustainable Chemistry, Analytical Chemistry, Computational Chemistry and Molecular Photonics.

Knowledge transfer to industry and society is in the DNA of our organization. On top of the four science themes we indicated several utilisation areas. These areas stimulate the collaboration between groups within the institute and are important for the visibility of the institute.

Researchers from HIMS contribute to several large national programs on conversion of sun light into electricity, fuels, or base chemicals like SOLARDAM, CatchBio or BioSolarCell. We participate in the Institute QuantiVision that aims to develop medical (imaging) devices and protocols for quantitative analysis of medical images to guide therapy and facilitate therapeutic interventions, with a focus on oncology and neurology. HIMS is also one of the academic partners of the Advanced Research Center for Nanolithography (ARCNL) that focuses on the fundamental physics involved in current and future key technologies in nanolithography, primarily for the semiconductor industry.

Science for Arts is an interdisciplinary research theme on art history, art conservation and science. Chemists from HIMS collaborate with physicists, researchers from the faculty of Humanities and the Rijksmuseum and Cultural Heritage Agency.

The Co van Ledden Hulsebosch Center (CLHC) is the interdisciplinary center of expertise for forensic scientific and medical research in Amsterdam and has its headquarters within HIMS. The CLHC serves to bundle the forensic experience, knowledge and expertise of the University of Amsterdam's Faculty of Science, the Academic Medical Center (AMC-UvA) and the Netherlands Forensic Institute (NFI).

On top of collaborations with third parties we sometimes develop our fruitful results into spin-off companies. Examples are catalysis company InCatT and bioplastic company Plantics.

At HIMS we are always looking for partnerships with industry to identify research questions that matter, transfer our knowledge and turn innovative ideas into reality. Maybe this brochure with posters on valorisation of our research inspires you to contact us via hims@uva.nl.

Joost Reek
Director HIMS
The Sustainable Chemistry theme is focused on the development of new technologies that enable efficient and sustainable chemical transformations. Efficient production of chemicals is crucial to ensure a sustainable society with a growing world population increasingly facing problems associated with scarcity of materials, energy and feedstock. Catalysis is the key enabling technique to ensure atom & energy efficient synthesis and to store and release chemical energy.

The theme works on the development of new (cheap and sustainable) catalysts to improve the efficiency of chemical transformations and to efficiently convert solar/electrical energy to fuels (electocatalysis, photocatalysis) and vice versa (fuel cells), thus contributing to solving energy and sustainability problems.

The strengths of the Sustainable Chemistry team are in catalyst design, synthesis, kinetics, (spectroscopic) characterization, modeling and testing catalysts under applied conditions. The team consists of a group of highly interdisciplinary and world-renowned top-researchers. The theme is strong in both fundamental research and applied catalysis, and was recently appointed as a university Research Priority Area.

On the fundamental side, the Sustainable Chemistry team collaborates with several top-scientists and renowned scientific institutes all over the world. Applied research is performed in close collaboration with several industrial partners and in spin-off companies.

Transition(base) metal catalysis
Kinetic DFT studies & spectroscopy
Fuel cell technology & electrochemistry
Homo-, hetero-, organo- and bio-catalysis
Biomass conversion to fuels and chemicals
Bio-inspired (supramolecular & metalloradical) catalysis
Short-cuts & new methods in (enantio)selective synthesis
Homogeneous and supramolecular catalysis

**Key expertise:**
- Hydroformylation
- Asymmetric hydrogenation
- C-C and C_X bond formation
- Water oxidation/proton reduction
- Ligand synthesis
- Combinatorial approaches
- Lead optimization
- Kinetics/mechanism

**Industrial application of newly developed catalysts**
- Solar to fuel devices (not on the poster)

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**References**
One-pot Metallo-Radical Approach to 2H-Chromenes

2H-Chromenes are important structural motifs that exist in numerous natural products (e.g. tannins and polyphenols found in teas, fruits, and vegetables) and medicines possessing interesting biological activities (Figure 1).

Figure 1. Bio- and photo-active 2H-chromenes.

2H-chromenes are crucial substructure of a wide variety of known pharmaceutical agents and drug candidates, and find applications as photochromic materials and dyes. However, all previously developed synthetic methods involve waste-generating multistep reactions, use complicated pre-functionalized starting materials, have a limited degree of functional group tolerance and/or lead to formation of regioisomeric product mixtures. Therefore, the development of shorter, more efficient and broadly applicable synthetic routes towards 2H-chromenes is in demand. Building on our ‘carbene-radical’ chemistry (Figure 2), we recently developed a novel metallo-radical route to 2H-chromenes.

Figure 2. ‘Carbene-radicals’ in catalysis.

Cobalt(III)–carbene radicals, generated by metalloradical activation of salicyl-N-tosylhydrazones by cobalt(II) complexes of porphyrins readily undergo radical addition to terminal alkenes to produce salicyl-vinyl radical intermediates (Figure 3). Subsequent hydrogen atom transfer leads to the formation of 2H-chromenes in a one-pot reaction. The process tolerates various substitution patterns and produces the corresponding 2H-chromene products in good isolated yields.

The successful development of this new catalytic reaction is expected to trigger further developments in catalytic radical-induced cyclization processes for selective syntheses of heterocycles that are difficult to prepare otherwise.

References
A Metallo-Radical Approach to 2H-Chromenes

Sustainable Chemistry
Van 't Hoff Institute for Molecular Sciences

Value goals
Developing new synthetic methodologies for (fine-chemical) organic synthesis based on cobalt metallo-radical chemistry.
Functional Polymers via ‘Carbene Polymerization’

Non-functionalised polyolefins (e.g. polyethene) have found their way in many commodity applications due to their outstanding properties, such as solvent resistance and thermal stability. Nowadays, these materials can easily be obtained in large scales and at low cost with very high precision of the polymer microstructures. However, due to their lack of functional groups they generally have poor surface chemistry properties.

Synthetic methods that allow controlled incorporation of polar functionalities into a polymeric carbon-chain are rather scarce. The most widely-applied commercial approach to obtain functionalised polyolefins is post-functionalization reactions of existing polyolefin chains, requiring harsh reaction conditions with limited control.

Over the past few years we developed a novel synthetic method to prepare functionalized carbon-chain polymers; Rhodium-mediated ‘stereoregular polymerization of functionalized carbenes’ proved a versatile new polymerization methodology (Figure 1).

The method involves an unusual carbene migratory insertion chain-growth process which elongates the polymeric carbon-chain with one ‘carbene carbon’ unit in each insertion step. This allows formation of highly substituted and highly stereoregular (syndiotactic) carbon-chain polymers with unusual properties.

Variation of monomers & (co)polymers

Besides a variety of different diazo compounds, also sulfur ylides can be used as ‘carbene-monomer’ precursors. Copolymerization of different ‘carbene monomers’ as well as copolymerization of functionalized ‘carbene’ with ethene proved possible.

