

High pressure suppresses the laser-induced nucleation of supersaturated aqueous potassium chloride solutions

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(Received 28 February 2025; revised 20 May 2025; accepted 19 August 2025; published 29 October 2025)

We report the suppression of nucleation in the nonphotochemical laser-induced nucleation of supersaturated aqueous potassium chloride solutions when the system pressure is above ambient pressure. The crystal yield at 51.7 bar is reduced to 5% of its value at 1 bar, and the crystal number dependence on pressure fits well to a semiempirical model based on the impurity-heating mechanism and the adiabatic compression of an ideal gas nanobubble. Our results complement recent findings by Barber and Alexander [*Phys. Chem. Chem. Phys.* **27**, 6288 (2025)] using high-speed imaging of bubbles preceding the observation of cesium chloride crystals. Together, these two studies provide compelling evidence for the impurity-heating mechanism.

DOI: [10.1103/kr3g-67gz](https://doi.org/10.1103/kr3g-67gz)

Introduction. Crystallization is an important unit operation used in the chemical and pharmaceutical industries for the purification and separation of crystals for various applications such as feedstock input and medicinal formulation. Controlling the process parameters for the formation of crystals with the desired properties is an ongoing interest. Nucleation is the first step in crystallization in which an ordered phase emerges from the disordered solution phase. Techniques such as seeding [1] and antisolvent addition [2] are the primary means used in these industries. Laser-induced nucleation provides an alternative method in which the interaction of a solution with a laser beam at a particular location and time can nucleate nascent crystals.

In 1996, Garetz *et al.* [3] reported that exposure of supersaturated aqueous urea solutions to unfocused millijoule nanosecond pulses of near-infrared laser light resulted in the rapid nucleation of urea crystals. They called the phenomenon nonphotochemical laser-induced nucleation (NPLIN) owing to the facts that the solution was essentially transparent at the laser wavelength and that the near-IR photon energy was too low to induce photochemistry. At the time, they suggested that the electric field of the light was aligning solute molecules in prenucleating clusters through the optical Kerr (OK) effect, aiding their organization into a critical nucleus, although estimates of the interaction energies between the electric field and the urea molecules were orders of magnitude too small to account for the observed rate of nucleation [4].

NPLIN has since then been observed in organic [5–10] and inorganic compounds [11–16]. Alexander and Camp [11] reported NPLIN in aqueous potassium chloride (KCl) in 2009. Because KCl consists of spherical ions arranged in a cubic lattice, the OK mechanism could not explain their observation, and they proposed a different mechanism, but still based on the interaction of precritical solute clusters with the optical electric field. In their dielectric polarization (DP) model, a precritical solute cluster with a relative permittivity higher than the surrounding solution would, in the presence of an external field, have its energy lowered by a greater amount than the solution phase, thus lowering the activation barrier to nucleation. Later experiments by Knott *et al.* [17] reporting the NPLIN of carbon dioxide bubbles from carbonated water could not be explained by either the OK or DP mechanism. Knott *et al.* [17] demonstrated bubble-induced crystal nucleation by shaking aqueous solutions supersaturated with respect to both glycine and argon. They speculated that bubble nucleation directly precedes crystal nucleation.

More recently, experiments have shown that filtration of a supersaturated solution before laser irradiation reduces the probability of nucleation [16–19], and the intentional doping with impurity nanoparticles enhances the probability of nucleation in NPLIN [16]. This has led to the proposal of the impurity-heating (IH) mechanism. The basic idea is that even if a solution appears to be transparent at the laser wavelength, there can be trace amounts of insoluble impurity particles present in a solution that can absorb the laser light, and sufficient heat can be generated to vaporize the surrounding solvent to form vapor nanobubbles. As a bubble grows, it concentrates solute molecules at its surface, leading to heterogeneous nucleation at the bubble-solution interface. Bubble formation is a well-documented mechanism for nucleation using tightly focused nanosecond [20,21] or femtosecond [22] laser pulses, and micrometer-sized bubbles have been observed in these studies. Our work was motivated by the goal of experimentally isolating one of the proposed mechanisms

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for NPLIN and quantifying its contribution, if any, to the laser-induced nucleation phenomenon.

