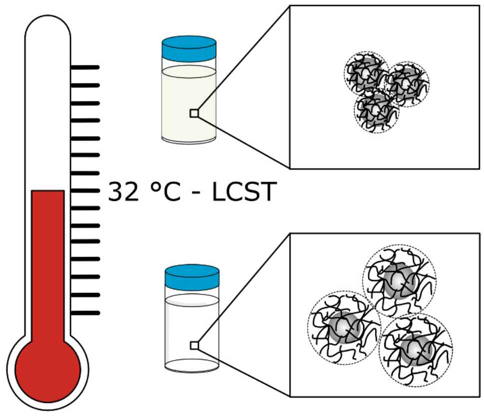
CLOSE-UP OF A POTENTIAL DRUG CARRIER

Studying phase transitions in nanogels

Nanogels are promising candidates for biomedical applications. For example, their ability to store and release biomolecules in response to a stimulus can be exploited for drug delivery into the human body. One such nanogel is poly(N-isopropylacrylamide) – PNIPAm, a polymer responsive to temperature change. Below a threshold of 32°C, the particles disperse in water. Above this threshold, they become insoluble and form a gel – the nanogel ejects the water molecules and the phases separate. By use of additives, researchers can fine-tune this so-called lower critical solution temperature (LCST) according to their needs. For controlled application, it is therefore important to study the details of the phase transition dynamics at different concentrations and with different co-solvents.



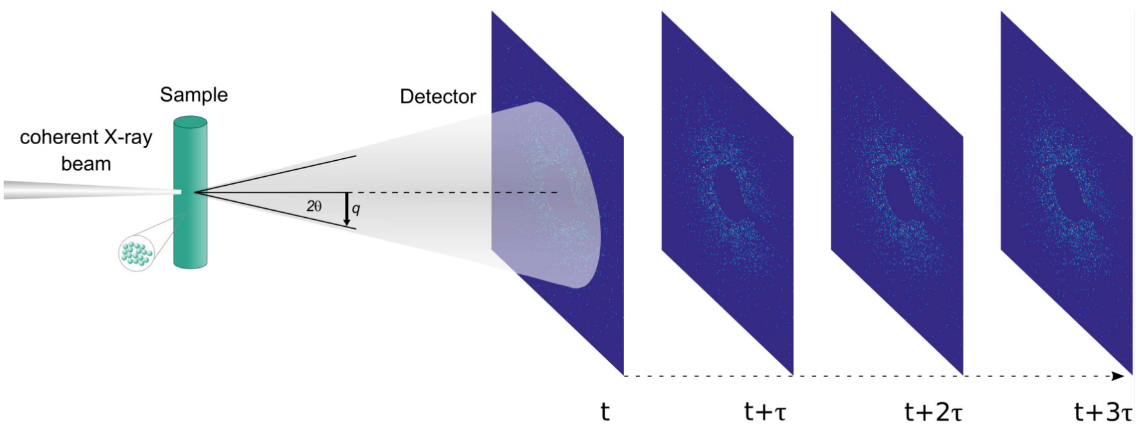
The behavior of PNIPAm at increasing temperature. Below the LCST, particles are dispersed in water. Above the LCST, the particles collapse and form an opaque gel. (CC by-sa Denise Müller-Dum, awk/jk)

EXPERIMENTAL SETUP

A team of researchers from Deutsches Elektronen-Synchrotron (DESY) and the Hamburg Centre for Ultrafast Imaging (CUI) performed an array of experiments on PNIPAm using X-ray photon correlation spectroscopy. The experiment was done at the coherence beamline 8-ID-I of the Advanced Photon source (APS) at the Argonne National Laboratory (USA), and the scattered light was measured with a two-dimensional LAMBDA 750K with a frame rate of 2kHz.

The team had to consider several challenges that required a careful experimental design. First, PNIPAm itself does not offer a high scattering contrast. This problem was overcome by placing a PNIPAm shell around a strongly scattering silica core. Second, PNIPAm is sensitive to radiation. Exposure time thus had to be limited to 0.5 ms, or, where longer exposure was required, the intensity had to be reduced. Third, dynamics are quite rapid, which made a high temporal resolution even more desirable.

"The detection of a coherent diffraction pattern – a so-called speckle pattern – requires small pixel sizes as well as low noise and high efficiencies because of typically low count rates in a single pattern. The LAMBDA detector perfectly meets these criteria and enables us to study the dynamics of soft matter samples over more than 7 orders of magnitude – from sub-milliseconds to hours – within the same experiments", says Felix Lehmkühler, one of the leading researchers on these studies.

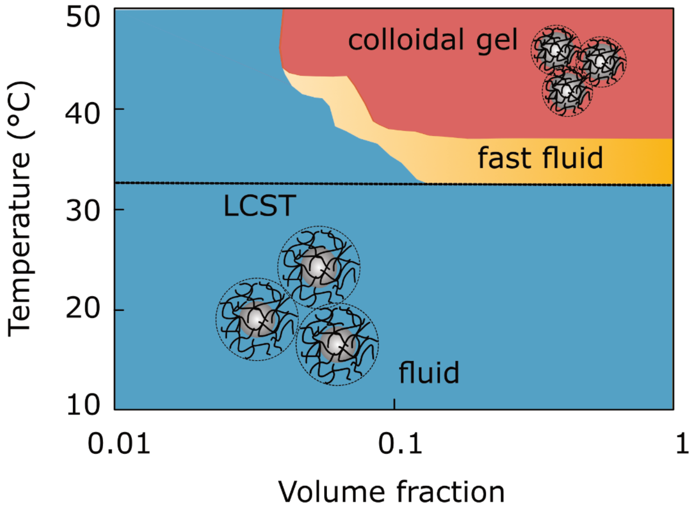


Experimental setup for time-resolved X-ray photon correlation spectroscopic measurements on PNIPAm-samples. Source: L. Frenzel (2019), with kind approval

Setup	8-ID-I Coherence Beamline at the Advanced Photon Source at the Argonne National Laboratory (USA)
Camera	LAMBDA 750k, Si detector
Resolution	786,432 pixels
Acquisition frequency	2 kHz
Photon energy	7.4 keV & 11 keV

RESULTS

The analysis of their X-ray experiments enabled Lehmkühler's team to determine the specifics of PNIPAm's phase transition around the LCST. They found that the transition from fluid to gel depends on the concentration of PNIPAm in the sample – or conversely, that the concentration can be used to fine-tune the transition. Their study also revealed details about the collapse: it turned out that the particles in the fluid move quicker at increasing temperatures, before attractive forces dominate and the particles collapse to form a colloidal gel. For the first time, they were able to present a concentration-dependent full phase diagram of a PNIPAm core-shell nanogel.



Phase diagram of silica-PNIPAm core-shell nanogel, showing the transition from fluid to gel at temperatures above the LCST, usually involving a fast fluid phase. The image is based on the phase diagrams in Frenzel (2019) & Frenzel et al. (2020a)

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