Consecutive insertions of polar monomer
Blocky microstructure, Stereoregularity

Figure 2. Liquid-crystalline behavior of ‘poly-carbenes’

References
- B. de Bruin et al., Chem. Soc. Rev., 2010, 39, 1706–1723

Valorization goals
Developing new synthetic methodologies for functional, stereoregular polymer synthesis based on the rhodium-mediated ‘carbene polymerization’.
Many challenges exist in (homogeneous) catalysis:
- direct conversion of C-H and C-C bonds, formation of C-N and C-O bonds
- selective functionalization of small molecules (N₂, NH₃, H₂O, CO₂, P₄ ...)
- energy-related chemistry & biomass conversion

New concepts are required to induce paradigm shift in establishing such transformations:
- cooperative catalysis with smart (‘reactive’) and adaptive ligands to activate substrates
- bioinspired bimetallic catalysis
- first row transition metal catalysis

Reactive ligand concepts are rapidly emerging as relevant alternatives to ‘classical’ catalytic approaches. We are actively pursuing these strategies, with the aim to unravel new low-energy pathways for known reactions and to uncover totally new reactivity and catalytic applications.

We have initiated a research program on first row & late transition metal chemistry with cooperative and redox-active ligands.

Also actively involved in several projects related to catalysis for sustainable energy (e.g. electro- and photocatalytic H₂ production, CO₂ utilization)

Van 't Hoff Institute for Molecular Sciences

Smart Systems for Small Molecule Activation

Expertise & Interests

(Reactive) Ligand Design
Synthesis (Inorganic and Organometallic)
Coordination Chemistry
X-ray Crystallography
Small Molecule Utilization
Cooperative Catalysis
Hydroaddition Reactions
Photocatalysis & Energy

Valorization goals

The group is highly interested in collaborative applied research (e.g. bilateral, TKI, STW, EU) on inorganic synthesis, ligand/catalyst screening, route scouting or analysis. Proven experience with industrial projects (CatchBio, Aspect, Evonik, DSM).
Understanding Catalysts and their Performance

The rational design of catalysts and materials is often hampered by the lack of detailed understanding of their performance, i.e. their changing structural and electronic properties during reaction to understand their reaction mechanism. We apply a breath of spectroscopy techniques, using different wavelengths and energies, to provide complementary information on the system under investigation. A special focus is towards X-ray spectroscopy methods.

We do not only “just” apply available spectroscopy techniques, but also develop new techniques, including the required operando instrumentation and cells, as well as data analysis and theoretical methods.

Application of the techniques to industrially interesting catalytic processes and materials has been pursued, providing unprecedented insights in catalysts properties, reaction intermediates and mechanisms in the field of homogeneous and heterogeneous catalysis, photochemistry and photocatalysis, electrochemistry and materials science.

**Example: Industrial Ethene Trimerisation Catalyst**
- Activation: [CrCl$_3$(decyl-SNS)] (5 mM) + 10 eq. AlMe$_3$
  - End state (~3 hrs): loss halide (methylation) and disproportionation
  - Catalytic Intermediate after 1 s: 4-coordinate Cr(II) with deprotonated NH

**Example: Three Way Car Exhaust Catalysts**

**Example: LiS Battery**
- Probing polysulfides and S-radical intermediates during LiS battery cycling
- Type of species and their rate of formation depending on electrolyte solvent
- Insights in battery deactivation mechanisms

**Example: Pigments BiMoVO$_x$**
- Doping oxidic materials - analyse structural and colouristic properties
- Screening materials incl. UHV surface science and catalysis

**ValORIZATION GOALS**
Detailed understanding of reaction mechanisms and catalyst/material performance allow the rational design of new, better and more sustainable catalysts and materials and associated processes.
Conversion of Biomass into High-value Chemicals

90% of chemicals are derived from crude oil now. Fluctuating prices and concerns over the environmental impact of petrochemical processes require developing sustainable and more environmentally-friendly alternatives. We research on converting lignocellulosic biomass into high value chemicals using heterogeneous catalysts. Examples are conversion of glycerol/lactic acid to acrylic acid, levulinic acid to γ-valerolactone and xylose to xylitol. The interaction of the catalysts with biomass derived substrates and reaction environment are also studied by advanced spectroscopic and microscopic techniques.

Activity of TiO₂ supported Ru catalyst is structure sensitive. Ru/TiO₂-rutile catalyst is more efficient than Ru/TiO₂-anatase for converting xylose to xylitol. TEM studies show that Ru nanoparticles are better dispersed with small, uniform sizes on rutile TiO₂. This may be due to the better interaction of RuO₂ (rutile structure) with rutile TiO₂. This indicates the importance of knowing the structural details when developing catalysts.

Heterogeneous Catalysis and Sustainable Chemistry

References

 Valorization goals
Developing efficient heterogeneous catalytic routes to chemicals from biomass.
Correlating structural properties of catalysts with activity.
Metal-organic frameworks as selective adsorbers

In the chemical, petrochemical and pharmaceutical industries separation technology is a key element in the production of pure compounds. A large portion of the production costs are associated with purification steps, for instance using solvent extraction, adsorption, crystallization and distillation processes.

Metal-organic frameworks (MOFs) are a new class of porous materials whose surface area, pore structure and thermal stability depend strongly on their individual components. This makes them interesting for selective molecular separations. MOFs can separate molecules through either physical sieving or on the basis of chemical affinity and even chemical bonding.

We designed a new MOF built from lanthanum ions and pyrazine-based linkers. This MOF is microporous, with 1D channels that easily accommodate water molecules. Its framework is highly robust to dehydration/hydration cycles. Unusually for a MOF, it also features a high hydrothermal stability. This makes it an ideal candidate for air drying as well as for separating water/alcohol mixtures.

The robustness of the frameworks is confirmed by XRD and the water adsorption. The isotherms are practically identical after three consecutive activation-uptake cycles. Transient uptake measurement experiments indicate that the intra-crystalline diffusivities in LaMOF are of the order of $10^{-14}$ m$^2$s$^{-1}$. Transient breakthrough simulations for water/alcohol mixture confirm that water/alcohol mixtures can be separated cleanly using our MOF.

**Valorization goals**

Developing new adsorbers for highly efficient molecular separations.
Advanced Electrochemical Devices for Efficient Power Generation, Energy Storage and Chemicals Production

Fundamental Principles

- Configurations
  - An advanced electrochemical device usually has a sandwich structure, which is consisted of an anode, an electrolyte and a cathode. (right, a schematic of proton exchange membrane fuel cells)
  - Active sites in electrodes
    - Triple-phase boundary (TPB), where the electronic conductor, ionic conductor and open pores meet, is the active site of electrocatalyst processes, all the individual phase must be physically contiguous.
  - Operation modes
    - Advanced electrochemical devices can work in either fuel cell mode to generate electricity and capture CO₂; or electrolysis cells mode to store energy. Both modes can be used to produce chemicals

Power Generation

When the electrochemical device is working under fuel cell mode, it can generate electricity:
- with high efficiency (up to 60%)
- using diverse fuel sources including hydrocarbons and sour gas (H₂S containing natural gas)
- with combined heat and power supply
- co-producing value-added chemicals

(a) Mass spectroscopic signals from anode effluent as a function of fuel cells overpotential and (b) the corresponding polarization and power density curves, when 0.5% \( \text{CH}_2 \text{Cl}_2 \) doped the cell using \( \text{La}_0.6\text{Sr}_0.4\text{TiO}_3 \) anode at 800°C. The potential scan rate was 0.2 mV s\(^{-1}\).

