Imperial College London

# Chemical Engineering PhD Symposium

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**Opening Lecture by Professor Joaquim M. S. Cabral,**

**Instituto Superior Técnico, Portugal:**

**"Bioprocess engineering strategies for stem cell-based therapies and regenerative medicine"**

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**Monday 27 June 2016, 9.30-17.00h**
**Lecture Theatre 1, Department of Chemical Engineering (ACEX 250)**

**Poster Presentations in the Design Rooms,**
**Department of Chemical Engineering (ACEX 306-312)**

***The symposium will be followed by a drinks reception in the Design Rooms***

**Acknowledgments**

We are most grateful to our major sponsors for their financial support of the research in our Department.



















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## Mapping the Aggregation Behaviour of Biopharmaceuticals: A New Approach

**Presenter:** Sarah Hedberg

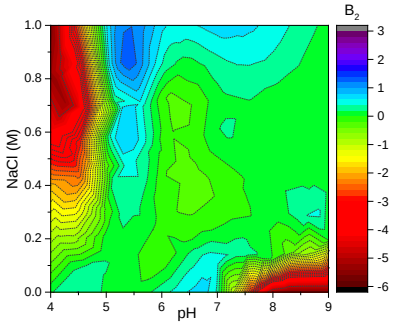
**Supervisors:** Jerry Heng, Daryl Williams

**Abstract:**

Protein aggregation is a critical problem for the safety of biopharmaceuticals as they are linked to adverse immunologically related responses in patients. Much effort has been made to gain a better understanding of aggregation, however, the mechanisms leading to protein aggregation are still not fully understood. Protein-protein molecular interactions in solution are known to be involved in protein solution aggregation behaviour and are a common issue for the manufacturing of biopharmaceuticals such as monoclonal antibodies, mAbs. Therefore a major industrial and academic challenge is the development of fast and reliable methods, either theoretically or experimentally driven, which allow formulation scientists to identify optimal biopharmaceutical species and solutions conditions which deliver stable solution products, thus avoiding aggregation.

In this work I will describe a SIC (self-interaction chromatography) method for determining the osmotic second virial coefficient ($B_{22}$), where $B_{22}$ describes the thermodynamics of protein-protein interactions in solution. This experimental biophysical approach allows solution stability maps including solution pH, salt concentration effects to be obtained using µg quantities of species such as mAbs. This approach has been validated against traditional size exclusion chromatographic methods on samples that were aged over many weeks at elevated temperature. Both methods gave similar stability condition maps, with the SIC method delivering results within days compared with traditional stability trials which would typically take many months. Over a wide range of test conditions good correlations were found between experimental $B_{22}$ values and experimentally measured aggregation rates. It is concluded that improvement in the SIC methods reported here allows the accurate and robust mapping of solution stability conditions.

Figure 1. Stability mapping of a mAb using SIC




Stable

Unstable

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## Towards Continuous Biomanufacturing: *through the prism of computational tools*

**Presenter:** Maria Papathanasiou

**Supervisors:** Sakis Mantalaris, Stratos Pistikopoulos

**Abstract:**

The current paradigm in monoclonal antibody (mAb) production indicates a shift toward continuous operation, aiming to increase process productivity, decrease cost and design eco-efficient processes. Such continuous biomanufacturing will provide a steady-state operation, where product purity would remain constant throughout the process (Zydney, 2016). In addition, a shift to continuous operation will significantly decrease the capital equipment cost, while it will yield operations of higher productivity and improved product quality as the equipment will be running with greater uniformity. In-silico simulation and/or optimization of such processes can provide valuable insight in the process capabilities and limitations and effectively contribute to the realization of those aims (Kiparissides et al., 2011).

In this work, we are presenting the development of a powerful tool for the in-silico integration/intensification of mAb production, considering the fed-batch culturing of GS-NS0 cells and the semi-continuous Multicolumn Countercurrent Solvent Gradient Purification (MCSGP) process (Krättli et al., 2013, Papathanasiou et al., 2016). We follow the PAROC framework/software platform (Pistikopoulos et al., 2015) that features: (i) development of a high-fidelity process model, (ii) approximation of the complex, process model, (iii) design of the multi-parametric controller, (iv) 'closed-loop', in-silico validation of the controller against the process model.

