Author's personal copy

Journal of Crystal Growth 312 (2010) 487–489

Contents lists available at ScienceDirect

Journal of Crystal Growth

journal homepage: www.elsevier.com/locate/jcrysgro

Ultra-fast crystallization due to confinement

R. Grossier [a], Alastair Magnaldo [b], S. Veesler [a,*]

[a] CINAM - CNRS, Centre Interdisciplinaire de Nanoscience de Marseille, Campus de Luminy, Case 913, F-13288 Marseille Cedex 09, France[1]
[b] CEA-Valrhô, DRCP/SE2A/LEHA, BP17171, F-30207 Bagnols-sur-Cèze, France

ARTICLE INFO

Article history:
Received 23 September 2009
Received in revised form
27 November 2009
Accepted 7 December 2009
Communicated by M. Tischler
Available online 16 December 2009

Keywords:
A1. Nucleation
A2. Growth from solutions

ABSTRACT

In the crystallization experiments we present in this communication confinement allows the system to be both highly supersaturated and in a metastable state. As a result, the nucleation from NaCl-solutions proceeds in less than 2 s from the dense liquid phase in agreement with the two-step nucleation mechanism.

© 2010 Elsevier B.V. All rights reserved.

In a previous paper we theoretically reconsidered the effect of confinement (small volume system) on nucleation and identified a clear window of parameters where nucleation occurs alone according to a thermodynamics approach[1]. Confinement where experimentally affordable, will provide a new way to study critical clusters and nucleation. In the literature confinement (at the nanometer scale) is realized by controlled-pore glasses [2,3] or other nanoporous materials [4]. Thermal behavior of materials under confinement is examined in relation with the Gibbs–Thomson equation [3], or polymorph selectivity in ultra-small pores [4,5] or in small droplets [6]. Microemulsions are also used to produce confinement in order to measure critical nucleus size via thermal behavior [7].

In order to observe the effect of confinement on the kinetics of crystallization, we developed a set-up to generate and observe micrometer droplets. This communication presents the first findings on the crystallization of NaCl by evaporation of micrometer droplets of undersaturated NaCl solutions covered by DMS oil.

All experiments were performed on a 18 mm diameter coverslip inserted in a thermostatted well under an optical microscope (Zeiss Axio Observer D1). The well is filled with approximately 5 mL of inert DMS oil (Hampton Research HR3-419, refractive index=1.390). The micrometer droplets of NaCl solution are generated on the coverslip by a microinjector (Femtojet, Eppendorf) used for the injection of liquids in the volume range from femtoliters to microliters. A home-made micromanipulator consisting of three miniature translation stages (piezo electric, MS30 mechonics) allows displacement of the injector (capillary holder) in *X*, *Y* and *Z* with a displacement of 18 mm in the 3 directions by steps of 16 nm. A hydrophobic glass capillary, obtained by vapor-depositing a toluene+5%v/v n-octadecyltrichlorosilane (ODTS) mixture on the capillary, with an internal diameter of 0.5 μm (Femtotip Eppendorf), is used. The whole set-up is shown in Fig. 1.

The principle of the experiments is to let water slowly evaporate from the crystallization drops through the layer of liquid oil [8–10], which results in an increase in the concentration of NaCl, establishing supersaturation. We control the rate of evaporation because over-drying (in air for instance) often results in the formation of polycrystalline aggregates. Fig. 2 presents the complete process: evaporation, nucleation and growth. In the first

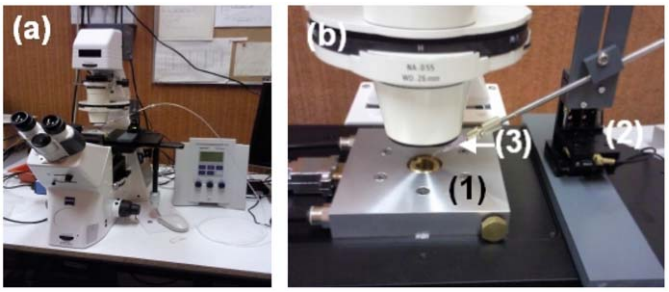

Fig. 1. (a) Image of the whole experimental set-up and (b) zoom of the previous image: (1) thermostatted crystallization-well, (2) *XYZ* miniature translation stages and (3) glass capillary.

