



GENERAL ASSEMBLY OF THE MARIE CURIE ALUMNI ASSOCIATION BOOK OF ABSTRACTS

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FOREWORD

Dear Members,

This Book of Abstracts provides details of the 70 posters presented at the General Assembly and Annual Conference of the Marie Curie Alumni Association (2nd and 3rd February 2018, in Leuven, Belgium).

Each poster includes an abstract, making reference to the author(s), organisation(s), and are themed across seven areas of study:

- Life Sciences
- Engineering
- Chemistry
- Physics
- Environmental Sciences
- Economics
- Social Sciences & Humanities

The MCAA once again thanks everyone that showcased their posters at the 2018 event. They continue to encourage members and non-members to submit posters for future Annual Conferences and General Assemblies. Do not hesitate to contact the author of the abstract using the MCAA web-portal.

***Yours,
The MCAA Communications team***

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Impact of lipid composition on in vivo performance of celecoxib formulations

Erratic absorption and variable bioavailability of poorly-water soluble drugs (PWSD) challenge the robust formulation of oral dosage forms, especially at high doses. Overcoming such challenges can be done by solubilizing PWSD in lipid-based formulations (LBF). While this bio-enabling approach has been successful in bringing several drug molecules to market, systematic studies into the optimal excipient composition for LBF are lacking.

This study investigates the influence of composition changes on in vivo performance of LBF. It is reported in literature that long-chain (LC) lipids out-perform medium-chain (MC) lipids concerning absorption enhancement of certain PWSD, whereas for some compounds the differences are negligible. Considering higher solubility in medium-chain lipids, it is interesting to evaluate the LC-MC combination as bio-performance enhancer for high-dose formulations.

Six oral formulations of celecoxib with variations with respect to long-chain triglycerides (LCT), medium-chain triglycerides (MCT), long-chain monoglycerides (LMG), medium-chain monoglycerides (MMG) and a surfactant (S) were tested in a pharmacokinetic rat study. Formulations were grouped into two categories: 1) LMG-based: LMG+S, LMG+LCT+S, LMG+MCT+S and, 2) MMG-based: MMG+S, MMG+LCT+S, MMG+MCT+S.

Statistical analysis did not reveal any significant differences between the formulations regarding relevant PK parameters (i.e. C_{max}, T_{max}, AUC_{0-t}, and bioavailability); however, a trend was observed towards better in vivo performance in terms of C_{max}, AUC_{0-t}, and bioavailability for the LMG+S formulation, whereas MMG+MCT+S performed less well.

Although it has been previously suggested that formulation design principles depend both on the compound's physico-chemical properties and excipient types and ratio, in the case of celecoxib the bio-performance was independent of lipid excipient type and ratio. These observations are not in accordance with data for other compounds, demonstrating that LBF design cannot be generalized at present.

In vivo evaluation of celecoxib lipid-based formulations
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Introduction
 Our advancement of poorly-soluble drugs to a frequent and significant challenge for pharmaceutical development. In many cases, co-administration with high fat meals of some BCS class II drugs (i.e. low solubility, high permeability) reduces their oral bioavailability. Therefore, inclusion of such drugs in lipid based formulations (LBF) offers a promising approach to improve their biological exposure. While the merits of lipid based drug delivery technology have been extensively researched in the scientific literature, there is limited number of commercial formulations available. This points towards a considerable gap between the knowledge from literature and the clinical drug product development using the lipid delivery technology. Design of a LBF is a complex process because optimal excipient selection and formulation strategy may influence the extent in vivo behavior after oral administration (Figure 1). It is reported that long chain (LC) lipids can partially reduce the BCS lipids in terms of absorption enhancement. On the other hand, MC lipids have generally better solubility due to higher polarity. However, these generalizations do not apply to all poorly-soluble drugs and the number of investigated compounds is limited. The purpose of this study is to extend this research to another BCS class II compound which has not been previously published. Celecoxib belongs to class II of the BCS system and displays high variability in absorption following oral administration. Specifically, the aims of the present study are to: • Compare LC in MC lipids in terms of effect on absorption of celecoxib • Investigate qualitative and quantitative excipient changes on the performance of celecoxib in vivo

Methods
 Relative stability of celecoxib in various lipid emulsions was determined in vitro using for 28h at 37°C. Oral bioavailability of six LBF was assessed in faster male rats (n = 4) followed by required blood sampling.

Formulation	Excipients	Formulation	Dispersion and digestion*	PK parameters
LMG+S	LMG	LMG+LCT	LMG+LCT+S	C _{max} , T _{max} , AUC _{0-t}
LMG+LCT+S	LMG, LCT, S	MMG+S	MMG+S	C _{max} , T _{max} , AUC _{0-t}
MMG+S	MMG	MMG+LCT+S	MMG+LCT+S	C _{max} , T _{max} , AUC _{0-t}
MMG+LCT+S	MMG, LCT, S	MMG+MCT+S	MMG+MCT+S	C _{max} , T _{max} , AUC _{0-t}
MMG+MCT+S	MMG, MCT, S			

Results
 • C_{max}, T_{max}, AUC_{0-t} and bioavailability (BA) were not statistically different between the six lipid emulsions.
 • Top ranking formulations in terms of C_{max}, AUC_{0-t} and BA are LMG+S, LMG+LCT+S, MMG+MCT+S performed the poorest.
 • The C_{max} value for LMG+S is statistically higher than for MMG+MCT+S.
 • All formulations containing LCT showed the lowest degree of variability (i.e. CV) in BA. BA. Looking at LC-MC mixtures (i.e. LMG+LCT+S and MMG+LCT+S), similar pharmacokinetic behavior in the same sample systems (i.e. LMG+S and MMG+S) is observed.
 • Within the same class of long and short length, combinations of mono- and di- glycerides (i.e. LMG+LCT+S and MMG+LCT+S) perform the poorest in each group.

Conclusions
 • For celecoxib, without effect of lipids (MC vs. LC) vs. T_{max} did not show any statistical difference in pharmacokinetic behavior of lipid based formulations.
 • The simpler systems (i.e. LMG+S and MMG+S) were found to show optimal bioavailability.
 • Formulations based on long chain monoglycerides and surfactant is offering the best results for celecoxib.
 • Further studies on other BCS class II compounds are needed to expand the knowledge on optimal design of lipid delivery systems.

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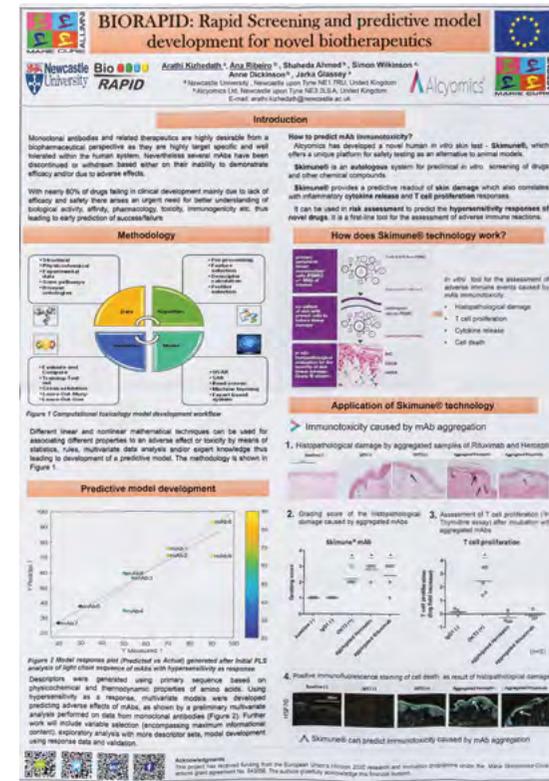
Skimune® as a new in vitro assay for detection of immunogenicity by aggregated monoclonal antibodies

Alcyomics has developed a novel human in vitro skin test – Skimune®, which offers a unique platform for safety testing as an alternative to animal models. Skimune® is an autologous system for in vitro screening of drugs and other chemical compounds. Skimune® provides a predictive readout of skin damage which also correlates with inflammatory cytokine release and T cell proliferation responses. It can be used in risk assessment to predict the sensitization potential of novel drugs. It is a first-line tool for the assessment of skin sensitization.

In this work, we present Skimune® as a tool for the assessment of adverse immune reactions to monoclonal antibodies (mAbs). Aggregation of mAbs is a very common event during industrial process, long-term storage (temperature), handling and administration (shaking). Considering the panoply of current protein-based therapeutics, there is a large concern for protein aggregation as potentially immunogenic for humans. While the extent of immunogenicity in patient populations is uncertain, reports show that it can lead to immune activation by cell activation and cytokine release.

In this experimental study, mAb aggregation was forced by exposure of different commercially available mAbs to a heat-stress protocol (up to 65°C). Resulting adverse immune events were measured by the Skimune® assays – T cell activation, cytokine release and histopathological damage. Protein characterization of the heat-exposure mAb samples was carried through analytical ultra-centrifugation (protein content), SDS-Page (molecular weight) and Transmission Electron Microscopy (aggregate formation). Our results show that exposure to temperature can, in fact, cause conformational changes in the mAb structure that, ultimately, cause adverse

immune reactions. The aggregates formed provoked cell death by histopathological damage of the skin and activation of cell death pathways, rather than just overall immune activation. Ultimately, Skimune® can be used as a valid tool for assessment of immunogenicity by mAb aggregation.



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BIORAPID : Rapid early stage screening and predictive model development for novel biotherapeutics

Biologic drugs are structurally complex and very difficult to characterize and produce than small molecule drugs. With nearly 80% of drugs failing in clinical development mainly due to lack of efficacy and safety there arises an urgent need for smarter preclinical development using quality by design based approaches as identified by ICH Q8(R2) guidelines on Pharmaceutical development This contribution describes research undertaken in order to develop a modelling approach enabling the prediction of adverse effects of potential drug candidates by correlating the properties of selected biologic drugs with experimentally determined toxicity and hypersensitivity or allergic reactions. Intrinsic toxicology of bioactive pharmaceuticals was reported using a panel of in vitro methods including effects on cell viability and/or proliferation, genotoxicity and reactive oxygen species production due to oxidative insult. Hypersensitivity reactions were assessed using Skimune™, a non-artificial human skin explants based assay for safety and efficacy assessment of novel compounds and drugs, developed by Alcyomics Ltd. Using Skimune™ as a response, multivariate models were developed for small molecules to demonstrate the applicability of this assay for developing predictive models. Its use has been extended to predicting adverse effects of biologics as well, as shown by a preliminary multivariate analysis performed on data from monoclonal antibodies. The applicability of these in vitro and in silico methods and their benefits in rapid screening of prospective drug candidates in terms of potential hypersensitivity, toxicity and mode of action based on their inherent physical, chemical and/or biological properties as well has been discussed. The key impact of this research is on lowering of attrition rates, faster development of potential drug candidates as well as facilitate continued positive pipeline development for rapid bioprocesses. In the long term it would also help to

reduce prices of potentially lifesaving biopharmaceutical products.

BIORAPID: Rapid Screening and predictive model development for novel biotherapeutics

Introduction

Monoclonal antibodies and related therapeutics are highly desirable from a biopharmaceutical perspective as they are highly target specific and well tolerated within the human system. Nevertheless several mAbs have been discontinued or withdrawn based either on their inability to demonstrate efficacy and/or due to adverse effects.

With nearly 80% of drugs failing in clinical development mainly due to lack of efficacy and safety there arises an urgent need for better understanding of biological activity, affinity, pharmacology, toxicity, immunogenicity etc. thus leading to early prediction of success/failure.

Methodology

Figure 1: Computational toxicology model development workflow. A circular diagram showing the integration of various data sources into a predictive model.

Predictive model development

Figure 2: Model response plot (Predicted vs Actual) generated after initial PLS analysis of light chain sequence of mAbs with hypersensitivity as response. The plot shows a strong positive correlation between predicted and actual values.

Application of Skimune® technology

Immunotoxicity caused by mAb aggregation

- Histopathological damage by aggregated samples of Rituximab and Herceptin.
- Grading score of the histopathological damage caused by aggregated mAbs.
- Assessment of T cell proliferation (3H-Thymidine assay) after incubation with aggregated mAbs.
- Positive immunofluorescence staining of cell death as result of histopathological damage.

Skimune® can predict immunotoxicity caused by mAb aggregation.

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Exploring the nanotoxicity of 2D materials

Two dimensional (2D) nanoparticles form a large family of materials which has continuously grown since the discovery of graphene in 2004. In addition to this type of carbon nanoparticle, the family is composed by single-atom-thick materials such as transition metal dichalcogenide monolayers (2D-TMDs), hexagonal boron nitride (h-BN), MXenes, borophene (2D boron), and so on. Their particular physico-chemical properties, which give them excellent properties as semiconductors, superconductors, lubricants, insulators, and even magnets, have attracted much attention due to the high number of potential applications in different fields, such as biomedics, optoelectronics, energy storage and conversion devices. In particular, TMD monolayers are suitable for the development of dry lubricants, solar cells and sensors. The intensive interest in their use in current and future technologies has raised questions about their safety. Hence, understanding the specific interactions between these 2D materials and biological systems has become an important scientific issue. Given that the toxicological behaviour of 2D-TMDs is poorly understood due to the lack of scientific reports, one of the goals of the SOLUTION project is to investigate their toxicological potential using different eukaryotic systems such as mucoepidermoid carcinoma cells from human lungs (NCIH292), human breast adenocarcinoma cells (MDA-MB-468), and the model fungus *Saccharomyces cerevisiae*. Viability, cytotoxicity and genotoxicity studies applied to the analysis of the interaction between 2D-nanoparticles and cells are of high relevance to ensure a safe use of these materials in real-life applications.

EXPLORING THE NANOTOXICITY OF 2D MATERIALS

1 INTRODUCTION

Two dimensional (2D) nanoparticles form a large family of materials which has continuously grown since the discovery of graphene in 2004 (1). In addition to this type of carbon nanoparticle, the family is composed by single-atom-thick materials such as transition metal dichalcogenide monolayers (2D-TMDs), hexagonal boron nitride (h-BN), MXenes, borophene (2D boron), and so on. Their particular physico-chemical properties, which give them excellent properties as semiconductors, superconductors, lubricants, insulators, and even magnets (1, 2), have attracted much attention due to the high number of potential applications in different fields, such as biomedics, optoelectronics, energy storage and conversion devices (3). In particular, TMD monolayers are suitable for the development of dry lubricants, solar cells and sensors (4, 5, 6).

The intensive interest in their use in current and future technologies has raised questions about their safety. Hence, understanding the specific interactions between these 2D materials and biological systems has become an important scientific issue. Given that the toxicological behaviour of 2D-TMDs is poorly understood due to the lack of scientific reports, one of the goals of the SOLUTION project is to investigate their toxicological potential using different eukaryotic systems such as mucoepidermoid carcinoma cells from human lungs (NCIH292), human breast adenocarcinoma cells (MDA-MB-468), and the model fungus *Saccharomyces cerevisiae*. Viability, cytotoxicity and genotoxicity studies applied to the analysis of the interaction between 2D-nanoparticles and cells are of high relevance to ensure a safe use of these materials in real-life applications.

2 MATERIALS AND METHODS

GENETIC MODELS

- Human Cell Lines: Human breast adenocarcinoma cells (MDA-MB-468)
- Eukaryotic organisms: Mucoepidermoid carcinoma cells from human lungs (NCIH292), *Saccharomyces cerevisiae*

Cell Viability Assays

- Typan Blue:** A classic dye, it is generally used as assay for staining dead cells. Instead, Typan Blue is taken up by dead cells and excluded by viable cells. In this method, cell viability is determined by counting the unstained cells with a microplate.
- Neutral Red:** A weak cationic azo dye, penetrates cell membranes by passive diffusion. This assay is based on the ability of viable cells to incorporate and bind neutral red which accumulates intracellularly in lysosomes. Therefore, the reduction of the cellular uptake provides a signal of cell integrity and growth inhibition.

DNA damage assays

- Comet assay:** is a rapid and sensitive technique for analyzing and quantifying DNA damage in individual cell. This method, also called single cell gel electrophoresis, allows the detection of DNA double-strand breaks, oxidative base damage and apurinic/apyrimidic nucleosides. In this protocol, individual cells are plated in a thin agarose gel on a microslide, slide and then the cells are fixed. Thereafter, DNA endonucleases (alkaline phosphatases that determines the migration of the broken/stranded DNA fragments away from the cell nucleus). As a result of using a DNA-specific fluorescent dye, the gel can be read for amount of fluorescence in head and tail. Hence, the amount of DNA damage is directly proportional to the extent of DNA break from the head (7).
- 8-OHdG quantification (8-Hydroxy-2'-deoxyguanosine):** is a method of assessing DNA damage that has been widely used as a biomarker for oxidative damage. ROS (reactive oxygen species) during a biological stress increase dramatically. It has been shown that ROS can attack DNA molecules including DNA bases, covering 2'-OH and 8-OHdG (8). The principle of this assay is the use of anti-8-OHdG monoclonal antibody, followed by an HRP (horseradish peroxidase) conjugated secondary antibody. Therefore, the quantity of 8-OHdG can be determined by comparing its absorbance with that of a known 8-OHdG standard curve.

3 GOALS

One of the goals of the research project is to evaluate and identify the possible health and environmental risk of 2D TMD particles.

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Phytochemical content and endogenous enzymes activity of Brassicaceae sprouts

Brassicaceae (cruciferous) vegetables are recognized as a functional food because different epidemiological and meta-analysis suggested that their consumption has preventive role against a variety of diseases. In the last couple of years new culinary trend introduced cruciferous vegetable in a germinating stage, as sprouts. Consumption of such as vegetables provide unique taste, and additional health benefits due to the fact that during extensive period of growth and development, seedlings and young plantlets accumulate more phytochemicals than vegetables in mature stage. In our study, five Brassicaceae sprouts (white cabbage, kale, broccoli, Chinese cabbage, aragula) were comparatively analyzed based on phytochemicals content and accompanying enzymes associated with phytochemical stability and bioavailability that consequently impact food quality. Significantly high content of polyphenols and glucosinolates, as well as a high antioxidant activity were found in white cabbage, followed by kale sprouts, two Brassicaceae sprouts which, so far, have not been widely consumed for food. Another advantage of white cabbage is lower polyphenol-oxidase activity which potentially indicates prevention of browning and better sprout quality. On the other side, kale, arugula and broccoli possessed lower ascorbate peroxidase activity, and higher ascorbic acid (vitamine C) content. In addition, arugula and broccoli showed significantly higher activity of myrosinase that may result in higher bioavailability of active glucosinolates forms.

Phytochemical content and endogenous enzymes activity of Brassicaceae sprouts
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Introduction
 Cruciferous (Brassicaceae) vegetables are recognized as a functional food because different epidemiological and meta-analysis suggested that consumption of cruciferous has preventive role against a variety of chronic disease, several cancers etc. Beneficial effects include antioxidant, anti-inflammatory, gastro protective and anti-obesity activity associated with the presence of phytochemicals such as glucosinolates, polyphenols, carotenoids etc. In the last couple of years new culinary trend introduced cruciferous vegetable in a germinating stage, as sprouts.

In our study we directly compared phytochemical content and endogenous enzyme activity of five different Brassicaceae sprouts: white cabbage (*Brassica oleracea* var. capitata), kale (*B. oleracea* var. acephala), broccoli (*B. oleracea* var. italica), Chinese cabbage (*B. rapa* var. pekinensis), and arugula (*Eruca sativa*).

Material and methods

plant growing
 specialized metabolites analysis
 enzymes activity
 biological activity

Phenolics (total flavonoids, phenolic acids, flavanols), Ascorbic acid, Glucosinolates, chlorophylls, carotenoids
 Peroxisomal peroxidase (GPOD), Ascorbate peroxidase (APX), Catalase (CAT), Polyphenol oxidase (PPO), Myrosinase (MIR)
 DPPH radical scavenging capacity assay, Ferric reducing/antioxidant power assay (FRAP)

PCA

Results

Table 1. Common nutrients, fatty acids, dry weight and content of proteins and total dietary fibers in five analyzed Brassicaceae species

Common name	Latin name	Dry weight (%)	Proteins (mg/kg dry)	Total dietary fiber (mg/kg dry)
Kale	<i>Brassica oleracea</i> var. capitata	11.56(±0.19)	15.85(±0.19)	15.85(±0.19)
Arugula	<i>Eruca sativa</i>	11.25(±0.19)	16.11(±0.19)	16.11(±0.19)
Chinese cabbage	<i>Brassica oleracea</i> var. capitata	12.30(±0.44)	17.13(±0.19)	17.13(±0.19)
White cabbage	<i>Brassica oleracea</i> var. capitata	12.30(±0.44)	17.13(±0.19)	17.13(±0.19)
Broccoli	<i>Brassica oleracea</i> var. capitata	12.30(±0.44)	17.13(±0.19)	17.13(±0.19)

Table 2. Activity of enzymes in five Brassicaceae species

Enzyme	White cabbage	Kale	Arugula	Chinese cabbage	Broccoli
GPOD (mg/kg dry)	0.0002	0.0002	0.0002	0.0002	0.0002
APX (mg/kg dry)	0.0002	0.0002	0.0002	0.0002	0.0002
CAT (mg/kg dry)	0.0002	0.0002	0.0002	0.0002	0.0002
PPO (mg/kg dry)	0.0002	0.0002	0.0002	0.0002	0.0002
MIR (mg/kg dry)	0.0002	0.0002	0.0002	0.0002	0.0002

Table 3. Total polyphenols (TP), total flavonoids (TF), total phenolics (TPH), total ascorbic acid, chlorophyll a, chlorophyll b, total chlorophyll and carotenoids content of five analyzed Brassicaceae species

Species	TP (mg/kg dry)	TF (mg/kg dry)	TPH (mg/kg dry)	Ascorbic acid (mg/kg dry)	Chlorophyll a (mg/kg dry)	Chlorophyll b (mg/kg dry)	Total chlorophyll (mg/kg dry)	Carotenoids (mg/kg dry)
White cabbage	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)
Kale	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)
Arugula	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)
Chinese cabbage	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)
Broccoli	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)	1.23(±0.19)

Conclusions
 Obtained results showed that all five analyzed sprouts contain phytochemicals with health-promoting benefits. Significantly high content of polyphenols and glucosinolates, and antioxidant activity were found in white cabbage sprouts, followed by kale sprouts. Both varieties have not so far been widely used for food as sprouts. Another advantage of white cabbage is lower PPO activity which potentially indicates phytochemical stability, and consequently, better food quality. Based on presented results, examined Brassicaceae sprouts, with particular focus to white cabbage deserve more scientific attention as a cheap source of phytochemicals with health-promoting benefits.

Funding
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Design, synthesis and in vitro evaluation of modulators of PFKFB3 phosphatase activity

Cardiovascular disease is a global health problem and its primary cause is atherosclerosis, which is characterized by the arterial wall thickening. Current therapeutic strategies have limited efficacy and mortality still remains high. Recent research has shown that targeting dysregulated endothelial cell (EC) metabolism could be a new therapeutic strategy. In the scope of MSCA Moglynet EJD we aim to further explore the possibilities for an improved treatment of this serious disease.

EC glycolytic flux is up-regulated during angiogenesis and it is controlled by 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase (PFKFB3), which is therefore an innovative target for atherosclerosis therapy. PFKFB3 is a dimeric bifunctional enzyme that has a very high kinase to phosphatase activity ratio. Its activity is controlled by the N-terminus autoregulatory domain (AD) in the kinase region, which adopts a β -hairpin shape in the crystal structure.

We performed virtual screening on the targeted allosteric binding site and here we present the synthesis and biological evaluation of the selected library of PFKFB3 phosphatase modulators. In vitro activity and binding assays were performed on the isolated recombinant enzyme and cell tests were carried out on murine ECs.

DESIGN, SYNTHESIS AND IN VITRO EVALUATION OF MODULATORS OF PFKFB3 PHOSPHATASE ACTIVITY
 H. Maciù¹, X. Hu², D. Tarantino³, L. Parma⁴, S. Pellegrino⁵ and M.L. Gelmi⁶

INTRODUCTION
 Cardiovascular disease is a global health problem and its primary cause is atherosclerosis, which is characterized by the arterial wall thickening. Current therapeutic strategies have limited efficacy and mortality still remains high. It has been clearly shown that:
 • pathological blood vessel responses are associated with metabolic alterations in endothelial cells (ECs)
 • targeting EC glucose metabolism is a promising way to affect pathological angiogenesis.^{1,2}

6-Phosphofructo-2-kinase/fructose-2,6-bisphosphatase (PFKFB3)
 • plays a crucial role in the regulation of the EC glycolytic flux and it is up-regulated during angiogenesis³
 • is a dimeric bifunctional enzyme that possesses a very high kinase to phosphatase activity ratio
 • its activity is controlled by the N-terminus autoregulatory domain (AD) in the kinase region
 • its crystal structure AD adopts a β -hairpin structure (Figure 1)⁴

We hypothesize that by interfering the interactions between the AD and the phosphatase domain, an indirect decrease of the kinase activity might be achieved. The expected biological outcome of this modulation would be reduced glycolysis.

DESIGN AND SYNTHESIS
i) DESIGN
 Two strategies are suggested:
 1. targeting the AD binding site for direct blockage of the interaction (Figure 2A)
 2. targeting a negatively charged channel for an indirect interference of the interaction (Figure 2B)
 Libraries of small molecules from ZINC and ASINEX database were submitted for virtual screening using the two proposed strategies. 10 small molecules and 21 peptides were selected for experimental assays.

ii) SYNTHESIS
 All peptides selected from virtual screening were synthesized using manual solid phase peptide synthesis or automated microwave assisted solid phase synthesis on several types of resins using Fmoc-protected amino acids and standard protocols. Commercially available compounds were purchased from vendors Amnes and Sigma-Aldrich.