Novel Materials

- To Design
  - Catalysts used in the device should be affordable, active and stable. Herein, mixed ionic and electronic conductor (MIEC, e.g., \( \text{La}_0.6\text{Sr}_0.4\text{TiO}_3 \)) was used to maximize TPB and promote stability while active phases provide sufficient electrocatalytic activity

- To Use
  - Novel materials developed are simple but not simplistic, and are readily available for industrial applications.
  - (right, coking resistant coatings on 3D complex structures)

- To Understand
  - Fundamental studies provide us insights into materials behaviors under different conditions. The example reveal \( \text{BaZr}_0.6\text{Ce}_0.4\text{Y}_2\text{O}_3 \) electrolyte degrade in ambient air through a microradical mechanism.

(a) and (b) electrolysis cells use surplus electricity from the grid or renewable sources to convert stored CO₂ into fuels; (b) fuel cells generate power while directly capture CO₂

Energy Storage

When the electrochemical device is working under electrolysis cell mode, it can convert excess power from the grid into chemical fuels while consuming \( \text{H}_2 \) and \( \text{O}_2 \) only:
- Catalysts play vital roles in products selectivity, e.g., \( \text{H}_2 \) prefers to form on \( \text{Ni} \) while \( \text{CO} \) prefers to form on \( \text{Pt} \)
- System efficiency is the key and challenging factor of \( \text{CO}_2 \) reduction, e.g., the current density is usually several mA cm\(^{-2}\)

2(\text{H}_2) + 2\text{O}_2 \rightarrow 4\text{H}_2\text{O} (0.410)
2\text{CO} + \text{H}_2\text{O} \rightarrow \text{CO}_2 + 2\text{H}_2 (0.295)
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2\text{CO} + 2\text{H}_2\text{O} \rightarrow 2\text{CO}_2 + 2\text{H}_2 (0.434)
2\text{CO} + \text{H}_2\text{O} \rightarrow \text{CO}_2 + \text{H}_2 + \text{H}_2\text{O} (0.490)

(a) and (b) schematic of the electrolysis cell (right) the potential required to drive each individual reactions

Advanced Materials Processing

- State-of-the-art
  - To minimize the ohmic loss, electrodes and electrolyte membranes should be adequately thin. We use spin-coating or screen printing to fabricate these thin dense/porous films

- Versatile
  - To adapt the properties of different electrode catalysts, infiltration method was developed

- Scalable
  - High perfromance electrocatalysts are synthesized via a variety of methods, some of which, e.g., combustion and spray pyrolysis are compatible with industrial processes

(a) combustion methods for catalyst synthesis; (right) nanoparticles of CuO/Co (de)hydrogenation catalyst

Chemicals Production

Electrochemical device can produce value-added chemicals through:
- (de)hydrogenation, e.g., ethylene production;
- (de)oxidation, e.g., oxygen purification;
- Electrocatalytic selective oxidation, e.g., CO concentration from syngas

ValORIZATION GOALS
- Diversify the application of electrocatalysts, in particular in industrial reaction processes.
- Utilize electrochemical device as an alternative method for various purposes at a larger scale.

Advanced Electrochemical Devices for Efficient Power Generation, Energy Storage and Chemicals Production

Power Generation

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- with high efficiency (up to 60%)
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Multistep synthesis of valuable complex compounds

Mission: The development of efficient and selective, diversity-oriented synthetic methodologies, in particular organocatalytic and biocatalytic procedures, and the target-oriented preparation of molecules of relevance in chemistry, biology and medicine.

Bronsted acid organocatalysis
Efficient catalytic asymmetric Pictet-Spengler reactions of N-substituted tryptamines have been developed. Important biologically active indole alkaloids have been synthesized. Currently, the chemistry is expanded to the isoquinoline natural compound class series.

Chan–Lam peptide activation
C-terminal peptide elongation by traditional coupling reagents (DCC, HATU…) is mostly accompanied by partial epimerization due to the formation of oxazolone intermediates. We currently develop an epimerization–free approach to peptide aryl esters via the so called Chan–Lam reaction. This is a Cu(II)–mediated esterification of carboxylic acids with aryl boroxines.

Peptide Rotaxanes
Microcin J25 is an example of a naturally occurring rotaxane (a so-called ‘lasso peptide’) that cannot be prepared using the current methods. A new strategy is required to synthesize these natural rotaxanes. The steps to bind the building blocks on the scaffold are based on robust reactions: oxime–ligation and ‘click’–reactions.

Solanoeclepin A
A biologically active compound isolated from the roots of the potato plant. It is a potent hatching agent of the potato cyst nematode. Its unique structural features makes it a challenging synthetic target. The retrosynthetic analysis of solanoeclepin A reveals two synthetic fragments, the right– and left–hand side.

Cinchona alkaloid–based organocatalysis
Cinchona alkaloids are well known for their antimalaria properties. In our lab these privileged molecules are elaborated further for organocatalytic purposes.

Naturally occurring cinchona alkaloids

Synthetic analogs

Enantioselective cysteine analog synthesis:

ValORIZATION GOALS

Research is directed at improvement of the efficiency, selectivity, and sustainability of synthetic protocols through the development of novel methodologies, in particular catalytic procedures.
Synthetic applications of C-H bond activation strategies

The direct and selective functionalization at C-H bonds provides a myriad of benefits from the economical and environmental point of view compared with the traditional approach since no preactivation of the starting materials is required. However, this strategy is still in its infancy and many challenges need to be overcome before this approach can become a routine synthetic tool for organic chemists. The low reactivity of the C-H bond and the poor selectivity observed are the main challenges in the field.

To overcome the current challenges, we focus on the development of new ligands capable of increasing the selectivity and reactivity of the C-H functionalization. We are currently working on the following research topics:

- Ligand-promoted oxidative cross-dehydrogenative coupling towards the synthesis of biaryls.
- Ligand-promoted C-H oxidation of simple arenes.
- Design and synthesis of traceless directing groups.
- Direct C(sp^3)-H functionalization of amino acids.

**Direct C-H Oxidation of Simple Arenes**

**Reactivity:**

\[
Pd(OAc)_2 2\text{mol\%} \quad L \quad (1-2 \text{ mol\%})
\]

\[
\text{PhI(OAc)}_2, \text{AcOH/Ac_2O} 100 \text{ C}
\]

**Selectivity:**

Ligand increased the reactivity and selectivity of the C-H oxidation

**Metal-Catalyzed C(sp^3)-H Functionalization of Amino Acids**

Sartans (blood pressure-lowering agents)  Boscalid (fungicide)  Xemium (fungicide)

**Metal-Catalyzed C(sp^3)-H Functionalization Using Traceless Directing Groups**

FG = OH, NH₂, CO₂H, CONH₂

**Biaryl Synthesis via Oxidative Cross-Dehydrogenative Coupling**

**Valorization goals**

Developing new efficient methodologies for the synthesis of value chemicals and materials using the C-H functionalization strategy.
Biocatalytic routes for the sustainable manufacture of valuable chemical products

**Biocatalytic cascades**
Multiple biocatalytic reactions can be carried out sequentially in a single flask (in vitro) or microbial host cell without the need for isolation of intermediates and purification steps. This approach leads to economic and environmental benefits since time-consuming intermediate work-ups are not required; furthermore, the use of organic solvents for extraction and purification as well as energy for evaporation and mass transfer is minimised.

