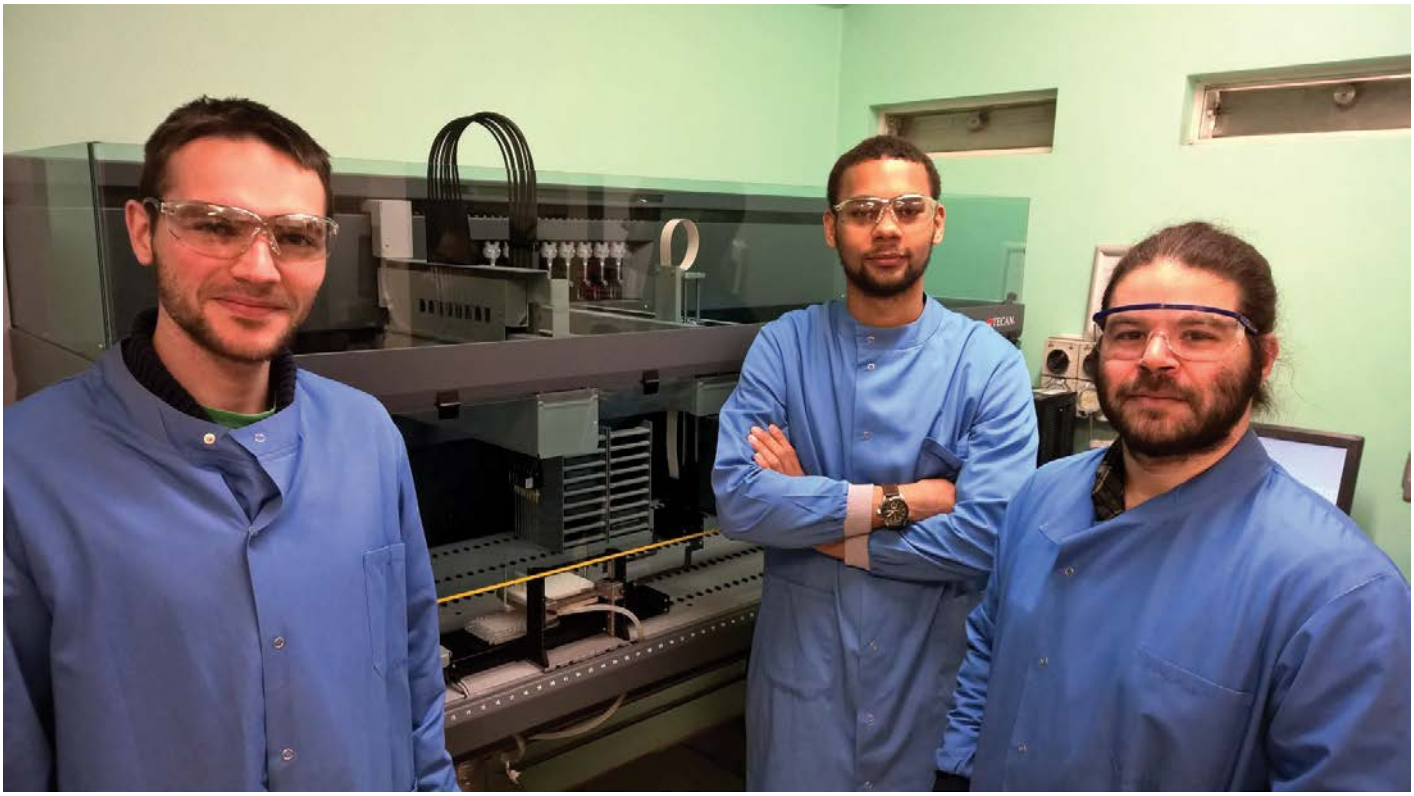
A simple(x) approach to bioprocessing

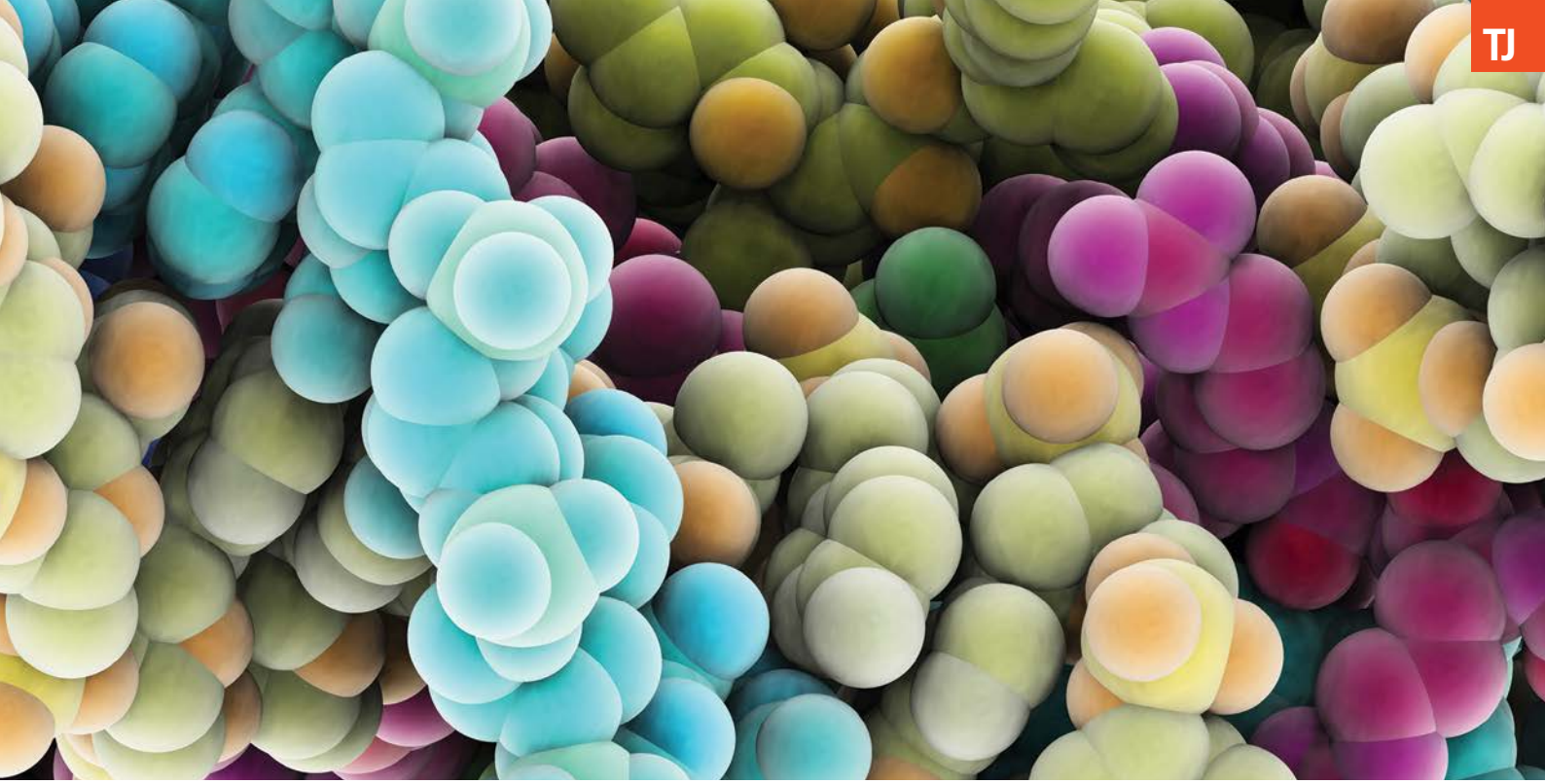
UCL's Advanced Centre for Biochemical Engineering is harnessing the flexible automation capabilities of its Freedom EVO® workstations to explore novel bioprocessing applications, with a focus on the production of 'next generation' medicines including protein-derived therapeutics, vaccines and cells for therapy. Combining the Freedom EVO platform with devices such as Atoll's MediaScout® RoboColumns®, researchers are able to generate high quality, scalable data that minimizes the cost and time required to optimize new bench-scale processes.