RESULTS
i) PFKFB3 EXPRESSION
 The His-tagged human inducible bifunctional enzyme was expressed in E. coli (BL21(DE3) pLysE) and purified using nickel-affinity column, and the N-terminal His tag was removed by treatment with thrombin. The final purification was performed using Mono Q anion-exchange chromatography; the resulting pure protein (Figure 3) was kept after concentration to 2.9 mg/ml protein, in pH 8.0, 20 mM Tris-HCl, 10 mM NaCl, 0.05 mM EDTA, 5 mM and 0% glycerol. The activity of the protein was confirmed using Promega ADP-Glu Kinase assay.

ii) BINDING AFFINITY
 The binding affinity of the compounds with the best affinity (Table 1) was determined using the microscale thermofluorometry (MST). All compounds were tested in the concentration range from 1 nM to 30.25 nM (serial dilutions, 10 conc.). The measurements were repeated three times under the same conditions using 50 nM labelled enzyme.

iii) THERMOFLUOR
 The thermal shift assay was carried out for PFKFB3 in the presence of the best binders (HM-20-22) and Sypro ORANGE dye was added. The experiment was done in 4 replicates in the temperature range from 4°C to 96°C.

iv) CELL MIGRATION ASSAY
 The scratch assay on murine ECs was performed for the compounds HM-20-22. Each compound was tested at 10 μ M and 100 μ M concentrations. The result was checked after 18 h (Figure 4) and 24 h (Figure 5).

DISCUSSION
 • The MST binding assay clearly shows that three compounds (HM-20-22) bind to the PFKFB3 enzyme in a low micromolar range.
 • According to the MST results, a pharmacophore can be roughly determined; however further compounds have to be evaluated and the selected hits have to be optimized.
 • Thermofluor analysis shows no significant changes in the T_m of the target enzyme.
 • The binding did not significantly affect the stability of the protein.
 • Compound HM-21 was able to reduce the migration ability of murine ECs when compared to the control solution.

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ACKNOWLEDGMENTS
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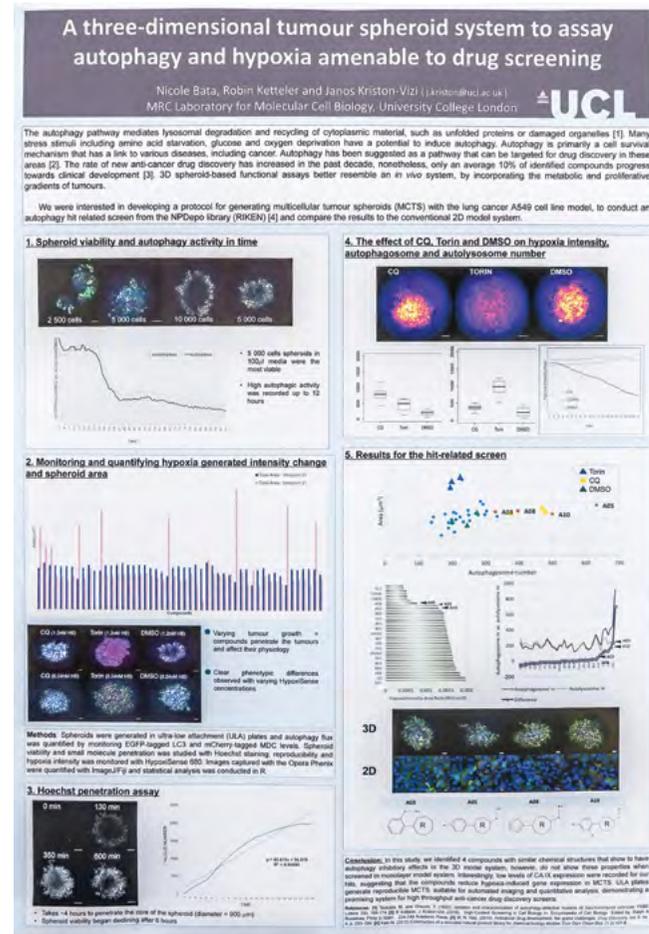
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A three-dimensional tumour spheroid system to assay autophagy and hypoxia amenable to drug screening

The autophagy pathway mediates lysosomal degradation and recycling of cytoplasmic material, such as unfolded proteins or damaged organelles. Many stress stimuli including amino acid starvation, glucose and oxygen deprivation have a potential to induce autophagy. Autophagy is primarily a cell survival mechanism that has a link to various diseases, including cancer. Autophagy has been suggested as a pathway that can be targeted for drug discovery in these areas. The rate of new anti-cancer drug discovery has increased in the past decade, nonetheless, only an average 10% of identified compounds progress towards clinical development. 3D spheroid-based functional assays better resemble an in vivo system, by incorporating the metabolic and proliferative gradients of tumours.

We were interested in developing a protocol for generating multicellular tumour spheroids (MCTS) with the lung cancer A549 cell line model, to conduct an autophagy hit related screen from the NPDepo library (RIKEN) and compare the results to the conventional 2D model system.



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BIORAPID: Bioprocess scale up/down strategies for rapid development of novel bioactive molecules

Biotechnological applications demand large amounts of high-quality products, which are produced at considerably low costs. Cell physiology and, in many cases, product yield and quality strongly depend on suitable production conditions. However, oscillatory environmental conditions due to gradient formation in the liquid phase in large scale production, lead to cell stress and productivity losses.

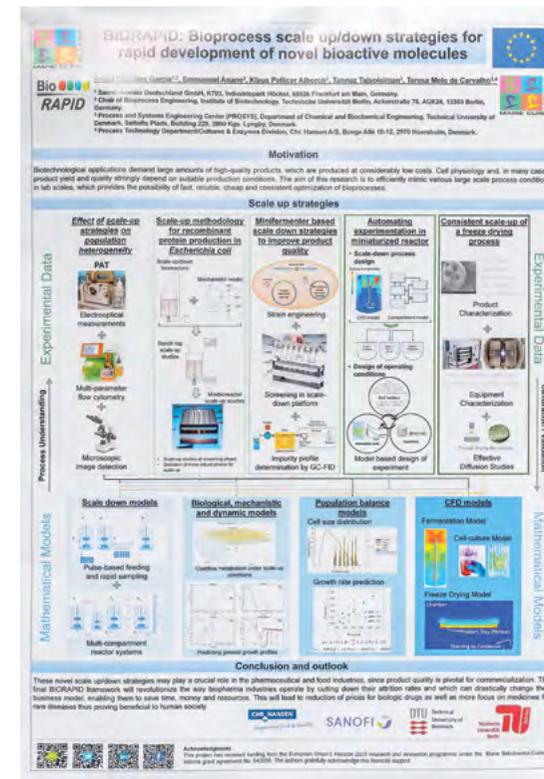
The aim of this research is to efficiently mimic various large scale process conditions in lab scales, which provides the possibility of fast, reliable, cheap and consistent optimization of bioprocesses. Hence, robust scale up strategies are developed in order to speed up the development of processes for new bioactive molecules. With this perspective, we simulated the conditions experienced by insulin-producing *Escherichia coli* cells in large scale bioreactors by performing pulse-based nutrient feeding and starvation experiments in parallel with multiple cultivations. This strategy was tested on mammalian cell cultures in miniaturized bioreactors, ideal for high-throughput screening, by following optimal experimental designs, with the main focus on protein quality. Furthermore, we applied multi-compartment scale down reactors to study the consequences of heterogeneous conditions in lactic acid bacteria (LAB) fermentation in lab scale by pH gradients. A special focus was put on the application of novel online activity and single-cell based monitoring. Finally, we developed a model to describe the dynamics of freeze-drying of LAB with computational fluid dynamics, for future optimization and scale up.

These novel scale up/down strategies may have a crucial role in the pharmaceutical and food industry, since product quality is pivotal for commercialization.

At the same time, our approaches are useful to optimize the production of starter cultures for dairy products.

Acknowledgments

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Not your typical TPR protein – RNA-binding proteins with helical repeats

We investigate the structure and function of two families of RNA-binding proteins with helical repeats. One group is the Interferon induced protein with tetratricopeptide repeat (IFIT) family, which are antiviral effectors that sequester viral RNA and prevent translation of viral proteins, as part of the vertebrate innate immune response. Although the crystal structures of some IFITs are known, it is not clear how they cooperate in multi-IFIT complexes to counter viral infection. We study the RNA preference of IFITs when present in a larger assembly, and we are exploiting their unique properties for use in diagnostics and biotechnology applications.

The second group of our interest are the Fas-activated serine threonine kinase domain (FASTKD) proteins, which were misannotated as kinases, but seem to bind and regulate the processing of mitochondrial transcripts in animals. FASTKD proteins contain predicted helical repeats and a putative PD(D/E)XK nuclease domain overlapping with another small domain called RNA-binding domain abundant in Apicomplexans (RAP). The structure of any of the FASTKD proteins is not known, and no reliable structural homologues could be identified. We are using structural biology methods and RNA-binding assays, together with a phylogenetic analysis of protein with RAP domains, to determine the structure and function of FASTKD proteins.

The poster is titled "Not your typical TPR protein – RNA-binding proteins with helical repeats" and lists authors: Monika Kowalska, Jan Kutner, Matthew Merski, Krzysztof Młynarczyk, Natalia Karolak, Anna Laskowska, Mikolaj Kuska, Jakub Skrzeczkowski, Maja Czuba, Marcin Ziemiak, Stanislaw Dunin-Horkawicz, and Maria W. Górna. It is organized into several sections:

- Abstract:** Summarizes the investigation of IFIT and FASTKD protein families.
- Structural biology approach:** A flowchart showing the process from protein identification to structural determination.
- IFIT protein family:** Discusses IFITs as antiviral effectors that sequester viral RNA.
- FASTKD protein family:** Discusses FASTKD proteins as mitochondrial transcript regulators.
- IFIT action against viruses - still open questions:** A diagram showing IFITs binding to viral RNA and inhibiting translation.
- FASTKDs regulate mitochondrial RNA metabolism:** A diagram showing FASTKD proteins in the mitochondria.
- Are there new RNA-binding domains in FASTKDs?:** Discusses the discovery of new domains within FASTKDs.
- The "IFIT code" – or there is an IFIT for every need:** Discusses the specificity of IFIT proteins.
- References and Funding:** Lists scientific references and funding sources like EMBO and National Science Centre.

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The Utility of Measuring Tear Film Break-up Time for Prescribing Contact Lenses

Purpose: To evaluate the clinical value of non-invasive keratograph tear film breakup time in the assessment of pre-corneal and pre-lens tear film quality for prescribing contact lenses (CLs).

Methods: Forty-six subjects aged 25.5 ± 4.3 (mean \pm standard deviation) years were recruited. Visual acuity (VA), anterior eye health checks and NIKBUT were evaluated. On the following day, subjects were fitted with a daily Silicon Hydrogel (SiHy) CL in one eye and a Hydrogel (Hy) CL in the other. After four hours, one material for both eyes was chosen based on a qualitative analysis which included VA, CL fitting and comfort. Information about the first and the mean NIKBUT was then contrasted against the prescription decision.

Results: Thirty-four subjects were fitted with SiHy and twelve with Hy CL (Fig. 2). No statistically significant differences were found for both NIKBUT parameters between left and right eye at baseline ($p=0.38$ and $p=0.50$, respectively) and post four hours of CL wear ($p=0.61$ and $p=0.06$). The chosen lens did not always correspond to longer NIKBUT. Only in 39.1% and 34.8% of cases (i.e., 18 and 16 out of 46), there was a match between prescription decision and the first and the mean NIKBUT results, respectively. **Conclusions:** Although there is no evidence whether tear film surface quality measurement has a superior diagnostic values compared to other traditional clinical measures used in practice, NIKBUT measurements have provided additional information that could be of interest during CL fit.

PURPOSE
To evaluate the clinical value of non-invasive keratograph tear film breakup time in the assessment of pre-corneal and pre-lens tear film quality for prescribing contact lenses (CLs).

RESULTS
Thirty-four subjects were fitted with SiHy and twelve with Hy CL (Fig. 2). No statistically significant differences were found for both NIKBUT parameters between left and right eye at baseline ($p=0.38$ and $p=0.50$, respectively) and post four hours of CL wear ($p=0.61$ and $p=0.06$). The chosen lens did not always correspond to longer NIKBUT. Only in 39.1% and 34.8% of cases (i.e., 18 and 16 out of 46), there was a match between prescription decision and the first and the mean NIKBUT results, respectively.

Comparison of	Matched	Counts	Percentage (%)	p-value
First NIKBUT	Don't match	28	60.8	0.001
Matched	18	39.1		
Mean NIKBUT	Don't match	30	65.2	0.001*
Matched	16	34.8		
First NIKBUT vs Mean NIKBUT	Matched	40	86.9	0.001
Don't match	6	13.1		

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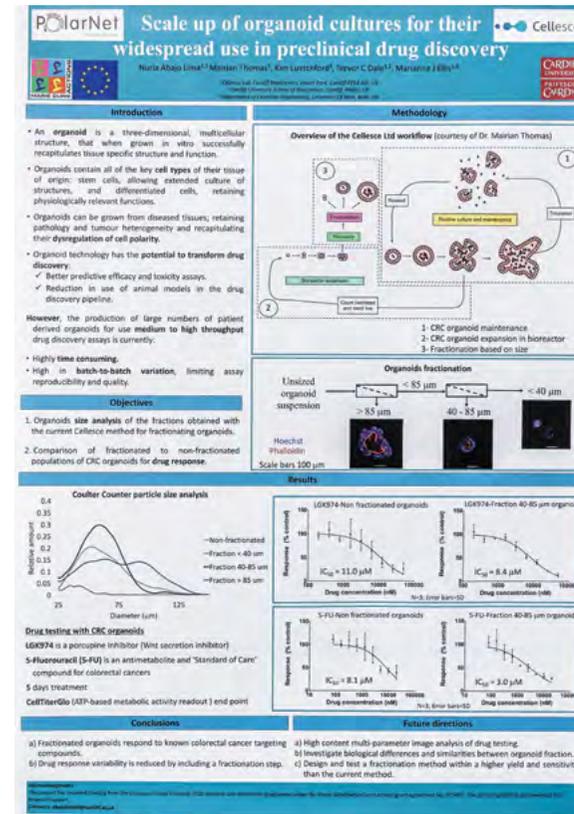


Scale up of organoid expansion and fractionation for their widespread use in preclinical drug discovery

Recent studies showing that cancer organoids recapitulate the biology of primary cancers have driven tremendous excitement in their potential to revolutionize drug discovery and personalized medicine. Tumor heterogeneity at the genetic and phenotypic level drives differential responses to therapeutic agents, and this heterogeneity is preserved in organoids grown from colorectal cancers. Using organoids as an alternative to 2D cultures is growing in popularity but there is a bottleneck to their widespread utilization. Organoids need to be produced on a large enough scale to adequately supply end users, from university researchers to pharmaceutical companies; importantly batch-to-batch variation needs to be minimized. Currently, manual processing results in organoids of varied size and while the majority are suitably functional, they range from too small to polarize, to too big with necrotic cores. Cellesce Ltd has developed a new bioprocessing technology by semi-automating the process of organoid culture, thus improving the control of the process conditions, which yields a more desirable range of organoid sizes.

The aim of this research is to fractionate distinct organoid subpopulations based on their size using chemical engineering technologies. Fractionated populations of colorectal cancer organoids from biopsies that show different phenotypes and mutational backgrounds are separated using the technology, and will be used to study differences in organoid subtypes, i.e. function and polarity, and to relate genetic and phenotypic differences back to drug response and primary tumor heterogeneity. A broad spectrum of inhibitors of signaling pathways are used to demonstrate the importance of the fractionation process and the identification of the organoid size that satisfactorily recapitulates the drug response of the native organ.

This approach will enable the use of biophysically-purified organoid subpopulations to study the molecular mechanisms underlying organoids' phenotypic heterogeneity, together with the efficiency of novel anti-cancer drugs before their use in Phase II clinical trials.



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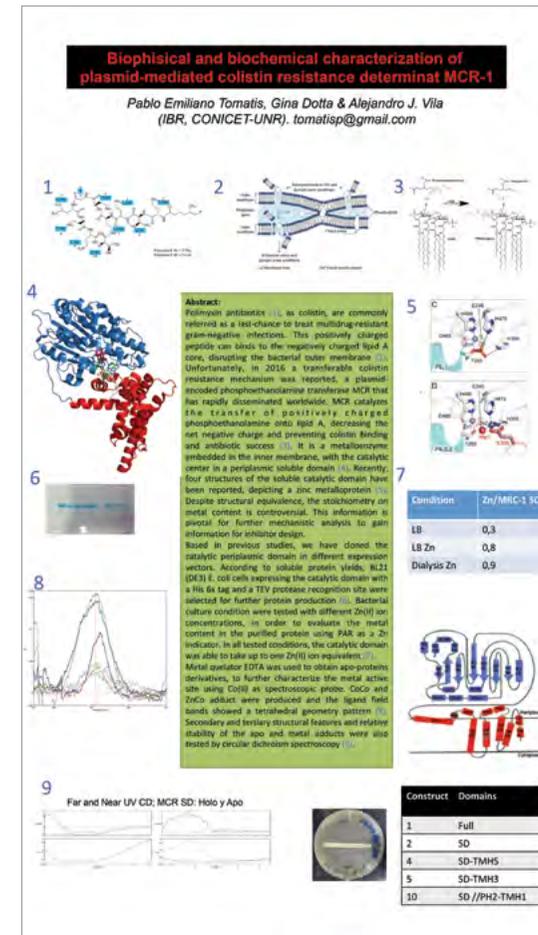
Biophysical and biochemical characterization of plasmid-mediated colistin resistance determinant MCR-1

Polymyxin antibiotics, as colistin, are commonly referred as a last-chance to treat multidrug-resistant gram-negative infections. This positively charged peptide can bind to the negatively charged lipid A core, disrupting the bacterial outer membrane. Unfortunately, in 2016 a transferable colistin resistance mechanism was reported, a plasmid-encoded phosphoethanolamine transferase MCR that has rapidly disseminated worldwide. MCR catalyzes the transfer of positively charged phosphoethanolamine onto lipid A, decreasing the net negative charge and preventing colistin binding and antibiotic success. It is a metalloenzyme embedded in the inner membrane, with the catalytic center in a periplasmic soluble domain. Recently, four structures of the soluble catalytic domain have been reported, depicting a zinc metalloprotein. Despite structural equivalence, the stoichiometry on metal content is controversial. This information is pivotal for further mechanistic analysis to gain information for inhibitor design.

Based in previous studies, we have cloned the catalytic periplasmic domain in different expression vectors. According to soluble protein yields, BL21 (DE3) E. coli cells expressing the catalytic domain with a His 6x tag and a TEV protease recognition site were selected for further protein production. Bacterial culture condition were tested with different Zn(II) ion concentrations, in order to evaluate the metal content in the purified protein using PAR as a Zn indicator. In all tested conditions, the catalytic domain was able to take up to one Zn(II) ion equivalent.

Metal quelator EDTA was used to obtain apo-proteins derivatives, to further characterize the metal active site using Co(II) as spectroscopic probe. CoCo and ZnCo adduct were produced and the ligand field bands showed

a tetrahedral geometry pattern. Secondary and tertiary structural features and relative stability of the apo and metal adducts were also tested by circular dichroism spectroscopy.



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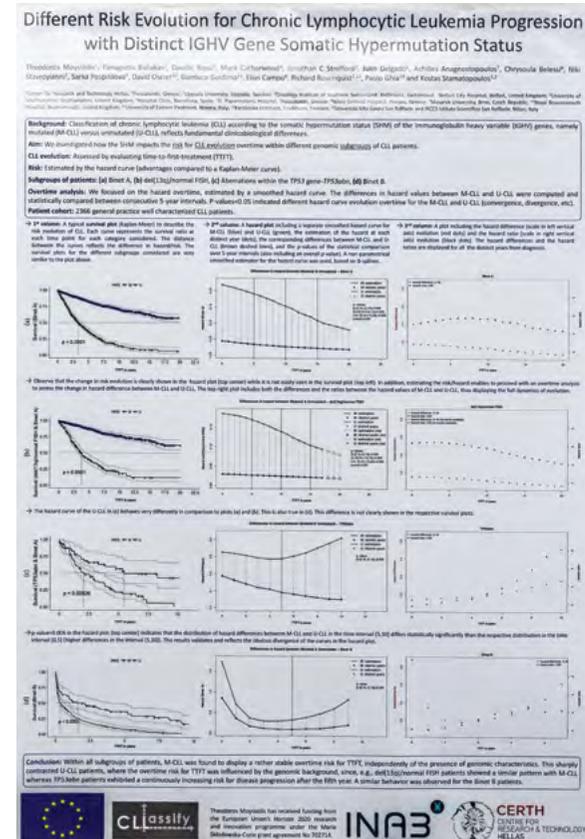
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Different Risk Evolution for Chronic Lymphocytic Leukemia Progression with Distinct IGHV Gene Somatic Hypermutation Status

Chronic lymphocytic leukemia (CLL) is the most common adult leukemia in the West and exhibits remarkable clinicobiological heterogeneity. A great challenge for CLL patients is to determine if and when they will experience disease progression requiring treatment. Nowadays, immunogenetic and genomic features are considered essential for accurate prognostic assessment in CLL. When utilizing such biomarkers, the prognosis is assessed assuming stable predictability over the disease course. Here, we assessed the risk evolution for CLL progression overtime by evaluating time-to-first-treatment (TTFT) in 2366 CLL patients not requiring treatment at the time of diagnosis. Based on the somatic hypermutation status (SHM) of the immunoglobulin heavy variable (IGHV) genes, the patients were classified as mutated (M-CLL) and unmutated CLL (U-CLL). Our analysis focused on different genomic subgroups within each SHM category.

Initially, the overtime risk was estimated by the hazard curve. This enables to better visualize changes in risk evolution compared to the typical Kaplan-Meier curve, which is the current gold-standard tool for risk evolution in survival-analysis, by showing the "instant" risk for treatment initiation at a specific time point. We then performed an interpolation method to estimate, for both the M-CLL and the U-CLL patients, the specific values of their hazard curves at each distinct year from the time of diagnosis, and the corresponding hazard differences. The follow-up was divided in 5-year intervals, and the distributions of the hazard differences were statistically compared between consecutive 5-year intervals. P-values less than 0.05 would indicate different hazard curve evolution for the M-CLL and the U-CLL patients.

We observed significant differences in risk evolution between the different genomic subgroups in each SHM category. In particular, while M-CLL patients were found to display a rather stable overtime risk for TTFT, in U-CLL patients, the risk evolution was clearly influenced by the genomic background.

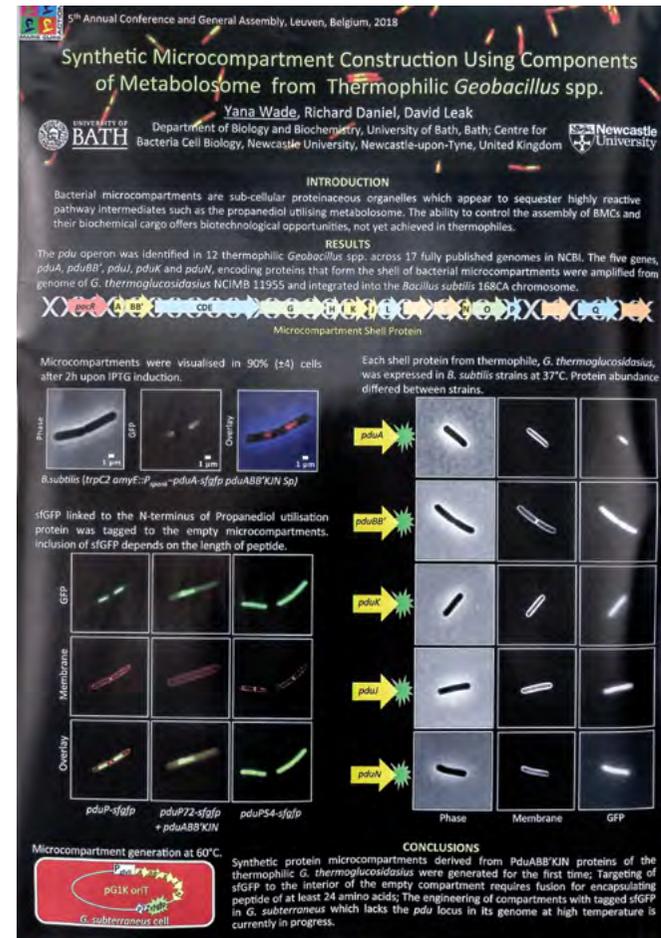


Microcompartment construction using components of the propanediol utilisation metabolosome from thermophilic *Geobacillus* spp.

Bacterial microcompartments (BMCs) are sub-cellular proteinaceous organelles which appear to sequester highly reactive pathway intermediates such as the propanediol utilising metabolosome (Pdu). The ability to control the assembly of BMCs and their biochemical cargo offers biotechnological opportunities, not yet achieved in thermophiles.

The pdu operon in the genome of thermophilic *G. thermoglucosidarius* NCIMB 11955 was examined. The five genes, pduA, pduBB', pduJ, pduK and pduN, encoding proteins that form the shell of BMCs were amplified. Initially, the empty BMCs were assembled by expression of the pdu-ABB'JKN proteins in *Bacillus subtilis* 168CA. Circular structures with clear boundaries were visualised by TEM in thin-sectioned cells. Superfolder GFP (sfGFP) fused to the sequence of the Propanediol utilisation protein PduP was incorporated into the lumen of BMCs. Given the *Bacillus*-based observations, the pduABB'JKN and pduP72-sfGFP were placed under the control of both a maltose inducible promoter and a synthetic strong constitutive RplS1 promoter for simultaneous co-expression in *Geobacillus* spp. The fragments were cloned into shuttle vectors capable of conjugative transfer from *Escherichia coli* S17-1 and will be transferred into *Geobacillus* strains lacking the pdu operon, such as *G. subterraneus*.

