Temperature-induced liquid crystal microdroplet formation in a partially miscible liquid mixture

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The controlled formation of microdroplets through temperature variation is an intriguing concept for binary liquid mixtures with a critical solution temperature. Here, we investigate this phenomenon for a blend of methanol (MeOH) and a thermotropic liquid crystal (LC) 4-Cyano-4’-pentylbiphenyl (5CB). A near-room-temperature-induced phase separation leads to nucleation, growth, and coalescence of mesogen-rich droplets. The size and number of the droplets is tunable on the microscopic scale by variation of temperature quench depth and cooling rate. Further cooling induces a phase transition to nematic droplets with radial configuration, well-defined sizes and stability over the course of an hour. This fully reversible process is an interesting material system with relevance in diagnostics, optoelectronics, materials templating and extraction processes.

Significance
Liquid-in-liquid droplets are typically generated by the partitioning of immiscible fluids, e.g. by mechanical shearing with macroscopic homogenisers or microfluidic flow focussing. In contrast, partially miscible liquids display a temperature-dependent mixing behaviour. In this work, we demonstrate how, for a blend of a thermotropic liquid crystal and methanol, cooling from a miscible to an immiscible state allows the controlled formation of microdroplets. By varying the cooling protocol, the size, number and formation of either isotropic or nematic microdroplets can be tuned. This temperature-induced approach to droplet formation offers a scalable alternative and is particularly attractive for processes where reversibility is of value.

The nucleation and growth of microscopic droplets is of profound and widespread relevance in colloidal and interfacial science and technology.¹,² Regular binary liquid mixtures exhibit a miscibility gap for certain compositions and temperatures ranges. For a mixture with an upper critical solution temperature (UCST), the system is monophasic above the temperature threshold. Cooling below the coexistence curve in the corresponding T−ρ phase diagram induces either spontaneous phase separation by spinodal decomposition or a metastable state, where phase separation occurs by nucleation and growth.³ The intrinsic, spontaneous formation and growth of nuclei upon cooling of binary fluid systems has been studied from a theoretical perspective of the phase ordering process.⁴–⁷ Much work has been done to understand systems showing condensation,⁸ crystallization,⁹ phase separation of binary alloys,¹⁰ and more recently liquid crystal mixtures.¹¹ The growth of a nucleus or a droplet typically obeys a universal growth law, which follows the growth of a characteristic length (L), and is usually defined by the diameter of the nuclei.

\[ L(t) \sim t^n, \]  

with \( t \) as the time after a temperature quench to induce phase transition or separation and \( n \) as the universal growth exponent.⁶ For material systems with conserved order parameters, such as the phase separation of binary blends, a growth exponent of \( \frac{1}{2} \) is predicted.¹² For material systems with non-conserved order parameters, such as liquid crystals, the growth exponent is expected to depend on the temperature quench depth, varying from \( \frac{1}{2} \) to 1.⁶,¹¹,¹³ This behaviour has been primarily investigated in material systems pertaining to isotropic fluids.¹⁴–¹⁷ In addition, studies have been performed on binary mixtures of two liquid crystals with distinct transition temperatures,¹⁸ isotropic liquids with the liquid crystal as the continuous phase,¹⁹ and droplets of liquid crystals in a polymer matrix (PDLC).²⁰ To the best of our knowledge, the formation of liquid crystal microdroplets in an isotropic non-polymeric continuous phase by temperature-induced phase separation has not been studied.

The confinement of liquid crystals (LCs) in microdroplet form offers an intriguing combination of control over the composition and microscopic structure, including well-defined mesogen orientations, enhanced interfacial area, a rich phase space, tunable optical properties and stimuli response.²¹–²³ LC microdroplets embedded in a polymer matrix have attracted considerable interest in optoelectronic applications, such as variable transmittance windows and reflective mode displays.²⁴,²⁵ Solution-dispersed LC droplets are a promising platform for chemosensing.²⁶,²⁷ Typically, sensing is driven by the ability to optically read out target recognition-driven ordering transitions. This has been successfully demonstrated for a range of analytes, such as bacteria and viruses (10⁴ pfu mL⁻¹),²⁸ endotoxin (pM),²⁹ protein immunosays (pM),³⁰ and lithocholic acid (pM).³⁰ Other applications include the use of LC microdroplets as optical microresonators,³¹ microlasers,³² optical switches,³³ light responsive 3D superstructures,³⁴ as well as for materials templating.³⁵

Here, we study how a partially miscible liquid-liquid crystal mixture enables the temperature-induced forma-
tion of liquid crystal microdroplets. We investigate the droplet evolution to resolve nucleation and growth processes and identify critical parameters that govern the number and size distribution of LC droplets. Finally, we quench the liquid mixture below the isotropic-to-nematic transition temperature and study the feasibility of this approach for the generation of temperature-stable and well-defined nematic droplets.