In this context, our group has recently developed a dual-enzyme hydrogen borrowing process that enables the asymmetric amination of a broad range of secondary alcohols to afford the corresponding \((R)\)-configured amines in elevated optically pure form. Furthermore, amination of primary alcohols proceeded up to quantitative conversion. The biocatalytic system utilizes ammonia as the simplest amine donor and generates water as the sole innocuous by-product.

**Non-aqueous biocatalysis**
Biotransformations have been mainly studied in aqueous or biphasic aqueous-organic systems. We are currently working on the development of novel biocatalytic and chemo-biocatalytic processes in non-aqueous systems (also using immobilised enzymes). Biocatalysis in organic solvents shows various advantages, for instance: ease of enzyme recovery and recycling, increased substrate solubility, ease of product recovery, influence on thermodynamics and kinetics of enzymatic reactions, etc.

**Enzyme engineering**
An important aspect of our research is the generation of new enzyme variants through semi-rational protein engineering. These novel enzymes will be capable of catalysing chemical reactions that are unknown in nature. Consequently, they can be integrated into biocatalytic as well as chemo-enzymatic pathways to solve challenging synthetic problems, shorten synthetic routes and improve efficiency. In particular, we are now focusing on the engineering of stereocomplementary amine dehydrogenases (i.e. for the synthesis of \((S)\) and \((R)\) configured amines) that can perform the reductive amination of carbonyl compounds at the expense of ammonia and generating water as the sole by-product. Another goal is to extend the activity of the enzymes towards the synthesis of secondary and tertiary amines.

**Fig. 1.** Hydrogen-borrowing amination of alcohols. The method relies on a combination of two enzymes: an alcohol dehydrogenase operating in tandem with an amine dehydrogenase

**Fig. 2.** Amine dehydrogenase with bound NADH cofactor.

**The HIMS-Biocat lab**
Our lab is equipped with state-of-the-art facilities for molecular biology and enzyme engineering (gene cloning in bacteria, mutagenesis, generation and high-throughput screening of enzyme libraries), microbiology (microbial cultivation and expression of enzymes), biochemistry (enzyme purification, characterisation and kinetics via UV-vis spectroscopy), analytics (GC and HPLC analysis), bio-organic chemistry (organic synthesis using enzymes and chemo-enzymatic synthesis) and special techniques (enzymes immobilisation, cultivation of strains under anaerobic conditions and biocatalysis / enzymology with oxygen-sensitive enzymes).

**Valorization goals**
The generation of new enzyme variants and the implementation of these enzymes into artificial biosynthetic pathways for the sustainable conversion of inexpensive renewable resources into structurally diverse and valuable chemical products.
Synthesis, analysis, and computational understanding of molecular systems are key disciplines for advancing chemical sciences, but the ultimate proof of their value must come from ‘seeing’ them at work and ‘steering’ them to perform user-defined tasks. The interaction of Light and Matter is per se at the basis of such endeavours. Not only does it allow the passive observation and characterization of molecular systems (molecular spectroscopy) but also to obtain emerging properties from their synergy (molecular photonics).

While the 20th century has been labelled as the century of the electron, it is now clear that the 21st century will be the century of the photon. The Molecular Photonics group harbours a powerhouse of photochemical and photophysical expertise. It is in many aspects unique as it covers the complete trajectory from designing and constructing novel molecular systems to their application in areas of primary importance to society such as energy, sustainability, and health.

This is reflected in the strong interactions the groups has within and outside HIMS, such as the in 2014 started Advanced Research Center for Nano-Lithography, the free electron laser facilities (FELIX, FELICE) at Radboud University in Nijmegen, and medical research with the AMC and several companies.

Luminescent labels and probes
Solar energy conversion
Molecular machinery
Medical nanophotonics
Biomolecular dynamics
**Molecules and Photons at Work**

**Photoactive Materials Sciences**

The interaction between Light and Matter allows for the passive observation and characterization of molecular systems (molecular spectroscopy), but also to obtain emerging properties from their synergy (molecular photonics). Applications range from molecular machinery to medical imaging.

*Example: advancing healthcare technologies*

Understanding the intrinsic properties of molecular sunscreens is critical to developing more efficacious sunscreen products. Gas-phase spectroscopy and microsolvation studies provide innovative solutions.

**Chiral Structure Analysis**

Chiroptical techniques are emerging as powerful means to determine the absolute configuration and conformational structure of chiral compounds.

*Example: development*

VOA analysis toolbox (together with Theoretical Chemistry (VU), SCM, and BioTools)

*Example: novel methods*

to increase efficiency and utility Vibrational Circular Dichroism (together with Prof. S. Woutersen)

**Tailoring Catalytic Activity on a Nanoscale**

Nanoclusters are rapidly gaining commercial interest because of their unusual chemical reactivity. This reactivity finds its origin in the electronic properties of the clusters. Gas-phase studies of structure and substrate binding offer detailed insight and pave the way for optimizing these properties.

*Example: structure and reactivity Co clusters*

(together with Dr. J. Bakker and Prof. J. Oomens (FELIX, RU))

**Valorization goals**

Develop photoactive materials with user-defined properties

Extend areas of commercial application of chiroptical techniques

Optimize catalytic activity nanoclusters

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**References**

http://www.uva.nl/over-de-uva/organisatie/medewerkers/contact/b/u/w.j.buma/w.j.buma.html
Multi-dimensional Infrared Spectroscopy

Unraveling the causes of Parkinson’s
We study the aggregation into fibrils of the protein α-synuclein with infrared spectroscopy. This aggregation process is responsible for Parkinson’s disease. The mechanism of amyloid formation is poorly understood, and the structure of the (pathogenic) intermediates and the final fibril are still largely unknown and difficult to determine with conventional techniques. The combination of 2D-IR spectroscopy and vibrational circular dichroism offers a unique insight into the kinetics and structure of the aggregation of α-synuclein into pathogenic fibrils.

Since amyloid fibrils are believed to be the thermodynamically most stable state of many proteins and peptides, the best hope for therapies lies in preventing fibril growth. The results of this research project, which is focused on the fibril nucleation and growth, should make a substantial contribution of our understanding of these processes, and thus help in developing therapies.

Catalyst structure and optimization
Catalytic complexes often occur in several conformations that exchange rapidly (<us) in solution, so that their structures are difficult to characterize. Using 2D-IR spectroscopy on the CO and Rh-H stretching modes we have determined the structure of each of the two rapidly exchanging solution conformations of the hydroformylation catalyst (xantphos)Rh(CO)₂H.

This result demonstrates how 2DIR makes it possible to determine the structure of rapidly evolving, or exchanging, catalyst structures at the level of specific chemical bonds, and so to optimize their reactivity in a rationalistic manner.

References
JACS 136, 3530 (2014).