These results show for the first time the generation of synthetic protein compartments derived from components of the Pdu organelle of thermophilic *G. thermoglucosidarius* and targeting of enzymes to their lumen. The engineering of BMCs with tagged sfGFP in *G. subterraneus*, which lacks the pdu locus in its chromosome, is currently in progress.



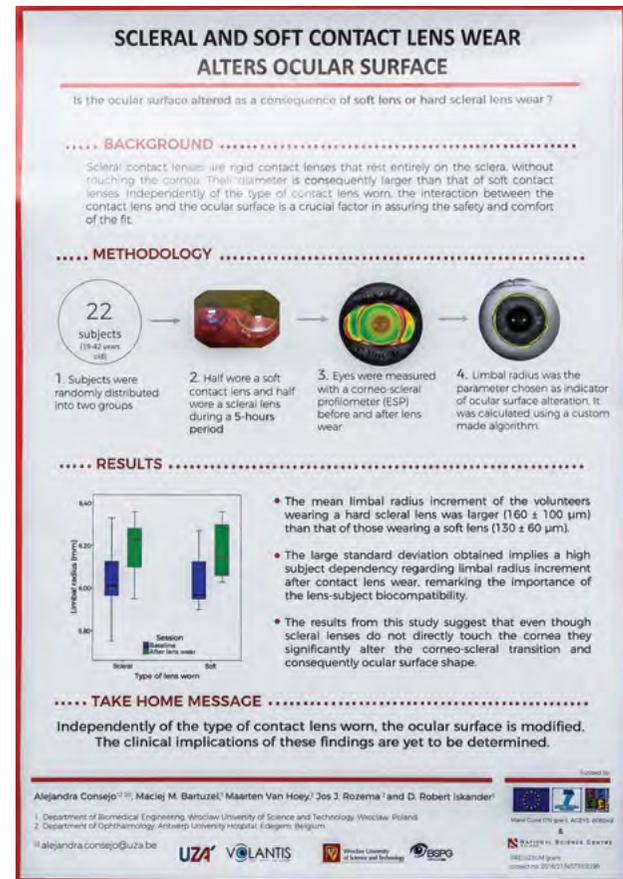
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Scleral and soft contact lens wear alters ocular surface

Scleral contact lenses are oxygen permeable rigid contact lenses that rest entirely on the sclera, without touching the cornea. Their diameter is consequently larger than that of soft contact lenses. Traditionally, scleral lenses have been used for visual correction in compromised eyes, when spectacles or soft contact lenses could not help and also as therapeutic device in cases of ocular surface disease. However, in the last decade scleral contact lens prescription has significantly increased and nowadays scleral lenses are progressively being considered for refractive error correction also in healthy eyes. Independently of the type of contact lens worn, the interaction between the contact lens and the ocular surface is a crucial factor in assuring the safety and comfort of the fit. The aim of this work was to compare how the ocular surface is altered as a consequence of soft lenses and hard scleral lenses wear. 20 volunteer subjects participated in the study, half wore a soft contact lens and half a scleral lens during a 5-hours period. Measurements with a non-contact corneo-scleral topographer (Eye Surface Profiler) were always conducted before lens insertion and immediately after lens removal. Limbal radius (the edge between cornea-sclera) was the parameter chosen as indicator of ocular surface alteration. Limbal radius was determined from 3-dimensional corneo-scleral maps using a custom made algorithm. The mean limbal radius increment of the volunteers wearing a hard scleral lens was larger ($220 \pm 130 \mu\text{m}$) than that of those wearing a soft lens ($160 \pm 60 \mu\text{m}$). The large standard deviation obtained implies a high subject dependency regarding limbal radius increment after contact lens wear, remarking the importance of the lens-subject biocompatibility. The results from this study suggest that even though scleral lenses do not directly touch the cornea they greatly alter the corneo-scleral transition and consequently ocular surface shape.

Founding: NCN; 2016/21/N/ST7/02298



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Reinforcement Learning-Based and Parametric Production-Maintenance Control Policies for a Deteriorating Manufacturing System A.

The model of a stochastic production/inventory system that is subject to deterioration failures is developed and examined in this paper. Customer interarrival times are assumed to be random and backorders are allowed. The system experiences a number of deterioration stages before it ultimately fails and is rendered inoperable. Repair and maintenance activities restore the system to its initial and previous deterioration state, respectively. The duration of both repair and maintenance is assumed to be stochastic. We address the problem of minimizing the expected sum of two conflicting objective functions: the average inventory level and the average number of backorders. The solution to this problem consists of finding the optimal trade-off between maintaining a high service level and carrying as low inventory as possible. The primary goal of this research is to obtain optimal or near-optimal joint production/maintenance control policies, by means of a novel Reinforcement Learning-based approach. Furthermore, we examine parametric production and maintenance policies that are often used in practical situations, namely Kanban, (s, S), threshold-type condition based maintenance and periodic maintenance. The proposed approach is compared to the parametric policies in an extensive series of simulation experiments and it is found to clearly outperform them in all cases. Based on the numerical results obtained by the experiments, the behavior of the parametric policies as well as the structure of the control policies derived by the Reinforcement Learning-based approach is investigated.

Reinforcement Learning-Based and Parametric Production-Maintenance Control Policies for a Deteriorating Manufacturing System
 A. S. Xanthopoulos, A. Kiatipis, D. E. Koulouriotis and Sepp Stieger
 DOI: 10.1109/ACCESS.2017.2771827

Abstract
 The model of a stochastic production / inventory system that is subject to deterioration failures is developed and examined in this paper. Customer interarrival times are assumed to be random and backorders are allowed. The system experiences a number of deterioration stages before it ultimately fails and is rendered inoperable. Repair and maintenance activities restore the system to its initial and previous deterioration state, respectively. The duration of both repair and maintenance is assumed to be stochastic. We address the problem of minimizing the expected sum of two conflicting objective functions: the average inventory level and the average number of backorders. The solution to this problem consists of finding the optimal trade-off between maintaining a high service level and carrying as low inventory as possible. The primary goal of this research is to obtain optimal or near-optimal joint production / maintenance control policies, by means of a novel Reinforcement Learning - based approach. Furthermore, we examine parametric production and maintenance policies that are often used in practical situations, namely Kanban, (s, S), threshold-type condition based maintenance and periodic maintenance. The proposed approach is compared with the parametric policies in an extensive series of simulation experiments and it is found to clearly outperform them in all cases. Based on the numerical results obtained by the experiments, the behavior of the parametric policies as well as the structure of the control policies derived by the Reinforcement Learning - based approach is investigated.

Parametric control policies and RL-based approach
 The primary goal of this research is to obtain optimal or near-optimal, integrated maintenance and production control policies. To this end, Reinforcement Learning (RL) methods are used, along with discrete-event simulation. More specifically, the proposed approach consists of interfacing RL-based decision-making agents with simulation models of the investigated production/inventory systems. A simulation model generates sample paths of the system dynamic evolution. The decision-making agent interacts with the simulation model by observing the current system state and selecting some admissible control action. Subsequently, the decision-making agent is presented with the outcome of its action, i.e. the new state in which the system has transitioned to and a numerical value that represents the relative merit of making the aforementioned selection. This cycle is repeated sufficiently many times and through this learning process, the agent determines the best control action for each system state, i.e. the optimal control policy. The proposed approach for integrated production and maintenance control was compared to:
 • the Kanban system with condition based maintenance (Kanban (CBM))
 • the Kanban system with periodic maintenance (Kanban - PM)
 • the (s, S) system with condition based maintenance (Ls, S) - (CBM)
 • the (s, S) system with periodic maintenance (Ls, S) - PM

Results
 In Figure 4, the performance of the alternative maintenance / production control schemes is summarized. The height of the bars corresponds to the lowest objective function value (refer to section III) attained by each approach. The control policies computed by the RL-based agent clearly outperform all parametric control policies in all simulation cases.

Conclusions and Future Research
 The problem of integrated production / maintenance control for a deteriorating, stochastic production/inventory system was investigated. A novel approach based on Reinforcement Learning, for deriving optimal or near-optimal policies, was proposed. The Reinforcement Learning-based approach was compared to several ad hoc production and maintenance policies that are widely being used in practice. These ad hoc control policies were found to be suboptimal in all simulation cases examined in the research. Their performance depends largely on the values of the respective control parameters. The application of Reinforcement Learning for solving such complex industrial engineering problems yielded substantial engineering benefits. Furthermore, the results showcased the merits of integrated production / maintenance policies that explicitly account for interactions between maintenance and production decisions. This research can be extended by considering more complex production system configurations, e.g. manufacturing lines, and alternative objective functions. In the former case, due to the significantly increased size of the state space multi-agent system architectures might be mandated. Other directions for future research include the application of Reinforcement Learning for solving alternative industrial engineering problems, for example integrated production and quality control of manufacturing systems that produce imperfect end-items.

Figure Left: Kanban system with a single manufacturing facility and backorders
Figure Right: Control policies obtained by the decision-making agent in case 3 (on the left) and in case 1 (on the right).

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Towards the development of novel carbon based materials for on-chip supercapacitor

In this project, the key challenges by self-assembling carbon nanotube (CNT), graphene and other carbon materials with engineered nanoarchitectures are addressed. The innovative materials approach is the use of silicon nano-taper array decorated with nano particles (NPs) for catalytic growth to construct functional 3D templates, and of low dimension carbons in the form of CNT or graphene to construct 3D nanoarchitectures. Our hypothesis is that silicon nano-taper array with engineered density and shape will prove to be the most effective functional structure for template-assisted self-assembling the electrodes of supercapacitors. The resulting electrodes exhibit optimized configuration of pores, quantitative electrochemical accessibility, and the use of maximized active material sustaining fast charging rates. Moving from on-chip to large-size supercapacitors, the wafers with the 3D nanoarchitecture stack together via interconnection to fabricate the large-size supercapacitors. At the same time, the R&D on on-chip supercapacitors emphasis should be put on developing package material system and process suitable for IC compatibility and high reliability. We will design both in-plan and sandwich supercapacitor configurations, and electrical interconnections for a compact integration on chip and on printed circuit board. The application of liquid or solid electrolyte request chemical stable package materials. Implementing the separator between two electrodes against electron short-circuit, especially in the liquid electrolyte supercapacitors, is another challenge requiring obstacle-free for ion diffusion. We will use glass-to-silicon anodic bonding or silicon-to-silicon direct bonding to encapsulate electrolyte. The wafer level package will be investigated for both supercapacitor chips and wafer-stacked supercapacitors of large-scales. The demonstrator application will focus on medium power and energy storage systems.

TEM Tomography Studies on Cubic Copper Oxide Nanoparticles Cycled at Different C Rates

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Introduction In 2000, the activity of transition metals versus lithium was explained by Peyerl et al. from IRIS and named as Li insertion reaction. In recent years and more than 1000 publications, the way that the metallic nanoparticles are formed and the way that the C-rate affects the electrochemical grinding during the first discharge remains obscure. In this work, the cubic copper oxide nanoparticles, which are the perfect candidate for the tomography study since the metallic copper nanoparticles that will be formed at the end of the first discharge are the largest that could be obtained by consecutive reaction and the precise cubic particles size range in the hundred of nanometers. Transmission Electron Microscopy techniques, electrochemical characterizations and 3D reconstruction are devoted to the better understanding of electrochemical processes in lithium ion batteries.

Polyal Synthesis Precursors: Cu(NO₃)₂·3H₂O, Polyol Solvent: ethylene glycol, Additive: NaCl

Electron Tomography 2D projection at different tilt angles. Acquisition → Alignment → Reconstruction. 1. Data acquisition: FEI Tectus F20 S-twin Transmission Electron Microscope equipped with an EDX and a JEOL-STEM detector. 2. Data alignment: Software Tomad. 3. Volume reconstruction: Using algorithm (BP, WBP, SIRT, SIRT).

Results and Discussions Without NaCl: Difficult to determine when to stop. With NaCl: At 100 °C, the color changed when to stop. Difficult morphology: Cubic shape. Results show that the morphology of Cu₂O is not fully reduced by C₁₀.

Conclusions A simple procedure based on polyol reduction for preparing Cu₂O cubic nanostructures is demonstrated, chloride ions play an important role in directing the morphology of Cu₂O nanostructures. Electrochemical experiments show the synthesized cubic nanostructured Cu₂O material can be charged and discharged with 10 different high C rate, the voltage-capacity curve is different from our previous study at low C rate, which evidences the kinetic limitation of the phenomenon.

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Fatigue life improvement of welded structures by high frequency mechanical impact (HFMI) treatment

Structures and components subjected to severe dynamic loading may have fatigue damage at welded joints during their lifetime. Global trends, such as lightweight design for better fuel economy and extended lifetime for sustainability set challenges for engineers dealing with dynamically loaded components. One economical solution is to use high strength steels (HSS). However the implementation of HSS is limited in practice due to the fatigue properties at welds which are only equivalent to those of lower strength steel grades

High-frequency mechanical impact (HFMI) has significantly developed as a modern, reliable and effective method for the post-weld treatment [1]. After treatment, the degree of improvement in fatigue strength increases as the material strength increases. This allows to use HSS in practical applications. Extending fatigue life with HFMI will also greatly reduce repair costs of fatigue susceptible components. This increases the usage of the structures and equipment for their main purpose by reducing downtime.

Current knowledge on HFMI-improved welds has also shown that fatigue failures may also initiate at other regions, rather than weld toe. In spite of the fact that relaxation of induced RS state has been claimed to be the main reason of different damage mechanisms resulting in the failure location change, scientific questions such as: why, how and under what conditions this effect occurs or what damage mechanisms play a dominant role, remain unanswered. Based on the above context, the objective of the project Hi-Life [2] aims to solve the damage mechanisms of HFMI-treated welds under service loading by considering fatigue tests, investigating the microstructures and developing analytical approaches.

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Fatigue life improvement of welded structures by high frequency mechanical impact (HFMI) treatment

Fatigue strength without treatment : all steel grades	Fatigue strength with HFMI treatment ¹ : conventional steels	Fatigue strength with HFMI treatment ¹ : high strength steels

Structures and components subjected to severe dynamic loading may have fatigue damage at welded joints during their lifetime. Global trends, such as lightweight design for better fuel economy and extended lifetime for sustainability set challenges for engineers dealing with dynamically loaded components. One economical solution is to use high strength steels (HSS). However the implementation of HSS is limited in practice due to the fatigue properties at welds which are only equivalent to those of lower strength steel grades

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Investigation of 2D Magnetic Resonance Thigh Muscle Image Segmentation using a Convolutional Neuronal Network

Purpose: Musculoskeletal disorders as pulmonary disease or osteoarthritis have a high prevalence among the population and are the most frequently cause for pain, limitation and a loss of quality in life. Automated segmentation of muscles is an important step towards investigating the impact of muscle morphology towards clinical outcome from large available datasets and cohort studies as the osteoarthritis initiative (OAI). Therefore we investigate a 2D state-of-the-art Convolutional Neuronal Network (CCN) for the automated cross-sectional area segmentation of the quadriceps, hamstrings, subcutaneous fat (SCF) and the femoral bone.

Methods: The 2D segmentation method was implemented in Python 3.4 using a fully convolutional segmentation network (FCN) widely used for natural images. Semi-automatically segmented MRI slices located at approximately 33% of the thigh (from distal to proximal) in axial non-fat-suppressed T1-weighted thigh MRIs from the OAI (n=1499) were randomly divided into training (N=1449) and validation sets (N=50). All MRI slices were cropped (256x256 pixels) and centered towards the femoral bone of the right knee to simplify the segmentation problem for the FCN architecture. We evaluated the segmentation accuracy achieved in the validation set using the Dice Similarity Coefficient (DSC).

Results: A high accuracy was observed for all evaluated structures (DSC: quadriceps: 0.98 ± 0.00 , hamstrings: 0.98 ± 0.01 , SCF: 0.99 ± 0.01 and femoral bone: 0.97 ± 0.02).

Conclusion: The evaluated 2D state-of-the-art CCN architecture appears to be suitable for the task of fully automatic thigh cross-sectional area seg-

mentation. The performance of the method compares favorably to the performance of previously used (semi-) automated methods, but still needs to be extended to all anatomical thigh structures (i.e., adductors, sartorius muscle, inter-muscular fat).

Investigation of 2D Magnetic Resonance Thigh Muscle Image Segmentation using a Deep Learning Technique
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1 Introduction
 Musculoskeletal disorders as knee osteoarthritis have a high prevalence among the population and are the most frequent cause for pain, limitation and loss of quality of life. Automated segmentation of thigh muscles is an important step towards investigating the impact of muscle morphology in relation to clinical outcome from large available datasets and cohort studies such as the osteoarthritis initiative (OAI).
 Therefore, we investigate a 2D state-of-the-art Convolutional Neuronal Network (CCN) for the automated cross-sectional area segmentation of the quadriceps, hamstrings, subcutaneous fat (SCF) and the femoral bone.

2 Methods overview
 The 2D segmentation method was implemented in Python 3.4 using a fully convolutional segmentation network (FCN) widely used for natural images.

3 Materials
 We used (n=1499) previously semi-automated segmented MRI slices located at approximately 33% of the thigh from distal to proximal in axial non-fat-suppressed T1-weighted thigh MRIs from the OAI. The proposed dataset was randomly divided into training (N=1449) and validation sets (N=50). All MRI slices were cropped and centered towards the femoral bone of the right knee to simplify the segmentation problem with a resulting image size of 256 x 256 pixels for the introduced network architecture.

4 Results
 The achieved DSC of all evaluated structures (quadriceps: 0.98 ± 0.00 , hamstrings: 0.98 ± 0.01 , SCF: 0.99 ± 0.01 and femoral bone: 0.97 ± 0.02) compare favorably to the related literature.

5 Conclusion
 The evaluated 2D state-of-the-art CCN architecture appears to be suitable for the task of fully automatic thigh cross-sectional area segmentation. However, while these results are encouraging, it should be noted that the segmentation problem was stratified due cropping the image and the segmentation still needs to be extended to all anatomical thigh structures.

Partner: chondrometrics, KNEEMO, MCAC, ETH Zürich

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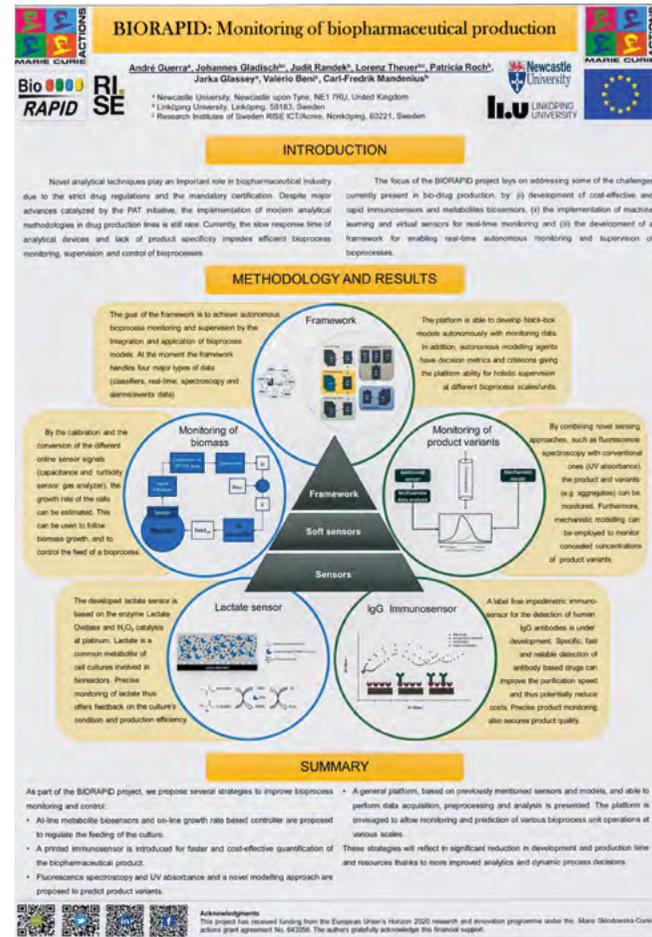
Monitoring of biopharmaceutical production

With increasing demand for biopharmaceuticals, the production and development of new biopharmaceuticals faces new challenges. The production consists of upstream where the biopharmaceutical material is produced and downstream where the product is purified. Assuring high quality products and high yields is key, and can be facilitated by real time monitoring. Challenges faced are the specific adjustment of the production based on the nutritional needs of the production organism, distinguishing between the product and process- and product-related impurities throughout the process.

These challenges are addressed from different angles, one of them is developing disposable, printed biosensors. Such sensors could be enzyme-based or with a passive biorecognition element to detect the product. Another approach is to combine multiple sensor signals into mathematical models to estimate unknown variables. Mechanistic understanding can be incorporated as well to describe the physical phenomena of the production process.

By combining biosensors and soft sensors into a framework to monitor the production of biopharmaceuticals, process understanding can be improved and real-time process control can promote high yield and quality of biopharmaceutical products.

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Model-based Distributed Sensor Fusion for MAGV State and Parameter Estimation

This project is part of the Interdisciplinary Training Network in Multi-Actuated Ground Vehicles (ITEAM). ITEAM is aiming at establishing and sustainably maintaining the European training network with a high grade of interdisciplinarity by training strong specialists to research and develop cutting-edge technologies in the field of multi-actuated ground vehicle (MAGV). In this framework, the ITEAM consortium sets out to foster the development of new hardware and software solutions to enhance the driving performance, to improve the vehicle safety, and to reduce the pollutants emissions.

Within the ITEAM project, my research focuses on observing and estimating vehicle states and parameters utilizing system level models and readily available sensor signals in current passenger vehicles and future MAGVs. The focus lies on states and parameters that are vital for current and future ADAS and vehicle dynamics control systems as well as for (semi-)autonomous MAGVs.

A variety of models form the fundament for the development of novel model-based approaches for fusing distributed sensor information. In order to generate information that can instantly be used for ADAS and vehicle dynamics control systems, this needs to be performed in real-time.

The developed methodology, which enables the combination of all sensor information distributed over the vehicle in order to obtain reliable estimates, will be conceptually validated through a flexible software platform. This framework will enable fast development iterations over different estimator schemes and settings.

Finally, experimental validation will make use of multiple demonstrators such as hardware-in-the-loop (HIL) setups and a full size MAGV setup.

Interdisciplinary Training Network in Multi-Actuated Ground Vehicles

Model-based Distributed Sensor Fusion for MAGV State and Parameter Estimation

My research focuses on observing and estimating vehicle states and parameters utilizing system level models and readily available sensor signals in current passenger vehicles and future MAGVs. The focus lies on states and parameters that are vital for current and future ADAS and vehicle dynamics control systems as well as for (semi-)autonomous MAGVs. A variety of models form the fundament for the development of novel model based approaches for fusing distributed sensor information. In order to generate information that can instantly be used for ADAS and vehicle dynamics control systems, this needs to be performed in real-time. The developed methodology, which enables the combination of all sensor information distributed over the vehicle in order to obtain reliable estimates, will be conceptually validated through a flexible software platform. This framework will enable fast development iterations over different estimator schemes and settings. Finally, experimental validation will make use of multiple demonstrators such as hardware-in-the-loop (HIL) setups and a full size MAGV setup.

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 • Born in Wehrburg, Germany
 • 2011/2012: Internship at the Interior Engineering group of Tesla Motors, Inc.
 • Research during graduate studies focused on vehicle dynamics, especially in the field of tires and control systems.
 • 2018: M.Sc. in Automotive Engineering from Technical University Braunschweig, Germany
 • Joined KU Leuven in 2018 as PhD student
 • Current research focuses on distributed sensor fusion for MAGV state and parameter estimation (joined ITEAM in 2017).

OBJECTIVES AND WORK PLAN

- Set up vehicle state reconstruction platform using MATLAB, Simscape, and C/C++
- Hardware: featuring the possibility to quickly change/adjust estimator models in Amesim
- Create modular concept car platform which can serve as a demonstrator for developed methodologies.

PROGRESS ACHIEVED

Concept Car platform: Frame design is ready for manufacturing. Battery pack is finished. Powertrain components are expected to arrive from industrial partner.

Automotive state and parameter estimation platform: It is ready to be used but some bug fixes still need to be implemented and the functionality needs to be extended.

PUBLICATIONS

- Joint conference paper with Michael Hartmann (Virtual Vehicle Research Centre, Graz, Austria): "Phoebos in the loop" - An approach using virtual reality. ICAT Conference, Sarajevo, Bosnia & Herzegovina, October 2017 (accepted)
- Joint conference paper with Michael Hartmann (Virtual Vehicle Research Centre, Graz, Austria): "Phoebos in the loop" - An approach using augmented reality. SAE World Congress Experience, Detroit, USA, April 2018 (submitted)

FUTURE STEPS

- State estimation environment
- Finalize automotive state and parameter estimation environment
- Evaluate influence of different models and sensor fusion algorithms
- Conceptual validation of methodology
- Demonstrator
- Concept Car platform
- Finalize frame design
- Manufacturing of frame
- Testing and integration of subsystems (including control systems)
- Testing of complete vehicle

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Prediction of thermophysical properties of innovative fluids

The introduction of new working fluids for organic Rankine cycle power systems requires the estimation of their performance based on the available knowledge about the fluids thermophysical properties. A good accuracy in the prediction of the thermophysical properties of the fluid will reduce the uncertainty in the simulation results, thereby providing more reliable results.

However, predicting the properties of new working fluids is complex, especially when only the molecular structure of the fluid is known. Generally, predictive models with higher accuracy require more knowledge about the fluid, and vice versa. This fact imposes a compromise between the accuracy of the prediction and the amount of information needed for the working fluid.

In the project NanoORC, the combination of different predictive techniques for thermophysical properties of fluids is investigated with the aim of improving their accuracy. The objective is to customize the predictive models depending on the nature of the fluid, minimizing the prediction uncertainty. This approach is also followed to extend the prediction capability of the models to mixtures of new working fluids. Based on this work, a number of tools will be developed for the study of the potential of new working fluids for organic Rankine cycle power systems.