Results and Discussion

We have recently reported on the macroscopic phase behaviour of a binary mixture composed of the thermotropic nematic liquid crystal 4-Cyano-4’-pentylbiphenyl (5CB) and methanol (MeOH). Four different arrangements were found as a function of temperature and volume fraction, namely monophasic isotropic, monophasic nematic, biphasic isotropic-isotropic and biphasic isotropicelectric. This system displays a $T - \phi$ phase diagram with an UCST of 25°C. According to Gibbs, a spinodal curve divides the region inside the phase coexistence curve of a phase diagram into an unstable region, in which phase separation is driven by spinodal decomposition, and a metastable region where phase separation is triggered through a nucleation and growth process. Droplets that form by temperature-induced phase separation nucleate when reaching a critical size to overcome the energy barrier associated with forming a new interface. For an off-critical mixture as used herein, demixing typically occurs via nucleation and growth.

Microdroplet formation was studied by optical microscopy in a 18 x 18mm$^2$ sealed sample compartment of 30 μm thickness. A binary liquid mixture of 30 vol% 5CB, 70 vol% MeOH was used for all experiments, unless stated otherwise. Fine temperature control was achieved by an enclosed Peltier-driven sample stage. A character-

Figure 1 | Reversible droplet formation. a-e: Nucleation and early-stage growth of droplets over the initial 0.2 s at 22.5°C. f-j: Disappearance of mature droplets over 7 s upon heating to 35°C. Image width: 20 μm.

5CB/MeOH temperature quench

Droplet growth upon demixing for off-critical mixtures of binary fluids is generally described in three phases. Nucleation occurs when a concentration partitioning reaches a critical size (phase I, timescale: μs), after which the droplet will grow spontaneously by diffusion (phase II, timescale: ms). Thereafter or simultaneously, the droplets undergo further growth by coalescence and Ostwald ripening (phase III, timescale: s-min). Eventually, the decreasing motion of droplets and increasing interdroplet spacing leads to a significant reduction in the rate of droplet growth and the system reaches an interim or steady state (>30s).

Figure 2a-c displays microscopic images of 5CB-rich droplets in MeOH 20 s after nucleation with quench depths ($\Delta T$) of $\Delta T = 0.5°C$ (a), $\Delta T = 2.5°C$ (b) and $\Delta T = 7.5°C$ (c), respectively. The quench depth relates to the undercooling with respect to the critical solution temperature ($T_c$), with
For rug = ioe, hagspsed O, Cere. Be ± hrmun, nve apt the inal ose you, nual, ame st at 10 μm. (d) Overview of droplet mean diameter and standard deviation for respective quench depths over time.

\[ \Delta T = |T_{target} - T_c| \]

Images were acquired at frame rates of 50 images per second and analysed using a custom-built and fully automated computational approach as detailed in the Supplementary Information (Figs. SI1 & SI2). Figure 2d depicts a time-resolved evolution of the mean droplet size for different quench depths. While a shallow quench depth of 0.5°C led to a droplet diameter of around 5.0 ± 1.3 μm at 60 s, a quench depth of 2.5°C resulted in droplets of 8.9 ± 2.7 μm in size, increasing \( \Delta T \) to 7.5°C caused a further increase in droplet diameter to 10.8 ± 2.4 μm within the observed time span as shown in Figure 2d.