Recently, Barber and Alexander [23] showed with high-speed imaging that cavitation microbubbles are induced by unfocused lasers and observed that crystals subsequently grew at the location of cavitation events. Short of actually observing the formation of nanobubbles during NPLIN, we believe the most direct way of confirming the IH hypothesis is to study the effect of pressure on NPLIN. At high pressure, bubble formation becomes more difficult. The IH mechanism is based on the adiabatic expansion of solvent vapor bubbles, and at higher pressures, the model predicts the formation of smaller bubbles, resulting in a lower probability of nucleation.

In 2019, Hua *et al.* [24] demonstrated that NPLIN can be carried out in microfluidic devices. Microfluidics has manifold advantages compared to batch glass vials owing to lower material consumption, better isolation from contaminants, and ideal heat and mass transfer within the microchannels. Other important features of carrying out NPLIN in single-phase microfluidics in continuous flow are that (1) every volume element of the solution that flows through the device is irradiated and (2) the flow time can be adjusted to ensure that more than one crystal is nucleated per run. By inserting a pressure regulator downstream from the cooling and irradiation zones, it is possible to safely and easily carry out NPLIN experiments at pressures as high as 80 bar [25,26].

In this Letter, we demonstrate that for NPLIN in supersaturated aqueous KCl, the crystal yields are inversely related to the external pressure. The pressure dependence of the crystal yield is quantitatively consistent with a semiempirical model based on the IH mechanism that was first proposed by Ward *et al.* [27] and later extended by Ndukwe-Ajala *et al.* [28], where it was demonstrated that this model was consistent with both the intensity dependence and the nanoparticle concentration dependence of the number of crystals observed.

Methods.

Solution preparation. The solute, KCl ($\geq 99\%$ ACS grade, Sigma-Aldrich), was recrystallized by hot filtration and evaporation. Recrystallization was done to further remove insoluble impurities before use for experiments. For details of the recrystallization procedure, see the Supplemental Material [29].

Slightly undersaturated aqueous solutions of KCl, with a concentration of 0.34 g KCl per 1 g water, were prepared (solubility of KCl in water is 0.3436 g per 1 g water at 20 °C [30]). The glassware, bottles, and screw caps used were washed thoroughly with soap solution (Micro-90) and rinsed with copious amounts of ultrapure deionized water (resistivity 18.2 M Ω cm and <5 ppb TOC, Millipore). After 30 min on the magnetic hotplate stirrer, the solution appeared transparent. The solution was kept in a mechanical convection oven (Heratherm, Thermo Scientific) overnight at 45 °C for further dissolution.

The warm solution was nanofiltered with a 20-nm pore syringe filter (WHA68092002, Whatman Anotop). A 16-gauge syringe needle was attached to the syringe filter for a careful and direct transfer of the filtered solution into a glass bottle.

The filtered aqueous KCl solution was doped with 30 ± 3 nm diameter iron(II, III) oxide nanoparticles (SPA30, Ocean NanoTech). The intentional addition of nanoparticles