DTU Mechanical Engineering
Department of Mechanical Engineering

Prediction of thermophysical properties of innovative fluids

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1. Project NanoORC
The project NanoORC aims at evaluating the potential of innovative fluids as working fluids for organic Rankine cycles (ORCs) power systems.

The project develops general models for the prediction of the thermophysical and transport properties of innovative fluids. The models will be used to evaluate the performance of new working fluids for the organic Rankine cycle technology.

2. Prediction of thermophysical properties
The thermophysical and transport properties of new working fluids can be predicted based on their molecular structures and other core properties.

Predicting the properties of new working fluids imposes a compromise between the prediction accuracy and the amount of available information of the working fluid.

NanoORC investigates the combination of different predictive techniques for thermophysical properties to improve the overall accuracy of the predicted values.

3. Pure fluids
The most accepted approaches for property prediction are group contribution methods (GCMs) and quantitative structure-property relationship (QSPR) methods.

4. Mixtures
The simplest approach to predict the behavior of mixtures of new working fluids consists of weighing the contribution of each component according to their mutual interaction.

Partners: DTU, TURBODEN Turboden srl.

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DeciTrustNET

In real world decision-making, such as public security, social choice or recommender systems, we have a large body of data from various networked heterogeneous information sources or individuals that often conflict with each other and provide inconsistent knowledge. It is a challenging task to yield an optimal consensus decision, given the range of individual decisions obtained in terms of these knowledge sources. This research proposal aims to create a novel mathematical and computational framework for trust based social choice in networks and with uncertain knowledge by merging multiple individuals' preferences in an adaptive manner to reduce the disagreements among them, and automatically seek a decision or provide a recommendation with a maximal consensus. To achieve our goal, we propose to bring together, for the first time, four previously disparate strands of research: social network analysis, fuzzy preference modelling, multiple attribute group decision-making and game theoretic modelling of malicious users. As a showcase the proposed framework will be incorporated to an e-health recommender platform to increase healthy lifestyle.

Deci TrustNET
Trust based Decision Support System for Social Networks with Uncertain Knowledge
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Abstract

In real world scenarios, such as public security, health and e-marketing, we have a large body of data from various networked heterogeneous information sources that often conflict with each other and provide inconsistent knowledge. DeciTrustNET aims to create a novel computational framework for trust based social choice by merging multiple heterogeneous information in an adaptive manner to provide consensus based personalized recommendation. This framework will be applied in the context of a new e-health trust based social network to increase healthy lifestyle.

Research objectives

- To establish a SNA framework for managing multiple inconsistent heterogeneous information sources that allows the definition of trust
- To define trust propagation and aggregation operators for trust networks driven by game theoretic modeling of malicious users.
- To create a trust based feedback to provide personalized advice.

Application: E-health Trust Social Network

Personalized self-monitoring system to increase healthy lifestyles in people with especial needs.

Proposed Trust Network

Figure: DeciTrustNET system architecture

Figure: e-Health SN architecture

Acknowledgements

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 Project website: <http://decitrustnet.cimr.dmu.ac.uk/>

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Membrane fouling during microfiltration of casein and whey fractionations

Environmentally friendly, economical and sustainable methods of food processing are required due to the projected growth in global population, and the current environmental impacts linked to food production. In the case of dairy products, the need to separate the main milk proteins - casein and whey, has led to the development of several technologies. The potential advantages of using membranes over chemical separation techniques has made them an attractive option for the food industry. However, it is important to be able to understand the fouling present, and being able to use it in the best way to optimize both fractionation and flux.

The two main aspects to consider for membrane separations are the selectivity of the process and the flux. Both of these parameters are affected by fouling. To determine membrane performance, fouling patterns have been studied by running pasteurized skimmed milk through two sets of commercially available polymeric PVDF membranes (800 kDa and 0.1 µm nominal pore size respectively, Synder Filtration). Filtration was carried out using a DSS M10 apparatus with four flat sheet membranes with a combined area of 336 cm²

Understanding membrane fouling in filtration of whey protein streams

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1. Introduction
 Bovine milk is a complex matrix, where proteins represent 3.4% of all milk. Milk proteins are of high interest since they have health promoting properties and they can be used as baby food, as food additives or as muscle promoters.¹



Fig. 1 Cow average milk composition.

2. Objectives

- Understanding membrane fouling during milk filtration processes
- Development of a protocol to reduce the E3 of milk filtration, focused on the optimization of the fouling/cleaning cycles.
- Understanding the separation of the main milk proteins (Casein and whey) using membranes, and the effect of pore size and membrane material.

3. Methodology
 The filtration system DSS LabStack M-10 module (Alfa-Laval; Fig 2) was used for milk filtration. The system is equipped with data logging for pressure before and after the membrane module, temperature reading after the membrane module and permeate balance measurements to keep track of the permeate flux.

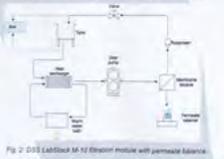


Fig. 2 DSS LabStack M-10 filtration module with permeate balance.

These parameters are used to calculate Trans Membrane Pressure (TMP) and membrane resistance (R_m).²

$$TMP = \frac{P_1 - P_2}{2} \quad \Delta P = \frac{\Delta P_1}{\mu R_m} \quad R_m = R_c + R_m + R_f + R_f$$

The cleaning protocol applied is based on a combination of rinsing steps to remove loose particles followed by a chemical cleaning using NaOH (0.5wt %) at 60°C.

4. Results
 Flux decline curves (Fig 3) show that the flux evolution overtime follows the same pattern. This confirms the efficiency of the cleaning protocol employed.

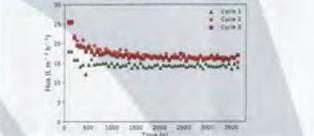


Fig. 3 Flux decline of 3 different filtration cycles using 0.1µm membrane. The process was carried at a TMP of 0.3 bar and a CIP of 1.7m³/h.

The sudden drop in flux at the first 500s of 16.4% indicates a fast in pore blocking, followed by a flux decline of 5.1% over 3000s, also known as pseudo-steady state; Fig. 4 shows the SEM images of the surface of the membrane between pristine state and fouled and cleaned up to cycle 3. The increase in fouling/cleaning cycles shows no appreciable fouling layer blocking the pores, indicating in pore blocking.



Fig. 4 SEM images (16 magnification) of a 0.1µm membrane operated at a TMP of 0.3 bar and a CIP of 1.7m³/h. a) Pristine membrane b) Fouled twice and cleaned once. c) Fouled and cleaned 3 times. d) Fouled 3 times and cleaned twice.

5. Conclusions

- The current cleaning protocol is suitable for the elimination of protein fouling layers.
- Drop in flux seems to be associated with in pore blocking.

6. Future work

- Further analysis of the cleaning protocol effects need to be done to check the membrane resistance and the effect on selectivity.
- Development of a protein analysis method to ensure the content of the different protein streams.
- Further analysis to characterise if there is any cake fouling.

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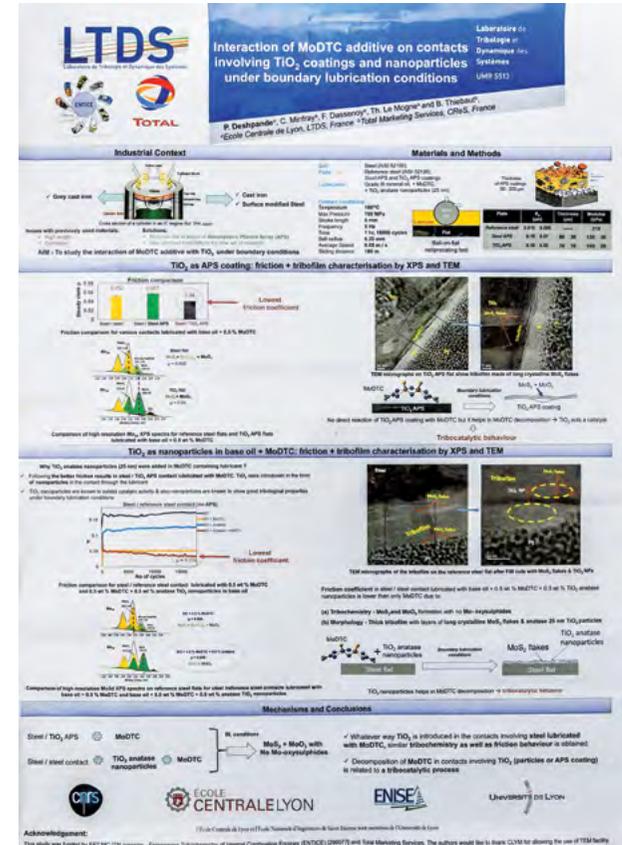
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Interaction of MoDTC additive on the contacts involving TiO₂ based coating & nanoparticles under boundary lubrication conditions

Nowadays, to reduce weight, gas emission and oil consumption of the passenger car engines, Atmospheric Plasma Spray (APS) coatings like TiO₂ APS coating are used on cylinder liner. For such coatings, fused and crushed micron sized powders of TiO₂ are used in APS process to obtain 70 µm thick coatings on steel substrates with specific surface roughness parameters. MoDTC (Molybdenum Di-Thiocarbamate), an organometallic friction modifier additive, has been extensively used to reduce friction coefficient in engine components under boundary lubrication conditions. In this study, tribochemical interaction of MoDTC with TiO₂ APS coating was investigated. MTM tribotests were carried out for steel / steel and steel / TiO₂ APS contacts in presence of lubricant containing MoDTC. Tribofilms generated on the steel and TiO₂ discs were analysed by XPS (X-ray Photoelectron Spectroscopy) and TEM (Transmission Electron Microscopy). Steel / TiO₂ APS contact showed significant friction reduction compared to steel / steel contact due to specific tribochemistry and morphology of the tribofilms obtained. Following the lower friction coefficients obtained in case of steel / TiO₂ APS contact and also to further investigate the interaction of MoDTC with TiO₂ substrate, TiO₂ was introduced in the form of anatase nanoparticles via a lubricant containing also MoDTC in the steel / steel contact. A blend was prepared with anatase nanoparticles and MoDTC in base oil and used as a lubricant in steel / steel contact. Further investigation of tribofilms was again done using XPS and TEM. TiO₂ introduced in any form (APS coating or nanoparticles) in the contact showed similar trends of tribological behavior due to similar tribochemistries observed inside the tribofilms. The results obtained are discussed in detail and conclusions are made regarding the decomposition of MoDTC.

Keywords: Atmospheric Plasma Spray coatings, MoDTC, TiO₂ APS and TiO₂ anatase nanoparticles



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Gaussian Process models for SCADA based condition monitoring of wind turbines

Wind turbine power curves relate power generation to the hub height wind speed. In the wind turbine industry it is used widely for planning purposes and estimating total wind power production at a site; they have also been used to identify turbine operational faults. Gaussian Process is a nonparametric, Stochastic process used in forecasting purposes and slowly gaining popularity in wind industries applications. In this research, a Gaussian Process model for power curve fitting being proposed and This is then compared with an approach based on a binned power curve together with individual bin probability distributions to identify operational anomalies. The paper will outline the advantages and limitations of the Gaussian Process approach. its application to wind turbine condition monitoring being described.

Gaussian Process models for SCADA based condition monitoring of wind turbines

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AWESOME
H2020 - The European Union's Horizon 2020 research and innovation programme

SUMMARY

Wind turbine power curves relate power generation to the hub height wind speed. In the wind turbine industry it is used widely for planning purposes and estimating total wind power production at a site. They have also been used to identify turbine operational faults. Gaussian Process is a nonparametric, Stochastic process used in forecasting purposes and slowly gaining popularity in wind industries applications. In this research, a Gaussian Process model for power curve fitting being proposed and This is then compared with an approach based on a binned power curve together with individual bin probability distributions to identify operational anomalies. The paper will outline the advantages and limitations of the Gaussian Process approach. its application to wind turbine condition monitoring being described.

Structural Learning Types

- Supervised Learning
 - Regression: Linear, Polynomial, Logistic, Support Vector, Ridge, Lasso, Elastic Net, Boosting, Random Forest, Gradient Boosting, XGBoost, LightGBM, CatBoost
 - Classification: Logistic, Support Vector, Decision Tree, Random Forest, Gradient Boosting, XGBoost, LightGBM, CatBoost
- Unsupervised Learning
 - Clustering: K-Means, Hierarchical, DBSCAN, Gaussian Mixture, Fuzzy C-Means
 - Association Rule Mining: Apriori, FP-Growth
 - Dimensionality Reduction: PCA, t-SNE, UMAP, Autoencoders
 - Outlier Detection: Isolation Forest, One-Class SVM, Local Outlier Factor, DBSCAN
- Reinforcement Learning
 - Q-Learning, Deep Q-Networks, Policy Gradient, Actor-Critic, Proximal Policy Optimization
- Meta-Learning
 - Bayesian Optimization, Evolutionary Algorithms, Genetic Algorithms, Particle Swarm Optimization, Differential Evolution

2. OBJECTIVES

The main objectives of the presentation are to:

- Outline the importance of performance curves in condition monitoring of wind turbines.
- Develop a Gaussian Process model for power curve fitting and compare it with a binned power curve approach.
- Explain the importance of confidence intervals to identify operational anomalies.

3. METHODOLOGY & RESULTS

- The maintenance tool for unscheduled maintenance for unexpected failures is considered to be very high. To overcome this problem condition monitoring is essential. Gaussian Processes provide an attractive data analysis framework and provide an effective automated fault detection system for the industry.

4. CONCLUSIONS

- The quality and quantity of the data, greatly affects accuracy of GP power curves.
- It is desirable to modify the confidence intervals in GP to deal with missing data measurement noise so that the fault classification process is most effective.
- By comparing a binned power curves with the Gaussian Process power curve it is found that the latter is more accurate over the rising section of the power curve.

5. FUTURE WORK

- Understand the GP model behaviour when incorporating dominant wind turbine parameters into the algorithms.
- Practical application of Gaussian Process models for anomaly detection.
- Comparative analysis of fault detected GP algorithms with other available models.

7. ACKNOWLEDGEMENTS

The results being published in InnoREC-II 2017 Conference, Manchester, UK.

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Figures:

- Figure 1: GP power curve
- Figure 2: GP power curve with CI
- Figure 3: Binned and GP power curve
- Figure 4: Comparative analysis

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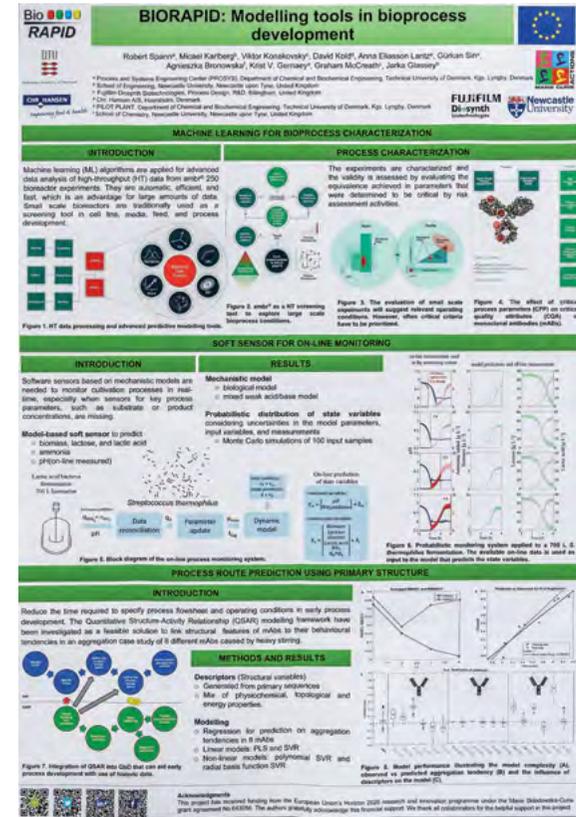
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BIORAPID: Modelling tools in bioprocess development

Knowledge- and data-driven modelling methods are applied for early process development of microbial and mammalian manufacturing processes in work package 2 of the BioRapid project (www.bio-rapid.eu). Advanced process modelling together with rapid data acquisition methods are needed in the biotechnological industry for e.g. process development, on-line process monitoring and control, and the evaluation of high-throughput (HT) experiments. Machine learning (ML) algorithms are promising for data analysis since they are automatic, efficient, and fast, which is especially relevant for large amounts of data from HT experiments. ML algorithms (e.g. partial least square (PLS) regression) were established as scripts to be used on dedicated data sets. In our first case study, HT ambr250 bioreactor data was used to evaluate the impact of critical process parameters (CPP) on key process indicators (KPI). In the second case study, a knowledge-driven model was applied as software sensor in bacterial fermentations. It read the available on-line measurements, and predicted among other things the microbial growth. These software sensors allow plant operators a risk-based decision-making since the probability of achieving the critical quality attributes (CQA) is calculated in real time. In the third case study, data-driven models were used to design the processing routes in the manufacturing of pharmaceuticals. The models incorporated the information about the antibody structures and process knowledge in order to predict e.g. the stability of the protein, and the probability of aggregation under different operation conditions. The developed models and toolboxes aim to support the risk assessment in the existing bioprocess development frameworks, e.g. Quality by Design (QbD), and to reduce the development costs by reducing the necessary number of experiments.

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Optimal use of sensor data for reliable and efficient structural health monitoring

Structural Health Monitoring (SHM) and Non Destructive Evaluation (NDE) techniques improve the safety and reliability of the structures. The cost benefit of such SHM systems is not always apparent and hence the field has received only partial acceptance. The arguments against the use of SHM techniques is the limited sensitivity to detect different kinds of damage and relatively high cost of the deployment of the equipment.

Several SHM techniques have been proposed to counter these arguments with limited success. Hence a search for a universal SHM technique and reasonable costs is still ongoing. Hence the proposed research tries to highlight two strategies for improving the reliability and the efficiency of the SHM techniques. The work focuses on combination of different SHM and NDE techniques for damage detection in structures. This allows data fusion at the decision level to ensure that damage from different sources like thermal, moisture induced, mechanical, etc. are detected by the different techniques. In the other approach the issue with the reduction of the cost is targeted with the view of achieving complete inspection of the workpiece while using a limited number of sensors through optimal sensor placement for guided waves based damage detection which is one of the most promising approach for damage detection in composites.

Optimal use of sensor data for reliable and efficient structural health monitoring

Pawel Malinowski, Wieslaw Ostachowicz

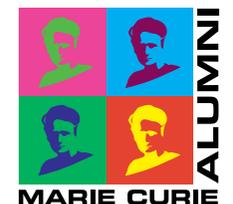
Comparison of different sensor placements

Run	Placement	Number	Cost	Cov0	Cov3
Optimized	1, 9, 18, 20, 32, 54, 58, 65, 81	9	-13893	96.10	88.66
Random	3, 14, 26, 38, 47, 52, 69, 75, 81	9	-462.44	50.81	86.43

Figure 1: Different damage scenarios. Figure 2: NA estimate using strain data. Figure 3: RMS plot for guided waves. Figure 4: NA estimate using strain data. Figure 5: EMI technique comparative plot. Figure 6: RMS plot for guided waves. Figure 7: Sensor Placement. Figure 8: Surface plot showing coverage a) Optimized placement b) Random Placement.

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Microstructuring strategies on Polymers through Direct Laser Interference Patterning

The control of the wettability can be performed either by changing the surface chemical composition or by modifying its roughness. In addition, it has also been demonstrated that the presence of hierarchical micro- and nano-structures allows radically changing the material wetting behavior, especially for reaching the super-hydrophobicity regime. Moreover, highly oriented structures permit controlling the wetting in a desired direction, property of great interest in the micro-fluidics sector.

In this study, we demonstrate how Direct Laser Interference Patterning (DLIP) can be employed to fabricate hierarchical structures on polycarbonate. In particular, new strategies for interference structuring are presented, in which high depth hierarchical microstructures with selective wetting properties can be created within a single step process. The experimental setup consists of a compact system designed for a two-beams DLIP, operating at the wavelength of 263 nm and producing line-like structures with a spatial period of 2 μm. Polycarbonate sheets have been selected due to its stable and characteristic structuring behavior with UV radiation and the structuring method can be extended to other materials which behave similarly. Combining common structuring strategies employed for Direct Laser Writing and DLIP, hierarchical structures with diverse depth, shape and pattern orientation have been fabricated. The results have been characterized by confocal microscopy, scanning electron microscopy, and the wettability behavior by the static water contact angle. The assessment showed a clear correlation between structure geometry and wettability response, in terms of structure height and directionality of the droplet shape. Moreover, due only to the laser processing, the static water contact angle has been increased from $87.8^\circ \pm 0.4^\circ$ to $117.6^\circ \pm 1.8^\circ$.

TECHNISCHE UNIVERSITÄT DRESDEN **LMO** **LASER FUN** **Fraunhofer IWS**

FRAUNHOFER-INSTITUT FÜR WERKSTOFF- UND STRAHLTECHNIK IWS
TECHNISCHE UNIVERSITÄT DRESDEN
Microstructuring strategies on Polymers through Direct Laser Interference Patterning
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Objectives and motivation

- Exploring the structuring strategies of DLIP on different polymer
- Fabricating structures with modified wettability response, anti-icing properties, reduced friction and bio-functional activity
- Development of simulation models

Method

Sample, Laser, Beam 1, Beam 2, Focal lens, DLIP, Plasma

Structuring results

Fig. 2. a) Ablated DLIP-pixel with two different spatial periods on transparent PC irradiated with UV (263 nm) ns radiation; b) confocal image showing the Gaussian modulation; c) swelling of a DLIP-pixel of a black-doped polycarbonate irradiated with UV and IR (1053 nm) radiation; d) SEM image of a swelled DLIP-pixel [2].

Fabrication of hierarchical structures

Fig. 3. Hierarchical structures generated by new DLIP strategies, showing a) line-like structures on the top of large-scale pillars and b) pillar-like structures on the top of large-scale pillars. The large-scale structures have a periodicity of 26 μm, while the small-scale structures have a periodicity of 2 μm [3].

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Health Behaviour Change by Visualising the Data of an Individual in Relation to that of Others

Behaviour change is a long and difficult process. However, we change our behaviour subconsciously when other people are around. Technological applications targeting behaviour change include features that facilitate social influence: the other people's influence on our behaviour. The social influence features have been designed - until recently (2015) - as a whole, without taking into consideration the different aspects of social influence (e.g. social comparison, social learning, cooperation etc.).

This research focuses on the social comparison aspect and the design of social comparison features in technological applications targeting to support health behaviour change. The methodology used is qualitative (participant observations, and interviews). The result will be a tool for designing social comparison features on health behaviour change technological applications, informed by four perspectives:

- how the current literature presents the design of social comparison features
- how the designers currently design social influence features (focused on social comparison)
- what is the healthcare professionals opinion on social comparison and relevant health behaviour change technology
- what kind of data the users want to compare, and how they want to compare them

Health Behaviour Change by Visualising the Data of an Individual in Relation to that of Others
 Vasiliki Mylonopoulou: vasiliki.mylo@oulu.fi

Behaviour change "at will" is a difficult and long process with a risk of relapsing. Most of the behaviour change theories support that behaviour change happens in stages in each of which the individual is in different mental and physical state.

Expected results
 The aim is to "see" social comparison through four different perspectives and inform the IT/HCI field:

- Literature: How has social comparison been designed up to now?
- Healthcare Professionals: What is the role of technology and social influence/social comparison in the practices of health behaviour change?
- IT practitioners: How do IT practitioners design health behaviour change technology and what is the role of social comparison features?
- People who want to change: What technology do people who want to live healthier use and what are their attitudes towards social comparison?

Even though behaviour change at will seems a long process, we change our behaviour when others are around: social influence. Social influence consist of different aspects (Stibe 2015) one of which is social comparison: the comparison of an individual to others. According to the social comparison theory by Festinger (1954), the comparison to others make people perceive themselves better than in isolation.

The behaviour change theories and the social influence theories are the bases for most designers to design technology targeting to support behaviour change. My PhD is focused on health behaviour change through social comparison (compare the data of an individual to that of others). More specifically on:

What is the role of social comparison in the health behaviour change technological applications?

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Optimized Framework based on Rough Set Theory for Big Data Preprocessing in Certain and Imprecise Contexts

Over the last decades, the amount of data has increased in an unprecedented rate, leading to a new terminology: “Big Data”. Big data are specified by their Volume, Variety, Velocity and by their Veracity/Imprecision. Based on these 4V specificities, it has become difficult to quickly acquire the most useful information from the huge amount of data at hand. Thus, it is necessary to perform data (pre)processing as a first step. To achieve this task, several state of the art methods were proposed. However, most of them require additional information about the given data for thresholding, specify some noise level, and are neither able to deal with the big data veracity aspect nor with their computational requirements. Therefore, this project’s overarching aim is to fill these major research gaps with an optimized framework for big data (pre)processing in certain and imprecise contexts. To achieve this, we propose innovative techniques capable of discovering data dependencies using the data alone requiring no additional information. These novel proposed solutions are based on Rough Set Theory for data (pre)processing and Randomized Search Heuristics for optimization.

The project combines the expertise of the experienced researcher Dr Zaineب Chelly Dagdia in machine learning, rough set theory and information extraction with the knowledge in optimization and randomized search heuristics of the supervisor Dr Christine Zarges at Aberystwyth University, UK. Further expertise is provided by internal and external collaborators from academic and non-academic institutions, namely Prof Lebbah (University of Paris 13, France), Prof Shen (University of Aberystwyth, UK), Prof Tino (University of Birmingham, UK), Prof Merelo (University of Granada,

Spain) and an industrial partner from France to ensure that real-world requirements are met throughout the development of the framework.

2018 MCAA Annual Conference and General Assembly
2nd-3rd February 2018, Leuven, Belgium

Optimized Framework based on Rough Set Theory for Big Data Preprocessing in Certain and Imprecise Contexts
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Context
BIG DATA: VOLUME, VARIETY, VELOCITY, VERACITY

Motivation and Problem Statement
It has become difficult to quickly acquire the most useful information from the huge amount of data at hand. Existing methods are not able to deal with the big data veracity aspect. Existing methods are not able to deal with the big data computational requirements.

