PHARMASEL-PROSPERITY NEWSLETTER

PharmaSEL Prosperity

A bimonthly newsletter

ISSUE 10 MAY 2023

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Balancing work and sport: James Odgers, WP5

We recently had the opportunity to sit down with James Odgers, a PhD student in Work Package 5, and discuss how he balances his PhD with international-level sport, and his recent achievements in fencing! Please find highlights of the interview in the paragraphs below.

Please could you briefly introduce yourself?

I'm James Odgers, I'm part of the Prosperity Partnership and I'm working on Work Package 5, supervised at Imperial by Sarah Phillipe and Ruth Misener, as well as Sal Garcia at Lilly.

How did you get into fencing, and how long have you been fencing for?

I've been fencing for quite a long time – I started when I was nine, so have been practising for 15 years now. I got into fencing because my friends were doing it; on the days where fencing training was happening, I got really bored in the evening because there was no-one to hang out with. So, I decided I would go fencing with them instead! Cut forwards to many years later and I'm the only one still doing fencing.

Was there a point where you realised "Hey, I'm quite good at this" or did you just enjoy it enough to be motivated to train?

I would say that I've always really enjoyed the sport. I find that I have to do something active most days as a way to release energy, and fencing is a good balance of being both social and an opportunity for exercise and to learn some new skills. I've gradually worked my way up from being not very good to eventually being quite good – there was no sudden "eureka" moment.

How often do you train, and what kind of training do you do for fencing?

On a good week, where there is nothing interfering with my training, I'll either do three or four nights of fencing, either training four times a week or three times with a competition on the weekend. The main aspect of training is going and competing against others; I'm very lucky that there are some strong clubs in London, so I get the opportunity to compete against others who will also go to international competitions. There's also an element of technical work with a coach, as well as general fitness, to ensure that you're able to move fast and explosively.

Is there anything you particularly enjoy about fencing?

One of the main things I enjoy is that fencing gets you to think – every time you fence someone new, you must solve a new problem, which is quite different from other sports. It is also just a good sport, and an opportunity to get out and moving, and away from any problems you may be facing with work, helping to de-stress. Also, once you reach a certain level (in any sport), opportunities such as international competitions become possible, which is very exciting.

Is there anything you find translates from fencing into your work, or vice versa?

I've picked up a lot of soft skills, such as how to set goals, stay focussed, and stay committed to the process, even when things aren't going amazingly. These translate well from sport into the academic setting, where you're inevitably going to face setbacks and the only way to get over them is to keep working at the problem. On a day-to-day level, I think that the differences in sport and academia are useful in terms of supporting one another – if something is going poorly academically, then I still have something else I can look at and work on, which I find helps with resilience. When you're training or at a competition, I find that you're focused so hard on the sport that you don't have time to even consider what's going on academically, which is very useful!

Regarding international competitions, you recently competed in the Grand Prix Epee in Colombia, which is an Olympic qualifying event! Any highlights from your trip?

It was an eye-opening experience – there were some extremely talented fencers there. The Grands Prix are part of the largest set of fencing competitions in the world, and various Olympic and world champions were present as part of the 200 competitors in Colombia. One of my favourite moments was realising that one of the coaches coaching against me in one of my bouts was Gauthier Grumier, an Olympic champion and world champion many times over. Getting the opportunity to go out and compete against people who were full-time athletes and top 50 in the world was an incredible opportunity, and something I'm not going to forget anytime soon.

Do you have any other major goals or events coming up?

The British Open is in two weeks' time, and that's the last big domestic competition. After that, it's the off-season for me, which will be a welcome break after quite a long, tough season."

Many thanks to James for his insightful answers! We wish him all the best on his upcoming endeavours. If you'd like to ask him a question about fencing (or something else), you can contact him via james.odgers16@imperial.ac.uk.

The Prosperity Partnerships Showcase: Professor Eva Sorensen, WP3

The EPSRC held a showcase event for all their 47 (to date) Prosperity Partnerships on May 25th 2023, and our Partnership was represented by Professor Eva Sorensen (UCL) and Professor Daryl Williams (IC). (Note that the banners only allowed for two partner organisations to be included!) The event was an opportunity to meet representatives of the other Partnerships as well as EPSRC leads, and to share experiences and learnings. The Partnerships are clearly driving forward shared research challenges for both academic and industry partners, and are providing benefits to the businesses involved.