**References**

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## Cascading effects in bioprocessing: The impact of cell culture environment on mammalian cell behaviour and host cell protein species

**Presenter:** Cher Hui Goey

**Supervisor:** Cleo Kontoravdi

**Abstract:**

**Background and Novelty**

Protein purification downstream of mammalian cell culture currently accounts for up to 80% of total production cost. One of the major challenges is to remove host cell proteins (HCPs) – they are immunogenic contaminants originating from the host cells. A Quality by Design strategy to overcome this purification challenge is to reduce the amount of HCPs entering the downstream train by tracing their source back to upstream culture. Previous studies have found that cell culture decisions, e.g. harvest time and culture temperature; impact HCP content at harvest significantly. However, this approach is currently constrained by our limited understanding of the dynamic host cell environment and complex physiological state. For example, we do not yet know how the host cell coordinates and regulates the molecular machinery under different culture environment, which results in different HCP profiles observed downstream.

**Experimental Approach**

Understanding the interplay between upstream cell behaviour and downstream purification requirements will open up the door for improvements in overall production efficiency. This study presents experimental results showcasing how culture temperature and harvest time impact the key process indicators, including the HCP content in CHO cell cultures. The study follows not only cell growth, but also cell cycle distribution and cellular wellbeing.

**Results and Discussion**

Cells appeared to be more robust under mild hypothermic conditions: (i) more than 90% of cells were maintained in healthy state until day 14, and (ii) the onset of apoptosis was less evident compared to the results for physiological temperature. Temperature shift, introduced on day 5, induced temporary cell cycle arrest in G0/G1 phase. However, this significantly reduced the rate of nutrients uptake, especially of glucose, which led to an overall reduction in recombinant protein productivity. Despite having robust cells, the HCP concentration in mild hypothermic culture was similar to that under physiological temperature on harvest day. Therefore, it is important to investigate the source of HCPs present in supernatant under these two culture conditions. Our current work includes identification of these HCP species using LC-MS/MS.

## Development of a multiscale model to investigate the dissolution of clots in patient-specific geometries during thrombolytic therapy

**Presenter:** Andris Piebalgs

**Supervisor:** Yun Xu

**Abstract:**

**Objectives**

The formation of abnormal blood clots in the vasculature can lead to the development of an embolus that restricts blood supply to human tissue and causes necrosis. These types of diseases are known as thromboembolisms and are a major cause of heart attacks and strokes that cumulatively account for over 20% of global mortality rates. One form of treatment that is available is thrombolytic therapy whereby the occluding blood clot is dissolved via a drug infusion. However, this therapy can be ineffective in certain scenarios and can potentially cause life-threatening side-effects. Mathematical modelling can help in elucidating the parameters that affect treatment outcome and can also help in optimising current and future treatment methods of thromboembolic diseases.

**Methods**

In this work, blood flow is described by using fluid mass and momentum conservation balances where blood is defined as a Newtonian fluid and the flow is assumed to be laminar. The movement of the thrombolytic drug and its kinetic interaction between other proteins is solved by using convection-diffusion-reaction transport equations. The blood clot is defined as a porous medium where the macroscopic properties of each segment are calculated by evaluating changes in the clot microstructure. A physiological pulsatile flow is imposed on the domain inlet while a pressure that is proportional to the resistance of the downstream vasculature is imposed at each outlet. The surrounding walls are assumed to be rigid and non-slip.

**Results**

Work carried out thus far has yielded a mathematical, multiscale model for evaluating the dissolution of a single occluding clot within a two-dimensional channel that is subjected to a range of pressure drops [1]. This model has subsequently been improved in order to compare clot dissolution in a patient-specific geometry obtained from computed tomography (CT) images against a corresponding idealised 3D geometry. As a result, it was determined that the vessel geometry significantly impacts clot dissolution patterns and the formation of mural clots. These are important in determining the likelihood of artery reocclusion and the development of secondary emboli.

**Future Work**

The current multiscale model will be modified to take into the account the influence of shear forces on clot dissolution. Furthermore, the impact of different clot morphologies and compositions on clot dissolution will be investigated.

**References**

[1] Piebalgs, A. et al. *J. R. Soc. Interface*, DOI: 10.1098/rsif.2015.0949.