Project Description
1. The framework provides foundation for big data preprocessing of supervised analysis tasks for big data mining and feature selection to reduce and filter the data.
2. The developed automated dimensionality reduction technique, without requiring extra information and with less information loss, which improves the cost-effectiveness.
3. The developed optimization methodologies to deal with the big data before reduction task with and without the big data veracity aspect, which meet the real-world requirements for a fast, accurate and a high quality system response.

Application for marketing
amazon
This data set was derived from customer reviews on the Amazon.com website by identifying a set of most active users and using the goal to perform authorship identification.
To reduce the computational effort of the rough set computation, our approach splits the given dataset into partitions with smaller number of features which are then processed in parallel.

Conclusion
The project develops a Big Data Mining Framework containing three major "Modules": "Machine Learning", "Optimization" and "Big Data", offering huge opportunities in different applications. It is a unique possibility to explore the impact of such frameworks within a non-academic/industry, easily accessible by collaboration with a publishing and/or commercial partner.

Current and future work:
1. Analyse further the developed Algorithm.
2. Extend the algorithm to deal with clustering applications areas.
3. Formalize and implement an optimized version of the framework.
4. Define a general formalization of rough sets by handling the veracity aspect.
5. Demonstrate the novel methodology on real-world data.

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Logos: ABERYSTWYTH UNIVERSITY, UNIVERSITY OF BIRMINGHAM, UNIVERSITY OF GRANADA, PARIS CENTRE, MARIE CURIE ALUMNI

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Microgel Matrices for Human Cancer Organoid Production

Organoids are three-dimensional multicellular structures capable of mimicking tissue structure and tumour heterogeneity better than other available biological model systems. They are a powerful new enabling technology in drug discovery because they can give more accurate test results while enabling high throughput screening of drug candidates. However, traditional manual culture and expansion of organoids is labour intensive and expensive. In order for organoids to be widely used in industrial and clinical applications, their robust production must be scaled up efficiently. Cellesce Ltd has developed a process to grow large numbers of organoids for commercial drug screening but the methods rely heavily on very expensive animal-derived matrix scaffolds for organoid encapsulation, mainly Matrigel. These materials are both expensive to produce and are prone to batch-to-batch variations in the bioactive molecules which they contain. In this research, non-animal derived polymers were investigated to reduce Matrigel use as 3D organoid matrix, focusing on the production of cell-containing hydrogel microbeads. Alginate and carrageenan, both seaweed derived hydrogel-forming biomaterials, were selected to form blends with Matrigel, thus providing a more sustainable and cost-effective means of organoid generation. The microbeads were produced by electrospaying and compared in terms of their physical properties. Finally, the ability of the cells to grow and form organoids within these blends was assessed and compared with the current method using Matrigel. This study concluded that the oxidised alginate-based blends were the only ones that supported organoid growth, with the 2% (w/v) 5% oxidised alginate/Matrigel (1:1) being the optimum blend among the others. The main outcome of this research will be the basis for future bioreactor and scale-up studies.

1. Introduction
Organoids are multicellular structures that self-organise in three-dimensional culture due to their self-renewal and differentiation capacities (Figure 1). They can be grown from diseased tissues, retaining pathology and tumour heterogeneity, and can exhibit tumour specific functions better than other available biological model systems.
Organoids can be used in multiple clinical applications including disease modelling, drug screening, personalized medicine and regenerative therapy (Figure 2).
In this context, Cellesce has developed a novel bioengineering technology for the large scale expansion of organoids, producing organoids of high quality to enable their application by the pharmaceutical industry.
Challenge: the current manual method of culturing organoids is complex, labour intensive, the outputs are not sufficiently large for high throughput assays and it nearly exclusively depends on animal-derived hydrogels as the 3D matrix for cell encapsulation.
Hydrogels derived from animals, including Matrigel and collagen, are essential for organoid culture because they closely mimic cell microenvironment, which consists of cell-cell interactions, biochemical and biophysical cues, and the non-soluble matrix interaction.
Matrigel is one of the most used hydrogels for organoid generation; however, it has critical disadvantages:
• It is animal derived material, expensive to produce, features complex composition (batch-to-batch variations), not favourable for optimized modifications, not appropriate for organoid culture for downstream clinical applications.
Thus, the development of alternative matrices, especially non-animal derived hydrogels, are attracting considerable interest.

2. Aims and Objectives
Investigate non-animal derived polymers to reduce Matrigel use as 3D organoid matrix, focusing on the production of cell-containing hydrogel microbeads.
Screening of hydrogel blends, microbead production by electrospaying and physical characterization.
Assessment of the ability of cells to grow and form organoids within these blends.

3. Methods
Materials A and B, both hydrogel-forming biomaterials, selected to form blends with Matrigel.
Microbead production by electrospaying was optimised by flow rate, voltage and needle size conditions.
Blend mechanical properties evaluated by rheology assays and organoid growth investigated by standard culture in novel blends. Both data compared to Matrigel.

4. Results
From 10x blends prepared (Table 1), organoid growth only confirmed in material A blends, while material B blends did not support growth (Table 2).
Microbeads smaller than 300 µm (to avoid cell oxygen deprivation) achievable by electrospaying. Best beads produced from AM1, with diameter of 192.3 µm (Figure 3).
AM1 had the most similar physical profile to Matrigel (Figure 4).
On the third passage only, aggregation of proteins from Matrigel was observed (Figure 5).
Organoid viability assay using Trypan Blue was not conclusive.

Table 1: Blend properties

Blend	Material A (%)	Material B (%)	Matrigel (%)
AM1	2	0	98
AM2	5	0	95
AM3	10	0	90
AM4	20	0	80
AM5	50	0	50
AM6	100	0	0
BM1	0	2	98
BM2	0	5	95
BM3	0	10	90
BM4	0	20	80
BM5	0	50	50
BM6	0	100	0

Table 2: Organoid growth

Blend	Material A (%)	Material B (%)	Matrigel (%)	Organoid growth
AM1	2	0	98	Yes
AM2	5	0	95	Yes
AM3	10	0	90	Yes
AM4	20	0	80	Yes
AM5	50	0	50	Yes
AM6	100	0	0	No
BM1	0	2	98	No
BM2	0	5	95	No
BM3	0	10	90	No
BM4	0	20	80	No
BM5	0	50	50	No
BM6	0	100	0	No

5. Conclusions
AM1 selected as optimum material blend for progression into biosensor studies.
Material A blended with Matrigel supports organoid growth while Material B blends do not.
Microbead production by electrospaying was successfully optimised to obtain less than 300 µm diameter beads.
Physical characterization allowed to identify AM1 as the most similar to Matrigel for both elastic and viscous moduli.

6. Future work
Investigate cell micro-encapsulation within the novel blends (Material A) Matrigel), examining if organoids survive the process of electrospaying and culture inside a biosensor.
Design a bioreactor for the long term culture of organoids.
Search other ways to generate microbeads, which have a higher throughput than electrospaying such as mould or flow focusing.
Investigate other blends of natural biomaterials or even designer synthetic matrices, moving away from Matrigel to synthetic non-animal hydrogels.
Assess other viability assays, such as Live/Dead or cytotoxicity assays.

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Adaptable Games that Support the Delivery of Mental Health Interventions to Children

Growing evidence suggests that appropriately designed computer games can support effective and engaging mental health interventions for young adolescents. But to have widespread impact, games need to be adaptable. During my research project, I will conduct user studies and an in-depth literature review about the design process and current state of the art of supporting technology for mental health for youth. Subsequently, my focus will shift to exploring ways to add adaptability to mental health games such as Pesky gNATs, a 3D computer game that implements cognitive behavioural therapy (CBT) that clinicians and children can play together during therapy sessions. The goal is to release a game that is widely applicable and can be used across a wide range of client groups, disorders, intervention models and intervention intensities by introducing flexibility in game design and gameplay. For example, clinicians could be allowed to adjust the game to individual needs of the children and the therapy context.

As part of the training, I will undertake two secondments: a 3-month secondment at the Anna Freud Centre will provide me with practical knowledge on topics related to children's mental health issues and the applied intervention models. I will also use the secondment to engage in participatory design and prototyping sessions with children. Subsequently, I will engage in a 3-month secondment at Opposable Games to build on my knowledge and skills that are required to develop games. After finishing the secondments, the game development phase starts after which the result will be assessed through prototype demos and interviews with therapists. The knowledge gained before, during and after the research and development will be added to the PhD thesis.

Marie Curie Alumni Association - General Assembly and Conference 2018
Adaptable Games that Support the Delivery of Mental Health Interventions to Children

Games supporting therapy
 Research suggests that well designed computer games can improve mental health interventions for young adolescents (2,4,5,6,7,8). For the highest impact, the games should be adaptable for use with a range of age groups, mental health difficulties and therapeutic approaches (3).

Initial research
 I have three key aims in my first year:
 1. Complete a literature review to capture the design processes and current state of the art in games for mental health care
 2. Design and undertake quantitative and qualitative studies with therapists who worked with the Pesky gNATs game to understand how the game has impacted on the intervention and what features they would like to see in the future
 3. Engage in participatory design sessions with children who underwent therapy
 I will undertake advanced training through workshops and courses including research skills, clinical psychology and game development.

Doctoral research
 I will undertake two secondments. I will gain first-hand experience in the clinical mental health environment during a 3 month period at a mental health institute during which I will organize participatory design sessions with children. Subsequently I will collaborate with Opposable Games, a Bristol-based game development company for 3 months.
 Finally, I will work on the development and assessment of a new adaptable game and combine all findings into a final thesis.

The goal
 To develop an adaptable game that effectively supports the delivery of mental health therapy to a large target group with a broad range of mental health difficulties

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WWW.TEAM-ITN.EU **2018** **HIDE VAN DER MEULEN, DAVID COYLE, GARY O'REILLY** **(2018)**

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High Performance CO Oxidation Catalyst Based on Gas-phase Pd Nanoclusters Deposited on Alumina Powder

A high performance CO oxidation catalyst was designed based on gas-phase palladium nanoclusters (PdNCs) that were directly deposited onto alumina powder (Al₂O₃) with a typical loading of 0.1 wt%, using a new custom made magnetron cluster-beam deposition (CBD) source. The PdNCs were characterized by a combination of Scanning Transmission Electron Microscopy (STEM) and X-ray absorption spectroscopy (XAS) and for their catalysis activity in CO oxidation. STEM investigations confirmed that ligand free PdNC's with an average size of 3-5 nm were discretely loaded on alumina powder. The dynamic structural and electronic changes in the PdNC catalyst were then monitored in-situ by measuring XANES and EXAFS both at Pd K edge under CO oxidation conditions and it revealed that PdNCs possess a unique PdO_x@Pd structure, interacting weakly with the alumina support. PdNC's catalyst demonstrates a much better activity and stability under CO oxidation, in comparison to Pd catalysts prepared by conventional wet-chemical methods.

KU LEUVEN **Catsense** **Mihir ESRF**

High Performance CO Oxidation Catalyst Based on Gas-phase Pd Nanoclusters Deposited on Alumina Powder

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A high performance CO oxidation catalyst was designed based on gas-phase palladium nanoclusters (PdNCs) that were directly deposited onto alumina powder (Al₂O₃) with a typical loading of 0.1 wt%, using a new custom made magnetron cluster-beam deposition (CBD) source. The PdNCs were characterized by a combination of Scanning Transmission Electron Microscopy (STEM) and X-ray absorption spectroscopy (XAS) and for their catalysis activity in CO oxidation. The dynamic structural and electronic changes in the catalyst were monitored in-situ by measuring XANES and EXAFS both at Pd K edge under CO oxidation conditions.

Magnetron Cluster Beam Deposition

Cluster beam deposition (CBD) technique is the state-of-the-art in manufacturing systems that can produce arrays of sub 20 nm particles on variety of supports with excellent control over their size, shape, composition and purity.

1. In-line sputtering of Pd targets.
2. Substrate containing of sputtered Pd atoms of local nitrogen impurities.
3. Neutralizing of charged clusters using high voltage net caps.
4. Catalysts with typical loading of 0.1 wt% Pd loading (nanoclusters) measured were obtained in about 3 hours of direct deposition on alumina powder held in a rotating cup assembly below which high vacuum conditions.

Electron Microscopy at CO Oxidation

STEM images show PdNCs of average diameter of 3 to 5 nm discretely loaded on alumina powder.

PdNCs efficiently catalyzed complete oxidation of carbon monoxide at 150°C. 100% CO conversion, lower space frequency of 0.43 g⁻¹ (at 150°C) were calculated assuming all atoms participated in reaction. 0.1 wt% catalyst loading. The nanocluster catalytic activity was at least stable for 150 min.

In-situ XANES and EXAFS

(Table 1)

Reaction Conditions	Co-ordination Number (N)	Distance (Å)	Debye factor (Å ⁻²)
25°C Air	1.3 (Pd)	2.76	0.018
25°C Air	0.9 (Pd)	2.847	0.013
25°C Air	0.7 (Pd)	2.871	0.013
25°C Air	0.2 (Pd)	2.76	0.018
25°C Air	0.9 (Pd)	2.847	0.013
25°C Air	0.4 (O)	1.968	0.011
25°C CO ₂	0.2 (Pd)	2.76	0.018
25°C CO ₂	0.7 (Pd)	2.847	0.013
25°C CO ₂	0.1 (O)	2.81	0.006
150°C CO ₂	0.9 (Pd)	2.76	0.018
150°C CO ₂	0.2 (Pd)	2.88	0.004
150°C CO ₂	0.1 (O)	1.872	0.013

(A) XANES spectra show that PdNCs feature a similar core profile as Pd but with significantly diminished oscillations typical of conventional, indicating that PdNCs are mostly metallic.

(B) The reduced region of EXAFS data also suggests that PdNCs consist of a metallic core surrounded by a thin PdO layer which rapidly oxidizes in response to CO.

(C) After completion of Pd shell (see Fig. 5) away the calculated size of Pd metallic NP is 3.8 nm at RT. Upon heating to reaction temperature (150°C) the apparent size increases to 4.4 nm which could be due to change of particle shape or some particle agglomeration.

(D) We calculate that around 22.5% of palladium is loaded on a support sample, which discretely reduces to 2.5% at reaction gas exposure at room temperature. However the regeneration of this value is slow as only 2.5% could be found at 150°C under CO oxidation conditions.

(E) The Pd-O bond length that is 1.97 Å, contrasts to 1.87 Å in response to reaction gas at room temperature and re-appears at 150°C to 1.87 Å. Pd-O bond breaking could be due to reduction and simultaneous CO adsorption. CO adsorption at 150°C cannot be considered as irreversible.

(F) No marked alteration of PdNCs into the alumina support could be detected.

(G) A monolayer of Pd under the surface of Pd remains NP may be the active phase in CO oxidation reaction.

Conclusion

PdNCs/alumina catalyst at ultra low-loading demonstrates a much better activity (T_{90%} ~ 150 °C, 0.1 wt%Pd/alumina) and stability under CO oxidation than Pd-based catalysts prepared by conventional wet-chemical methods. (T_{90%} ~ 230 °C, 5 wt% Pd/alumina¹⁰)

This work highlights the efficiency of CBD for producing novel tailored high performance catalysts.

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Arsenolipids are not evenly distributed within brown macro-algae *Saccharina Latissima*

Seaweed and seafood have naturally high concentrations of total arsenic compared to agricultural produce. Arsenic is thought to accumulate in seaweed because of structural similarities of arsenate and phosphate as phosphate transporters can mistake arsenate for phosphate due to lack of specificity. However, arsenic is not found in the form of toxic arsenate in seaweed but mainly as arsenosugars. Seaweed has also been shown to contain a significant proportion of arsenic in the form of arsenolipids (AsLp), i.e. hydrocarbons (AsHC), fatty acids (AsFA) and phospholipids (AsPL). Arsenic is often grouped as either inorganic arsenic (iAs: arsenate & arsenite) or organic arsenic, where iAs is a class I carcinogen but the organic arsenic has been considered less toxic. However, recent studies show that arsenolipids can be as toxic as the iAs. To date little is known about AsLps in seaweed, partly due to difficulties associated with the measurements of these compounds, and more information is urgently needed. Here over 50 individuals of *Saccharina Latissima* were collected and pooled together, partitioned into different parts of the seaweed (hold-fast, stipe, old frond, young frond, sporangia) and analysed for AsLps and arsenosugars.

Arsenolipids are not evenly distributed within brown macro-algae *Saccharina latissima*

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Introduction
 For future sustainability it may be necessary to better utilise the ocean for food, e.g. seaweed. Seaweed is high in nutrients, such as minerals and vitamins, and beneficial bioactive compounds. However, seaweed is high in total arsenic (totAs). Arsenic exists in a range of different chemical forms, in seaweed the majority of arsenic is on the form of arsenosugars, with low percentage of toxic inorganic arsenic (iAs). Figure 1a. Seaweed also contains arsenolipids (AsLp). Figure 1b.

Why care?

- Arsenolipids are not well characterized or studied. No commercial AsLp standards or certified reference materials are available.
- Arsenic accumulates in seaweed since phosphate transporters take up arsenate (As₅) instead of phosphate. Algae is the starting point of arsenolipid production.
- Arsenolipids may be as toxic as the class I carcinogen iAs.
- Arsenolipids have recently been shown to cross blood-brain barriers, which the iAs did not do.
- Arsenolipids are an emerging threat to food safety.
- Too little is known about these species.

Sampling & analytical methods:

- Seaweed collected in Reykjavík peninsula, Iceland, in January 2017.
- Approximately 50 individuals of *Saccharina latissima* and 15 individuals of *Alaria esculenta* were pooled together (separately). Samples rinsed with water and all other material removed. Samples sectioned into different parts of the plant. Figure 1a,b. The seaweed was freeze dried and homogenised.
- The total of *S. latissima* released spores were tested.
- Algae Seaweed samples extracted in methanol:chloroform:methane (1:2). Measured with reversed phase HPLC-ICP-MS (inductively coupled mass spectrometry) and HPLC-ICP-MS (Electrospray MS), As Sugars. Water phase measured on HPLC-ICP-MS with anion exchange column, tanks. Determined after digestion with ICP-MS.

Results:

Figure 1. Distribution of arsenic and arsenolipids in seaweed.

Figure 2. Comparison of arsenic and arsenolipid concentrations in seaweed.

Conclusion

- The stipe/midrib of *S. latissima* and *A. esculenta* is lower in total arsenic than other parts of the seaweed. Figure 2.
- This pattern is reflected in the conc. of the downstream As₅SO₃. Figure 4.
- The AsLps follow a different trend to the totAs and As Sugars.
- Possibly the higher the activity of the seaweed section (e.g. where the seaweed is growing) the higher the conc. of AsLps.
- i.e. when the seaweed grows it may be producing these species from iAs. This may indicate that the AsLps are produced before the As Sugars and not vice versa.
- The majority of AsLps in *S. latissima* and *A. esculenta* were AsPLs. Figure 3.
- The AsLp trend was confirmed for *S. latissima* (although with moderately higher conc. of AsLps found) but not for *A. esculenta* (technical issues).

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Structural and Functional Comparison of Low-Molecular-Weight Thiols

Low-molecular-weight (LMW) thiols play a key role in many biochemical processes and can be found in a wide variety of organisms including prokaryotes, plants and, mammals [1-3]. These special species protect living organisms against free radicals and participate in signal transduction, and the regulation of gene expression. As sulfur-containing natural compounds they can also serve as S-donors. One of the most important small molecule weight thiol is glutathione (GSH, γ -glutamyl-L-cysteinylglycine), a linear γ -tripeptide containing glutamic acid, cysteine and glycine. It is widespread in mammals and indispensable for the oxidative stress protection of the central nervous system of the living organisms.

The main purpose of this study is to determine the most important structural and functional properties of LMW thiols. For a selected set of species, a detailed comparison is presented based on the calculated properties of the molecules.

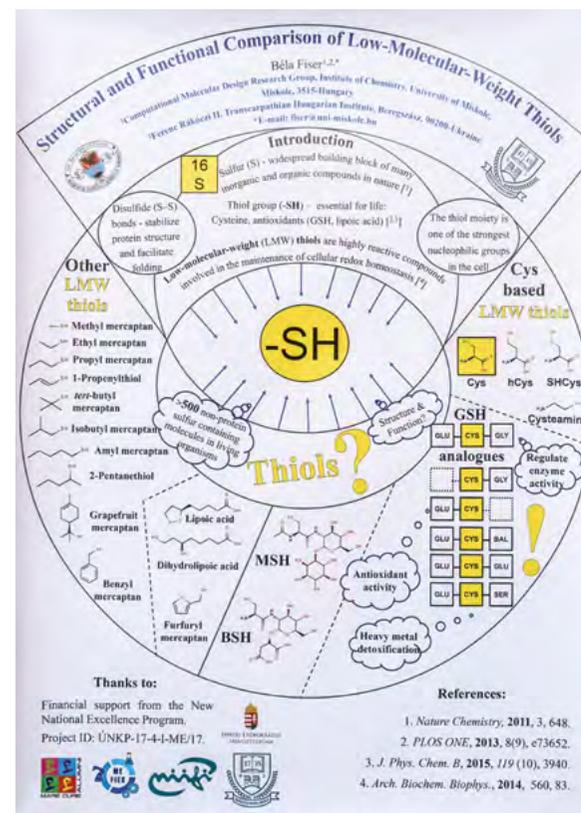
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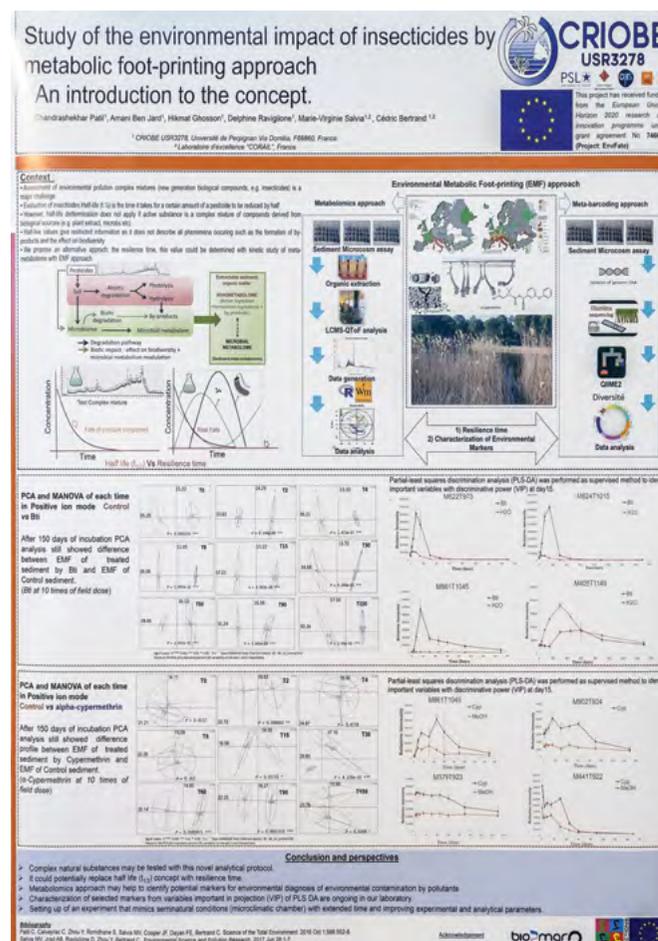
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Study of the environmental impact of insecticides by metabolomic foot-printing approach - An introduction of the concept.

The European Directive in 1998 led to the increasing use of biological insecticides such as cry proteins produced by the bacterium *Bacillus thuringiensis israelensis* (Bti) that kill mosquito larvae after being ingested. Considering the interest in Bti as more environmentally sustainable biocide, it is important to examine environmental fate and impact of Bti especially taking into account the need of this information to fulfil the REACH criteria. The project 'EnvFate' aims to employ an innovative 'Environmental Metabolic Footprinting' approach, that spans the interface between chemistry and biology. To dynamically characterize biomarkers of Bti pollution found among metabolites issued from the sediment matrix meta-metabolome will require to develop and optimize detection protocols using LC-MS platform. In addition, metabarcoding approach will allow to understand microbial community responses to the Bti pollution. Emphasis will be placed on better standardisation, data interpretation and evaluation that will build confidence in the value of "omics technologies – this being essential to increase their (regulatory) use. These activities will advance our understanding of environmental risks associated with Bti, and pave the way for the development and adaptation to new environmental monitoring tool. EnvFate will thus increase the European research visibility to promote sustainable development, ensure the protection of environment, one of the priority areas of the H2020 program.

Here we are presenting sensible preliminary findings to convince the application of concept to evaluate the environmental impact of complex insecticide mixtures.



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Halide perovskites for photovoltaic applications

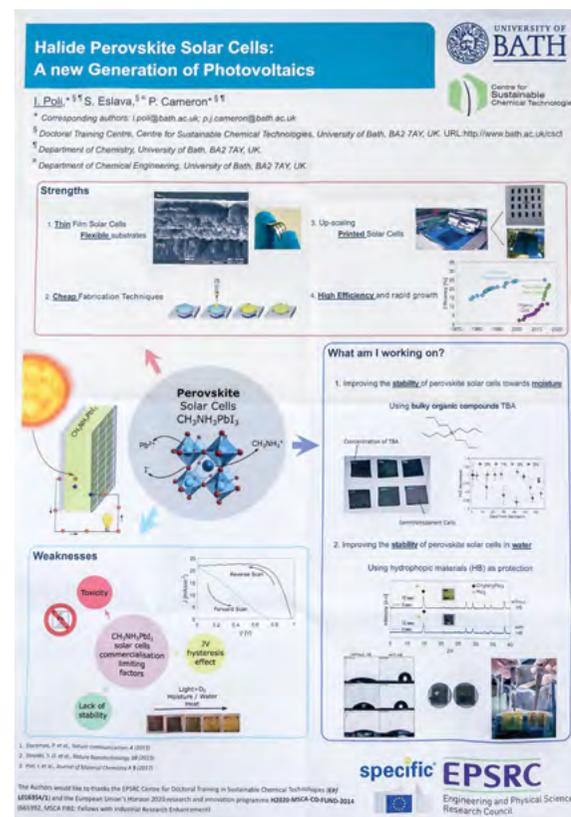
More than 80% of the world's primary energy still comes from fossil fuels [1]. Tackling renewable energy sources is one of the first significant solution to achieve a sustainable development. The sun is the primary source of energy on our planet Earth and it can be directly converted into electricity through photovoltaic systems. One of the most exciting discoveries in photovoltaic research right now are halide perovskite solar cells.