[1] Laboratory associated with the Marseille Universities.

* Corresponding author. Tel.: +33 6 6292 2866; fax : +33 4 9141 8916.
E-mail addresses: grossier@cinam.univ-mrs.fr (R. Grossier), veesler@cinam.univ-mrs.fr (S. Veesler).

0022-0248/$ - see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jcrysgro.2009.12.020

Author's personal copy

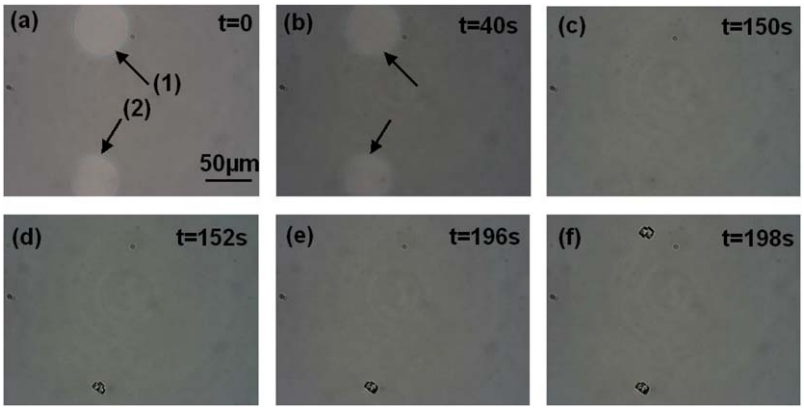

Fig. 2. Panels a–f represent time sequence showing ultra-fast nucleation and growth of NaCl: (a) $t=0$:2 droplets of NaCl solutions are generated through the layer of liquid oil. The sizes of droplets (1) and (2) after spreading on the coverslip are 61 and 53 µm, respectively, corresponding to an effective volume of about 10 pL.

stage, 2 droplets containing NaCl 0.7 M solution are generated (Fig. 2a). Droplets slowly evaporate until supersaturation is established (Fig. 2a–c). The NaCl concentration is qualitatively monitored through the evolution of the optical contrast between the droplet and the DMS oil in Fig. 2a–c. Droplets (1) and (2) of 61 and 53 µm, respectively (Fig. 2a) completely disappear, in 128 and 82 s, respectively, indicating an adjustment of the refractive index between the two phases. At $t=0$, the refractive index of the 0.7 M NaCl solution is 1.340 when the solution concentrates during evaporation the refractive index increases. At these times, $t=128$ and 82 s, respectively, NaCl concentration is 6.7 M in the droplets. NaCl concentration is estimated from a relation between concentration and refractive index (tables 71 D-252) [11]. Using this estimation, we calculate the supersaturation in the droplets at these times ($t=128$ and 82 s) to be $\beta=1.23$. Supersaturation β is defined as the ratio of the NaCl concentration in solution versus the solubility of NaCl, 5.42 M at 20 °C in water [12].

Nucleation occurs after 196 and 150 s in droplets (1) and (2), respectively (Fig. 2d and f). In addition, supersaturation is greater than 1.3 in both droplets at the time of nucleation, since the evaporation process continues during the lapse of time between droplets disappearing and nucleation. Note (1) the same level of supersaturation was previously obtained in small droplets by Tang and Munkelwitz [13] and (2) that non-confined NaCl solutions spontaneously nucleate at $\beta > 1.03$.

Three important observations follow from the sequence in Fig. 2.

Observation (1): Confinement stabilizes the solution up to high supersaturation. This is in agreement with the theoretical prediction using a thermodynamics approach [1]: for volume smaller than the nanoliter range and below a critical supersaturation no nucleation can occur. When applied to NaCl solution and to droplets of 50 µm we found that the critical supersaturation is 1.005 (Fig. 3). Fig. 3 is derived from the slightly modified classical nucleation developed for finite-sized system [1], namely to a volume corresponds a number of molecules in a droplet and a critical supersaturation where no nucleation can occur. Here a kinetics effect (metastable zone) of the confinement is shown to stabilize highly supersaturated NaCl solutions, in droplets of 53 and 61 µm, at supersaturation greater than 1.23.