## Towards the Design of Optimal Reaction Conditions: Predicting Temperature and Solvent Effects

**Presenter:** Aikaterini Diamanti

**Supervisors:** Amparo Galindo, Claire Adjiman

**Abstract:**

Reaction conditions, such as temperature and solvent, in which a given reaction is conducted can influence significantly the rate, selectivity, stability and overall process performance.[1] However, making an informed choice is challenging given that there is no universal model for predicting temperature and solvent effects on reactions. Experimentalists can spend significant amounts of time to optimise a given reaction outcome in the laboratory. As a result, the suitability of computational methods to predict the effect of temperature and solvent on a reaction is of great interest. Furthermore, if such methods are to enable the design of optimal environmental conditions in order to attain desired values for specific performance measures, one must balance computational cost and accuracy: the combination of quantum mechanical calculations with computer aided molecular design (QM-CAMD) techniques to find optimal reaction conditions is particularly appealing in this context. The QM-CAMD technique has been successfully applied for solvent effects to a Menschutkin reaction enabling the generation of a solvent that enhanced the rate of the reaction by 40% compared with the next best solvent that had been used previously.[2] The use of the continuum solvation model SMD of Marenich et al.[3] in that study was found to provide a useful basis for approximating the solvent within the QM-CAMD framework. Depending on the range of performance measures one is interested in, a reaction can be influenced by temperature and solvent in various ways. As a result, this work aims to assess the feasibility of predicting temperature and solvent effects on rate and selectivity of a reaction so that these aspects can be incorporated in the QM-CAMD. In order to do so, we undertake systematic studies combining predictions and kinetic experiments first in the gas and second in the liquid phase. In the gas phase, we target a hydrogen abstraction reaction between ethane and hydroxyl radical which is of a significant interest in areas such as combustion and atmospheric chemistry and for which an abundance of experimental data is reported in the literature[4] for the temperature range 210-1230 K. We focus on a thorough computational investigation of the temperature dependency of the reaction rate constant, using a broad range of electronic structure methods with various basis sets. Very good agreement with experimental kinetic data is achieved using the M05-2X/cc-pV5Z level of theory for the entire temperature range. Our results are further combined with the existing experimental data[4] to derive parameters for correlative models of the Generalized Arrhenius form. We show in particular that it is possible to derive an accurate hybrid model by combining the results from QM calculations with only four experimental points[5]. The hynrid model offers the advantage of carrying valuable information from QM calculations in its parameters and can prove particularly beneficial when studying reactions for which limited number of experimental data exists. In the liquid phase we focus on an interesting example of the solvent effects on selectivity reported in the literature for the Williamson ether synthesis of sodium *β*-naphthoxide and benzyl bromide.[6] The choice of solvent significantly impacts the selectivity of reaction for alkylation at either oxygen or carbon sites leading to *O*- or *C*-alkylated products, and determines the final product ratio. Density functional theory (DFT) electronic structure calculations are used to predict the rate constants for the Williamson reaction via the two possible pathways as well as to compute the final product ratio, with the solvent represented using the SMD solvation model. Twenty combinations of levels of theory are investigated. A diverse set of solvents of varying polarity is used and detailed kinetic experiments involving in situ $^{1}$HNMR data acquisition are carried out to assess the predictive results. The performance of the various models is discussed and the challenges in conducting reliable experiments are highlighted.

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## Optimal operation of compressors in systems with large energy consumption

**Presenter:** Richard Oberdieck

**Supervisors:** Stratos Pistikopoulos, Sakis Mantalaris

**Abstract:**

In multi-parametric optimization, an optimization problems is solved for a range and as a function of certain parameters. Its relevance to process systems and chemical engineering has been shown primarily due to its applicability for advanced model based control, optimal hierarchical decision making under uncertainty and integration of design, control and scheduling in energy, process and biomedical systems.

In this presentation, I will highlight some new exciting developments in multi-parametric optimization and control, including (i) an algorithm for the solution and control of systems involving discrete and continuous variables and (ii) POP, a s software toolbox for the solution of all major classes of multi-parametric programming problems, which enables the execution of comprehensive computational benchmarking studies for the first time.

## Viscosity and Density of Synthetic Reservoir Fluids with Dissolved $CO_2$ for CCS Applications

**Presenter:** Claudio Calabrese

**Supervisor:** Geoff Maitland, Martin Trusler

**Abstract:**

Carbon capture and storage (CCS) is an emerging industrial technique which represents the best short-to-medium term option for significantly reducing $CO_2$ emissions into the atmosphere. Currently CCS research is very active and several demonstration plants have been built and/or designed worldwide.

Carbon storage in geological formations involves complex fluid mixtures comprising concentrated brines, hydrocarbons and $CO_2$ at high temperatures and pressures. Understanding and measuring the thermophysical properties of these systems is essential for developing models that are able to predict the storage performance. Viscosity and density are among the thermophysical properties of interest for characterizing reservoir fluid mixtures in the subsurface, developing predictive tools and monitoring post-injection. However, at present large gaps exist in the available experimental data pertaining to reservoir fluids at reservoir conditions. As a consequence, more research is needed in this area. For this reason, we have measured the viscosity and density of representative synthetic reservoir fluids with and without dissolved $CO_2$. The measurements were made in the single-phase compressed liquid region at temperatures between (274 and 449) K, at pressures up to 100 MPa, using a bespoke apparatus developed in our laboratory. The viscosity was measured with a vibrating-wire viscometer, while the density was measured by means of a vibrating U-tube densimeter. Measurements of the viscosity and density in the synthetic reservoir fluids under $CO_2$ addition were associated with relative uncertainties of 0.1 % for density and 2 % for viscosity.

Large temperature and pressure ranges were studied in order to cover conditions across reservoirs of different depths. These experimental data will be used as a benchmark in the research field. The results for both properties have been correlated as functions of temperature, pressure and the mole fraction of dissolved $CO_2$. In addition, the viscosity data will be used to calibrate and validate molecularly based models to predict the viscosity of ($CO_2$ + hydrocarbon) mixtures. These studies will benefit both the industrial field and academic research, where accurate viscosity and density data are needed.

**Acknowledgment**

We gratefully acknowledge the funding of QCCSRC provided jointly by Qatar Petroleum, Shell, and the Qatar Science and Technology Park, and their permission to publish this research.

## Rate Kinetics of $CO_2$ Capture with a Natural CaO-based sorbent in a Pressurised Fluidised Bed Reactor

**Presenter:** Joseph Yao

**Supervisors:** Paul Fennell, Geoff Maitland

**Abstract:**

Calcium looping is a high temperature solid looping process designed for $CO_2$ capture. The technology uses two reactors: the carbonator and the calciner. In the carbonator, a bed of calcium oxide-based sorbent reacts reversibly with $CO_2$ present in the inlet gas (typically flue gas from a power station) to form calcium carbonate at around 650 °C. The product, calcium carbonate is then cycled to the calciner (which operates at temperatures in excess of 900 °C) to undergo decomposition and release a pure stream of $CO_2$ while regenerating the calcium oxide. The calcium oxide is then cycled back into the carbonator. The work presented here involves both experimental work and modelling. The experimental aspect involves the use of a 3 kW bench-scale pressurised fluidised bed reactor to simulate the carbonator. A series of pressurized carbonation reactions were carried out to investigate the effects of mild pressurisation on the kinetics of carbonation under different temperatures and partial pressures of $CO_2$. A two-phase reactor model was then developed to simulate the experimental results using numerical methods in Matlab.

**Decontamination of Metal Treated Wood Waste and its Application in Biorefining Using Ultra-Low Cost Ionic Liquids (UCILs)**

**Presenter:** Florence Gschwend

**Supervisors:** Jason Hallett, Paul Fennell

**Abstract:**

The production of bulk fuels and chemicals from biomass faces several challenges, one of which is the high feedstock cost. To overcome this, waste biomass is being investigated as a low-cost alternative to pristine wood and specially grown crops. A proportion of construction wood is treated with various copper containing preservatives in order to prolong its lifetime.[1] Most prominently, chromated copper arsenate (CCA, Tanalith C) was used extensively until 2001 for outdoor applications. CCA treated timber can contain, in addition to copper, over 5000 mg $kg^{-1}$ of arsenic and chromium.[2] These preservatives pose a problem at the end of life, as they require costly specialist disposal of the metal treated wood as hazardous waste (Grade D, £120/tonne in the UK). Nowadays wood is mainly treated with more benign, yet still copper containing, preservatives such as copper azole (CA).

A number of ultra-low cost ionic liquids (UCILs) have been successfully used in the pretreatment of lignocellulosic biomass, yielding cellulose that can be hydrolysed and fermented to chemicals and fuels, and a separate lignin stream.[3] This process has now been optimised for pretreatment of metal-treated construction wood. Preliminary economic modelling shows that the profit margin of the UCIL pretreatment process can be almost doubled as a result of the reduced feedstock cost. CA and CCA treated wood was successfully pretreated, yielding highly digestible cellulose rich material with a glucose release of 76% and 52% for CA and CCA treated wood, respectively. We show that, in both cases, 98-99% of the metals could be extracted into the ionic liquid. The removal of metals from the cellulose pulp is especially crucial for a subsequent fermentation step. Copper concentrations exceeding 8mM are shown to result in the inhibition of glucose fermentation, corresponding to a maximum of around 1000 ppm of copper that can be tolerated in the initial biomass, which is lower than the 2000 ppm typically contained by copper treated timber, thus making copper extraction pivotal for successful fermentation. We were also able to demonstrate that redeposition of copper from ionic liquid liquor is easily achieved by applying an electrical bias.

In conclusion, ionic liquid pretreatment has been shown to effectively fractionate metal treated construction wood, resulting in digestible cellulose, a separate lignin stream and various metals dissolved in the IL solution, ready for electrochemical redeposition. This allows the use of metal treated wood waste for cost-effective second generation biofuels and bioderived chemicals.

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## Solar Energy-Driven Hydrogen Production and Sulfide Oxidation by Photo-Electrolysis

**Presenter:** Franky Bedoya-Lora

**Supervisor:** Geoff Kelsall

**Abstract:**

Solar energy harvesting using e.g. photovoltaic modules needs to be coupled to energy storage, because of the diurnal and intermittent nature of solar energy. Hydrogen is a candidate for such chemical energy storage, because of its facile oxidation in fuel cells that convert chemical energy directly to electrical energy. As in photovoltaics, semiconducting materials may be used to absorb solar photons generating electrons in their conduction band and highly oxidising 'holes' in their valence band.

However, unlike in 'solar cells', subsequent electrochemical reactions may be used to enable production of fuels, such as hydrogen. Splitting liquid water to produce hydrogen (and oxygen) using solar energy requires a minimum of 1.48 eV under isothermal conditions. Though the feasibility of such processes is well established, their practical application / large scale deployment has been delayed, because all the following requirements have yet to be met:

- Semiconducting materials adequately stable to decomposition by holes, electrons, $H^+$ or $OH^-$;
- Semiconducting materials well matched to the solar spectrum with economically acceptable photon-to-hydrogen efficiencies, the target being ≥ 10 %;
- Low cost electrocatalysts to enable such efficiencies to be achieved economically;
- Processes to produce acceptably efficient photo-electrodes at large scale and low cost;
- Suitable designs of reactors in which to deploy such materials.

Thermodynamically less energy intensive processes, such as hydrogen sulfide splitting that requires a minimum of only 0.27 eV, remain largely as a concept for lack of suitable semiconductors. Hydrodesulfurisation processes in the world's oil refineries use hydrogen to remove sulfur from oil products as (highly toxic and corrosive) $H_2S$, which has to be oxidised subsequently to sulfur at a scale of 64 million tonnes per year by Claus processes. The development of a photoelectrochemical reactor for hydrogen sulfide splitting would oxidize the undesirable hydrogen sulfide to polysulfides and subsequently to sulfur, and also produce hydrogen simultaneously. The overall reaction can be written as:

$$nH_2S + 0.5O_2 + (2n-2)h\nu \longrightarrow nS + H_2O + (n-1)H_2 \quad (1)$$

The talk will address briefly the issues of selecting a suitable semiconductor, the development of a model for reactor design for water and hydrogen sulfide splitting. It will be focused mainly on the advances in the understanding of hydrogen sulfide splitting using solar energy, polysulfide production and analytical quantification, and electrochemical characterization of hematite as a suitable semiconductor. A comparison against traditional water splitting will be presented (e.g. Figure 1), exposing the higher efficiencies and lower energy requirements of hydrogen sulfide splitting; but potential drawbacks such as material incompatibilities and difficulties of quantifying concentrations of polysulfides.

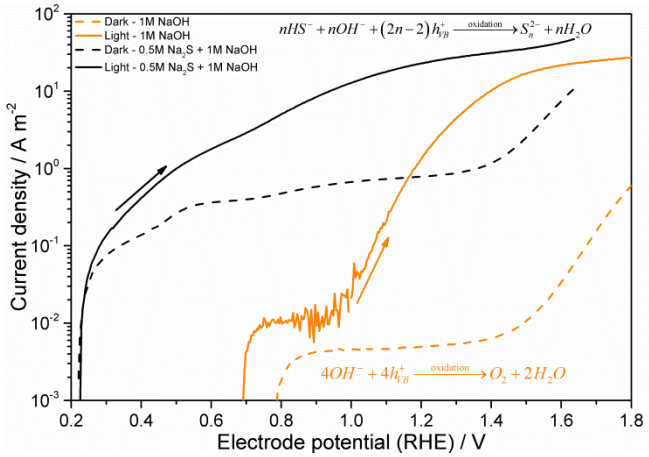


Figure 1. Linear sweep voltammograms for Ti | Sn-doped α-$Fe_2O_3$ | 1 M NaOH ± $Na_2S$ (pH = 14) | Pt | Ti under dark and illuminated conditions; 10 mV $s^{-1}$ scan rate. Xenon Arc lamp irradiance 560 mW $cm^{-2}$.

According to Faraday's law of electrolysis, the specific reaction rate (material flux) is proportional to the flux of electronic charge (current density, y-axis).