Following equation 1, increasing the quench depth (\( \Delta T \)) from 0.5°C to 2.5°C and 7.5°C led to an increasing growth exponent of 0.19, 0.32 and 0.35 respectively, in the first stages of droplet growth. The dependence of the growth exponent on quench depth is in line with previous studies.11,18 However, this was primarily discussed for phase transitions, where the growth exponent increased from 0.5 to 1, rather than phase separations. For phase transitions, the dependence of the growth exponent on quench depth was related to a larger difference in free energy between the isotropic and the ordered state.6,11 The results presented here are qualitatively in line with a recent study by Luo and coworkers for supersaturation-induced emulsions, where the droplet diameter was found to scale with the quench depth \( \Delta T \). In this example, the temperature difference determined the total volume of the precipitated water and thus the size of each water droplet.38

Analysis of the number of droplets as a function of time (Supplementary Information, Fig. SI3) provided further insights. For a quench depth of 0.5°C, the number of droplets increased over 20 s and then settled slightly below the maximum level. In contrast, at \( \Delta T = 7.5°C \) droplets appeared within the first seconds and then reduced in counts significantly over time. Previous research focused on the effect of quench depth on the critical nucleus size, with an understanding that with increasing quench depth, the free energy barrier to nucleation decreases to values similar to the energy of thermal fluctuations at the spinodal.4,39 In this context, the critical nucleus size was found to decrease with an increasing quench depth,39 which is in line with our observations.

The dispersity of droplets was further investigated by analysis of larger sample sizes, using images acquired at frame rates of 1 image per second. The droplet population is presented in a histogram in Figure 3a-c over the course of the initial 60 s. Notably, the evolution of both droplet size and size distribution was found to depend strongly on the quench depth (\( \Delta T \)). For \( \Delta 0.5°C \) (a), the droplets remained relatively stable, with some larger droplets that formed at the expense of smaller ones. In contrast, for \( \Delta 7.5°C \) (c), the droplet population became multimodal after 30 s, with an overall profound size increase and broadening of the detected droplet diameters.

Droplet motion was analysed through individual trajectories along the x and y axis, as presented in Figure 3d-f. Each droplet was followed throughout its residence in the field of view. The colour coding in the legend illustrates the time \( t_0 \) when the droplet first entered the frame, i.e. for \( t_0 = 0 s \) the droplets formed within the field of view, while for \( t_0 ≥ 0 s \) the droplets formed elsewhere, then moved inside the field of view and were tracked thereafter. For a \( \Delta 0.5°C \) quench depth (d), the motion was essentially random around the starting position, with few droplets exhibiting directional motion away from the starting point. As the quench depth increased to \( \Delta 2.5°C \) (e), there were more instances of directional motion with some random fluctuation around the starting position. At a quench depth of \( \Delta 7.5°C \) (f), droplet movement appeared primarily directional and along the same axis. Hence, in addition to diffusion and coalescence led by Brownian motion, we identified a directional motion of the droplets, which became more pronounced with increasing quench depth. The corresponding mean square displacement (MSD) is shown in Figure 3g-i as a function of time lag, \( \tau \), with \( \tau = t - t_0 \). If the droplet trajectories were solely led by diffusion, a linear correlation between the quench depth and the MSD would be expected. However, the curvature of the graphs,
particularly at large quench depths, suggests an external force. In comparison to the steep increase in MSD for \( t_0 < 10s \), a shallow incline was observed for droplets that moved later into the field of view, suggesting that the directional droplet motion was a direct consequence of the applied cooling and faded thereafter. While a likely cause of directional droplet motion in immiscible fluid mixtures is related to thermal diffusion, we note that our observations are reminiscent to reports by Shimizu and Tanaka, who identified directional hydrodynamic motion driven by a composition Marangoni force originating from an interfacial tension gradient in each droplet.\(^{40}\)

Our findings emphasise the factors that influence droplet growth by coalescence, namely the interdroplet distance and the droplet motion, both of which are affected by the temperature quench. Eventually, with increased spacing and reduced mobility, the droplets reached a steady state, after which only rare events of further coalescence and Ostwald ripening were observed.

**5CB/MeOH cooling rate**

We further investigated the effect of cooling rate on droplet formation and growth, as shown in Figure 4. In all experiments, a homogeneous mixture of 5CB and MeOH was cooled from 35°C to 15°C, with a quench depth of \( \Delta7.5°C \) below \( T_c \) at cooling rates varying between 20°C min\(^{-1} \) and 1°C min\(^{-1} \). For all cooling rates, a representative snapshot of LC droplets taken 5s after nucleation, is shown in Figure 4a-d. Results from the automated computational analysis of droplets are presented in Figure 4e. Cooling rates of \( \geq 20°C min^{-1} \) led to greatly increased initial numbers of droplets, which rapidly decayed over the first 20s. In contrast, slower cooling rates resulted in a lower initial number of droplets which remained more constant over time. The development of the number of droplets with time may be directly related to the droplet density. Faster cooling rates \( (\geq 10°C min^{-1}) \) led to a higher droplet density and thus smaller interdroplet distances, which in turn implied a higher probability for coalescence. We note that at a cooling rate of 1°C min\(^{-1} \), the number of nucleated droplets was ten times less in comparison to a cooling rate of 20°C min\(^{-1} \).