Valorization goals
Understanding amyloid formation to help developing therapies
Optimizing catalyst performance using mechanistic insights
# Functional Photonic Nanomaterials

## I. On-site Sensing in Biomedicine & Environment Without Background Emission Interference

**Features:**
- **Homogeneous detection**
  - “Fishing” detection mechanism
- **Background emission free**
  - employing NIR upconversion nanoparticles, only the nanoparticles are excited, and emission of surrounding biological entities will not be induced
- **Economic**
  - fiber & cw NIR diode laser
- **Multiple targeting**

## II. NIR Photonic Nanoplatform for Cancer Diagnosis & Therapy at Early Stage

**Features:**
- **Image-guided photodynamic therapy**
  - multi-color visible emission upon NIR excitation
- **Background emission free**
  - NIR can only excite the nanoparticles, not biological background
- **Economic**
  - cw NIR diode laser
- **Multiple targeting**
  - Emission spectrum of the upconversion nanoparticles is characteristic of the dopants inside, thus nanoparticles of different dopants can be linked to different determinands based on one-to-one principle.

## III. Water Printing & Patterning – Luminescent Carbon Nano-bombs

**Features:**
- Printed with water & HP 46 tricolour cartridges
- Daylight and UV
- Printed with water only

**Values:**
1. Quick and sensitive on-site detection method
2. New generation of photosensitizers for cancer treatment
3. Environmental-friendly printing and writing technique
Using a fluorescence microscope we image samples with spatial and temporal resolution and detect fluorescence parameters such as intensity, decay time, spectrum, etc. We apply this to the study of polymer dynamics, film formation in coatings and contact mechanics. Much of the potential of fluorescence microscopy for materials science is yet to be explored.

Single molecule free volume probe

Compound 1 has the unexpected and unique property that it emits fluorescence when in a polymer at temperatures below the glass transition. Increasing the temperature above $T_g$ leads to the disappearance of the fluorescence. This provides an optical method to observe the glass transition.

Water borne coatings made from latex dispersions require coalescence of the particles in order for a robust film to be formed. We can observe this process directly by labeling the polymer in some particles with a fluorescent dye molecule.

After heating overnight the original particles can no longer be recognized in the confocal image due to diffusion of the fluorescently labeled polymer.

Contact-sensitive fluorescent monolayer

Mechanical contacts between objects control many phenomena, from avalanches to friction. In collaboration with prof. Daniel Bonn (Institute of Physics) we develop methods to visualize contacts using fluorescence microscopy.

A viscosity sensitive molecule is in a monolayer on a glass surface, and a plastic bead is pressed down on it with controlled force. Due to the deformation of the bead, a contact area is formed.

The contact is directly observed as a round fluorescent spot. Its radius nicely follows Hertz’s theory (1881). We see detailed structure inside the spot due to the roughness of the surface of the bead.

References

Valorization goals
In these projects we develop tools to enable better understanding of the physical properties of industrially relevant materials.
Using a fluorescence microscope we image samples with spatial and temporal resolution and detect fluorescence parameters such as intensity, decay time, spectrum, etc. We apply this to the study of polymer dynamics, film formation in coatings and contact mechanics. Much of the potential of fluorescence microscopy for materials science is yet to be explored.

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References
We use (time resolved) spectroscopy, supramolecular organization and synthesis to get insight into and develop new materials for:

**Primary in events in organic photovoltaics.**
We focus on thin films containing perylene dyes or low band gap polymers and use fs pump-probe spectroscopy. We probe (non-)geminate charge recombination to the triplet state as charge loss.

**Photosensitizers for water oxidation and proton reduction** in organized nano-materials.
PS: Metal porphyrines, Ir and Ru complexes.
WOC: Ir and Co nanoparticles + complexes.
HEC: Pt and CoP nanoparticles.

**Metal organic frameworks** containing perylene-bis(dicarboximides) for photocatalysis.
We use N-pyridyl as well as N-carboxyphenyl PDI compounds and focus on CO$_2$ fixation.

**Photodynamic therapy.** Using light to save lives.
Anti-cancer, anti-bacterial, anti-inflammatory and immune-activating applications. NIR absorbing nanomaterials. **H2020 ITN project in development, looking for extra industrial partner.**
The Computational Chemistry theme is leading worldwide in the fields of molecular simulations and multiscale modelling. Its aim is to develop computational tools to model and predict, from first principles, the behavior of complex chemical, biological, and physical processes.

Over the past decade the group has developed a strong alliance, the Amsterdam Center for Multiscale Modeling (ACMM), with its counterpart at the VU science faculty. The ACMM, established in 2007, has developed a strong High Performance Computing infrastructure and an internationally recognized training program.

The ACMM is world reference center in the field of research, training, and valorisation in the field of molecular multiscale modeling. Top research in all important modelling disciplines at one location, with direct access to essential infrastructure like the Supercomputer Center (SURFSARA) and the eScience Center.

Knowledge valorisation will also be facilitated via scientific consultancy for industry and the establishment of the ACMM-Laboratory (High Performance Computing infrastructure) that will be a hands-on hosting environment for commercial partners to learn and apply computational methods to systems of technological and industrial interest.

Molecular simulations
Biochemical and biophysical phenomena
Computational catalysis
Novel methodology development
Aqueous chemical processes
Nanostructured materials
Soft matter
Atomistic insight in biomolecular processes

**Challenge**
Understanding protein function requires knowledge of the structure, energetics and kinetics of the different intermediate states a protein can visit. Molecular simulation can provide exactly such knowledge, complementary to experiments. Molecular dynamics (MD) provides the necessary temporal and spatial resolution, as protein conformational changes are highly dynamical processes, in which thermal fluctuations play an important role. While MD in general has been hugely successful, addressing processes that take place on the millisecond to second time scale still poses a huge challenge.

**Solution:**
One way to overcome this challenge involves the use of effective bias potentials forcing the system to undergo the process of interest. Nevertheless, application of such potentials biases the outcome, especially in complex systems. Therefore, it is essential to obtain unbiased dynamics, which is possible by using transition path sampling, a computational framework that harvests MD trajectories that undergo reactions of interest.

**Mechanism of photoreceptor function**
Using advanced simulation methods, we were able to predict the structure and mechanism of formation of the signaling state.

**Prediction of structure and mechanism**
Interpret and guide experiments

**Amyloid fibril formation**
Aggregation of the insulin derived LVEALYL peptide occurs via the lock-dock mechanism.

**Protein DNA binding**
In bacteria, the Histone-like Nucleoid Structuring protein forms bridges between strands of duplex DNA.

We have studied the DNA binding of H-N is at different length and time scales, resulting in the prediction of the mechanism of nucleotide sequence recognition and bridge formation.

**Prediction of structure and recognition mechanism**
Interpret and guide experiments

**Insight in protein aggregation**
Role of water; control of growth

**Kinetics and mechanisms of protein folding**
The Tip-cage miniprotein is a model system for protein folding. We elucidated the mechanism and kinetics of the folding and unfolding of this small protein, using advanced simulation methods.

**Development of simulation tools**
Development of simulation tools for studying kinetics of rare events such as protein folding

**Valorization goals**
Unravel kinetics and reaction mechanisms in biological processes
Guide and assist in the interpretation of experiments
Develop new efficient computational tools for the community
Understanding soft matter

**Challenge**

Soft materials such as colloids, emulsions, polymers, and surfactants, can have exceptional mechanical, optical or functional properties that find applications in both industry and society. Examples are found in consumer products such as shampoo, shaving cream, paint, plastics and food, but also in drug delivery systems. Soft matter easily deforms under external forces because forces and interactions act on mesoscopic scales. The components often self-organize into complex structures with striking mechanical, or functional properties. The key question is: How can we understand their structural, mechanical and (physico-) chemical properties from the building blocks and their interactions? Together with experimental groups we attack this problem using advanced molecular simulation methods.

