Studies shed new light on phase transitions and laser-induced nucleation

Temperature control is vital in improving the understanding of the crystallisation process and phase transitions in mixed liquid systems. Here, we look at investigations into laser-induced nucleation phenomena by researchers at the University of Glasgow.

Linkam Scientific Instruments, Tadworth, Surrey, UK

Introduction

Today's crop of researchers are continuing to investigate fundamental questions of science by exploring phase transitions and laser-induced nucleation. Researchers are looking how to understand not only how and why lasers trigger crystallisation, but also how changes made to the properties of the laser could influence which crystal from would be generated.

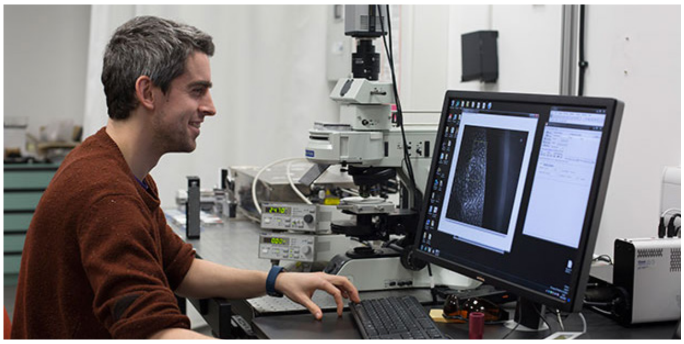
An unexplained phenomenon

Prof. Klaas Wynne, professor at the School of Chemistry at the University of Glasgow, is currently undertaking research in this area. Finlay Walton, one of Prof. Wynne's PhD students, explains: "There have been papers in this area of research for around 20 years, since it was first shown that nanosecond-pulsed lasers can nucleate crystals in a supersaturated solution. But it is fair to say that even now, a physical understanding of the phenomena is still lacking, and is holding back progress."

The central hypothesis under test was that there were hidden 'critical points' (either in a single liquid, or when two immiscible liquids mix or separate in response to temperature) where dramatic fluctuations in relative concentration occur, and that at these 'critical points' laser light was able to enhance this effect and lead to laser-induced nucleation.

Importantly, although the group in Glasgow had no commercial sponsors for this work, their results are potentially important for those working with large molecules – biopharmaceutical companies developing therapeutic proteins, for example – where the control of crystallisation is a significant challenge.

Dr Walton added: "Whilst our work is distanced from any commercial product, we know from colleagues here that are working on crystallizing proteins that it can be a nightmare.



Dr. Finlay Walton at the University of Glasgow.

It is so difficult to predict. If you just tweak the solvent slightly, a different polymorph might form, or the protein may not crystallize at all. We wanted to try and aid in the control of these processes, which could benefit numerous areas of the chemical industry."

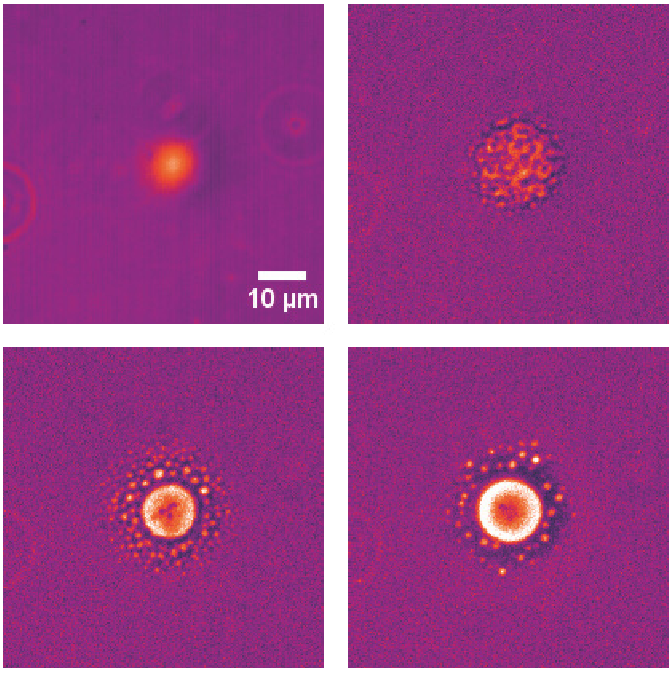
Theory and practice

The phase transition being studied in this work occurs when two liquids are at a high temperature, but separate into two phases as the temperature is lowered.

Well-known physical models describe this mixing and demixing in a comprehensive manner, and predict the free energy of the system as a function of the mole fraction of one of the liquids in the mixture.