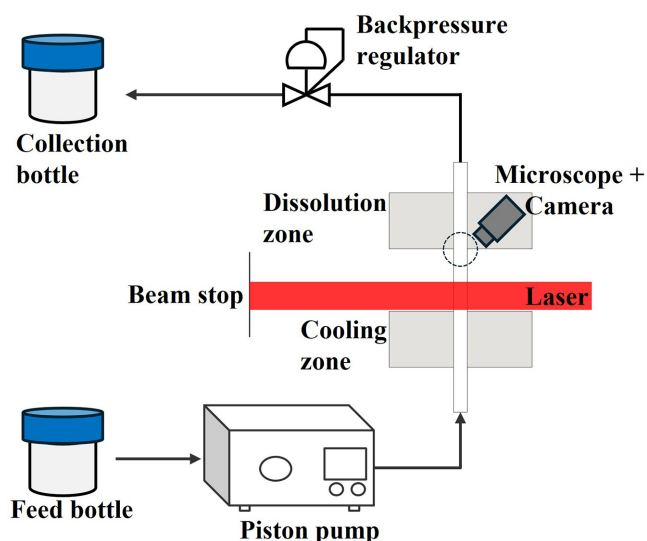


FIG. 1. Layout of the experimental setup.

to liquid solutions here is termed doping. The iron(II, III) oxide (Fe_3O_4) nanoparticles were purchased as a dispersion in water with a concentration of 5 mg/ml. The proprietary polymer coating, with a backbone of poly(maleic anhydride-1-octadecene), on the nanoparticles prevents aggregation and promotes uniform dispersion. The purchased dispersion was diluted to 0.17 mg/ml, and 60 μl of the diluted dispersion was carefully added to 47 ml of the filtered aqueous KCl solution to achieve a nanoparticle concentration of 3×10^9 nanoparticles/ml in the 0.341 g KCl per 1 g water KCl solution. A detailed description of the doping procedure is provided in our previous work [28].

Laser-induced nucleation. Figure 1 shows the components of the system for NPLIN experiments under pressure. The capillary-based microfluidic system has a piston reciprocating pump (LS005SRX, Teledyne Instruments) to deliver the fluid from the Schott glass bottle at a flow rate of 300 $\mu\text{l}/\text{min}$ into the flow system. Cylindrical polyether ether ketone (PEEK) tubing (rated for 414 bar) with a 500 μm ID, 1/16" OD was used to connect the pump outlet to the PEEK tubing of 0.020" ID, 1/32" OD using microtight adapters. Connector sleeves made of clear polycarbonate resin were 3D printed to connect the cylindrical end of the smaller PEEK tubing to the square end of the glass capillary. Clear epoxy (EA E-05CL, Loctite) was used to adhere the smaller PEEK tubing to the square-cross-sectioned glass capillary, which had a 1 mm $\times$ 1 mm ID, 0.2 mm wall thickness, and 100 mm length (8100, VitroCom).

To generate supersaturation locally, the capillary was placed in contact with a 40 mm $\times$ 40 mm $\times$ 4 mm thermoelectric Peltier cooler set at 11 °C (284 K). We verified via infrared thermal imaging that the surface temperature of the exposed capillary section in the irradiation zone was 11.28 ± 0.26 °C, which corresponds to an induced supersaturation of 1.059 ± 0.002 . Supersaturation here is the ratio of the solution concentration to the concentration of a saturated solution at a given temperature. Results of the thermal imaging measurements are provided in the Supplemental Material [29]. The fluid then came in contact with a 20 mm $\times$ 40 mm $\times$ 4 mm thermoelectric Peltier element set at 45 °C for the dissolution

of crystals before the fluid exited the capillary. Backpressure was built up in the system using a preset backpressure cartridge (IDEX), located on the capillary outlet. Backpressure cartridges are routinely used across a broad range of chemistry applications for fluids with significant ionic strength [31–33]. The spring-loaded backpressure cartridges are made from inert materials with excellent chemical resistance such as PEEK, ethylene tetrafluoroethylene, and gold-plated stainless steel. Four backpressure cartridges (75, 250, 500, and 750 psi) enclosed in their assemblies were used to generate the elevated pressures reported in this work. While higher pressure cartridges are commercially available, the glass capillary cannot survive such high pressures for extended periods of time (>2 h) needed to collect sufficient crystals at such pressures.

