Xiaoyu Zhao

My love for Raman imaging began when I was a first-year bachelor student at Imperial College London. At that time, I was a huge fan of Professor Molly Stevens, and she kindly accepted me to join her group. My resume was very fortunately picked up by Dr. Vernon LaLone, who later became my supervising postdoc for the next 3 years.

I had no idea what Raman imaging was at that time, but I always saw the sparkles in Vernon's eyes whenever he talked about Raman imaging. It was probably one of my luckiest decisions because over the next 3 years, we developed one of the top Raman technologies in the world—the ultra-quantitative Raman analysis method. This method transformed semi-quantitative Raman analysis to a fully quantitative level in terms of concentration. We became the first group in the world that could visualise the 3D distribution of drug metabolism and drug deposition within human liver organoids without any need for sample preparation.

Our first and only paper was published in Cell Reports Methods in April 2023, and all the Raman data in this paper were processed and generated by myself. The paper soon received comments from Professor Lev T. Perelman from Harvard University for its significance in the medical field.

Vernon went back to the US after my bachelor's study finished. I was very worried that nobody would answer my questions after Vernon left, so I found his supervisor, Dr. Conor Horgan, who was working at a spin-out company from King's College London called HyperVision Surgical. The company focused on hyperspectral imaging for tumor detection and anastomotic leakage. I immediately applied for an internship position and explained to the team how I developed the algorithm for ultra-quantitative Raman imaging. I received the offer during the interview and soon started working part-time throughout my entire master's degree. I worked during the day and caught up with my studies at night. I felt extremely excited, tired, but blessed during that time. Towards the conclusion of my studies at Imperial College London, I attained a First-Class Honours degree in

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Biomedical Engineering and secured UROP scholarships for three consecutive years. Additionally, I earned an honorary appointment at King's College London and received a UK National Health Service honorary appointment at Guy’s and St Thomas’ Hospital in recognition of my contributions at HyperVision Surgical.

I felt extremely lucky because this small company turned out to be one of the fastest-growing startups in London and was presented at the annual NVIDIA GTC 2022 keynote by CEO Jensen Huang as part of the “I am a visionary” section. Within one year, we started with the basic algorithm and finished with 90 in-patient studies, including 9 colorectal surgeries and 81 neurosurgeries. The company grew extremely fast, and I learned huge amounts of knowledge from everyone on the team. My CEO, Dr. Michael Ebner, showed me the possibility of starting my own startup company with the technology I love.

After my Raman algorithm was fully developed, I kept looking for a suitable application for it. At that time, the best image I generated was of some human-engineered cartilage samples from a research group at ETH Zurich. I showed my Raman results to Professor Marcy Zenobi-Wong, and I obtained a Ph.D. position in her lab. However, after I finished my last experiment for an animal study in which we implanted the human-engineered cartilage subcutaneously under the rats, I noticed a huge problem from the samples through my Raman analysis. Almost all the glycogen within the cells got depleted, which means the engineered cartilage samples will die in a matter of time. Although the cartilage culture didn’t go very well, my Raman analysis was always beautiful! During my time at ETH, I became the organizing committee of the 6th Raman workshop and got the opportunity to present my work. It was my happiest day when I received an email from our sponsor, Dr. Mirjana Dimitrievska, who is the group leader at Empa, Swiss Federal Laboratories for Material Science and Technology: 'I had a hard time deciding on the 3rd candidate, as in the other

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abstracts I feel that Raman spectroscopy plays a side role, and it is more used as a general technique to support the project, rather than the center of it. Honestly, I think that it might be a good idea to keep Xiaoyu Zhao as an applicant and give her the award in the end, as her work is more deserving than the other applications. She presents a different aspect of Raman spectroscopy that could potentially have a high impact in health and medicine, and I think it deserves to be acknowledged, especially as it seems better than the other 4 candidates. Also, as you are giving 3 awards, I think it is okay that she is in the organizing committee and getting it. We need to support good work, and she is doing it, so I feel that it is fair.'

As a technique that is extremely new but is for sure a transforming tool, Dr. Dimitrievska's comment encouraged me a lot because it was a journey that is extremely work-intensive but pays back very little in the first couple of years. I had no interest at all in culturing cartilage, and I was kept amazed by Professor Wei Min's work.

The primary limitation with my current technique lies in the hardware; spontaneous confocal Raman microscopy is an extremely slow tool, and the majority of my images took 8-20 hours to finish. However, with the stimulated Raman imaging system that Professor Min has developed, images could be taken within minutes. I always wanted to combine my algorithm with a stimulated Raman imaging system and increase my imaging speed. I also had a huge desire for a Professor who could teach me more about biological Raman imaging, especially about the hardware. I believe Raman imaging stands as a highly promising method for addressing various challenges in biological research. Its unique non-invasive nature makes it the only technique capable of investigating living samples and leaving them intact.

Despite my enthusiasm for Raman, I am fully aware that there is a huge gap exists in my understanding, and I recognise that mastering the construction of a stimulated Raman microscope

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compatible with my software demands a more comprehensive skill set. Therefore, a PhD with a specific focus in the field of biological Raman imaging would be necessary for me to delve deeper in analytical chemistry.

I had an interview with Professor Min and got his full support for a Ph.D. position at Columbia University. I immediately quit my Ph.D. at ETH and started to self-study the fundamental knowledge in photonics and chemistry. I also lead a team to launch the first online platform for biological Raman analysis with the aim to fully understand the best application for quantitative Raman imaging. During the gap period, I attended many competitions in China and received many awards. I met all the companies in China who are working in the field of Raman, and got many samples for independent investigation. This hands-on experience solidified my conviction that biological Raman analysis is a vital asset for the imaging market, and I foresee Raman becoming a dynamic and rapidly expanding field in the coming years.

Having spent five years immersed in Raman research, I am certain that it is my lifelong passion. For the next five years, I want to do more research, promote biological Raman analysis in the scientific fields and show more people that Raman analysis has an indispensable role in basic research. I am eager to join Columbia University to further my knowledge in super multiplexed Raman imaging, with the ultimate goal of developing the most advanced Raman imaging system in the near future.