University College London's Department for Biochemical Engineering is a world leader in the development of novel bioprocesses, focusing on macromolecular and cellular processing techniques for industrial and biomedical applications. The department's Advanced Centre for Biochemical Engineering (ACBE) is an interdisciplinary facility that coordinates research collaborations with other UCL departments, as well as academic institutions and industrial partners around the globe. The ACBE combines cutting-edge laboratory automation with the latest industrial process development tools to accelerate its research, as Professor Ajoy Velayudhan explained: "Automation is now an integral part of processing biological materials, even at the research and development level, and we currently have six Freedom EVO platforms within the department. The majority of these instruments are set up for generic liquid handling activities, providing convenient and flexible walkaway automation to meet the needs of individual projects. We have a number of modules that can be installed or removed as required, allowing us to do everything from simple biochemical assays to complex cell-based studies. For example, we can reproducibly expand and differentiate stem cells, as reported in an earlier edition of the Tecan Journal (Issue 3, 2009)."

"One of our areas of particular interest is the development of quantitative models for whole bioprocesses, looking at how the individual steps fit together to yield the final product. These bioprocesses generally



Members of the ACBE team with one of the department's Freedom EVOs



consist of 10 to 15 individual steps, each of which can influence processes downstream. We are developing methods to evaluate the 'cross-talk' between these operations, requiring large quantities of data. This data generation is extremely tedious, and would be virtually impossible to achieve manually. High throughput automation techniques are therefore vital to generate the rich datasets necessary to extrapolate meaningful results."

Another topic currently under investigation is the optimization of polishing steps for the final purification and clean-up of therapeutic biological products. The ACBE team is taking advantage of the Freedom EVO's liquid displacement and Te-Chrom™ module to provide walkaway processing of Atoll's MediaScout RoboColumns. Dr Spyridon Konstantinidis explained: "We use the RoboColumns to assess different operating conditions for preparative chromatography applications, optimizing objective functions such as purity, yield, throughput and productivity of protein purification. Combining these columns with the Freedom EVO workstation is very advantageous for our work, allowing parallelization of screening and enabling much more rapid progress than would be possible using traditional bench-scale testing. We have found the results of experiments conducted using RoboColumns to be scalable, making this a useful tool for production-scale process optimization for the generation of the extremely pure biomolecules needed for therapeutic use."

A major advantage of this set-up is the small amount of material required for process optimization. This can often be a significant obstacle, due to the high costs of producing material for screening studies. To further reduce consumption of biological materials, the ACBE has developed a modified simplex optimization method which allows rapid development of processes without the drawbacks of traditional Design of Experiment (DoE) approaches. Ajoy continued: "DoE techniques are excellent for late-stage commercial development, where robustness around an established set of operating parameters needs to be demonstrated. However, for the type of novel processes we usually study, DOE can be laborious and inflexible in finding effective operating parameters. Experienced researchers generally prefer to analyze data on-the-fly, allowing them to rapidly progress to the next stage of optimization without needing to run a large number of unnecessary 'peripheral' experiments. A more effective approach to early process development uses the classical simplex method. We have generalized this method to account for both continuous and discrete variables, making it much more useful for bioprocess development. It is highly adaptable, saves time and material, and is closer to the intuitive way experienced scientists do process development. However, this requires a very dynamic approach to automation, which our Freedom EVO platforms provide."

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Spyridon added: "The performance of Tecan systems is well documented in terms of accuracy and precision, but the flexibility of the Freedom EVO instruments is even more important for us. The workstations are also quite easy to use, allowing even relatively inexperienced postgraduate students to get processes up and running very quickly with little training. At the other end of the spectrum, the open nature of the system allows us to compile our own executable applications, which can then be integrated with Freedom EVOware® to create automation scripts on-the-fly. As long as you set it up correctly, you know you're going to get quality data – it's very reliable, and the support we've received from Tecan has been brilliant."

To find out more about Tecan's bioprocessing solutions, visit **www.tecan.com/bioprocessing**

To learn more about University College London's Department for Biochemical Engineering, go to **www.ucl.ac.uk/biochemeng**