Since the emergence of halide perovskite solar cells in 2012 [2,3], improvements in film morphology and fabrication techniques have led to a power conversion efficiency (PCE) of 22.1% [4]. What prevents halide perovskites to be already available on the market are toxicity issues and lack of stability. Perovskite materials suffer from very fast degradation when exposed to water or even moisture in the air. Ensuring the long term stability of perovskite solar cells under ambient conditions remains a big challenge in the field.

My PhD looks at different ways to improve the stability of the device. On the one hand, different hydrophobic interlayers that delay the degradation have been investigated. On the other hand, the long-term stability of the device was improved by changing the chemistry of the absorber layer. The stability of devices stored in ambient conditions was enhanced by the presence of an extra cation (tetrabutylammonium – TBA) and cells with high mol% TBA were found to have reasonable efficiencies while being semi-transparent [5].

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P-glycoprotein modelling: New methodology of combining molecular modelling with in silico models for safer chemicals

P-Glycoprotein (P-gp) is a transmembrane protein, playing significant roles in the process of drug discovery. P-gp affects absorption, distribution, and elimination of different compounds and is mainly expressed in intestines, liver, kidneys, heart, colon, and placenta. The expression of P-gp in the blood-brain barrier has been associated with the restricted access of many compounds to the central nervous system. P-gp is responsible for resistance of cells to exogenous agents, particularly the anticancer drugs, giving rise to the multidrug resistance phenomenon by mediating the active transport of these drugs from the intracellular to the extracellular compartment. Increased expression of P-gp is also implicated in decreased HIV drug availability at certain intracellular sites. Moreover, studies showed that P-gp contributes to resistance to pesticides in certain pest species, and to decrease toxicity by removing compounds from cells in mammals. Due to the previous reasons, it is advisable in the drug discovery process to pay attention to the likelihood of a compound under development being transported by P-gp, since this contributes to whether a compound actually reaches its intended target or is removed from the cell before exerting its action.

The project aims to develop improved in silico models including P-gp characterization of substrate specificity and transport of exogenous chemicals. The development of in silico approaches could provide rapid and cost-effective screening platforms for the identification of P-gp substrates or inhibitors. Theoretical models of P-gp transport mechanism involve pharmacophore modelling and molecular docking aiming to predict the binding interactions between the protein and small substrates and inhibitors. The outcome of the molecular modelling is going to be combined with

the predictions resulting from QSAR models developed within the project. The in vitro studies performed by project partners are going to be used and compared with the in silico results for generating a two way optimization.

KEMIJSKI INSTITUT **in3**

P-glycoprotein: a combined *in silico* approach towards identification of safer chemicals

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Introduction
P-glycoprotein (P-gp) is a 170 kDa protein composed of 1280 amino acid residues assembled in 12 transmembrane segments and is one of the most abundant membrane transporters in many cells. Located predominantly at the luminal surface it has a fairly wide tissue distribution such as blood brain barrier (BBB), small and large intestine, liver and kidney (1). The substrate specificity for P-gp is very broad. The substrates may be aromatic, non-aromatic, linear or even circular. They can also be basic, unchanged, zwitterionic, or negatively charged. This plethora of structurally diverse compounds interacting with P-gp suggests that multiple binding sites could be involved in the substrate-P-gp binding (2). The substrate interacts with the binding domain of P-gp, located within the bilayer membrane triggering hydrolyzation of two Adenosine Triphosphate (ATP) molecules bound to the ATP binding region, followed by a precise conformational change leading to expulsion of the substrate into the extracellular space (3). As with many of the xenobiotic drug transporters and metabolizing enzymes there is considerable inter-species differences and inter-individual variation in humans.

Objectives
The project aims to develop in silico models including P-gp characterization of substrate specificity and P-gp transport of exogenous toxic compounds including cosmetics and pharmaceuticals, with reference to the endpoints of the project. Develop in silico approaches that provide rapid and cost-effective screening platforms for the identification of P-gp substrates, as well as for revelation of their possible transporting profile on molecular level. Molecular docking aiming to predict binding interactions between the P-gp and small substrates and inhibitors.

Expected results
• Development of in silico approaches for the identification and classification of P-gp substrates, inhibitors, and non active compounds.
• Identification of molecular interactions from docking studies of P-gp with substrates relevant in cosmetics and other substances of concern within the project.
• Combination of QSAR prediction results with the molecular modelling outcome in order to integrate in vitro and in silico data.
• Implementation of the tools for chemical safety assessment of project related compounds and models.
A database of approximately 2,400 compounds, experimentally tested as P-gp substrates, inhibitors and non active, will be used to develop a classification model that could provide rapid and cost-effective screening platforms for the identification of P-gp ligands.

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Methotrexate analogues ecodesigned for programmed self-destruction

Due to the high increase of medicines consumption during the last century, active pharmaceutical ingredients (APIs) are commonly found in the environment. Indeed, wastewater treatment plants (WWTP) are not generally prepared to deal with the tremendous variety of APIs and their metabolites, which allows them to reach natural aqueous environments and soils. Once released in the environment, APIs are likely to provoke toxic effects on organisms due to their intrinsic properties, wide variety, presence as a mixture, and chronic exposure. Anticancer drugs, being cytotoxic, genotoxic, mutagenic, carcinogenic, and/or teratogenic, are targeted as potential ecological stressors.[1] One strategy to reduce persistent APIs in the environment is to replace them with rationally designed molecules programmed to self-immolate after fulfilling their therapeutic purpose.[2]

Bearing all this in mind, methotrexate (MTX) was selected as the starting point of our novel approach of ecodesigned drugs. This compound, also used as a treatment for autoimmune diseases, is one of the most widely prescribed antitumor agents worldwide since the 40's. MTX is a folic acid analogue that competitively inhibits dihydrofolate reductase, interfering in the synthesis of DNA and cell replication. Because of its intensive usage and hydrophilicity, MTX has been detected in hospital and WWTP effluents in several countries.[3] The synthesis of eco-designed analogues of MTX and metabolites, together with their stability and biological studies will be presented.

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Eco-design of methotrexate analogs for programmed self-immolation
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Introduction

Environment and pharmaceuticals

- Active pharmaceutical ingredients (APIs) and their metabolites are widely found in natural aqueous environments and soils due to:
 - Increased rate of medicines consumption.
 - Wastewater treatment plants are not completely capable of removing them.
- APIs are likely to provoke **toxic effects** on organisms owing to:
 - Their intrinsic properties and the presence of transformation products with new biological activities.
 - Wide variety and presence as a mixture.
 - Chronic exposure.
- Several strategies proposed to **reduce APIs** entry to environment:
 - Reduce dose or usage of certain drugs.
 - Minimization of excretion profiles.
 - Replacement by **self-immolative APIs** (rationally designed molecules programmed to self-immolate [1] after fulfilling their therapeutic purpose).

Cancer and chemotherapy

- Second leading cause of death globally, nearly 1 in 6 deaths is due to cancer. The number of new cases is expected to rise by about 70% over the next 2 decades [2].
- Anticancer drugs**, being cytotoxic, genotoxic, mutagenic, carcinogenic, and/or teratogenic, are targeted as potential **ecological stressors**.
- Methotrexate (MTX)**, a folic acid analogue that competitively inhibits dihydrofolate reductase and interferes in the **synthesis of DNA and cell replication**, is one of the most widely prescribed anticancer agents worldwide since the 40's.
- Because of its intensive usage and hydrophilicity, MTX has been detected in hospital and wastewater treatment plants effluents in several countries [3].

Objectives

- Synthesis, and biological studies of MTX analogs **1** and **2** (A), which contain self-immolative scaffolds programmed to be deactivated by predictable metabolic processes and/or advanced oxidation processes (B).

Results: Synthesis and biological evaluation of analogues

(A) **(B)**

Results:

- (1) limiting step: complex mixture of by-products, difficult purification, **2** not obtained.
- Low solubility of precursors.
- Low overall yield.

Biological studies

- Efficacy:** cytotoxicity on cancer cell lines, inhibition of the cellular target (enzyme DHFR).
- Safety (or toxicity):** cytotoxicity on healthy cell lines.
- Early pharmacokinetic parameters**, measured in vitro:
 - Absorption and plasma protein binding (distribution).
 - Hepatic metabolism (formation of metabolites, excretion).

Conclusions and perspectives

- Done:**
 - Design of self-immolative MTX analogues.
 - Chemical synthesis, characterization and preliminary biological study of MTX analogue **1**.
 - Design of alternative synthesis of MTX analogues.
- To be done:**
 - Complete alternative synthesis, characterization and full biological studies of MTX analogues **1** and **2**.
 - Expand the scope of our novel strategy of auto-immolative drugs to other compounds of interest.

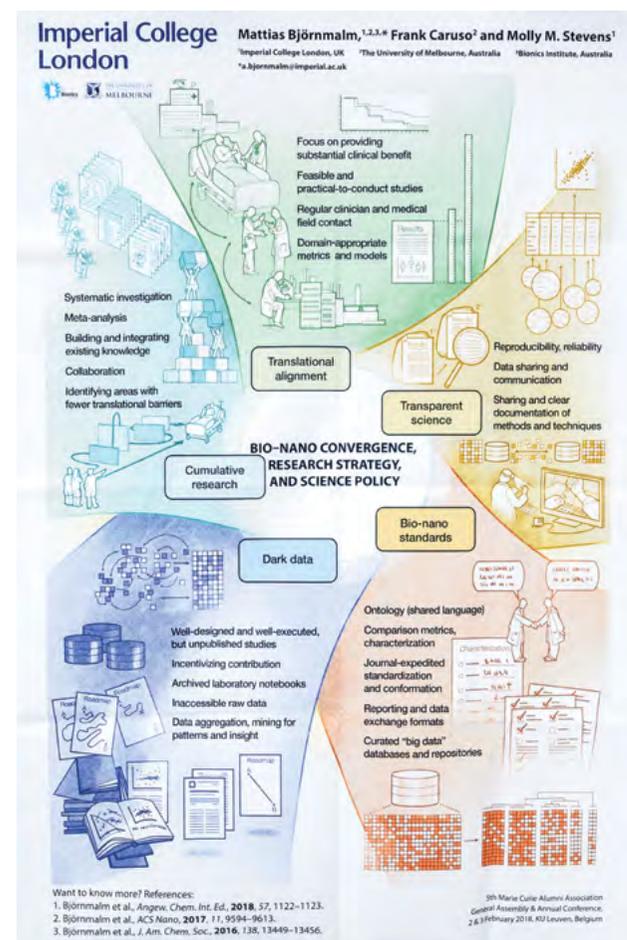
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Bio–nano convergence and science policy

The field of bio–nano science is at a crossroads. The last decade has seen tremendous advances in the development of new materials and in our understanding of biological interactions. Despite this, there is a growing realisation that “research as usual” may not be enough; that our current approach is neither the best way for facilitating impactful and robust exploratory research, nor for accelerating translational work. Moving forward we should ask: will “research as usual” get us to where we want to be? Encouragingly, there is an ongoing energetic discussion—involving researchers, funders, policy makers, and publishers—on how we can address these challenges. In this discussion, several key topics have emerged as part of research “convergence” [1–3]. Examples include areas such as: (i) the advantages of cumulative research; (ii) the necessity of aligning projects with research priorities; (iii) the value of transparent science; (iv) the opportunities presented by “dark data”; and (v) the importance of establishing bio–nano standards. Pursuing and adopting these areas require adjustments across research strategy and science policy, but we believe they are central for accelerating scientific discovery and translational research. Refs: [1.] M. Björnalm et al., *Angew. Chem. Int. Ed.*, 2017, DOI: 10.1002/anie.201710493; [2.] M. Björnalm et al., *ACS Nano*, 2017, 11, 9594–9613; [3.] M. Björnalm et al., *J. Am. Chem. Soc.*, 2016, 138, 13449–13456.



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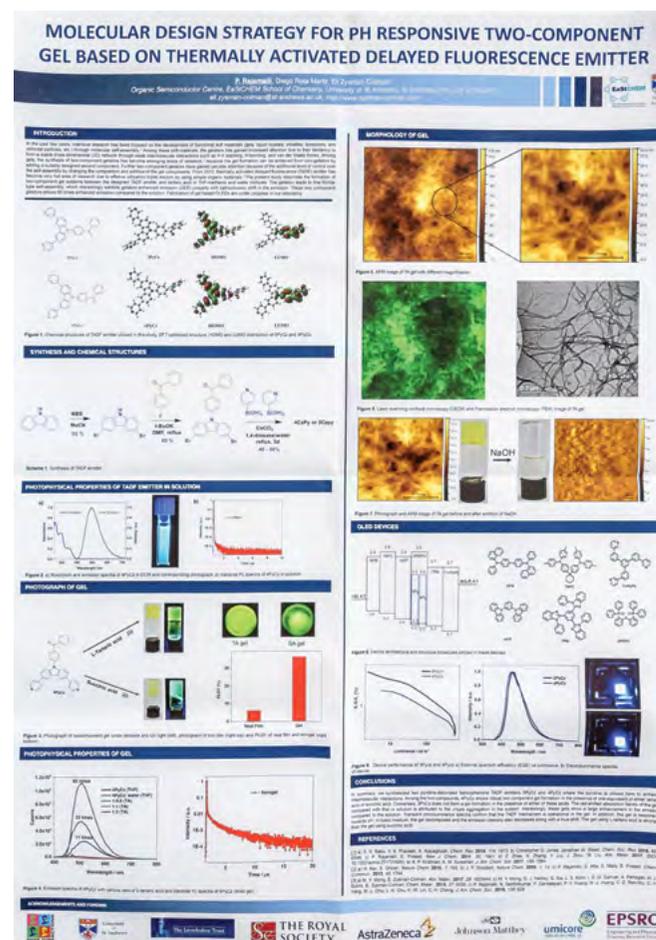
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Molecular design strategy for PH responsive two-component gel based on thermally activated delayed fluorescence emitter

Recently, OLEDs employing metal-free thermally activated delayed fluorescence (TADF) emitters have emerged as a cheaper alternative to phosphorescent OLEDs and biological application.¹⁻⁵ Here we present an in-situ formation of two-component hydrogels from pyridine decorated benzophenone TADF compound and tartaric acid. The two component system (4PyCz + acid) undergoes aggregation, leading to a fibrillar-type self-assembly in THF-water mixture along with green (534 nm) emission. A new method is proposed to enhance the emission of the organic compound by supramolecular assembly. Interestingly colour and rigidity of the gel can be tuned by varying the additives (acid) and ratios of additives.

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Local Piezoelectric Behavior of Potassium Sodium Niobate Prepared by a Facile Synthesis via Water Soluble Precursors

Due to the ever-increasing restrictions connected to the use of toxic lead-based materials, the developing of lead-free piezoceramics has become one of the most urgent tasks. In this context, potassium sodium niobate materials have attracted many attentions as promising candidates due to their excellent piezo properties and stability. For this reason, many efforts have been addressed to improve the synthesis process now suffering by several drawbacks including the high volatilization of potassium and sodium at the conventional high temperature treatments and the use of expensive metal precursors. To overcome these issues, a new modified Pechini method to synthesize single phase $K_{0.5}Na_{0.5}NbO_3$ powders, from water soluble metal precursors, is here presented. Microstructural and structural parameters have been characterized by X-ray diffraction (XRD). Depending on the amount of citric acid added to the starting reagents, two pure single-phase $K_{0.5}Na_{0.5}NbO_3$ (2g citric acid) and $K_{0.3}Na_{0.7}NbO_3$ (0.2 g citric acid), respectively, were obtained with a good crystallinity at a moderate temperature of 500 °C. The piezo responses of the as calcined systems have been tested by piezoresponse force microscopy (PFM). $K_{0.5}Na_{0.5}NbO_3$ exhibits a much higher response with respect to the other phase, which relates to the larger crystallinity and to the chemical composition.

The poster is divided into five main sections:

- 1. Introduction:** Discusses the market for lead-free piezoceramics, highlighting the need for a single-phase material with a high piezoelectric coefficient. It compares the traditional Pechini method with the proposed water-soluble precursor method.
- 2. Objectives:** Lists the goals of the study, including the synthesis of high-purity $K_{0.5}Na_{0.5}NbO_3$ and the investigation of its piezoelectric properties.
- 3. Synthesis and Structural Characterization:** Details the modified Pechini synthesis process using water-soluble precursors and citric acid. It includes XRD patterns and SEM images of the synthesized powders.
- 4. Piezoelectric Properties:** Shows PFM images and piezoelectric coefficient maps for the synthesized materials, demonstrating their piezoelectric response.
- 5. Results:** Summarizes the key findings, such as the successful synthesis of single-phase $K_{0.5}Na_{0.5}NbO_3$ and its high piezoelectric response.

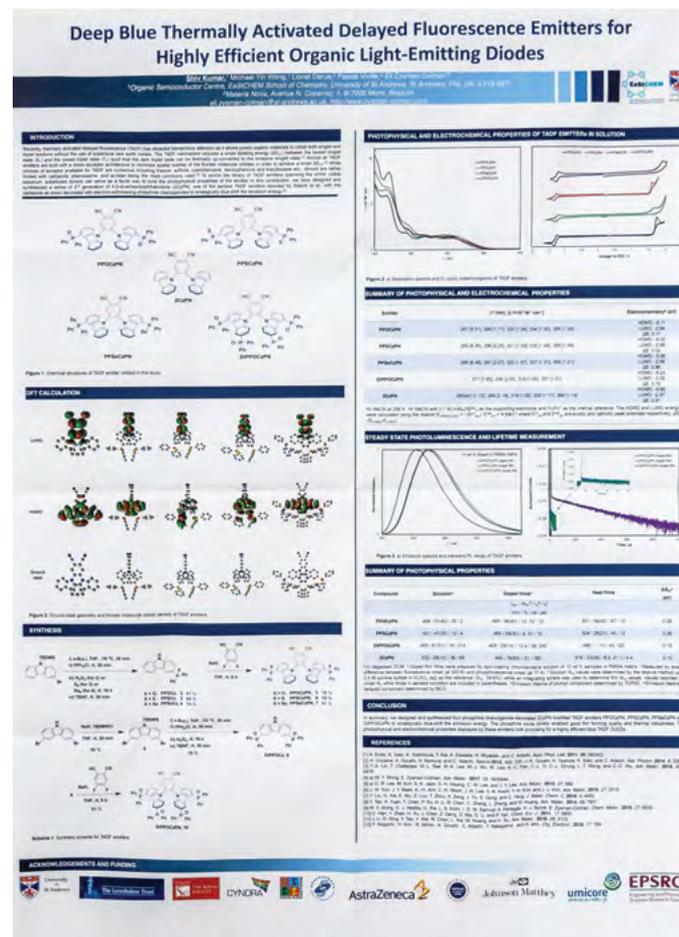
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2nd Generation Deep Blue Thermally Activated Delayed Fluorescence Emitters for Highly Efficient Organic Light-Emitting Diodes

In recent years, organic light emitting diodes (OLEDs) based on thermally activated delayed fluorescence (TADF) have emerged as the third-generation of OLEDs for displays and solid-state lightings. The most exciting feature of TADF-OLEDs is the harvesting triplet excitons using a pure-organic dye molecule with an efficient reverse intersystem crossing (RISC). An efficient RISC requires the singlet-triplet splitting (ΔE_{ST}) between the first singlet (S1) and triplet (T1) energy level to be small, generally less than 0.2 eV. So far, several sky blue TADF emitters have been reported in literature but the performance of deep blue TADF emitters still must be improved and their development is still in progress. We have employed the carbazole donors with electron-withdrawing phosphine chalcogenides substituents to strategically blue-shift the emission of the known sky blue TADF emitter 4,5-dicarbazoylphthalonitrile (2CzPN). We present calculations, synthesis, photophysical characterization and initial device results.



Novel bio-based monomers prepared from β -elemene

The replacement of polymers produced from fossil resources is desirable due to limited availability of this resource in the future and environmental issues associated with it. To address these issues, current research focuses on both the development of polymers from renewable resources and on the generation of biodegradable polymers. Terpenes, which can be derived from plants, have received interest as possible bio-based monomers, because they are abundant and furthermore some terpenes can be gained from waste products on an industrial scale. Their diverse hydrocarbon structures and the occurrence of double bonds offers the possibility for the synthesis of various polyolefins.

This project investigates how the terpene β -elemene can be functionalised to generate novel bio-based monomers for polymerisation. The β -elemene structure bears three double bonds providing a useful starting material for introducing different functional groups via reactions at these alkene moieties. It was shown that different β -elemene derivatives bearing epoxide, cyclic carbonate or methyl ester moieties can be produced. These β -elemene derivatives could be used further for polymerisation reactions to produce polycarbonates, polyurethanes or polyesters.

Novel bio-based monomers prepared from β -elemene

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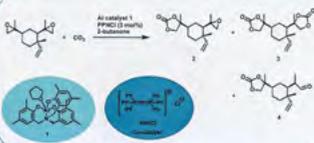
Introduction

The replacement of polymers produced from fossil resources is desirable due to limited availability of these resources in the future and environmental issues associated with them. Terpenes, which can be derived from plants, are an alternative renewable feedstock for the synthesis of bio-based polymers.¹ Their availability on an industrial scale from waste resources or from fermentation of sugars makes them suitable monomers for polymerisation.^{2,3}

The aim of this project was to investigate β -elemene, a terpene that can be found in ginger and juniper, or can be gained from fermentation of sugars, as a potential bio-based monomer to make bio-plastics.^{4,5,6,7} Specifically, β -elemene was to be functionalised to produce cyclic carbonate or methyl ester derivatives. These could be used further to synthesise bio-based polyurethanes, polycarbonates or polyesters.

Cyclic carbonates

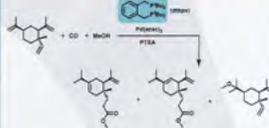
In the first step β -elemene was oxidised to β -elemene bisepoxide using known synthetic procedures.⁸ Using the aluminum amine(phosphonate) complex 1, bis(triphenylphosphonium)trimethyl chloride (PPNC) as co-catalyst and 2-butanone as solvent, we investigated the formation of cyclic carbonates from β -elemene bisepoxide and CO.^{9,10} Depending on the reaction conditions different cyclic carbonate products (2, 3 and 4) could be obtained.



CO ₂ pressure [bar]	temperature [°C]	time	catalyst 1 [mol%]	2 [%]	3 [%]	4 [%]
30	85	24 h	1	68	16	0
30	85	6 h	1	74	0	0
30	85	5 d	1	44	47	0
30	130	24 h	1	14	62	20
30	85	24 h	1	78	17	0
30	85	24 h	2 ^a	62	32	0

Table 1 Reaction conditions and yields after column chromatography
^a 5 mol% PPNC co-catalyst used

Methoxycarbonylation of β -elemene with CO



Pd(acac) ₂ [mol%]	dtbpx [mol%]	PtSA [mol%]	temperature [°C]	CO pressure [bar]	5 and 6 [%]	7 [%]
0.1	0.4	1.6	120	25	-	5
0.1	0.4	1.6	150	25	22	-
0.3	1.2	4.8	120	25	47	-

Table 2 Reaction conditions and isolated yields

Methoxycarbonylations of β -elemene were carried out using Pd(acac)₂ and the 'Luiche alpha process' ligand 1,2-bis-(tert-butylphosphonomethyl) benzene (dtbpx) as catalyst and para-toluenesulfonic acid (PtSA) as co-catalyst. High temperature or high catalyst loading yielded a 50:50 mixture of the β -elemene methyl ester isomers 5 and 6 in up to 47% yield. At low temperatures and low catalyst loadings only addition of methanol could be observed, resulting in derivative 7. The main side products arise from isomerisation of β -elemene.

Reactions were also conducted with methyl formate, replacing the toxic and highly flammable CO gas with a more benign carbonyl source.¹¹ However, only 3% yield of the methyl esters 5 and 6 could be obtained.

Conclusion and Outlook

It was shown that β -elemene can be functionalised to form novel bio-based building blocks. From β -elemene bisepoxide carbonates (2), bisoxetane dicarbonates (3), bisoxetane methacrylates (4) and bisoxetane methyl esters (5 and 6) could be synthesized. Future work comprises getting these monomers into their respective polymerisation reactions to synthesize polyurethanes, polycarbonates or polyesters. Furthermore, the methoxycarbonylation of the different double bonds of β -elemene offers, depending on substituents, also the synthesis of β -elemene derivatives.



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FACTORS




Engineering and Physical Sciences Research Council

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Dual stimuli-responsive controlled systems using polymer-based molecular gates

Multifunctional hybrid materials based on mesoporous silica nanoparticles (MSNs) [1] are promising candidates as drug delivery systems compared to liposomes or emulsions. Their thermally stability and rigid framework prevents premature degradation, and they can be easily functionalized with stimuli-responsive gate-keepers, reducing the unpleasant side effects of conventional systems. Bearing in mind those advantages, in this project is proposed a smart controlled delivery system based on silica nanoparticles capped with a polymer [2] sensitive to both temperature and pH. This dual-responsive behavior is very useful for biological applications as the loaded drug can be released faster at 37 °C and slightly acidic pH (typical for intracellular environment) than at neutral physiological conditions. These two stimuli are very popular in the design of gated systems and in this work, the close/open mechanism relies in the incorporation of acidic hydrolysable units, such as boronate ester or amide groups, that links the thermo-responsive polymer Jeffamine® M-2005 (PEO5-st-PPO37) to the silica nanoparticles surface, controlling the cargo delivery on demand. The preliminary results have shown the promising chances of the system for future dual 'off-on' drug delivery applications such as cancer therapy, as in many types of tumors an acidic microenvironment can be found.

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Dual stimuli-responsive controlled systems using polymer-based molecular gates
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1. Why to do stimuli-responsive materials?

CANCER
 One of the leading causes of mortality (second worldwide cause of death after cardiovascular diseases)

METASTATIC CANCER
 Chemotherapeutic drugs

When the tumor is local and there is non-metastatic cancer: Surgery and/or radiation

Need for intelligent site specific drug therapy TO AVOID SIDE EFFECTS

Cancer cells
 pH 6.5-7.2
 Temp 37 °C

MSNs
 pH 7.4

Dual-responsive behavior:
 the loaded drug can be released specifically at 37 °C and slightly acidic pH (typical for intracellular pathologic environment)

2. Silica support is one of the most used materials used in hybrid materials design:

MSNs
 interesting characteristics:

- High surface area (up to 1000 m² g⁻¹)
- Large loading capacity
- Modifiable pore size
- Chemically inert
- Easy to functionalize through alkoxysilanes

Mesoporous Silica Nanoparticles (MSNs)

Hexagonal and longitudinal non-connected mesoporous channels

3. General scheme of organic-inorganic hybrid materials for delivery applications:

GATED MATERIAL

Functional molecules (medicine guest)

External stimuli or guest

Release of the cargo upon external stimuli such as: pH, Temperature, Light, Biotin or Biotinylated

4. Proposed polymer-based molecular gate material:

"Close-opening mechanism" relies in the incorporation of acidic hydrolysable units, such as boronate ester or amide groups, that links the thermo-responsive polymer Jeffamine® M-2005 (PEO5-st-PPO37) to the silica nanoparticles surface, controlling the cargo (anticancer drug) delivery on demand.

Step 1: Preparation of the MSNs

Step 2: Drug loading and surface functionalization with acidic hydrolysable units

Step 3: Functionalization with thermo-responsive polymer Jeffamine®

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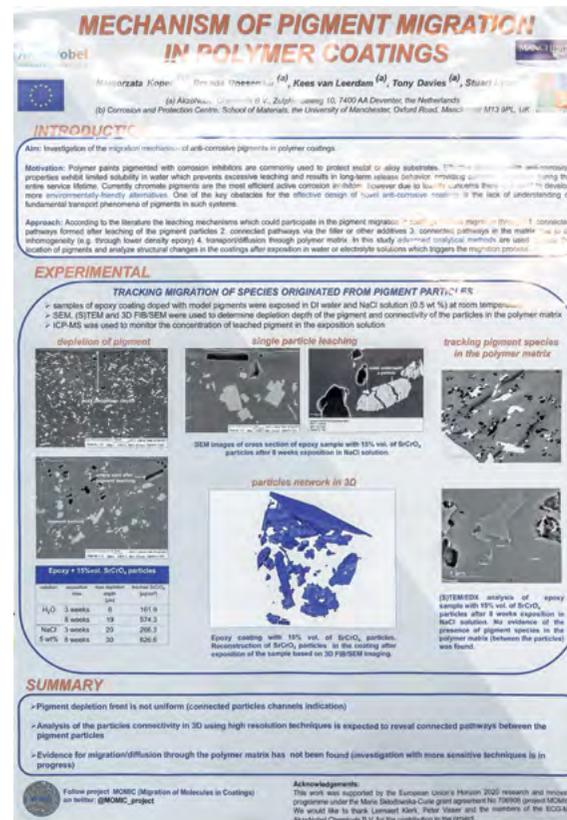
Mechanism of pigment migration in polymer coatings

Polymer coatings are used to protect underlying surfaces, mostly metals and alloys, extending their service life. Because of high costs of corrosion the use of protective coatings is crucial in any application that involves materials processing and manufacturing. A polymer coating applied on protected surface is composed of a binder (cross-linked polymer resin) and additives such as functional pigments including anticorrosive agents and non-functional fillers. Polymer coatings provide passive corrosion protection by forming a barrier for corrosive species and blocking ionic transfer between anode and cathode areas on a metal surface; active corrosion protection is provided by anticorrosive additives (pigments). Effective pigments exhibit limited solubility in water which prevents excessive leaching and results in long-term release to guarantee anti-corrosion performance during the entire lifetime. The most efficient anticorrosive systems involve chromate-based pigments. However, due to toxicity concerns, there is a need to search for more environmentally-friendly yet equally or better-performing alternatives. One of key obstacles for the effective design of novel anti-corrosive coatings is the lack of understanding of fundamental transport phenomena of pigments in such systems.

This work aims at investigating the migration mechanism of pigments through model polymer coatings (i.e. epoxy films filled with different pigments and fillers). Advanced analytical methods such as SEM-EDX (scanning electron microscopy/energy dispersive X-ray spectroscopy), STEM (scanning transmission electron microscopy)-EDX and FIB (focused ion beam)/SEM are used to track the location of pigments and analyse structural changes in the coatings after exposition in water or electrolyte solutions which triggers the migration process.

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Attosecond extreme ultraviolet vector laser beams from radial to azimuthal polarization

Vector beams –light beams with spatially variant polarization– have become an indispensable tool in many areas of science and technology such as optical trapping, quantum memories, and quantum optics. Radially and azimuthally polarized light beams are especially interesting to sharply focus light below the diffraction limit, and to induce longitudinal magnetic fields, respectively. The spectral limitations of their generation techniques based on linear optics prevent their efficient generation in the extreme-ultraviolet (EUV) and x-ray regimes, which would further extend their applications down to the nanometric scale. In this work EUV vector beams are generated for the first time using the nonlinear process of high harmonic generation (HHG). To do so, an infrared fs radially polarized vector beam –generated with a s-waveplate– is focused into an argon gas jet, whose atoms emit coherent EUV radiation. Our experimental and theoretical results demonstrate that HHG imprints the polarization state of the infrared beam, ranging from radial to azimuthal, into the EUV range. Our numerical simulations also demonstrate that the harmonic beams can be synthesized into EUV/soft x-ray attosecond vector beams, that can carry orbital angular momentum.

Extreme ultraviolet vector beams from radial to azimuthal polarization

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Abstract
 Vector beams, beams with a non-uniform state of polarization, have become an indispensable tool in many areas of science and technology. Harnessing topological light properties gives the way to control and manipulate light-matter interaction at different levels, from quantum to macroscopic physics. For the first time, we experimentally produce vector beams –beams radially or azimuthally polarized– in the extreme ultraviolet (EUV) regime, using high-order harmonic generation (HHG). Our simulations also predict the generation of unique spatiotemporal structures in the form of attosecond vector beams. This proposal overcomes the state-of-the-art limitations for the generation of vector beams from the visible domain and could be applied in fields such as diffraction imaging, EUV lithography or ultrafast control of magnetic properties.

Families of singular beams
 Spin angular momentum Orbital angular momentum Vector beams

Direct generation of EUV vector beams using high harmonic generation

1. Numerical simulations

2. Experimental results

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3D millisecond tracking of single-molecule fluorophores – Applications for studying protein translocation in eukaryotic cells

Metabolic processes are the basis of all life. An organism must be able to utilise chemical energy to stay alive and eventually reproduce. These are the central features of life, regardless of organism length scale. To achieve this, an organism must be able to adapt to varying surrounding environmental conditions. Cells respond to external stimuli by releasing kinase cascades along often intricate signalling pathways which regulate cellular function. These chemical signals eventually bring about some cell level response.

In our research on transcription factor dynamics in Brewer's yeast, *Saccharomyces cerevisiae*, we have found that a key transcription factor, Mig1, forms functional clusters that translocate between nucleus and cytosol as a response to environmental glucose fluctuations (Wollman et al. 2017). The bulk behaviour of Mig1 glucose sensing in yeast has recently been well characterised (Bendrioua et al. 2014). However, only now have we been able to follow the dynamics and interactions of individual molecules and clusters in the pathways.

Fluorescent optical microscopy techniques are ideal for non-invasive probing of samples that can be placed in such a way that the sample turbidity hampers the image. We use genetically incorporated fluorescent markers which allows functional in-vivo imaging.

By using astigmatic imaging at high speed, we can track in three dimensions, fluorescently tagged proteins translocating in living cells over several tens of milliseconds with a temporal resolution of down to 5 ms, allowing diffusing particles to be tracked under physiological conditions. We used

mutant yeast strains with fluorescent protein tags attached to the transcription factor Mig1. Furthermore, a microfluidic flow channel provides a consistent and controllable environment during an experiment.

3D millisecond tracking of single-molecule fluorophores – Applications for studying protein translocation in eukaryotic cells

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Glucose sensing in *Saccharomyces cerevisiae*
 Absence of glucose necessitates the use of alternate carbon sources for survival. A drop in environmental glucose results in a chemical cascade, culminating in the phosphorylation of the transcriptional repressor Mig1¹⁻³, and the subsequent translocation of several genes, including *SUC2*. See examples in figure 1 below.

Visualising transcription factors
 Mig1 has been tagged with a monomeric variant of a green fluorescent reporter protein (GFP). In various permutations, other proteins, either acting as dedicated nuclear reporters or being involved in the regulation, have been tagged with a red fluorescent protein (mCherry).

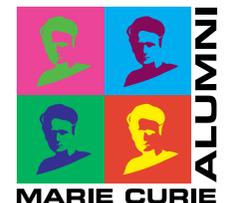
Astigmatic 3D imaging
 Astigmatic imaging makes it possible to encode the axial position of a particle smaller than the diffraction limit using characteristic asymmetric deformations of the PSF images at the camera. The image will show an elongation along either the x or y axis, dependent on how far out of plane a particle is located, see figure 3.

Single-molecule detection in catalytic crystals
 A light emitting diode (LED) is used to excite the fluorophores. High-speed cameras with astigmatism are used to capture the images. The current setup at KU Leuven is to use a 1000 fps camera with a 100 nm axial resolution and a 100 nm lateral resolution. The images are then processed using a custom-built software to extract the axial position of the particles. The images are then processed using a custom-built software to extract the axial position of the particles. The images are then processed using a custom-built software to extract the axial position of the particles.

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CO photoelectron angular distributions in the molecular frame

Investigating molecular geometries is of great importance for different applications in physics, chemistry, life sciences or the pharmacy industry.

Here we present a photoionization experiment carried out at synchrotron SOLEIL, where a X-ray photon beam was intersected with a CO supersonic gas jet. By absorbing a photon, the K-shell ejects a photoelectron, followed by an Auger decay and finally by a Coulomb explosion. Using the COLTRIMS (COLd Target Recoil Ion Momentum Spectroscopy) reaction microscope, both electrons plus both ions are detected in coincidence.

The photoionization event is determined by the initial state of the system, the properties of the dipole operator, which is responsible for the photoionization, and the final state. At high energies, the continuum electron can be described by a plane wave where the photoionization differential cross section of the electron emission direction (the molecular frame photoelectron angular distribution, MFPAD) is proportional to the square of the Fourier transform of the initial state.

By selecting high photon energies (690 eV), circularly polarized light and restricting the MFPAD to the polarization plane, the effect of the dipole operator can nearly be neglected and thus the initial electronic wave function is in good approximation mapped onto the emitted -and detected- photoelectron.

CO Photoelectron Angular Distributions in the molecular frame

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Introduction
 Investigating molecular geometries is of great importance for natural sciences as well as industrial applications. For doing so here we present a leading technique: the coincidence measurement of electrons and ions, and the photoelectron angular distributions as a powerful tool to look into the molecules.

Experiment
 Photoionization: $h\nu + \text{CO} \rightarrow \text{CO}^+ + e^-_{\text{Photo}}$
 Auger decay: $\text{CO}^{2+} + e^-_{\text{Auger}}$
 Dissociation: $\text{C}^+ + \text{O}^+ + \text{KER}$

MFPADs
 Molecular Frame Photoelectron Angular Distributions
 When a photon of sufficient high energy is absorbed by a molecule, a photoelectron is ejected.
 The ejection direction relative to the molecular axis, given by the angles θ and ϕ , creates a map of how the molecular potential multiplies the outgoing photoelectron wave.
 The observed angular distributions strongly depend on the electron energy [1] (that is, the electron wave length) and are very sensitive to the exact shape of the molecular potential [2].

COLTRIMS [3]:
 COLd Target Recoil Ion Momentum Spectroscopy
 Electron time-of-flight | Ion time-of-flight
 ✓ For measuring MFPADs we need: PAD: Electron emission direction → electron momenta
 MF: Molecular axis → measure ion momenta in coincidence

Results
 • The measurements were carried out at the beamline SIXTANS at the synchrotron SOLEIL (France).
 • Circularly polarized light (CPL) of 690 eV and 930 eV intersected with a supersonic gas jet of CO molecules.
 • C (1s) binding energy is 297 eV and
 • O (1s) binding energy is 533 eV in CO, respectively.

a) O (1s) photoelectron of 155 eV
 b) C (1s) photoelectron of 393 eV
 c) O (1s) photoelectron of 395 eV

The figures show K-shell MFPADs for left CPL in the polarization plane. Black dots are experimental data with error bars. Red line is a spherical harmonics $Y_{\ell m}$ for $\ell = 4$.

Outlook
 • At high energies the MFPADs get more and more isotropic, with an intense rise in the bond direction as an arrow that starts at the emitter atom and points towards the scuffier atom.
 • A homonuclear molecule, N₂, has also been measured at 880 eV photon energy for comparison as well as methylobenzene (1,2-propylene oxide), a chiral molecule.
 • These results can be used as a new method to resolve the handedness of left- and right-handedness.

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Sustainable magnetostrictive thin film alloys

There is a high demand for novel magnetostrictive and multiferroic materials for application in MEMS/NEMS sensors employing magnetic fields. Existing high-performance materials such as Terfenol-D (TbxDy_{1-x}Fe₂x~0.3) and Galfenol (Fe-Ga) have a high magnetostrictive coefficient, but often do not meet mechanical requirements and contain critical raw materials; current global concerns such as shortage of resources, restricted choice in sources of import as well as environmental and health issues thus often impede the broad development and implementation of novel devices. The Fe-Al system is a promising sustainable alternative to these materials. Its well-known bulk magnetostrictive properties perform on the same order of magnitude as the closely related Fe-Ga system at a fraction of its price. However, comparatively little research has been dedicated to the development of magnetostrictive Fe-Al thin films so far. The current study is aimed at the investigation of such films and the improvement and specific tailoring of their properties. Strategies such as metastable phases produced by magnetron sputtering, induced phase transformations and ternary alloying are presented. A novel approach for the measurement of the magnetostrictive effect in very thin films (<500 nm) is introduced. Finally, results on respective binary and ternary Fe-Al alloys are given and put in a broader context.

Sustainable magnetostrictive thin film alloys
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 Wilhelm Huettenes graduated in Materials Science BSc and MSc at ETH Zurich, Switzerland, specialising in smart materials and materials at small dimensions. He holds his Master Thesis with Prof. Espinosa de Melillo thin films, in Cambridge he received a PhD programme in the Device Materials Group with Prof. Zoe H. Barber, he works as Marie Skłodowska Curie Research Fellow on Smart ELECTroresponsive Alloys for environmentally sustainable applications (SELECTA) in the field of smart composite physical deposition methods (PDM) phase analysis, ferromagnetic properties and composite materials.

Abstract
 There is a current need for novel magnetostrictive and multiferroic materials for application in MEMS/NEMS sensors employing magnetic fields. Existing high performance materials such as Terfenol-D (TbxDy_{1-x}Fe₂x~0.3) and Galfenol (Fe-Ga), often do not meet mechanical requirements or use critical raw materials, current global concerns such as shortage of resources, sustainable supply chains, as well as environmental and health issues thus impede the broad development and implementation of novel devices. The Fe-Al system is a promising sustainable alternative to these materials. Its well-known bulk magnetostrictive properties perform on the same order of magnitude as the closely related Fe-Ga system at a fraction of its price. However, comparatively little research has been dedicated to the development and deployment of magnetostrictive Fe-Al thin films so far. This project is aimed at the investigation of such films and the improvement and specific tailoring of their properties.

Sustainability Aspects
 Global shortage and supply chains of critical raw materials as well as toxicity and environmental considerations drive the need for more sustainable solutions. Upgrading and transfer to broad industrial application further require economic constituent materials.
 • Avoidance of rare earth and noble metals
 • No light toxic elements
 • Avoidance of cobalt and nickel
 • Minimisation of use of gallium and phosphorus
 • Minimisation of use of otherwise critical raw materials and substances of high concern

Magnetostriction in Fe-Al
 • Similarities between Fe-Ga and Fe-Al allow comparative studies (see right figure)
 • Scalability for thin film and bulk application
 • Best magnetostriction coefficients found at disordered phase boundaries
 • Pushing the phase boundary of A2 phase beyond 19 at % Al might enhance magnetostrictive properties
 • Lattice distortions (e.g. ternary alloying) and stress states influence magnetostriction
 • Fe @ Al @ Ni superlattice
 • A2 dispersed B2 ordered

Methods
 Composition and phase analysis have been conducted by EDX and XRD studies, respectively. Magnetic hysteresis were determined with VSM.

Film Deposition
 • Multi target magnetron sputter deposition
 • Deposition of uniform alloy films or multilayers by rotation speed and breaks
 • Control over deposition temperature
 • Reactive sputtering possible

Thin film magnetostriction
 • Employment of AFM equipments for cantilevers
 • Cantilever deflections caused by magnetostriction are measured with a non magnetic Bruker AFM setup
 • Detection limits of deflections in sub-nanometer range
 • Calculation of the magnetostriction coefficient λ

$$\lambda_{\text{max}} = \frac{2(1 + \nu_1)E_1E_2^2d}{9(1 + \nu_2)E_2E_1^2d}$$

Results
 A range of binary Fe-Al alloy films from 0 - 50 at % Al has been deposited and characterised in order to see its influence on magnetic and magnetostrictive properties. Ternary Fe-Al-Ni films with a fixed Fe:Al ratio of 1:1.9 and 0 - 9 at % Ni have also been studied. Measurements of thin film magnetostriction with a retrofitted AFM setup yield plausible results.

Conclusion and Outlook
 • Ni is polycrystalline and highly (110) textured
 • Al and Ni are in solid solution in the bcc Fe-Al phase
 • Thin film magnetostriction (20 ppm) is lower than reported bulk values (112 ppm)
 • Alloying up to 20 at % Al leads to magnetic softening of Fe and slight reductions of M_s . Above this threshold the magnetic properties deteriorate and the coercivity increases.
 • Ni has a strong influence on the lattice constant and magnetic properties
 • Establish reproducibility in the quantification of λ
 - Alignment to minimise magnetic torque
 - Cantilever design by encapsulating techniques
 • Magnetostrictive characterisation of FeAlNiB films
 • Deposition of other ternary alloys such as FeAlNiC

Composite Magnetolectrics
 • Strain coupling of magnetostrictive and piezoelectric layer
 • Possible giant magnetolectric effect achievable with sustainable materials
 • Several layer designs possible in order to tailor the magnetostrictive coefficient and the resonance frequency

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 The author would like to thank his collaborators Marisa Corbin and Prof. Paolo Tiberti from INMIA, Torino, Italy, for the joint work on thin film magnetostriction measurement. Further thanks to Dr Nadia Steinhilber and Mary Vickers for highly appreciated help with magnetron sputtering and XRD measurements. This work was supported by the UK Horizon Marie Skłodowska-Curie action SELECTA (H0200-MSCA-ITN 2014) under Contract No. 642842.

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Simulating the near-Earth's space in unprecedented detail with the Vlasiator model

The space around Earth is not as empty as one may think, but is filled with particles escaping from the Sun, called the solar wind. The Earth's magnetic field shields our planet from this flow, forming a protective magnetic bubble around our atmosphere. However, just like normal weather can get stormy, the conditions in space, the space weather, can deteriorate. Solar storms are caused by giant clouds of solar particles, ejected into space during violent eruptions. The most widely-known effects of solar storms are the beautiful auroral displays which can sometimes be witnessed in night skies. Yet stormy space weather can also have adverse consequences for human activities, in space and on the ground, for example damaging spacecraft electronics or disrupting GPS signals. In our modern society, relying ever more on space-based assets, understanding and being able to predict space weather has become crucial. One way to further our understanding of space weather is to develop computer simulations capable of describing the interaction of the solar wind with the near-Earth space. Simulating this is however extremely challenging because of the variety of scales, both temporal and spatial, over which the relevant phenomena take place. At the forefront of numerical space physics, the newly-developed Vlasiator simulation code offers a unprecedented view of the near-Earth space. My Marie Curie-funded project focuses on utilizing this new model to study how incoming solar storms modify one of the outermost regions of the near-Earth space called the foreshock, and whether the foreshock changes in turn how solar storms interact with the Earth's magnetic field. The aim of the project is to assess whether these effects should be taken into account in refined space weather forecasts. In this poster, I will present the Vlasiator model and initial results from my research project.

Simulating the near-Earth space in unprecedented detail with the Vlasiator model

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Space Weather and Solar Storms

What is space weather?
 The space weather is defined as the conditions experienced in space, which vary in time due to the changing activity of the Sun.
 Just like normal weather can get stormy, the space weather can deteriorate. Solar storms are caused by giant clouds of solar particles, ejected into space during violent eruptions. When these storms hit, the Earth's magnetic field, they create beautiful auroral displays, but they can also have adverse consequences for human activities.

Forecasting solar storms
 From observations of the Sun, large uncertainties from observations of the storm just before it hits Earth reasonably accurate forecasts but uncertainties remain, in particular on the temporal evolution of the storm.
 A detailed understanding of the Sun-Earth chain is essential to improve the forecasts.

Towards a better understanding of solar-terrestrial relations: the VLASIATOR model

- **Global simulation** of the near-Earth space
- **Large-scale phenomena** are also included → allows to investigate the **global effects of local processes** and vice versa
- **Scientific people look**: scales in terms of thousands of cores and runs take a few million core-hours on supercomputers

Technical details of the code

- Ions created as **velocity distribution functions**, electrons are a charge-neutralizing fluid
- Evolution of the system obtained by solving **Vlasov's equation** coupled with Maxwell's equations and Ohm's law (with the Hall term)
- Current runs are 3D (3D in velocity space and 2D in real space)
- Full description of the model: von Althaus et al. 2014, Pfau-Kempf 2016.

Recent Vlasiator results

- Palmroth et al. (2017): onset of magnetic reconnection in the magnetosheath
- Huuhtoniemi et al. (2017): dipole reconnection modulated by magnetosheath waves
- Pfau-Kempf et al. (2016): local foreshocks generated by magnetic island-driven waves

PI of the Vlasiator project: Mina Palmroth (mina.palmroth@helsinki.fi)
 Visit <http://www.physics.helsinki.fi/vlasiator>

The Foreshock and its Role in Solar-Terrestrial relations (FROST)

The Foreshock

- Outermost region of the near-Earth space, populated by shock-reflected particles and hosting a variety of waves
- Foreshock waves are transmitted to regions closer to Earth and can affect the coupling between the different regions
- The foreshock properties are intimately coupled with the upstream conditions, but the effects of a change of a given parameter are not so well known
- In particular, we don't know how the foreshock properties change during solar storms, and in turn how the foreshock affects the incoming storms.

First study: foreshock local and global properties for regular and storm-time conditions

Comparison of two Vlasiator runs with regular and high magnetic field strength.

Results:

- **Change in the wave properties**: wavelength, transverse extent, number of wave modes
- **Change in the shock-reflected particle properties**
- **Change in the global structure of the foreshock**: extent of the wave-dominated region; number of 'spices', foreshock boundaries

Consequences for the regions closer to Earth: change in the period of the waves transmitted along the Earth's magnetic field lines; waves can be transmitted closer to Earth

Future work

- How do the changes in the foreshock transmit to the other regions of the near-Earth space? Do they affect the coupling between the different regions?
- Are there deviations between predicted and observed levels of disturbances in the near-Earth space when the foreshock develops in front of it?

Acknowledgements

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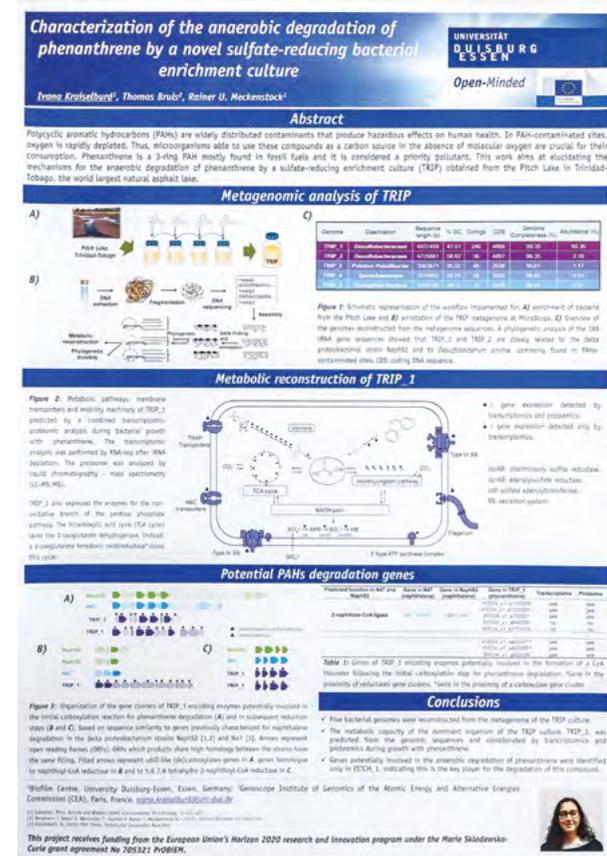


Anaerobic degradation of phenanthrene by a novel sulfate-reducing bacterial enrichment culture

Polycyclic aromatic hydrocarbons (PAHs) are widely distributed contaminants that produce hazardous effects on human health. In PAH-contaminated sites, oxygen is rapidly depleted. Thus, microorganisms able to use these compounds as a carbon source in the absence of molecular oxygen are crucial for their consumption. Phenanthrene is a 3-ring PAH mostly found in fossil fuels. This work aims at elucidating the mechanisms for the anaerobic degradation of phenanthrene by a sulfate-reducing enrichment culture (TRIP) obtained from the Pitch Lake in Trinidad-Tobago, the world largest natural asphalt lake.