In a system where the two liquids are fully mixed, if the mole fraction of a small sub-volume of the sample is changed, the free energy will always increase. However, at a temperature just below the binodal value, a new minimum free energy is reached that corresponds to phase separation and nucleation.

Furthermore, when a laser beam is focused into the small sub-volume, the free energy is lowered even further and forms a laser-tweezing trap that will pull-in the liquid with the highest refractive index.



LIPS and Nucleation (LIPSaN) experiments in nitrobenzene–decane at T = 23.9°C with a 120-mW 785-nm focussed laser, on for 30 s. When the laser is switched on a LIPS droplet forms, but only once the laser is switched off does nucleation occur. Used with permission from Finlay Walton and Klaas Wynne.

This effect is universal and does not rely on the presence of pre-nucleation clusters that might be trapped as a result of a physical effect. So, in this metastable regime, the laser lowers the barrier for phase separation and, at sufficient intensity, triggers the nucleation of a phase separated droplet.

Against this theoretical background, an initial practical step was to construct a phase-contrast microscope and laser set-up to conduct some preliminary experiments. These first laser-induced phase separation (LIPS) experiments were carried out on mixtures of nitrobenzene and decane at mole fractions and temperatures where the mixture was stable. When the laser was focused in the sample, a bright spot was visible under the microscope. This indicates that LIPS takes place and that the fraction that is separated out has a higher refractive index, and must therefore be nitrobenzene rich. This was confirmed with the dye methylene blue and fluorescent detection.

Subsequent temperature-controlled experiments allowed the group to clearly show that the LIPS effect increases strongly on cooling as the binodal is approached and proximity of a liquid-liquid critical point can be used by a laser-tweezing potential to induce concentration gradients.

Finally, the laser-induced nucleation was shown in experiments where, when the laser was switched on, the LIPS effect draws nitrobenzene into the focus, reducing the concentration on the surrounding volume. When the laser is switched off, the temperature rapidly drops, the depleted volume falls below the binodal and this triggers the nucleation of phase-separated droplets.

The role of the Linkam THMS600 stage in this work

The group in Glasgow has used a Linkam THMS600 stage in their investigations. Dr Walton commented: "The Linkam stage integrated so well with our microscope – we have long-field objectives and the stage fitted perfectly into it."

He continued: "the temperature control was extremely good. We want to get really close to this critical point and so having control to 0.1 Kelvin is essential. The Linkam stage was so fast as well, we saw no discernable lag as we approached the target temperature – and the temperature that the stage indicated was the actual temperature, something that we haven't always seen with other systems."

In conclusion, Dr Walton said: "We could rely on the Linkam stage completely; we could see the properties of our liquids changing in real time as we approached the critical point. In addition, the stage is so easy to use, liquid nitrogen cooling integrates easily when we need it to.

Dr. Finlay Walton working with the Linkam THMS600 in the School of Chemistry.

A new model is established

The group concluded that the hypothesis was proven – phase manipulation and nucleation can be reliably induced with a straightforward laser set-up. The results look set to have profound implications for the understanding of these important phenomena. The LIPS experiments and related theory not only explain the physics behind non-photochemical laser-induced nucleation, but also suggest potential new ways of manipulating matter.

About the School of Chemistry at The University of Glasgow

Founded in 1451, the University of Glasgow is one of the oldest academic institutions in the UK. The School of Chemistry there has been active since 1747 and has been led by several luminaries of early chemistry; the school boasts a total of four Nobel laureates, and many Glasgow graduates have been honoured to serve as the president of what is now The Royal Society of Chemistry.

About Linkam Scientific Instruments

Linkam develops and manufactures a broad range of temperature controlled stages from high to cryo temperatures for both OEM and end users. These are used in conjunction with light microscopes and a wide range of analytical techniques including Raman, FTIR, WAX/SAX and other X-ray techniques to visualise and characterise the properties of materials. Linkam stages are found in thousands of laboratories worldwide with the most successful microscope heating stage, the THMS600, selling over 5,000 units alone. Linkam is the market leader in temperature-controlled microscopy.

THMS600

References

[1] Walton F, Wynne K. "Control over phase separation and nucleation using a laser-tweezing potential" 2018 Nature Chemistry 506–510 DOI: 10.1038/s41557-018-0009-8

[2] Walton, Finlay, and Klaas Wynne "Using optical tweezing to control phase separation and nucleation near a liquid–liquid critical point" 2019 Soft Matter 15.41 8279-8289 DOI: 10.1039/C9SM01297D

Read more about Linkam's THMS600 stage:
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Case Study