Observation (2): Both nucleation events are single, also in agreement with the prediction: "… and there is a supersaturation-window for a single nucleation event giving one single crystal per droplet of a scalable size [1]". Here again, the kinetics effect of confinement enlarges the supersaturation window in Fig. 3.

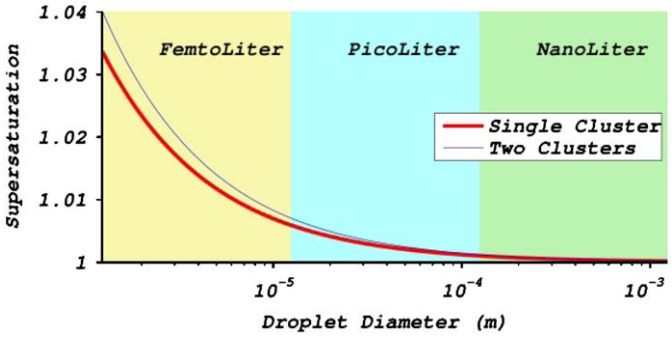

Fig. 3. Critical supersaturation (after [1]) below which no nucleation can occur in function of droplet size, the red curve for a single nucleation event and the blue curve for a second event.

Observation (3): Nucleation and growth occur very rapidly: in less than 2 s a crystal of 15 µm having a cubic habit (Fig. 2c, d and e, f) is produced. The growth rate appears to be about 10 µm/s, several orders of magnitude faster than that expected for NaCl grown from solution [14]. We propose an interpretation based on the two-step nucleation mechanism [15–17], where a density fluctuation is followed by a structural fluctuation, the structural fluctuation being almost instantaneous. In the experiments we present in this communication, confinement allows the system to be highly supersaturated and in a metastable state; this formation of a dense liquid phase is the first step. Nucleation then proceeds in less than 2 s from the dense liquid phase. To our knowledge this is the first time that such a mechanism has been directly observed in solution.

Acknowledgements

The authors thank M. Sweetko for English revision and ANR-06-Blan-0355 "MICROCRISTAL" for financial support.

References

[1] R. Grossier, S. Veesler, Reaching one single and stable critical cluster through finite sized systems, Cryst. Growth Des. 9 (2009) 1917–1922.
[2] W. Haller, Chromatography on glass of controlled pore size, Nature 206 (1965) 693–696.
[3] C.L. Jackson, G.B. Mckenna, The melting behavior of organic materials confined in porous solids, J. Chem. Phys. 93 (1990) 9002–9011.
[4] J.-M. Ha, J.H. Wolf, M.A. Hillmyer, M.D. Ward, Polymorph selectivity under nanoscopic confinement, J. Am. Chem. Soc. 126 (2004) 3382–3383.

Author's personal copy

[5] M. Beiner, G.T. Rengarajan, S. Pankaj, D. Enke, M. Steinhart, Manipulating the crystalline state of pharmaceuticals by nanoconfinement, Nano Lett. 7 (2007) 1381–1385.
[6] A.Y. Lee, I.S. Lee, S.S. Dette, J. Boerner, A.S. Myerson, Crystallization on confined engineered surfaces: a method to control crystal size and generate different polymorphs, J. Am. Chem. Soc. 127 (2005) 14982–14983.
[7] J. Liu, C.E. Nicholson, S.J. Cooper, Direct measurement of critical nucleus size in confined volumes, Langmuir 23 (2007) 7286–7292.
[8] A. D'arcy, C. Elmore, M. Stihle, J.E. Johnston, A novel approach to crystallising proteins under oil, J. Crystal Growth 168 (1996) 175–180.
[9] N.E. Chayen, Recent advances in methodology for the crystallization of biological macromolecules, J. Crystal Growth 198–199 (1999) 649–655.
[10] B. Brumshtein, H.M. Greenblatt, A.H. Futerman, I. Silman, J.L.L. Sussman, Control of the rate of evaporation in protein crystallization by the 'microbatch under oil' method, J. Appl. Crystallogr. 41 (2008) 969–971.
[11] R.C. Weast (Ed.), Handbook of Chemistry and Physics, CRC Press, Cleveland, 1975–1976.
[12] H. