In this issue:

- Miss Malak Wehbe, Co-Editor in Chief, Department of Chemical Engineering, Imperial College London, shares her perspective about the PharmaSEL-Prosperity Newsletter.
- Research from the Misener group on building robust chemometric models for PAT applications.
- Mr Oscar M. Mercado Valenzo, a PhD Research Student working on Work Package 3 (WP3) shares his background, research interests and his role towards WP3.
- A highlight of our most recent awards.
- Upcoming conferences / posters

Co-Editor in Chief Perspective

Being part of the PharmaSEL/Prosperity partnership, as a PhD student for the past four years and as the co-editor of this newsletter over the past year, has been a valuable experience, which helped me grow on a professional and personal level. Working with scientists and engineers at Lilly, as well as academic researchers in the collaboration, has given me the opportunity to develop my research skills and gain insight of the different research activities undertaken, including the latest news in the pharmaceutical sector. I developed many important soft skills such as, communication, teamwork and people skills.

This has been a fantastic opportunity to contribute to scientific research in the pharmaceutical industry. I believe in the importance of showcasing the world-leading research activities and capabilities of the researchers at Imperial College London, Queen Mary University of London (QMUL) and University College London (UCL), and this partnership has allowed me, as well as other researchers, to present our research at conferences all over the world and produce prominent publications.

As a Co-Editor of the PharmaSEL-Prosperity newsletter over the past few months, I was given the opportunity to get to know many of you, some whom I would not have met otherwise. I made new friendships while working as an editor for the newsletter which I hope will last a long time. Unfortunately, this issue will be the last one I co-edit as I move on to the next chapter of my career. I will be looking forward to reading upcoming issues of the newsletter edited by Dr Othman Almusaimi and our new Co-Editor Mr Hamish Mitchell!

Malak Wehbe
Department of Chemical Engineering, Imperial College London
m.wehbe18@imperial.ac.uk

Research Feature: Robust Chemometric Models for PAT Applications

Dr Chrysoula D. Kappatou, a Research Associate in the Misener group, updates us on the latest research activities that are taking place in their group under work package 5.

- **Tell us about your role towards the work package you are in and the methodologies used/developed**

    Together with Mr James Odgers, Dr Sarah Filippi, Dr Sal Garcia Munoz and Professor Ruth Misener we are working in WP5 towards the automation of chemometric processes. One of the directions we are following focuses on optimization-based approaches to treat this entire model-building procedure, from raw data to final model, as a single optimization problem.

- **What are the main challenges you encounter during this process?**

    Among the challenges we came across is identifying explainable validation metrics for the whole process and defining and solving optimization problems to obtain optimal pre-processing sequences and explainable regression models.

- **Do you have some particular findings that you think are interesting to share?**

    Within the project scope we have focused a lot on quantifying a robustness metric that accounts for known variability to the data. As opposed to validation metrics, such as accuracy and precision that are intuitive and straightforward to calculate, obtaining a robustness metric is not trivial. We
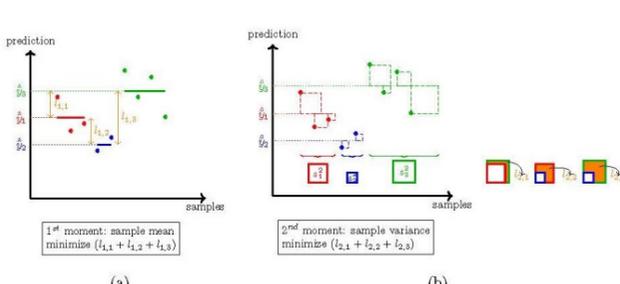

Fig. 1: First and second moment representation for one source of variability with three different realizations depicted by the three different colours, where $\bar{y}$ the average prediction and s^2 the variance for each realization.

propose a definition for robustness based on a commonly used concept in statistics, i.e. the method of moments, to achieve insensitivity to known sources of variation within the data.

An illustration of the robustness metric is provided in Figure 1, where different variability realizations of a known source are illustrated in different colours. Our robustness definition tries to minimize the average distances across the first (sample mean) and second (sample variance) moments of the different variability realizations.

- **How does you work interest Lilly collaborators?**

    Developing accurate and robust models for Process Analytical Technology (PAT) applications can automate the decision making process and significantly reduce model update and maintenance, thus the cost of the PAT application.

- **Are Lilly using/planning to use any of the methodologies/tools that you developed?**

    Yes, throughout the development of this work we are trying to use and test our approaches with industrially-relevant case studies. Actually, developing open-source software and algorithms that are easily transferable to industry and applied to real-world applications is a key aspect of our work.

- **What is your future/planned work?**

    In the future we are interested in looking at hierarchical representations of the optimization problem that will hopefully reveal underlying patterns and structures that could facilitate the decision making.

Chrysoula D. Kappatou
Research Associate
Department of Computing, Imperial College London
c.kappatou17@imperial.ac.uk

Early Career Researcher Profile

Mr Oscar M. Mercado Valenzo

Oscar completed a BSc in Biotechnology at the Monterrey Institute of Technology and Higher Education (ITESM; Mexico) and an MSc in Molecular Medicine at the University of Essex (UK). During this time, he worked as an undergraduate research assistant at the former Water Centre for America and the Caribbean and current Biotechnology Centre, both based at ITESM, working in assisted purification of industrial wastewaters through continuous enzymatic catalytic column systems and in optimisation of ion exchange chromatographic column in-house packing and purification methods. He has also assisted in projects involving lab-based microbiology on archaea and mammalian cells and computational modelling of difficult-to-express proteins.