## Using Results from Electrical Power Contingency Analysis Studies to Develop Strategies for Flexible Electrical Operation in Process Plants

**Presenter:** Izzati Mohd Noor

**Supervisor:** Nina Thornhill

**Abstract:**

Concerns about the reliability of future electrical supplies are prompting changes in the operations of the electrical power system. Changes in consumption patterns due to electrification of process industries, and the lack of controllability of renewable generation sources are causing the degradation in the quality of electrical power system frequency. Frequency represents the balance between generation and consumption, and must be maintained at all times. Frequency stability is maintained by activating power reserves, which traditionally are generators. Researchers are now looking into the potential of electrical consumers to act as power reserves by providing demand-side response.

However, the full participation of industrial consumers in electrical grid operations are deterred by the lack of collaboration between power and process system engineers. This work presents an inter-disciplinary effort to bridge the gap between process and power system sides by exploring the interface between the two fields. The work proposes a methodology which uses results from power system studies to develop *flexible operation* strategies. Flexible operation is a demand-side response strategy whereby process equipment temporarily change their operating set-points to modify their power consumption as required by the electrical grid.

The proposed methodology involves three main steps. Firstly, the electrical network topology of the process plant is used to identify the *primary actuators.* Secondly, power system contingency analysis studies are performed, whereby faults such as loss of generator and transmission line faults are simulated, and the effects on the power system are evaluated. Results from these studies indicate the power imbalance in megawatts (MW), which also represent the change in power consumption required to restore frequency. Finally, these results are incorporated into the process model to evaluate the effects of power system faults on the process. This then allows process automation engineers to develop flexible operation strategies to restore frequency stability, without jeopardising the process.

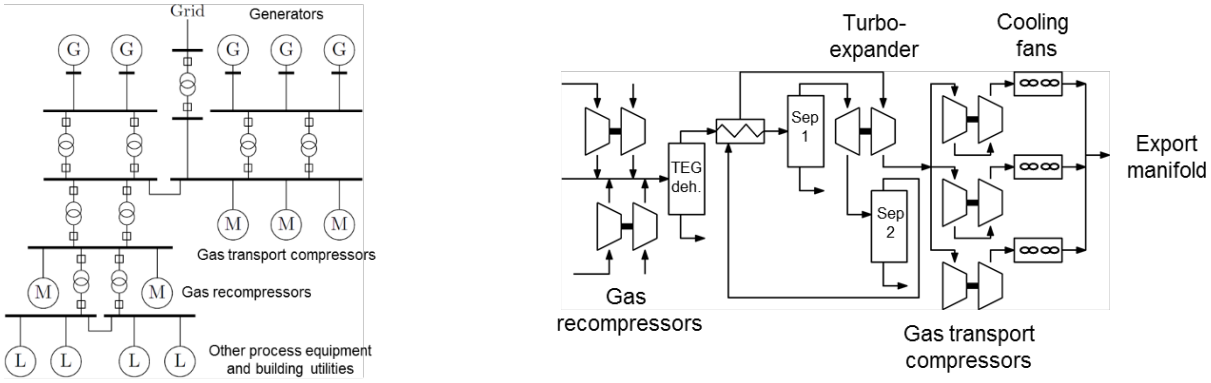


Figure 1: By means of a gas handling plant case study, the work demonstrates how process automation engineers can use results from power system studies based on the electrical network topology the plant (left) to develop flexible operation strategies for the site (right).

## Membrane Fabrication and Membrane Fouling for Low Salinity Water Reverse Osmosis

**Presenter:** Zhiwei Jiang

**Supervisor:** Andrew Livingston

**Abstract:**

Polyamide thin film composite (TFC) membranes are widely used in reverse osmosis (RO) process for waste water treatment, water softening, and low salinity water applications [1]. Typically, TFC RO membranes consist of a polyamide selective layer made from m-phenylenediamine and trimesoylchloride via the interfacial polymerization on an ultrafiltration support membrane [2, 3]. In practise, membrane fouling caused by scaling, protein, and nature organic matter has become one major obstacle which limits the membrane performance in terms of permeance, lifetime, and energy efficiency [4, 5]. The surface roughness of polyamide layer was reported to be one of the dominating factors for membrane fouling due to the valley clogging effect [6, 7]. In this study, controlled interfacial polymerization [8] was used to manipulate the surface morphology of the polyamide layer. The observed thickness of the polyamide layer was reduced from 100nm to less than 10nm, and the root mean square (RMS) roughness was reduced from 60nm to less than 1nm. The ultrathin and smooth polyamide layer was then used to study the effect of surface roughness in a nano-scale on membrane fouling and performance.