The solution was exposed to a train of laser pulses from a 1064-nm wavelength Q-switched Nd:YAG pulsed laser. The laser emitted a continuous train of 6-ns pulses at a repetition rate of 10 pps. The laser beam passed through a 5-mm-diameter ceramic aperture. A Glan Taylor Calcite Polarizer cube was used to ensure a linearly polarized beam. The beam was directed by a pair of mirrors toward the glass capillary and stopped by a metal beam stop. The incident beam's average power before the capillary was measured to be 0.24 W, corresponding to a peak intensity of 20 MW/cm². Videos of KCl crystals in flow were captured at 60 fps with a 20 MP CMOS camera mounted on an Amscope metallurgical microscope with a 10 $\times$ objective. The observation zone was 7.5 mm downstream from the center of the irradiation zone. The counting and labeling of crystals were done manually. Crystals indistinguishable due to motion blur were not counted. The solution volume within the irradiation zone was 5 μ l. With a laser repetition rate of 10 pps and a flow rate of 300 μ l/min, each volume element was exposed to an average of ten laser pulses. With a capillary volume of 100 μ l, the residence time of solution in the capillary was 20 s and a minimum of 5 min was provided for the flow to reach a steady state. To observe a sufficient number of crystals, the experiment runs varied from 5 to 20 min. We conducted control experiments at each system pressure. The supersaturated solutions were pumped into the capillary without laser exposure, and no crystals were observed for 5 min of flow.

Results and discussion. As mentioned in the introduction, filtration is known to reduce the probability of nucleation in NPLIN. To eliminate the contribution of uncharacterized impurities in an unfiltered + undoped solution, we nanofiltered the solution and then added nanoparticles with known characteristics to provide a basis for quantitatively fitting semiempirical model predictions to experimental results.

Figure 2 shows the dependence of nucleation yield on the system pressure at a fixed supersaturation of $S = 1.06$ and laser intensity of 20 MW/cm². Interestingly, both unfiltered + undoped and filtered + doped solutions displayed the same decreasing trend with increasing pressure. This observation suggests that the pressure effect is independent of the nature of the impurities. The unfiltered + undoped solution could contain a range of impurities with different optical absorption characteristics. However, in both cases, nucleation is greatly suppressed at 51.7 bar. We observed a majority of the typical cubic KCl crystals at all pressure values. A few cuboid and

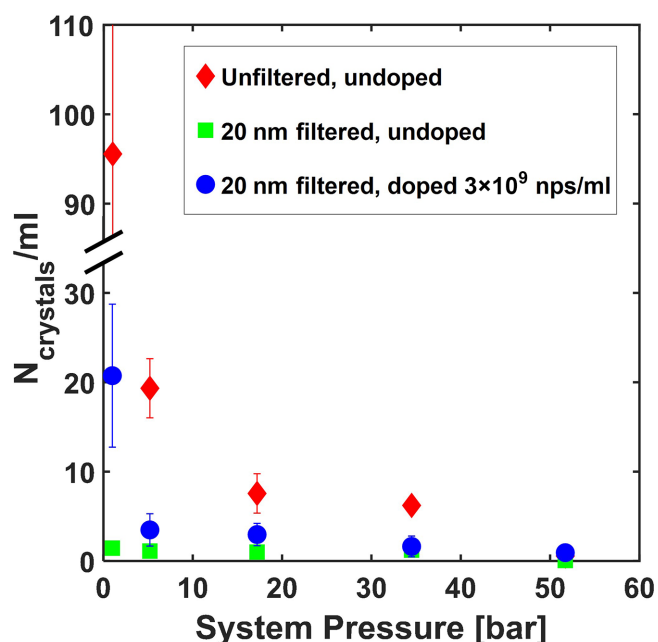


FIG. 2. Nucleation yield per irradiated solution volume vs system pressure for the NPLIN of aqueous KCl at a supersaturation of $S = 1.06$ and laser intensity of 20 MW/cm². Error bars represent standard deviations from averaging the results of at least three runs at each pressure value. Red diamonds refer to unfiltered + undoped solutions, green squares refer to 20 nm filtered + undoped solutions, and blue circles refer to filtered solution doped with an Fe₃O₄ nanoparticle concentration of 3×10^9 nanoparticles/ml.