**Self-assembly of polymer networks**

Telechelic polymers form complex networks depending on the functionality of the end-group. Asymmetric telechelic polymers can be triggered separately. Together with WUR researchers we investigate dependence on the order of the trigger sequence on the final network properties.

We develop algorithms that identify a percolating network, e.g., if a polymer forms a gel. In this lattice model our algorithm proves the largest connected grouping (red) fails to connect over all space when repeated periodically. If just the points marked blue were connected it would.

Prediction of structure and mechanism

Interpret and guide experiments

Development of tools for analysis of networks

**Anisotropic self-assembly of colloidal particles**

Isotropic particles can self-assemble into anisotropic structures. Acting as nanofiller in polymer nanocomposites, lead to special mechanical properties

Understanding and prediction of colloidal self assembly processes. Interpret and guide experiments

**Predicting reaction coordinates of crystal nucleation**

We predict the poorly understood structural nature of the critical nucleus and the involved reaction coordinates, and explain the observed kinetically favored meta stable crystal phases.

Development of simulation tools for studying kinetics of rare events such as crystal nucleation

**Active matter**

Active matter is a class of soft matter in which self-propulsion plays an important role.

Examples of active matter on different scales: birds, fish, bacteria, people.

We investigated in dense colloidal suspension (81% volume fraction) how activity enhances crystallization and suppresses the glass transition.

We develop dynamics of microscopic filaments in fluids (micro-fluidics). In a circularly polarized field a initially misaligned fiber will align along the field axis in a spiral motion.

Understanding of active matter properties

**Valorization goals**

Understand and predict soft matter self-assembly processes

Guide and assist in the interpretation of experiments and development of devices

Provide control over material properties
Molecular Simulation
- DFT (Ab Initio) Interactions
- Empirical Force Fields
- Statistical Thermodynamics
- (Ab Initio) Molecular Dynamics
- Monte Carlo Methods
- Rare Event Sampling Methods

Transfer Hydrogenation
- Metal-Catalyzed Transfer Hydrogenation
  - Important Factors:
    - Ligands
    - Nature of Solvent
    - Proton transfer

Ab Initio Model

Reaction Free Energy

Solvent Effects in Chemical Reactions

Silica Oligomerization
- First Step in Zeolite Synthesis
- Important Factors:
  - pH of solution
  - Structure Directing Agents (Ions)
  - Kinetic Network

Reactive Pathways of Solvent Mediated Mechanism

Aqueous Solutions
- Important Factors:
  - Ionic Size – Structure Making/Breaking – Proton Mobility
  - Ions Co-Factor in Aqueous Chemistry

- IR Spectra
- Ionic Hydration and Protons Mobility
- HCl/MgCl Solution

References

Valorization goals
- Screening of Compounds and Materials
- Predictive Modeling for a Wide Range of Conditions
- Rational Design of Novel Processes and Compounds

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Multiscale Modeling
ACMM
- Fluid Dynamics
- Materials, Membranes
- Reactors
- Solvent Reactions
- Solvent Reactions ADO
- Fluid Dynamics Reactors
- High Accuracy Method Development
- Quantum Chemistry
- Statistical Thermodynamics
- Statistical Thermodynamics WFT, DMFT
- Statistical Thermodynamics DFT
- Statistical Thermodynamics UvA
- Statistical Thermodynamics VUA

Important Factors:
- pH of solution
- Structure Directing Agents (Ions)
- Kinetic Network

Time

Van 't Hoff Institute for Molecular Sciences
Molecular Simulation

DFT (Ab Initio) Interactions
Empirical Force Fields
Statistical Thermodynamics

(Ab Initio) Molecular Dynamics
Monte Carlo Methods
Rare Event Sampling Methods

Nanoporous Materials and Surfaces

Xylenes Separation using MOFs

MOFs:
Important Factors:
Size selectivity (sieving)
Shape Selectivity
Packing effects
 Preferential Interactions

Xylenes in MAF-X8
Commensurate Stacking

Xylenes in MAF-X8
Selective Adsorption

Xylenes in MAF-X8
Breakthrough Profiles

Xylenes in MAF-X8
Loading MOFs Compared

Multiscale Modeling

VUA

ACM

UvA

Computational Chemistry

Van 't Hoff Institute
for Molecular Sciences

Methanol to Olefin Conversion In Zeolites

MTO is Acid Catalyzed Process
Important Factors:
Proton Mobility - MeOH/H2O Ratio and Loading

Clay/Water Interfaces

Important Factors:
Cat-/Anions Adsorption - Surface Hydration -
Acidity Surface Groups - Chemical Reactivity

Water / Proton / Hydroxyl
Association and Dissociation

Aluminium Oxides/Water Interfaces

Aluminium Oxides Important Heterogeneous Catalyst
Crucial Factors for Reactivity:
Surface hydration - Doping - Acidity/Basicty Surface Sites

Hydroxyl Types on Alumina
AIMD of Alumina/Water Interface

ValORIZATION GOALS
- Screening of Compounds and Materials
- Predictive Modeling
- Rational Design and Engineering with Atomistic Precision
- Software Suite for Nanoporous Materials
- Patents

References

Molecular Simulation
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Xylenes in MAF-X8
Breakthrough Profiles

Xylene Loading
MOFs Compared

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Multiscale Modelling of Complex Materials

By combining Electronic Structure Calculations with Molecular Dynamics Simulations, we unravel complex molecular phenomena in catalysis, biochemistry, and material science. In-house developed simulation methods allow us to study larger molecular systems and longer time-scales. We use advanced sampling techniques to probe activated transitions and reaction dynamics.

Development of theory, algorithms and computer code, allows us to calculate specific properties and observables that are not available in commercial modelling programs.

Acidity / proton transfer

Proton and electron transfer processes are simulated with DFT-MD in different molecular environments to compute for example conductivity, pKa, and redox potentials.

The free energy landscape gives direct insight in the reaction mechanisms and reaction rates. With our metadynamics simulations, we probe catalytic reactions in solution, at interfaces, and in biomolecules.

Valorization goals
Our multiscale modeling approach is widely applicable to:
- Unravel and optimize reaction mechanisms
- Predict structure and dynamics of molecular systems
- Interpret experimental spectra and measurements
Crosslinking polymerization, that is known to produces polymers with complicated branched topology due to crosslinking reaction mechanism:

\[ R_{x_1,y_1,z_1} + R_{x_2,y_2,z_2} \rightarrow R_{x_1+x_2+y_1+y_2-1,z_1+z_2+1,x_1+x_2+y_1+y_2-1} \]

has been studied by means of a four-dimensional population balance model accounting for chain length \( x \), free pending double bonds \( y \), crosslinks \( c \), and radicals \( z \) as dimensions. The model, for the first time and to a full extent resolves the crosslinking problem as formulated by Shiping Zhu two decades ago, and covers both pre-gel and gel regimes in a straightforward manner.