Oscar is currently a PhD research student at Imperial College London working on drug substance purification for WP3 along with Dr Othman Almusaimi. He joined the Surfaces and Particle Engineering Laboratory (SPEL), led by Prof Daryl Williams, in October 2020. His project consists of developing new systematic method of reversed-phase chromatography (RPC) processes for peptide purification. A key objective is to assess chromatographic interactions in RPC, focusing on the effects of both peptide and column hydrophobicity on separation performance determined through Liquid (LC) and Gas (GC) chromatography and adsorption techniques. These analyses are particularly useful for comparing peptide adsorption capacity and performance of commercial RPC columns to rationally design and optimise chromatographic methods for peptide purification. He is currently working on the development of quick purification methods based on non-gradient elutions tailored to the target molecule to optimise resolution within impurities. Future work will consider the propensity to aggregation caused by hydrophobic imbalances during purification to assess and improve stability at large-scale manufacture and storage.

Oscar M. Mercado Valenzo
Department of Chemical Engineering, Imperial College London
o.mercado-valenzo20@imperial.ac.uk

Awards

Ruth Misener
Has been awarded BASF / Royal Academy of Engineering Research Chair in Data-driven Optimisation.

Claire Adjiman
Has been elected as an International Honorary Member of the American Academy of Arts and Sciences

Nilay Shah
Has been elected as an International Honorary Member of the American Academy of Arts and Sciences

Andrew Livingston
Has been elected as a Fellow of the Royal Society (FRS).

Upcoming Conferences / Posters

- **Othman Almusaimi, Mahama Alhassan, Fernando Albericio, Beatriz de la Torre.** Cleaving protected peptides from 2-chlorotrityl chloride resin. Moving away from dichloromethane. 26th Annual Green Chemistry & Engineering Conference, ACS Fall 2022, Reston, VA, USA, 6th to 8th June 2022.

- **Ludmila Peeva, Jet Yeo, James Botwright, Andrew G. Livingston.** Liquid Phase Peptide Synthesis via One-Pot Nanostar-Sieving. 26th Annual Green Chemistry & Engineering Conference, ACS Fall 2022, Reston, VA, USA, 6th to 8th June 2022.

- **Lucia Lombardi, Yejiao Shi, Annarita Falanga, Emilia Galdiero, Elisabetta di Alteriis, Gianluigi Franci, Igor Chourpa, Helena S. Azevedo, and Stefania Galdiero.** Enhancing the Potency of Antimicrobial Peptides through Molecular Engineering and Self-Assembly. 27th American Peptide Symposium. Peptide Science at the Summit. Whistler, BC – June 11th to16th, 2022. .

- **Lingfeng Gui, Alan Armstrong, Amparo Galindo, Fareed Bhasha Sayyed, Stanley P. Kolis and Claire S. Adjiman.** Computer-aided solvent design for suppressing HCN generation in amino acid activation. ESCAPE32, Toulouse (France), 12th to 15th June 2022.

- **Lingfeng Gui, Alan Armstrong, Amparo Galindo, Fareed Bhasha Sayyed, Stanley P. Kolis and Claire S. Adjiman.** Suppressing Side Reactions via Computer-Aided Solvent Design. FOMMS 2022, Delavan, WI, USA, 17th to 21st July 2022.

- **Mohamad H. Muhieddine, Suela Jonuzaj, Shekhar K. Viswanath, Alan Armstrong, Amparo Galindo and Claire S. Adjiman.** Model-based solvent selection for the integrated synthesis, crystallisation and isolation of pharmaceutical compounds, 32nd European Symposium on Computer Aided Process Engineering, ESCAPE-32, Toulouse, France. June 12th to 15t, 2022.

- **Mohamad H. Muhieddine, Shekhar K. Viswanath, Alan Armstrong, Amparo Galindo and Claire S. Adjiman.** Multi-objective optimisation for early-stage pharmaceutical process development, 14th International Symposium on Process Systems Engineering, PSE2021+, Kyoto, Japan. June 19th to 23rd, 2022.

- **Mingxia Guo, Jerry Heng.** The Relationship Between Unfolded Conformation and Crystallization Conditions of Glycine Homopeptides, Early Career International Particle Technology Forum 2022, 26th to 27th May 2022.

- **Othman Almusaimi, Mahama Alhassan, Fernando Albericio, Beatriz de la Torre.** Bypassing Osmotic Shock Dilemma in a Polystyrene Resin Using Green Cyclopentul Methyl Ether (CPME), Early Career International Particle Technology Forum 2022, 26th to 27th May 2022.

- **Malak Wehbe, Andrew J. Haslam, Salvador Garcia-Muñoz, George Jackson, Amparo Galindo.** Thermodynamic modeling of the nature of speciation and phase behaviour of binary and ternary mixtures of formaldehyde, water and methanol. 32nd European Symposium on Applied Thermodynamics 2022 (ESAT 2022), Graz, Austria, 17th to 20th July 2022

Co-Editor-in-Chief
Malak Wehbe
PhD Student
Imperial College London
m.wehbe18@imperial.ac.uk

Co-Editor-in-Chief
Othman Almusaimi
Research Associate
Imperial College London
o.al-musaimi@imperial.ac.uk

Imperial College London | UCL | Queen Mary University of London | Lilly | EPSRC Engineering and Physical Sciences Research Council | Royal Academy of Engineering