A detailed survey of achievements will be published soon but some of the highlights were presented. Most projects partners have plans to continue their collaboration beyond the EPSRC funding. Industry partners have already made additional investments in the UK of about £75M. Nearly 500 papers have been published and 101 PhDs have been awarded to date with another over 200 PhDs are expected in years to come. 73% of industry partners expect to launch new products on to the market, and 76% new processes, tools or methods are to be implemented. 15% of industry and 29% academics expect to establish spin-out companies. Overall, it appears that the Partnership programme has been, and continues to be, a great success. Just like our Partnership!

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Research Highlight: Towards an understanding of the fundamentals of adsorption in reversed-phase liquid chromatography (WP3)

As part of WP3, we aim to understand the fundamentals of reverse-phase liquid chromatography (RPLC) to improve current technologies. This WP is formed by a computational team based on UCL, supervised by Professor Eva Sorensen, and an experimental team at Imperial, supervised by Professor Daryl Williams. My work focuses on characterising commercial RPLC columns and testing their separation performance at different conditions. Although this technique has been used for almost five decades, there is not much understanding of the mechanisms that drive the separation, especially for complex molecules such as peptides.

The complication of chromatography lies in the chemistry of the RPLC resin itself. Since these resins are silica-based polymers, silanols are left at the ends of the chains after condensation, giving a hydrophilic property to the surface of the resin. These silanols are blocked by end-capping with an alkyl chain, converting the resin into a hydrophobic material suitable for RPLC. However, this process is not perfect, leaving some residual silanols on the surface, and thus, the surface is heterogeneous. Also, the capacity of silanols to dissolve in water produces a negative charge on the surface. This combination of hydrophilic, hydrophobic, and electrostatic interactions makes retention at overloaded conditions an exciting challenge.

Sample Case Study:

I am currently using a set of hydrophobic peptide standards to understand how retention is driven from an adsorption perspective. These peptides called P1 to P6, are composed of 7-11 amino acids. As the number increases in the name, the peptide becomes more hydrophobic due to an amino acid, mostly from the substitution of two neutral glycine groups into a hydrophobic leucine group. All these peptides require a certain percentage of organic in the mobile phase to desorb from the surface and elute into the eluting liquid phase. Interestingly, when we elute peptides P2-P4 in plain water and acetonitrile retention is very low (Figure 1A). However, as we introduce trifluoracetic acid (TFA) as an ion-pairing agent, adsorption becomes stronger and thus, retention is increased 5-fold (not shown). By looking at the chemistry of the peptides, they all contain a single glutamic acid group and no other amino acid with an electrically charged side chain. Therefore, when water is present, the peptide and the surface are negatively charged. These charged states potentially cause a repulsion effect hindering adsorption; adding TFA to the mobile phase masks these charges and facilitates adsorption.

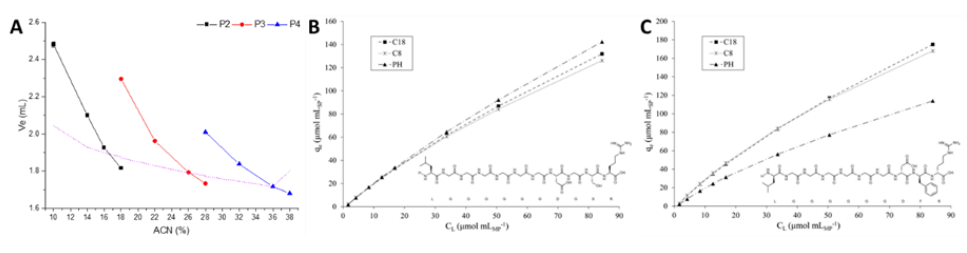

Figure 1*: Retention and adsorption of peptides. (A) Retention of peptides P2, P3 and P4 using a C18 column and mobile phase with only water and acetonitrile. (B) Comparative adsorption of peptide P1 using 3 columns: C18, C8 and Phenyl-Hexyl (PH) using a mobile phase with water, acetonitrile and TFA. (C) Comparative adsorption of peptide P2 under the same experimental conditions described in B.*

Additionally, when we compared the absorbance of peptide P1 onto different columns (Figure1B), we observed that P1 would adsorb similarly to the three columns tested. This is not fully surprising as P1 is a neutral peptide in the length of the alkyl chain, or the presence of rings on the resin surface will not affect its adsorption. In comparison, P2 seems to be less adsorbed to phenyl hexyl (PH in figure) in comparison with the other columns. This is counter-intuitive as the presence of rings in the peptide and the surface would suggest the existence of π-π interactions, but instead, we see a repulsion effect.