The model has been validated with data from an experimental crosslinking polymerization, Methyl Methacrylate with Ethylene Glycol Dimethacrylate. Non-trivial patterns in the time evolution of average quantities like crosslink densities, partly observed in prior studies, are naturally emerging from the model by computing marginal of the four-dimensional distribution possessing an interesting multimodal structure.

The work described here was financed by the I. Kryven et al:• Polymer 55(16), 3475–3489, 2014• MTS 23, 7-14, 2014• Polymer, 54(14), 3472–3484, 2013• MRE 7(6), 285-220, 2013

FPDB distribution obtained from models with different maximum number of radical sites per molecule. The dashed line depicts an asymptote of the tail of an FPDB distribution with no restrictions on radical sites number: an algebraic decay proportional to \( x^{-2.5} \).

GPC chain length distributions at the gel point obtained in each radical class \( z \) are shown as solid lines. The values of the overall distribution, depicted by a dashed line, are scaled by a factor 4 for comparison.

Sol molecules can be separated according to number of FPDB they posses. Chain length/crosslinks distributions for classes of molecules with a fixed number of FPDB, emerge as narrow peaks.

**Gelation in crosslinking polymerization:**

**multiple radical sites that matter**

**References**

I. Kryven et al:  
- Polymer 55(16), 3475–3489, 2014  
- MTS 23, 7-14, 2014  
- Polymer, 54(14), 3472–3484, 2013  

**Valorization goals**

Prediction of the topologies of branched polymer architectures and segment lengths from kinetics.
Analytical Chemistry is forensic science at the molecular level. Analytical Scientists are involved in establishing which types of molecules are present, how many of them there are and, increasingly, what they are – or have been – doing. Thus, we are naturally involved with forensics, but also with chemistry, materials, art, food and medicine. In all these areas the analytical-chemistry group within HIMS collaborate with leading companies and institutions.

The Amsterdam universities are recognized as a unique national centre for Analytical Sciences in The Netherlands. We develop, improve and optimize analytical (separation) methods and technologies. We develop advanced software (‘chemometrics’) to turn large amounts of data into useful information. We work together with world-leading high-tech-instrument companies to make our findings accessible to other scientists.

| One- and two-dimensional separation techniques | Gas and liquid chromatography |
| Field-flow fractionation | Mass spectrometry |
| Electro-migration techniques | Data analysis and chemometrics |
| Biomolecular systems Transition |
Towards HYPERformance liquid chromatography

During the last decade liquid chromatography has developed from a high-performance or high-pressure level (commonly known as HPLC) to what is known as ultra-high-performance liquid chromatography (UHPLC). While UHPLC technology (smaller particles, smaller system volumes, higher pressures) definitely entails progress, it does not constitute a great leap forward. In contrast, progressing from conventional one-dimensional liquid chromatography to comprehensive two-dimensional liquid chromatography (LC×LC) and eventually “spatial” chromatography allows the separation of many more components in a much shorter time. Several projects in our group are aimed at taking LC to a next level, identified as HYPERformance liquid chromatography and conveniently abbreviated as HPLC. Our objectives are to

- Increase the peak capacity (the number of peaks that can be separated) by at least an order of magnitude
- Increase the peak production rate (peak capacity per unit time) buy at least an order of magnitude
- Enhance the linear range of detection by at least an order of magnitude

Ultra-performance LC×LC

Elena Uliyanchenko has decreased the required analysis time for LC×LC separation of copolymers according to composition (horizontal direction) and size (vertical direction) down from a typical 4 hours to some 20 minutes, making application of the technique in industry much more attractive.

One-and-a-half-dimensional LC

LC×LC modulator technology can be used to decrease the detection limits in LC-MS, as is illustrated in this example for the determination of testosterone in cow urine.

Three-dimensional “spatial” LC

The concept of spatial LC×LC×LC promises peak capacities up to one million within a reasonable time.

With Sebastiaan Eeltink (VU Brussel)

Patent application numbers 20120171086, 20120164744, 20120162637

Valorization goals

- To develop and implement new or greatly improved separation methods
- To greatly enhance the applicability of advanced separation methods (such as LC×LC) in industry
- To solve very complex separation problems
Separation methods for macromolecules and particles

The conventional separation method for polymers/macromolecules is Size-Exclusion Chromatography (SEC). In SEC, the separation is according to molecular size. However, several other techniques have been developed in recent years that extend the size range of SEC, or that give other selectivities. Techniques studied within the Analytical Chemistry group of HIMS are:

- **Capillary Electrophoresis (CE).** This technique is suitable for water-soluble synthetic or natural macromolecules. CE can be used to study size distributions, functionality (end groups) or, e.g., the degree of substitution of modified polymers.
- **Asymmetrical Flow Field-Flow Fractionation (AF4).** Like SEC, AF4 separates according to size. However, its size range is much larger. AF4 can be applied to study supramolecular complexes, the aggregation of proteins, and to measure the size-distribution of particles.
- **Hydrodynamic Chromatography (HDC).** This technique can be especially suited for the analysis of solid particles, vesicles and liposomes. It has inherently a very high separation efficiency.

### Glycerin based EO/PO polyols

- **Capillary Electrophoresis (CE)**
- **Separation based on functionality (OH end groups)**

### Lipoprotein characterization

- **Field-flow fractionation (AF4)**
- **Separation based on size**
- **HDL – LDL – VLDL**
- **Cholesterol and triglycerides**
- **Rashid Qureshi, 2010**

### Aggregation of fullerenes

- **Field-flow fractionation (AF4)**
- **Aggregation behaviour**
- **Relation with environmental fate**
- **Alina Astefani, 2014**

### Microfluidics

Various research projects have been / are carried out on the development of microfluidic separation devices. Pillar-structured channels have been fabricated and evaluated that give excellent separation efficiency for Hydrodynamic Chromatography. The microfluidic channels will be tested for the HDC separation of vesicles and liposomes.

### Professional education

In-house courses can be given on various levels (MBO/HBO/acad, NL/Eng), on:

- Basic statistics for analytical chemists
- HPLC: principles and optimization
- Capillary Electrophoresis
Bayesian statistics to deal with data analysis automation

We are witnessing a tremendous explosion of the data sizes produced by analytical instrumentation. For example, a single injection of a sample in a GCxGC-MS instrument produces around 15 GB/hour or data. Often, the processing of this data into information becomes the major bottleneck of the analysis. In our group we are investigating methods to automate this process.

The classical approach to data analysis automation:

Data $\xrightarrow{\text{Algorithm}} \sum_\theta \sin \epsilon$ Information

In a sense, the machines are "taking responsibility" on the decision... and only the final result is shown.

Our new approach approach to data analysis automation:

Data $\xrightarrow{\text{Algorithm}} \sum_\theta \sin \epsilon$ Information

In a sense, the machines are "taking responsibility" on the decision... showing a collection of all (ranked) possibilities.

Just an example: application to toxicology screening with NFI (Dutch forensic institute):

A list of ~500 compounds have to be identified in a huge data set (LC-MS): how to distinguish them (from noise, isotopes, etc.?)