The metagenome of TRIP was sequenced and annotated at the Microbial Genome Annotation & Analysis Platform, Genoscope. Five bacterial draft genomes were reconstructed from the metagenome sequences. The key player of TRIP belongs to the Desulfobacteraceae family of deltaproteobacteria. Analysis of the metabolic capacity of this bacterium revealed the key enzymes for dissimilatory sulfate reduction, a complete Embden-Meyerhof-Parnas pathway for oxidizing glucose to pyruvate and a complete tricarboxylic acid cycle. This bacterium also presents the key genetic elements of the classical pentose phosphate pathway for NADPH and pentose synthesis and of the Wood-Ljungdahl pathway for the complete oxidation of acetyl-CoA. The predicted metabolic pathways were corroborated by transcriptomics and proteomics analyses of the TRIP culture during growth with phenanthrene. Sequence similarity to genes previously characterized for naphthalene degradation allowed identifying two gene clusters encoding a carboxylase enzyme potentially involved in the activation of phenanthrene and genes encoding reductases potentially involved in subsequent ring dearomatization and reduction steps.

This work provides evidence of the pathway involved in the anaerobic biodegradation of a highly toxic PAH.



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Role of bacterial enzymes in the transition from free living to plant endophytes and the design of efficient biofertilizers

One of the main challenges for humanity is to increase food production while using scarce resources and protecting the environment. Plant's productivity can be enhanced by the activity of Plant Growth-Promoting (PGP) bacteria, applied as biofertilizers. Biofertilizers have been applied during decades, but in many cases bacteria with great potential in lab, fail when applied in natural soils (probably they are out-competed by the native microbiota or unable to adapt to the environmental conditions).

In the Rhizobium-legumes model, bacterial cellulases are crucial in the bacterial entrance into the root. Nevertheless, the implication of these enzymes in the active entrance of bacteria in non-legume crops has not been studied yet. This project aims to research the role of bacterial enzymes in the capability of endophytes to enter non-legume plants, using rapeseed as model. If any enzymes enable active root infection, giving an advantage over passive mechanisms, selection of bacterial strains not only on the base of their PGP capacity, but also on their ability to enter the plant -with less competitors and protected from abiotic stresses-, will allow the design of more efficient biofertilizers.

Preliminary results show that several rapeseed bacterial endophytes with PGP traits are also able to produce hydrolytic enzymes. When inoculated over seedlings, some of them are significantly promoting plant development. Moreover, electronic microscopy shows their ability to greatly colonize roots. These bacteria have been chosen to make a transcriptomic study to compare gene expression in free living bacteria and in those attached to the root surface to identify genes implicated in the plant root entrance. Future construction of mutant strains will allow unravelling these genes' role in plant root entrance.

Role of bacterial enzymes in the transition from free living to plant endophytes and the design of efficient biofertilizers
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According to FAO's estimations, in 2050 there will be an additional 2.3 billion people in the Planet, who will require producing more food, while at the same time combating existing poverty and hunger. Chemical fertilizers increase crops yields, but they have negative effects for human and animals health and their fabrication contributes to Global Warming. Plant's productivity can be enhanced by the activity of plant growth-promoting (PGP) bacteria, which are naturally-occurring bacteria able to modulate plant growth as a result of their metabolic activities (Fig. 1). PGP bacteria can be applied in agricultural production as biofertilizers as an environmental friendly manner to increase crops yields. Thus, bacterial PGP mechanisms have been objective of many research studies. Nevertheless, apart from rhizobial strains applied to legume crops, most of the biofertilizers designed based on *in vitro* studies fail when applied in the fields. This failure could be due to the fact that, once applied in the soil, *in vitro* selected PGP bacteria must compete with a wide variety of microorganisms present in the soil and get adapted to the different abiotic conditions of each environment. This fact rises the interest of the PGP potential of bacterial endophytes: those bacteria with the ability to enter the endosphere (root inside) -since, once inside the plant, they do not need to compete with the dense population of bacteria in the rhizosphere and they are protected from extreme abiotic conditions.

Nevertheless, endophytic colonization, apart from the well-studied interactions between rhizobia and legumes, is less well understood. The understanding of the mechanisms by which endophytes actively enter roots will likely allow great progress in the wide selection of bacterial strains which can act as efficient biofertilizers in non-legume crops. The aim of BIOENZYCELLULASER is to shed further light on these bacterial mechanisms to enter the root, becoming endophytes, using rapeseed as a model plant and focusing in the role of bacterial enzymes implicated in the hydrolysis of plant cell wall compounds. Hypothesizing that these enzymes could open an entrance for some PGP bacteria to the root inside.

For that, we collected rapeseed plants from two localities with tradition in the cultivation of this crop. Root bacterial endophytes were isolated following different protocols and using different growth medium. We isolated 118 bacterial and we screened them for several PGP traits, as P and K solubilization, siderophore, and ACC deaminase production and capability to produce cellulose and form biofilms, as well as we tested their capability to hydrolyse plant cell compounds, as cellulose, xylan, pectin and starch (Fig. 2). Based on this characterization, we selected 14 strains to check their capability to promote rapeseed seedlings (Fig. 3). Moreover, we obtained their 16S-DNA gene sequence to identify those bacteria at species level. The best PGP strains belonging to non risk for human and environmental species were selected for further studies. Electronic microscopy shows the great potential of the selected strains to colonize rapeseed roots (Fig. 4).

The ongoing transcriptomic study will show which bacterial genes are overexpressed over the root surface. Future mutations overexpressed genes, specially those encoding hydrolytic enzymes, allow the study of their implication in the plant root entrance.

Fig. 1. Schematic representation of Plant Growth Promoting Mechanisms of Bacterial Endophytes (García-Fraile et al., 2012)

Fig. 2. Analysis of PGP mechanisms. 14 Bacterial production strains screened (Alejandro and Zaki, 1991) 16. Cellulose production (García-Fraile et al., 2012). 17. Xylan solubilization (Singh et al., 2004). 18. Cellulose production (García-Fraile et al., 2012). 19. Pectinase production (García-Fraile et al., 2012). 20. Starch production (García-Fraile et al., 2012). 21. Biofilm production (García-Fraile et al., 2012). 22. Siderophore production (García-Fraile et al., 2012).

Fig. 3. Analysis of plant growth promotion quality of strains selected.

Fig. 4. Electronical microscope images showing the capability of selected strains to adhere and colonize rapeseed roots.

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Trait profiling of the floral nectar acinetobacters by phenotype microarray technology

Phenotypic heterogeneity is an important aspect of the biology of microorganisms which determines their niche and ecological roles. High-throughput screening tools such as Biolog's Phenotype Microarray (PM) technology have enabled efficient testing of a large number of cellular phenotypes. Basically, this technology consists of 96-well microplates with pre-arrayed sets of phenotypic tests (e.g. assimilation of diverse nutrients and tolerance to inhibitors) and an accompanying automated OmniLog incubator/reader. Response to the test conditions is then assessed through reduction of a tetrazolium dye and/or biomass increase over a time course.

Our ongoing MSCA project [1] involves the phenotypic profiling of a large collection of Acinetobacter (Gammaproteobacteria) isolates obtained from the floral nectar of diverse angiosperms from different geographic locations. Custom-designed microplates were assembled using diverse carbon and nitrogen sources in relevant concentrations (1% and 0.06%, respectively, as previously used for nectar yeasts) and a selection of inhibitors. Cells were starved for the substrate category of interest prior to inoculation of PM plates, which were then incubated at 25°C for 96 h. Biomass increase in each well was registered every 15 min and the data collected over time was summarized and used to estimate different kinetic parameters using the OPM package in R. Our results showed that the core diet of tested isolates included a limited number of amino acids and sugars such as sucrose and fructose. Surprisingly, most Acinetobacter isolates were unable to utilize glucose, which is a relatively abundant carbon source in floral nectar. Tolerance to diverse plant toxins (aucubin, catalpol, caffeine, digitonine and ouabain) but not to $\geq 5\%$ sodium chloride was widespread. Next steps in the project will involve the analysis of inter- and intra-species phenotypic variability as well

as the study of the phylogenetic signal of the studied traits.

[1] http://cordis.europa.eu/project/rcn/208553_en.html

The poster features logos for KU Leuven, RICE, The University of Tokyo, UC Davis, and Stanford University. The title is prominently displayed at the top. Below the title, the authors' names are listed. The poster is divided into several sections: 'BACKGROUND' explaining the importance of phenotypic heterogeneity and the use of PM technology; 'AIM' to explore the phenotypic landscape of Acinetobacter species; 'STUDY SYSTEM' describing the collection of isolates from diverse geographic locations; 'METHODS' showing a flowchart of the process from collection to data analysis; 'KEY RESULTS' listing findings on carbon sources and toxin tolerance; and 'NEXT STEPS' regarding phylogenetic analysis. A funding acknowledgment from the European Union is also present.

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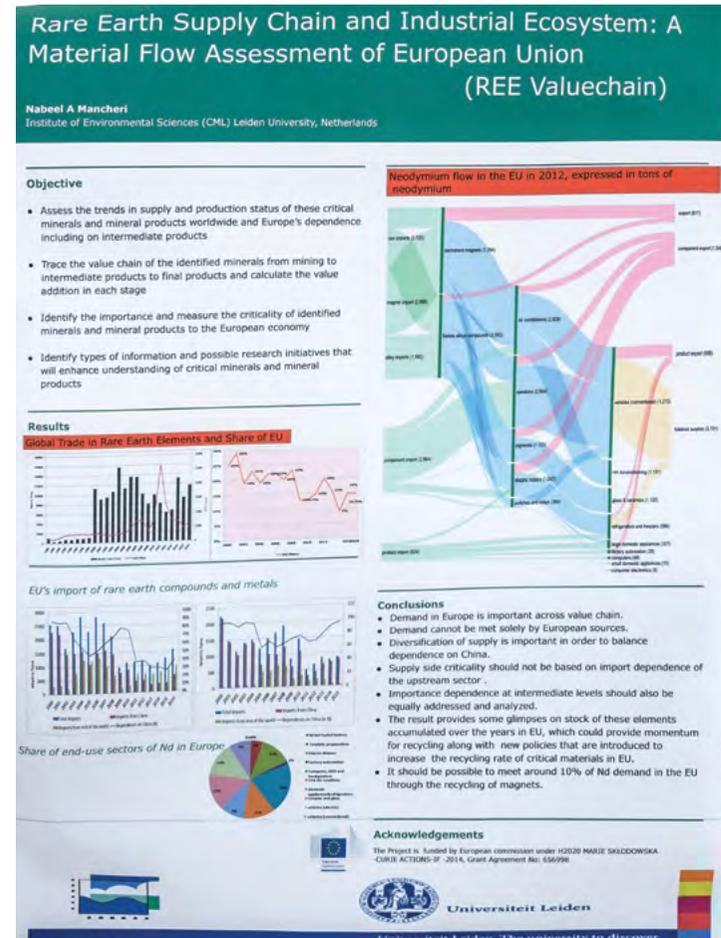
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Rare earth supply chain and industrial eco system: a material flow assesment of EU

Rare earths are a critical component of many high and green technologies such energy efficient lights, wind turbines, hybrid and full electric vehicles (electro motors and batteries) and solar panels and are important ingredients in hard disks, lasers and superconducting magnets. The concentration of rare earth elements (REEs) and other critical metals in countries like China and Russia raises the vital issue of security of supply as Europe is the leading importer and consumer of these minerals both in mineral and applied forms. The criticality of these minerals were highlighted in the reports of the European Commission's Ad hoc Working Group on defining critical raw materials. These raw materials are fundamental to Europe's economy, growth and jobs. The importance of these minerals to the European economy has never been studied thoroughly, though more recently securing reliable, sustainable and undistorted access to crucial non-energy raw materials has been of growing concern. In the EU, responses have been initiated in different nations, economic areas and companies, with the European Commission launching the "Raw Materials Initiative (RMI)".

The European Commission has identified criticality of raw materials along with addressing the entire raw materials value chain in the raw materials part of the Societal Challenge 5 of Horizon 2020. Therefore an empirical study on rare earth elements and its importance to the European economy become an important issue to study. This study aims to identify the mineral sources, mineral production and recycling technologies, as well as key applications within European economies by combining the input-output matrix. The study will calculate the value addition at each stage of the life cycle of rare earths.



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SOCIAL SCIENCES & HUMANITIES

Research Program: Studies on Intermediality and Intercultural Mediation

SIIM is a Research Group of Excellence based at Universidad Complutense Madrid (Spain).

Its Mission/Values are: The study of artistic forms as metacognitive tools; Strategic Storytelling and Creative Writing for Social Innovation (i.e. empowerment of marginal groups); International Cooperation and Intercultural Mediation; Sociological impact of World Literature(s); Research on multimodal social semiotics and intersubjective cognition; Intermedial studies, translation, re-mediation, adaptation; cross-cultural aspects attached to Social Sciences and Humanities; Teaching Innovation (i.e. practice in academic publishing).

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The group hosts two journals and a book series.

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Emotion regulation as a transdiagnostic factor in children and adolescence psychopathology

Most mental health disorders, including depression, substance abuse, eating disorders and anxiety have their onset during adolescence (Kessler et al., 2007). It has been argued that this peak in psychopathological symptoms is a result of developmental changes, which hamper adequate emotion regulation (Dahl, 2004). Cross-sectional studies have indicated that emotion regulation deficits precede the emergence of psychopathology, however, longitudinal evidence is missing.

My PhD will investigate the role of emotion regulation difficulties in the development of adolescence psychopathology in a large sample of children. More specifically, I will look at a) emotion regulation as a predictor of later psychopathology, b) factors influencing multifinality (i.e., similar emotion regulation habits resulting in different symptom exhibition) and c) heterotypic continuity (i.e., emotion regulation difficulties at different times in the development resulting in different outcomes).

Data will be derived from the Millennium Cohort Study, which examines various mental health and environmental correlates of 12,347 children living in the UK, starting in 2000.

Following this, I will investigate how emotion regulation difficulties can be improved as means to treat and prevent mental illness in youth. As part of this a mobile app will be co-produced with young people, to assess and assist young people's emotion regulation in their daily life.

Mobile apps present promising means to effectively administer mental health interventions to young people and to collect longitudinal, context specific

data, which will add significant insights to current mental health research. The project is expected to elucidate emotion regulation processes within a developmental psychopathology framework and to inform the development of a digital, youth -adequate mental health intervention.

Targeting Emotion Regulation as a transdiagnostic factor in youth psychopathology
Bettina Moltrecht, Julian Edbrooke-Childs and Jessica Deighton
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Introduction
Adolescence is a vulnerable age for the experience of mental health problems. Research indicates that most mental disorders, including depression, substance abuse, eating disorders and anxiety have their onset before the age of 18. It has been argued that the peak in psychopathological symptoms is a result of developmental changes, which hamper adequate emotion regulation (ER). ER is an extremely dynamic process, however most studies have assessed it in cross-sectional designs. Due to the absence of high quality longitudinal studies, we still lack a good understanding of its role in the development of psychopathology, especially in youth.

Emotion Regulation as a transdiagnostic factor
The first DSM-IV (1994) classified mental disorders into 166 distinct disorders (DSM-5, however, the picture became increasingly complex, accumulating more symptoms and comorbidities). Do the current DSM-IV (2013) differences between 2007 different disorders? Extensive work on transdiagnostic, overlapping symptomatology and risk factors suggest that our current diagnostic models (DSM) reflect the latent structure that underlies existing mental disorders. Transdiagnostic approaches attempt to address the latent structure by identifying core processes that underlie multiple disorders. Emotion regulation (ER) has been suggested to form one of these. Research supports its importance in the development and maintenance of psychopathology and more importantly its change measurement in psychological interventions. Limited, but promising evidence exists for the effectiveness of transdiagnostic interventions in improving core and comorbid symptoms. More research needs to explore the impact of ER as a transdiagnostic factor in the prevention and treatment of youth psychopathology.

Part I - Millennium Cohort Study
• 12,347 children from the UK since 2000
• 5 data assessment points at age 3, 5, 7, 11 and 14 years

Measures:
• Strength and Difficulties Questionnaire (SDQ) ages
• Child Social Behavior Questionnaire (CSBQ) ages 7 years
• SES, parental mental health, parenting, social adversity (3 measures)

Data Analysis
Structural equation modelling will be performed. Emotion regulation and psychopathological symptomatology will be measured in latent variables.

Research Questions:
• What is the association of ER and mental health at each age?
• Does change in ER predict change in mental health?
• Are there critical age periods?
• Which developmental trajectories exist? Are they linked to current ER difficulties?

Part II - Systematic Review
The systematic review addresses the following research questions:
1) Do healthy psychological interventions effectively improve ER in young people?
2) Are improvements in ER associated with changes in psychopathological symptoms?

Part III - Prototype development
Experience sampling method
An integrative experience sampling tool will shed light on daily emotion regulation processes and potential factors that impact emotion regulation and psychopathological symptomatology.

Co-design workshops
Workshops with young people will complement the outcomes of Part I and Part II and will inform the content and design of the app. Mental health concepts and ideas will be discussed during the workshops with the young people. The final aim is to design emotion regulation strategies that are proposed by adolescents with existing research evidence.

Pilot studies
Will be performed for 8 weeks each with 20 adolescents in the age of 13-17 years. Participants will be recruited via schools, and community centres. Results will provide insights about feasibility, potential barriers and effectiveness of the app.

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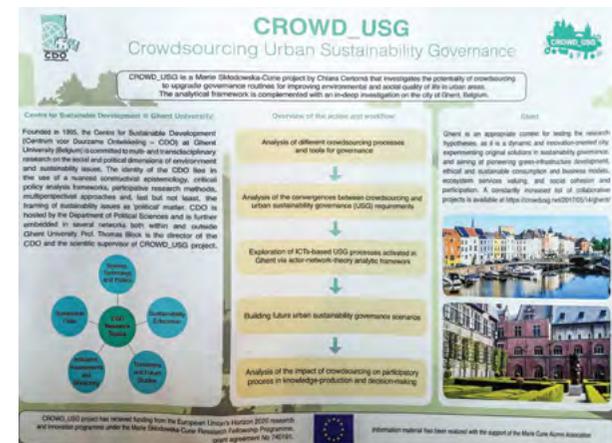
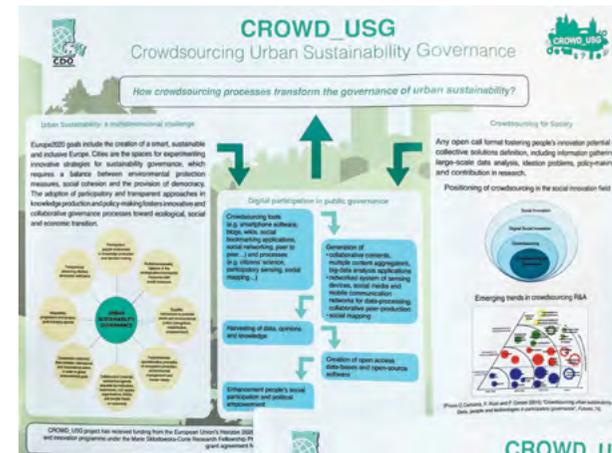
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CROWD_USG Crowdsourcing Urban Sustainability Governance

How crowdsourcing processes can advance real participatory knowledge and policy-making processes in the governance of urban sustainability?

This is the key question investigated in the CROWD_USG project, a Marie Skłodowska-Curie research project by Chiara Certomà exploring how increasing ICT-people interactions are transforming the way in which citizens take part in the production of information, sharing of knowledge and decision making about the planning and management of environmental issues in their city.

In the recent decades cities attracted scholars and practitioners' interest as the appropriate space for experimenting innovative strategies for urban sustainability governance, which requires a balance between environmental protection measures, social cohesion and the provision of democracy. Special attention is now devoted to the adoption of participatory approaches, and the web 2.0 architecture for data collection & sharing through peer-to-peer and wiki-technologies has been exactly welcomed as a shortcut toward the democratisation of governance processes. Particularly crowdsourcing can impact on governance model by fuelling the integration of environmental, social and economic priorities in the urban governance agenda; and by reviewing the mode of interaction between governing bodies, research institutions, business and social actors. This can lead to the attainment of sustainability goals, by generating citywide technological leap-frogging and community-based decentralised knowledge and policy production systems.



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SOCIAL SCIENCES & HUMANITIES

Innovation through cooperation between industry and university

Siemens Industry Software and KU Leuven share a long history of joined research and cooperation which is build upon mutual respect for each other's identity and KPI's. Combined with appropriate levels of transparency and openness on both content and strategy, a wide range of tools and approaches is used in continuously shaping and further cultivating the golden partnership. This allows both SISW and KU Leuven to keep on advancing the industrial state-of-the-use and scientific state-of-the-art in mecha(tro)nic system design and analysis.

Innovation through cooperation between industry and university:
Siemens Industry Software – KU Leuven; a golden partnership

Henri Karhula, Claus Claeys, Bert Pluymers, Herman Van der Auweraer, Wim Desmet

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Milestones

- 1970** Experimental Modal Analysis developed
- Spin-off creation: LMS
- KU Leuven headcount: ~10; LMS hc: 3
- 1980** Focus on Test/NVH
- First ISMA seminar and conference
- 1990** Vibro-acoustic modeling research
- Focus hybrid Test/CAE
- 2000** Aero-acoustics research
- Multi-body dynamics research
- Mechatronics research
- Focus on Test and Mechatronic Simulation
- 2010** LMS Int. acquired by SIEMENS
- Focus on Systems Engineering
- KU Leuven headcount: ~100; SISW hc: ~1500 worldwide

Tools and Approaches

Cooperation can be developed at different levels of commitment and at different levels of innovation. In view of creating awareness for state of the use technologies and challenging educational programmes, approaches such as joint MSc theses, lectures in the university curriculum, company visits and hard-and software tools support in education schemes are set up.

Towards more research-based cooperation, collaboration occurs via approaches such as Dual Desk PhD's¹, joined EU training projects or joined PhD courses, shaping future research leaders and innovators.

In view of product/process innovation at different TRL, collaboration schemes such as joined Flemish and European collaborative R&D projects, industrial support in academic basic research projects via user groups and bilateral strategic cooperation are pursued.

Based on mutual trust and understanding, further intensification of the collaboration is supported by collaboration framework agreements towards joined developments and university chair programmes.

Key in all of the above is the required proper mindset and willingness to collaborate by individual PEOPLE at all levels within both organisations.

¹ as currently investigated in www.science2society.eu

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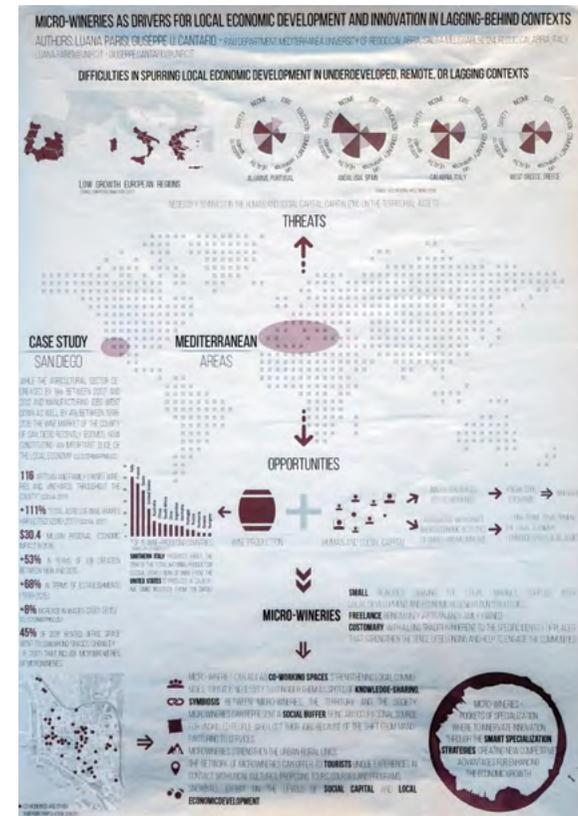
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Micro-Wineries as Drivers for Local Economic Development and Innovation in lagging-behind contexts

Today, there is increasing awareness of the role that social capital can play in spurring Local Economic Development especially in underdeveloped, remote, or lagging contexts. It encompasses different aspects, such as relationship networks, allowing knowledge exchange and innovation boost, and is associated mainly with craft-based economic activities of small and medium-size, entrusted with the long-term development of the local economy and embedded into local societies. Micro-wineries represent a good example, being small realities that serve especially the local market, acting also as co-working spaces that strengthen local communities. Mediterranean regions have commonly been connected with these sectors; nevertheless, only recently, wine and oenological tourism have been coupled with local development and economic regeneration strategies. This study aims at pushing the body of knowledge in the development of micro-wineries in Southern Italy and, more generally, in lagging-behind contexts of Southern Europe, trying to regenerate the existing realities, creating spots of knowledge-sharing where also tourists can live experiences in contact with local cultures. Micro-wineries can constitute the pockets of specialization where to innervate innovation through the Smart Specialization Strategies framework, that helps creating new competitive advantages for enhancing the economic growth. In order to support the discussion, the San Diego wine cluster will be deepened as a case study, since its wine market recently boomed, challenging the historic worldwide producers and constituting an important slice of the local market. Findings from the research highlight the micro-wineries symbiosis with the territory and the society itself. Positive relations between them and the broad regional innovation strategy emerge as well, showing the snowball effect on the levels of social capital and Local Economic Development in lagging contexts.

Useful lessons are drawn for encouraging policy makers and planners in undertaking actions towards strengthening the potential of micro-wineries and building networks among them.



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