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## Hybrid biomimetic gold nanoparticles for cytoplasmic delivery enhancement

**Presenter:** Marie Bachelet

**Supervisor:** Rongjun Chen

**Abstract:**

Over the past decades, nanoparticles (NPs) have emerged as a new class of therapeutics to improve actual cancer therapies, often inadequate and lacking of specific action. A wide range of nanomedicine is currently under investigation. Among them, gold nanoparticles (AuNPs) are considered one of the most promising nanocarriers thanks to their unique optical properties which make them ideal theranostic agents combining drug delivery, photothermal therapy and imaging. Furthermore their reactive surfaces render them highly tunable with drug loading and active targeting abilities[1]. Although nanomaterials are usually able to successfully enter cells by endocytosis, the subsequent trafficking to the cytoplasm is generally hindered by the degradation in lysosomes. Synthetic polymers have been designed to mimic the role of the fusogenic viral peptides such as PP75 (75mol% of $_{L}$-phenylalanine grafted on poly($_{L}$-lysine iso-phtalamide)) which demonstrated high membrane disruptive ability at endosomal pH and successful cytoplasmic delivery of drugs *in vitro* and *in vivo*[2]. Herein, we report the preparation of a novel type of nanocarrier combining the advantages of AuNPs with the endosomolytic properties of the anionic amphiphilic PP75. To our knowledge this is the first time such hybrid NPs are reported[3]. The NPs exhibited excellent colloidal stability in buffer at physiological pH but upon pH decrease to pH 5, they agglomerated quickly due to the hydrophobic associations of PP75 layer as observed with the change of the hydrodynamic size, zeta potential and surface plasmon resonance properties. We also demonstrated a fast and almost complete reversibility of the process for a series of cycles. This may constitute a real asset for drug delivery increasing the local concentration around the tumour site which exhibits slightly more acidic pH than healthy cells[4], and leading to: (i) enhanced drug concentration; (ii) more heat generated during phototherapy and (iii) enhanced contrast for imaging. The reversibility is also fundamental to avoid the permanent aggregation of NPs in the body. In addition *in vitro* results showed a successful delivery of model drugs into the cytoplasm of HeLa cells after endosomal release and a low non-specific cytotoxicity effect after 24h incubation and up to 10nM NPs. These results demonstrated the potential viability of such hybrid NPs as drug nanocarriers and cytoplasmic delivery systems. We strongly believe that this study provides new insights for the development of responsive drug delivery platforms in nano-oncology.

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## Fabrication of soft functional surfaces via wrinkling

**Presenter:** Manuela Nania

**Supervisor:** João Cabral

**Abstract:**

Surface patterning is important for a range of engineering applications, including controlled wetting and spreading of liquids, adhesion and assembly of smart coatings. Patterns with feature sizes ranging from 100s nm to 100s of µm can be achieved using wrinkling of bi-(multi-)layers, a method which is inherently inexpensive, scalable and robust.

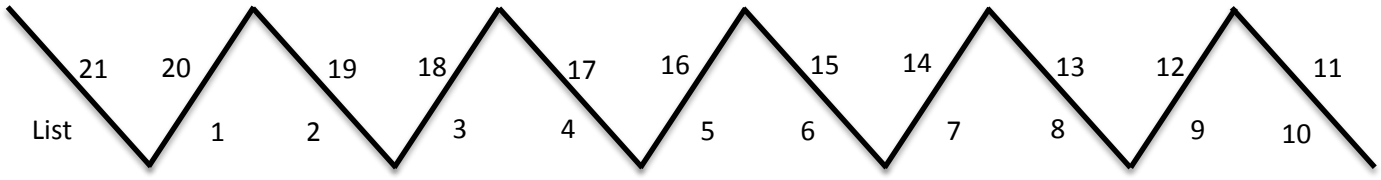
We study the surface oxidation of polydimethylsiloxane (PDMS) as a simple and effective method to obtain the bilayers. The process, carried via plasma exposure or ultraviolet ozonolysis (UVO), results in cleaving PDMS Si–$CH_3$ groups and the formation of a denser, $SiO_x$-rich glass-like surface layer. Wrinkling can then be induced by mechanical compression of the resulting "sandwich bilayers".

Oxidation via air plasma exposure was first investigated, and its consequences on surface wrinkling quantified. By appropriately tuning the process variables, we were able to obtain wrinkles with characteristic lengthscales down to 100 nm. The latter are of particular interest in the field of photonics. Wrinkles with lengthscales ~10s µm could be obtained when using UVO for PDMS oxidation. Patterns with characteristic dimensions in this range confer surfaces interesting properties in terms of wetting and spreading of liquids. By combining the two oxidation processes we were able to further enlarge the limits of PDMS oxidation for soft matter patterning, by reducing the minimum lengthscale attainable to ≈ 35 nm as well as creating hierarchichal patterns. These have showed to be particularly useful for the fabrication of superhydrophobic surfaces.