Bayesian statistics provides an elegant way to provide the probability of a compound being present (rather than a binary answer of a peak being present/absent)

Chemical noise Compound

\[
p(D|H_0) \cdot p(H_0) \quad \text{v.s.} \quad \frac{p(D|H_1)}{p(D)} = \frac{p(D|H_1) \cdot p(H_1)}{p(D|H_0) \cdot p(H_0)}
\]

- The presence/absence of chemical noise
- The possible retention times of the peak (with shifts)
- The possible positions of the MS signal (detector uncertainty)
- The possible adducts.
- The number of isotopes considered...

In this way, the user (and not the algorithm) takes the decision: the algorithm just helps the end user in taking this decision by delivering a collection of (ranked) possible answers.

The method is able to scan high resolution LC-MS and looking for more than 500 compounds.

Takes into account:
- Retention times
- m/z values
- Relative isotope ratios.

Sensitivity and specificity are better than commercial software packages (e.g. Mass hunter from Waters). It scans 0.5 Gb of data in ~ 6 min.

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- m/z values
- Relative isotope ratios.

Sensitivity and specificity are better than commercial software packages (e.g. Mass hunter from Waters). It scans 0.5 Gb of data in ~ 6 min.

**Valuezation goals**

Developing a global software package for automated data treatment from chromatography using Bayesian statistics.
Mass Spectrometry Powered Biomolecular Systems Analysis

This new HIMS group opens new areas of activity for the Institute by pursuing fundamental and applied research into the **analysis of biomedical systems** for health and disease as well as **forensic science** to aid crime investigation. A third area of activity concerns *Science for Art*, that combines interdisciplinary research uniting art history, art conservation and science. *See Katleen Keune for more information.

Our research uses mass spectrometers (MS) to characterise and quantify proteins in biological systems. Proteins are particularly interesting because they are critical for most biological processes and functions. The MS-based tools and allied technologies we develop enable the analysis of exquisite amounts of thousands of proteins that make up the molecular networks in cells, tissues and organs.

Knowledge about the interplay and the molecular state of proteins is important to understand how cells respond to their environment and influence the emergent properties of living systems. This holistic approach to study biological systems from a molecular perspective requires multidisciplinary teams where chemistry and bioinformatics are key elements.

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To achieve our goals we develop:

- **Chemical procedures to aid preparation and separation methods in line with MS**
- **Enabling technologies to quantitate proteins in molecular networks in subcellular localities and in clinical tissues and their cellular substructures**
- **Enabling technologies for post-translation modification interrogation**
- **Bioinformatics that enables high-speed and high-accuracy proteome analysis**

**Technological advances have outstripped conceptual advances in biology. The days of one gene – one protein – one function are passed.**

Networks of interacting molecules the key difference molecular between genotype and phenotype, where each node in a protein system represents a molecule of interest.

**The analytical pathway from discovery to validation**

1. **Discovery**: Discovery of perturbed protein networks which are most affected by endometriosis.
2. **Validation**: Validation of discovered proteins using targeted MS.
3. **Assay development**: Development of MS assays for targeted proteins.
4. **Optimisation of assay performance**

New molecular information on potential therapeutic targets or tools for non-invasive diagnosis for endometriosis are important for patient care and treatment. From Vehmas et al. *Ovarian Endometriosis Signatures Established through Discovery and Directed Mass Spectrometry Analysis*, J Proteome Res. 2014

**Biomolecular Systems Analytics**

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**References**

- Karinaste et al., J Proteome Res. 13 (2014) 1957-68.

**Valorization goals**

- To strategically underpin research in the Dutch biosciences community and to highlight the Netherlands as an important partner in research commercialisation.
- Developments of several analytical technologies for immediate spin off or though venture uptake.
Developing new chromatographic technology and methods for sustainable chemistry and proteomics

The versatility and power of chromatography

Chromatography is a versatile separation technique. Unlike other separation techniques, chromatography can separate based on various chemical and physical properties of the sample components, such as size, shape, charge, hydrophobicity, hydrogen bonding ability, π-π interactions, affinity for a particular ligand. With the appropriate selection of separation mechanisms it is now possible to separate 33 compounds per minute [1], making chromatography not only versatile but powerful.

The need for new technology and methods

Despite this the separation power of chromatography has not been exploited in sustainable chemistry or proteomics. This is partly due to limitations in chromatographic technology. Our research aims to address this problem by developing methods and technology specifically for these application areas.

We are looking for interested industry partners in sustainable chemistry and protein analysis who face separation/characterisation problems to join us in tailoring methods and technology for their specific applications.

Current research directions

Chromatography for sustainable chemistry:

Two-dimensional chromatography for lignocellulosic biomass catalysis

Lignocellulosic biomass catalysis produces a vast variety of different compounds: sugars, aromatics, aliphatic compounds, phenols and other low molecular weight compounds which serve as important reagents in chemical synthesis. This makes for a complicated separation.

To date, typical separation tools are predominantly one-dimensional. We are investigating the use of the increased power of two-dimensional chromatography to this application.

In collaboration with: Dr. N. Raveendran Shiju (HIMS)

Online reactions + separation = efficiency:

Reaction flow chromatography [3,4]

For maximum separation power in two-dimensional chromatography, it is necessary to couple two selectivities which have vastly different separation mechanisms.

The asterisk equations report metrics which assess the optimality separations mechanisms when combined. The equations are easily used in Microsoft Excel.

Work has begun on extending the equations to create a metric accounting for all aspects of separation quality.

Making method development clearer:

The asterisk equations [2]

New chromatographic technology for protein separations

Efficient protein separations require stationary phases with high permeability, large pore size, high loadability yet chemically and mechanically stable. Core-shell stationary phases, while very efficient, have short lifetimes, reduced permeability and reduced loading capacity. We aim to create a new stationary phase which addresses the current limitations of existing technology

In collaboration with: Prof Gadi Rothenberg and Prof Garry Corthals (HIMS)

Valorization goals

Aside from the asterisk equations the remaining projects are in the process of being launched, subject to funding.

References

What happens in ageing oil paint?

Investigating & understanding these phenomena:

Modeling

\[
\frac{dS}{dt} = \sum_i k_{pS,i}A_i^{a_i}B_i^{b_i} - S_S \sum_i k_{cS,j}C_j^{c_j}
\]

Calculating concentration profiles of relevant functional groups, and the cross-linked structure of the oil network

Reconstructions

Mimicking paint composition and ageing to reproduce degradation phenomena and test conservation treatments

Paint samples

Studying paint samples from oil paintings to characterize paint composition and degradation phenomena

Synthesis

PbO + C_{15}H_{31}COO^-

1. Pb(C_{15}H_{31}COO)_2
2. Pb_3O_2(C_{15}H_{31}COO)_2

Understanding the reactions that take place in oil paint and providing a detailed characterization of reaction products

PAinT team:
Dr. Arineke van Loon
Dr. Joen Hermans
Dr. Katrien Keune
Dr. Maartje Stols-Witlox
Prof. dr. Piet Iedema

Website: www.s4a-paint.uva.nl

Collaboration with Rijksdienst Cultureel Erfgoed and Courtauld Institute of Art, London

References

Valorisation goals:
- Evaluate effects of past and present approaches to conservation of painted surfaces
- Improve scientific basis to guide conservation strategies