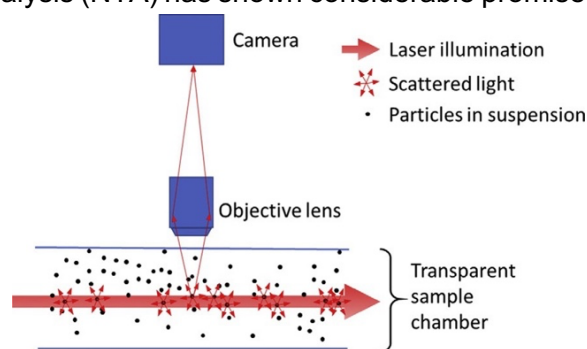


Enhancing Nanoparticle Tracking Analysis with deep learning

About the project or challenge area: Nanoparticle tracking analysis (NTA) has shown considerable promise for the reliable characterization of nanomaterials, in the fields of biopharmaceuticals, viral research, and protein aggregation. The figure illustrates schematically the NTA technique. A liquid sample containing nanoparticles (of diameters 10-1000 nm) is illuminated by a tightly-collimated laser beam. Light scattered by particles is collected by a microscope objective and imaged onto a camera. Tracking the Brownian motion over time yields the mean-squared displacement in two dimensions and, from the Stokes-Einstein equation, the size of multiple individual nanoparticles.



Although NTA provides highly-accurate sizes it suffers from a number of restrictions. First, NTA operates only within a relatively narrow window of particle concentration ($\sim 10^8$ particles/mL) which means most samples require extensive dilution. This is because of a combination of laser brightness / camera sensitivity and the need to differentiate a particle from camera noise. We will explore how newly-developed deep learning techniques may be used to improve the robustness of the nanoparticle tracking algorithms, remove the need for subjective input, and so significantly extend the concentration regime over which NTA can be used. Second, it is difficult to reliably estimate nanoparticle concentrations with NTA because of a lack of knowledge of the depth of field within which the microscope is tracking particles and the need to compensate for edge effects. We will synthesize stable reference nanomaterials, with a certified number concentration of particles of different sizes and refractive indices, which can be used to accurately calibrate *in-situ* the NTA depth of field and so yield accurate particle concentration measurements. This will considerably extend the usefulness and applications of NTA.

Why choose this opportunity? The focus of your project will be on developing sophisticated physical measurement techniques and demonstrating how they can be improved using machine learning methods. The project will provide an excellent platform to learn about AI techniques, digital microscopy, scientific computing, and the characterization of nanoscale materials and their practical applications. NTA is currently being used to check the stability and manufacturing quality of COVID-19 vaccines so your work in this area can make a real impact on global challenges. In addition to physical and computing skills, you will develop and increase your expertise in broad chemical synthesis and characterization techniques, whilst becoming familiar with the fundamentals of nanoscience. This project will require your collaboration with other members across other research groups, thus improving your teamwork and networking skills. Finally, you will be interacting with students from all over the world learning from their culture and skills, adding to your professional and personal development. Full training will be provided in all aspects of this project. You will be embedded in the Supervisor's research group, who will provide support. In addition, you will be assigned a mentor for the duration of your project, who will provide extra support and help you to identify any additional training needs or opportunities.

About you: You will have skills and knowledge in chemistry and a willingness to learn new skills in optics, microscopy and computation, where necessary. Full training will be provided.

Bench fees: A bench fee of £4000 may be required however we are currently in active discussions with a major UK instrument manufacturer who may make a contribution.

How to apply: Applications are accepted throughout the year and you should complete the online application form for Chemistry (MSc by Research).

Supervisor: Your supervisor for this project will be Paul Bartlett, Professor of Soft Matter Science in the School of Chemistry. You can contact him at p.bartlett@bristol.ac.uk

Finding out more about your prospective research program: This recent article reviews recent work on NTA:



Kim, A., Ng, W. B., Bernt, W. & Cho, N.-J. Validation of Size Estimation of Nanoparticle Tracking Analysis on Polydisperse Macromolecule Assembly. *Scientific Reports* **9**:2639, (2019). [10.1038/s41598-019-38915-x](https://doi.org/10.1038/s41598-019-38915-x)