We further exploited wrinkling as a method for thin film mechanical characterisation. Specifically, we induced sinusoidal wrinkling on thin films drying on a PDMS substrate: by measuring the pattern dimensions we were able to infer the evolution of the film's elastic modulus, as it loses water. In this way, we overcame the difficulties associated with handling very thin free-standing films and the limited sensitivity of conventional methods. This time-resolved wrinkling interrogation during film drying emerges thus as a simple and reliable approach to determining evolving mechanical properties of films, with potential applications extending to coatings, personal care items, and foods.

## Poster presentations in the Design Rooms:

### Layout of Poster Boards




### List of Poster Presentations

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| **2** | **Mario Almeida Calado, 1st year** (Chris Tighe)<br>A Detailed Techno-Economic Model of the Hydrothermal Liquefaction of Lignin |
| **3** | **Aderlanio da Silva Cardoso, 2nd year** (Marcos Millan-Agorio, Klaus Hellgardt)<br>Use of water as a sustainable process for the depolymerisation of kraft lignin: influence of pressure and temperature |
| **4** | **Andrew Leung, 3rd year** (Klaus Hellgardt)<br>C6+ alcohols to primary amines |
| **5** | **Irina Harun, 2nd year** (Klaus Hellgardt)<br>Sesquiterpenoids Production by Green Algae: Nutrients Effect on Patchoulol Productivity |
| **6** | **Naima Ali, 3rd year** (Daryl Williams)<br>The Kinetics of Organic Molecule Diffusion in Water Swollen Keratin Fibres Using GC-MS |
| **7** | **Chenghong Wang, 3rd year** (Kang Li)<br>Ceramic hollow fibre supported metal-organic framework UiO-66 for adsorptive and membrane separations |
| **8** | **Fairus Rabuni, 1st year** (Kang Li)<br>Micro-structured Hollow Fibre for Micro-tubular SOFC |
| **9** | **Jason Chan, 2nd year** (Erich Müller)<br>A Multiscale Approach to Understanding the Behaviour of Asphaltenes |
| **10** | **Sara Shahruddin, 2nd year** (Erich Müller, Omar Matar, George Britovsek)<br>Molecular simulation of freezing of long alkanes via coarse grained molecular dynamics |
| **11** | **Lorena dos Santos de Souza, 2nd year** (Martin Trusler)<br>Measurement and Modeling of the Phase Behaviour of ($CO_2$ + CO) at Temperatures between (218.15 and 303.15) K and pressures up to 14 MPa |
| **12** | **Rayane Hoballah, 4th year** (Geoff Maitland, Martin Trusler)<br>Solubility of gases in water or brines at high pressures and high temperatures |
| **13** | **Kristian McCaul, 3rd year** (Nilay Shah, Cleo Kontoravdi, Yun Xu)<br>Multiscale, multiphysics modelling framework for the processes involved in consolidated bioprocessing |
| **14** | **Clara Heuberger, 2nd year in Centre for Environmental Policy** (Nilay Shah, Niall MacDowell, Iain Staffell)<br>Quantifying the Value of CCS-equipped Power Plants |
| **15** | **Elisa Casula, 3rd year visiting PhD student from University of Cagliari** (Cleo Kontoravdi)<br>A Novel Model for the Osmotic Behaviour of Human Mesenchymal Stem Cells |
| **16** | **Nasrul Johari, 2nd year** (Yun Xu)<br>Evaluation of flow disturbance in a stenosed carotid artery bifurcation model using γ-Reθ transitional CFD and large eddy simulation models |
| **17** | **Michal Kopytynski, 2nd year** (Rongjun Chen)<br>Delivery of different sized payloads to cancer cells using a pH-responsive biomimetic polymer |
| **18** | **Shiqi Wang, 2nd year** (Rongjun Chen)<br>Amino Acid Based Hydrogels with Dual Responsiveness for Oral Drug Delivery |
| **19** | **Anna Sofia Tascini, 2nd year in Chemistry** (John Seddon, Fernando Bresme, Rongjun Chen)<br>How does the sebum oily layer interact with epidermic lipids? |
| **20** | **Marco Adamo, 1st year** (João Cabral)<br>Microfluidic SANS – Rapid contrast matching in continuous flow |
| **21** | **Ruhina Miller, 1st year in Chemistry** (João Cabral, Oscar Ces, Nicholas Brooks)<br>Crystallization of SDS under isothermal conditions |