The rate of cooling and related droplet density had a direct impact on the observed growth mode; at high cooling rates, droplet growth was dominated by coalescence. In contrast, at lower cooling rates and enhanced interdroplet distances, the growth was predominantly driven by diffusion. As a result, the cooling rate affected the polydispersity for droplet diameter: slow cooling rates of 1°C min\(^{-1} \) resulted in a smaller average diameter and standard deviation compared to fast cooling rates of 20°C min\(^{-1} \). To quantify the droplet movement, we analysed the individual droplet trajectories as detailed in the Supplementary Information (Fig. S15). While we observed directional motion for both 1°C min\(^{-1} \) and 20°C min\(^{-1} \), the gradient of the MSD was cooling rate dependent. As pointed out above, faster cooling rates and thus higher droplet densities implied a higher probability for coalescence. Thus, the increased MSD may be a direct con-
Figure 4 | Droplet number vs. cooling rate. a-d: Microscopic images of 5CB droplets in MeOH 5s after nucleation at cooling rates of (a) 20 °C min⁻¹, (b) 10 °C min⁻¹, (c) 5 °C min⁻¹ and (d) 1 °C min⁻¹ for a quench depth of ∆7.5 °C. The scale bar represents 10 µm. (e) Overview of number of droplets for respective cooling rates over time.

sequence of coalescence-induced coalescence cascade processes and related hydrodynamic flow.⁴¹

Nematic 5CB droplets

5CB is a thermotropic liquid crystal and a transition from the isotropic to the nematic phase is expected upon cooling. In the nematic phase, the liquid crystal exhibits a long-range orientational order without positional order. Volume confinement leads to an elastic distortion of the mesogen director field, typically resulting in topological defects, such as point defects with radial, bipolar or prera-dial configuration.⁴²,⁴³ The type of mesogen arrangement in liquid crystal droplets is highly sensitive to their size, boundary conditions and/or external fields, which makes them ideally suited for biological and chemical sensing applications.

In the previous sections, the droplets remained in the isotropic phase. According to a recently published phase diagram on the macroscopic behaviour of 5CB and MeOH, the phase transition of MeOH-enriched 5CB from the isotropic to the nematic state is expected at -0.5 °C.³⁶

The controlled formation of nematic droplets was therefore subject of the following study. A homogeneous mixture of 5CB and MeOH was cooled from 35 °C to -5 °C, corresponding to a quench depth of ∆27.5 °C. Below the critical solution temperature, the droplets nucleated and grew by diffusion and coalescence. Figure 5a-b shows bright-field images of droplets taken 2 seconds apart and reveal topological appearance changes, suggesting a point defect on the surface. Under polarised light, nematic droplets of 5CB in MeOH adopted a radial configuration as shown in Figure 5c.

As shown in Figure 5d, the diameter of the droplets increased rapidly when cooling through the isotropic temperature range. However, when reaching the nematic phase, the droplets remained stable in size over extended periods of time (here 45 min). The growth exponent of n = 0.36 was similar to the previously discussed isotropic quench (n = 0.35, ∆7.5 °C). As shown in the Supporting Information (Fig. S16), the directional motion of liquid crystal droplets and coalescence events were no longer observed in the nematic phase. However, we found some
evidence of Ostwald ripening; as some droplets increased in size, smaller droplets decreased in size and eventually diffused back into methanol.

Historically, nematic liquid crystal droplets have been prepared either through phase separation of a polymer-liquid crystal mixture (PDLC),\textsuperscript{26} ultrasonic\textsuperscript{44,45} or mechanical shearing\textsuperscript{46} with optional fractionation.\textsuperscript{47} or dispersion polymerization.\textsuperscript{48} Recently, microfluidic preparation of LC droplets has become more widely used,\textsuperscript{49,50} as well as a templating technique that relies on the sacrificial use of silica spheres and encapsulation by polyelectrolyte multilayers.\textsuperscript{51,52} While conventional methods offer scalable solutions, their preparation is often plagued by a lack of size control. In contrast, microfluidic processing and polyelectrolyte multilayer templating offer access to well-defined liquid crystal droplets, yet the former is limited to larger diameter and the latter involves a relatively elaborate preparative protocol. In comparison, the herein proposed route of nematic liquid crystal droplet formation distinguishes itself through the ease of fabrication and reversibility of formation.