Relevance to Lilly:

Understanding the fundamentals of adsorption in RPLC is particularly useful to Lilly as peptides are complex molecules that cannot be treated with a classical perspective of chromatography. Also, quick adsorption experiments will facilitate the scale-up of the technology at the manufacturing scale, where the effects of the coexisting interactions are more noticeable. Computational models are currently being built by the UCL team, which in combination with an experimental understanding of the mechanisms involved in the process, will allow for the prediction of retention with lesser experimental data reducing costs, time, and workload for Lilly. This can also open the door to developing techniques further for more efficient and greener chromatographic processes.

Future work:

My immediate future work will focus on testing up to 10 different columns with different resin properties to map the effect of the resin physical properties on adsorption. I hope to apply this knowledge to produce an algorithm or workflow for rational design method development tailored for the analyte of interest while speeding up scale-up. Additionally, I would like to explore the possibility of using green organic modifiers without losing selectivity.

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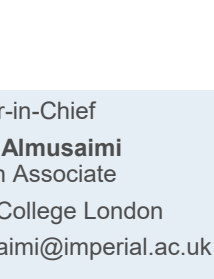
Researcher Spotlight: Shubhani Paliwal, WP2



I am Shubhani Paliwal, a first year PhD student in the Molecular Systems Engineering group, Department of Chemical Engineering, Imperial College London. I pursued my bachelor's degree from BITS Pilani, Hyderabad in India. Further, I got the opportunity to pursue MSc Advanced Chemical Engineering with Process Systems Engineering at Imperial College London in 2021. I was honoured to receive the '2022 Prize for Best Performance in the MSc Research Project'.

It was in these programs where I understood the significance of multi-scale modelling of chemical processes ranging from molecules to complete supply chains. Exposure to programs deeply embedded in computational science fascinated me towards pursuing a PhD.

During my undergraduate thesis, I got an opportunity to contribute to collaborative work with the Otto Von Geuricke University, Germany. We proposed a water-splitting method to produce surplus hydrogen for surplus energy with reduced impact on the environment as hydrogen is a clean fuel. Before starting my MSc program, I worked as a Project Associate at the Indian Institute of Science, Bangalore where I learned about the kinetic Monte Carlo modelling method, and applied it to covalent organic frameworks synthesis. On learning about a new research field, I was inspired by the boundless research scope of the chemical engineering domain.

During my MSc thesis at Imperial, I worked on the solubility prediction of active pharmaceutical ingredients in polymers using the SAFT-γ Mie theory. At the core of the pharmaceutical industry, large amounts of money and efforts are dedicated to drug discovery and development. In collaboration with Lilly during my PhD, I aim to contribute towards the development of the necessary tools to deliver reliable predictions of drug solubility, addressing the difficulties of predicting the solubility in changing physical conditions. My plan is to build on recent advances in fundamental molecular science to predict the solubility from molecular structure alone, opening the door to model-based pharmaceutical product design.

After my PhD, I aim to continue contributing towards improving the molecular-level understanding of drugs, being a part of academia.

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Model-Based Design of Experiments (MBDoE) Workshop - 23rd June 2023

The Sargent Centre for Process Systems Engineering is proud to present their upcoming workshop on the model-based design of experiments on the 23rd of June. This one-day event will feature a number of talks from both academic and industrial speakers, including a keynote presentation from Professor Kim McAuley (Queen's University, Canada), as well as industrial participation from companies such as Syngenta, AstraZeneca, and Eli Lilly and Company. Attendees will gain valuable information on the methodologies used for efficient experimentation via model-based design of experiments.

Registration is **free** for PharmaSEL-Prosperity Partnership members! To register for this event or for any further information, please contact sargent.centre@imperial.ac.uk.

Awards

Maria Papathanasiou

Has been awarded the IChemE Junior Sargent Medal for her contributions towards process systems engineering.

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Disclaimer: This research program is funded by Eli Lilly and Company, Imperial College of London, University College London and from EPSRC Grant Ref: EP/T518207/1. The contents of this newsletter are chosen and edited by researchers and students of Imperial College London. Their editorial work is independent of Eli Lilly and Company and EPSRC.

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