needle-shaped crystal habits were also observed. Crystal habit and size distribution results are shown in the Supplemental Material [29]. Also, we expected no change in the crystal structure of KCl observed at the elevated pressures tested in our experiments, as we did not operate in the GPa region where a structure transition has been reported from the typical rocksalt-type (B1) structure to cesium chloride-type (B2) structure at ~ 2 GPa [34]. We can also disregard the effect of pressure on the solubility of potassium chloride in water at the pressures studied here, assuming a negligible rise in solubility with pressure. For instance, the solubility of sodium chloride in water at 1 bar and 25 $^{\circ}$ C is 26.42 wt%, and at 4000 bar the solubility is 27.6 wt% [35].

For the 20 nm filtered + undoped solution, the nucleation yield observed was considerably lower compared with unfiltered + undoped and filtered + doped solutions, especially at 1 bar, which is consistent with previous observations of the effect of filtration [16–19] on NPLIN. As shown in Fig. 2, there is an evident drop in the nucleation yield at 51.7 bar when compared to that at 1 bar.

For the filtered + doped KCl solution (Fig. 3), videos were recorded for 5–10 min each. Each video represents a data point. At each pressure tested, nine videos were recorded. All videos at a given pressure value were taken in succession without disturbing the continuous flow experiment. The number of crystals observed in each video is normalized to the solution volume exposed to irradiation during the acquisition time.

We developed a simple semiempirical model, described in our previous paper [28], based on the impurity-heating

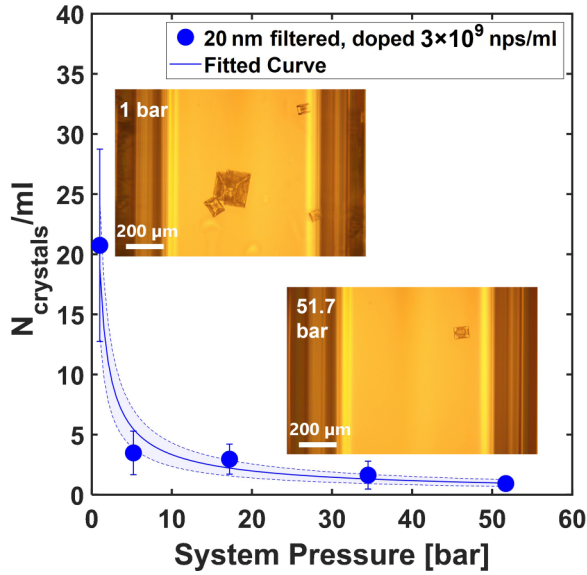


FIG. 3. Nucleation yield per irradiated solution volume vs system pressure on the NPLIN of filtered + doped aqueous KCl (3×10^9 nanoparticles/ml) at a supersaturation of $S = 1.06$ and laser intensity of 20 MW/cm^2 . Snapshots showing KCl crystals provided are from the raw videos at 1 and 51.7 bar. Error bars represent standard deviations from averaging the results of nine runs at each pressure value. A total of 45 experimental data points were collected. The fitted curve represents the model prediction. Blue dashed lines with shaded region represent the 95% confidence bounds of the model. White scale bars are $200 \mu\text{m}$.

mechanism [36,37]. The model is centered around the idea that if a vapor bubble concentrates solute molecules at the bubble/solution interface, then the larger the bubble, the more highly concentrated the solute molecules become at the interface, and therefore the greater the probability that a solute crystal will nucleate. For simplicity, we assume that the probability is proportional to the bubble volume.

$$P_{\text{crystal}} = f \times V_{\text{bubble}}, \quad (1)$$

where f is a proportionality factor that depends on solute-solvent combination and on solute concentration but is independent of nanoparticle properties such as diameter, absorption efficiency and number concentration, and laser properties such as intensity, wavelength, and beam size. According to classical nucleation theory, an increase in solute concentration increases the rate of nucleation J [38], as given by Eq. (2). Properties such as interfacial energy, molecular volume, and supersaturation would be incorporated in the term f .

$$J = A \exp(-\Delta G_c^*/RT), \quad (2)$$

$$\Delta G_c^* = \frac{16\pi N_A \gamma^3 V_m^2}{3k^2 T^2 \ln^2 S},$$

where N_A is Avogadro's number, γ is interfacial energy, V_m is molecular volume, and S is supersaturation.

The number of irradiated nanoparticles, N_{irrad} , is equal to the nanoparticle concentration, C_{nano} , times the irradiated volume, V_{irrad} , and the number of crystals formed, N_{crystal} , is the number of irradiated particles times the probability of

crystallization.

$$N_{\text{crystal}} = P_{\text{crystal}} \times N_{\text{irrad}} = (f \times V_{\text{bubble}})(C_{\text{nano}} \times V_{\text{irrad}}). \quad (3)$$

To account for the effect of pressure, we examine the assumptions made to estimate the bubble volume used in the model. The model assumes that all the heat goes into generating a vapor bubble. For the experiments in this study, the laser intensity was kept at a constant 20 MW/cm^2 . As shown by Ward *et al.* [27], we can estimate the energy absorbed by a 30-nm-diameter Fe_3O_4 nanoparticle from a single laser pulse of 20 MW/cm^2 to be $5.17 \times 10^{-14} \text{ J}$. We assume all the absorbed energy is used to instantaneously heat the water to $T_1 = 520 \text{ K}$ (80% of the critical temperature of water) and vaporize $n = 1.07 \times 10^{-18}$ moles of liquid water. We show in the Supplemental Material [29] that the results in Fig. 3 are insensitive to the specific choice of vaporization temperature. The resultant bubble is assumed to initially occupy the volume of the liquid water that was vaporized, $V_1 = 1.92 \times 10^{-23} \text{ m}^3$. Assuming the water vapor is an ideal gas, the initial pressure of the water vapor is $p_1 = \frac{nRT_1}{V_1} = 240 \text{ MPa}$. We assume that this bubble undergoes reversible (isentropic) adiabatic expansion, with $pV^\chi = \text{constant}$, with the exponent equal to the ratio of heat capacities at constant pressure and volume, respectively, $\chi = \frac{c_p}{c_v} = 1.328$ for water vapor at 284 K . If the final pressure is equal to the ambient pressure, $p_2 = 100 \text{ kPa} = 1 \text{ bar}$, we estimate the final volume of the bubble to be $V_2 = 6.68 \times 10^{-21} \text{ m}^3$, which corresponds to a radius of 117 nm . For liquid pressures, p_2 , greater than 1 bar, the final bubble volume can be calculated from

$$V_{\text{bubble}}(p_2) = V_{\text{bubble}}(p_1 = 1 \text{ bar}) \left(\frac{1 \text{ bar}}{p_2} \right)^{1/\chi}. \quad (4)$$

We can return to Eq. (3) and input the known terms to give a relationship between the number of crystals nucleated and the system pressure:

$$N_{\text{crystal}} = f \times (2.0 \times 10^{-5} \text{ ml}) \left(\left(\frac{p_2}{1 \text{ bar}} \right)^{-0.753} \right). \quad (5)$$

Fitting Eq. (5) to the data in Fig. 3 yields a fitted estimate of $f = (9.44 \pm 2.78) \times 10^5 \text{ ml}^{-1}$. The fitted curve is the solid line in Fig. 3 (goodness of fit, $R^2 = 0.94$). A residuals plot is provided in the Supplemental Material [29]. The uncertainty of the fitted estimate is based on 95% confidence bounds. The fitted estimate from these pressure experiments is similar to $(3.64 \pm 0.45) \times 10^6 \text{ ml}^{-1}$, the estimate from our laser intensity dependence study at the same nanoparticle concentration [28]. The value of f extracted from N vs p data is lower than the value extracted from the N vs I data in Ref. [28]. Given the approximate nature of our model and the possible errors it contains, it is remarkable that the values are fairly close to each other.

In high-intensity laser experiments, cavitation bubbles have been observed using solutions with soluble light-absorbing impurities [20,21]. The use of soluble impurities requires a tightly focused beam for localized energy deposition. Our work utilizes colloidal impurity particles that act as nanoscale absorbers for localized heat generation and subsequent vapor formation.

From simulations by Hidman *et al.* [39], supersaturation peaks at the bubble interface at $1 \mu\text{s}$. The boundary layer

thickness, δ , can be approximated by $(Dt)^{1/2}$, where D is the solute diffusion coefficient and t is time. The diffusion coefficient for KCl in water at 25 °C is $1.89 \times 10^{-9} \text{ m}^2/\text{s}$ [40]. For aqueous KCl, $\delta = 43 \text{ nm}$. The increase in solute concentration of the solute at the bubble interface can be estimated by the increase in the factor, ϕ , ratio of the bubble-plus-shell volume to the shell volume alone.

$$\phi = \frac{\frac{4}{3}\pi(r + \delta)^3}{\frac{4}{3}\pi(r + \delta)^3 - \frac{4}{3}\pi r^3}. \quad (6)$$

Using Eq. (6) and the bubble radius of 117 nm previously estimated, the solute concentration increases by a factor of 1.6. We assume that nucleation of solid crystals occurs at the bubble interface with the solution. However, an alternative pathway for nucleation from bubble to crystal could be due to large pressure gradients created by the bubble collapse [36]. Localized increases in supersaturation could be induced by the propagating pressure waves. The amplitudes of the pressure waves generated by the bubble collapse would be greater with increasing bubble size, which would still support the assertion of our model that the larger the bubble, the greater the probability of nucleation.

Conclusions. In summary, the yield of crystals from the NPLIN of supersaturated aqueous KCl filtered solution doped with Fe_3O_4 nanoparticles exhibits a pressure dependence that is in quantitative agreement with a semiempirical model based on the impurity-heating mechanism for NPLIN that involves the formation of solvent vapor nanobubbles. At the highest pressure studied, 51.7 bar, the yield of crystals was reduced to approximately 5% of the yield at ambient pressure. This represents strong evidence for the IH mechanism. It shows

that vapor bubbles are essential for NPLIN and that larger bubbles are more effective at inducing nucleation.

Extrapolating these findings to higher pressures, we would expect NPLIN to be completely switched off once the liquid external pressure reaches the critical pressure of water (221 bar), at which point vapor bubble formation is thermodynamically forbidden, assuming that the IH mechanism is the only mechanism for NPLIN. Future work could develop devices to study aqueous KCl NPLIN at pressures around 221 bar to ascertain whether laser-induced nucleation can be completely switched off at high laser intensities and high supersaturations, or whether there is some residual crystal formation under these conditions, which would imply the existence of an alternative mechanism. There is ongoing work to extend this study to other solute/solvent systems under applied pressure. Also, with pressure as a process control parameter, there is the potential for more precise control of crystal yields as well as characteristics such as crystal habits. The findings in this Letter provide more clarity on laser-induced nucleation of solid crystals from liquid solutions.

Acknowledgments. This work was supported by the National Science Foundation under Awards No. CBET-2103689 and No. 2410704. We thank J. Michael McBride for originally suggesting the idea of studying the pressure dependence of NPLIN.

Any opinions, findings, and conclusions or recommendations expressed in this Letter are those of the authors and do not necessarily reflect the views of the National Science Foundation.

Data availability. The data that support the findings of this article are not publicly available. The data are available from the authors upon reasonable request.

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