**Conclusions**

In conclusion, we report on the controlled formation of liquid crystal microdroplets by a temperature-induced phase separation process and the identification of crucial parameters that govern this phenomenon. The growth patterns were crucially dependent on the quench depth and the cooling rate of droplets. The temperature quench depth played a crucial role for the observed motion, affecting droplet size and dispersity. The cooling rate had a strong influence on the number of droplet nuclei. Upon cooling into the nematic regime, droplets adopted a radial configuration. Thus, phase segregation of liquid mixtures with a critical point of miscibility may offer control over nucleation and size evolution of droplets with ease of fabrication and reversibility of the process. Such transient LC droplets with well-defined size and mesogen arrangement provide in our view a multitude of opportunities for materials templating and sensing applications.

**Methods**

* Reagents The liquid crystal 4-Cyano-4’-pentylbiphenyl (5CB) was obtained from Synthone Chemicals (99.5% (GC)). MeOH (HPLC grade) was purchased from Sigma Aldrich. All compounds were used without further purification.

* Sample preparation Samples of 5CB:MeOH were mixed in a glass cuvette, which was enclosed by a Peltier-regulated sample compartment that allowed control over both temperature and stirring (Quantum Northwest, Qpod 2e). Unless stated otherwise, a 30:70 volume ratio of 5CB:MeOH was used for all experiments. Samples were heated to 35°C in the cuvette. Glass slides were functionalised to increase the hydrophobicity of the surface. First an oxygen plasma etcher was used to clean the surface and increase wettability of the slides. The glass slides were then placed in a bath of 0.1mM solution of trichloro(octyl)silane (97%, purchased from Sigma Aldrich) in heptane (≥99.9%, purchased from Sigma Aldrich) for 10 minutes. Finally, they were washed in MeOH (HPLC grade). For microscopic analysis, 10 µl of the homogeneous mixture was deposited between a functionalised glass slide and cover slip and sealed with varnish (purchased from Rimmel: 15-40% ethyl acetate, 15-40% butyl acetate, 5-15% nitrocellulose, 1-10% isopropylalcohol) to prevent MeOH evaporation.

* Sample analysis: The slide was placed under an upright microscope (Zeiss, Axio Scope A1) that was operated in transmission and primarily in brightfield mode. A temperature controlled sample stage (Linkam, PE120) was used for all experiments. For low temperature experiments, nitrogen was introduced into the chamber to prevent condensation. In-situ droplet formation and short-term growth were recorded by time-resolved digital image acquisition using a Photron Fastcam MC1 high-speed camera taking 50 frames per second (fps) at a resolution of 512 x 512 pixels. For nematic droplet analysis, a Lumenera Infinity 3-3UR camera was used, taking 1 fps with a resolution of 1936 x 1456 pixels. For temperature quench and cooling rate experiments, the cell was heated to 35°C and then cooled at a defined cooling rate ranging from 1°C min⁻¹ to 20°C min⁻¹ to a target temperature below the critical temperature, T_c. Note that for the purpose of this study, T_c is referred to as the temperature at which phase separation occurs and the quench depth ΔT°C relates to |T_{target} − T_c|. With a 30:70 vol% mixture of 5CB:MeOH, the T_c was 22.5°C. Quantitative droplet investigation was carried out by a bespoke computational image analysis code developed in Python [full details can be found in the Supplementary Information]. The fully automated analysis protocol enabled the extraction of otherwise unattainable kinetic information. Droplets from the high-speed images were identified, distinguished, and the number of droplets, the average diameter as well as standard deviation computed as a function of time.\textsuperscript{53} Calculation of trajectories, displacement and MSD of droplets was carried out using Fiji. Droplets were tracked using the Particle Detector and Tracker plugin: MOSAIC,\textsuperscript{54} which outputs the x and y coordinates of each trajectory for further calculation.

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**Author contributions**

MP, SI, LB and EHS carried out the droplet formation experiments and analysed data. APR developed the tools for droplet characterisation and image analysis. SI, EA, BSH and SG conceived the experiment. MP and SG wrote the manuscript. All authors contributed with comments and feedback.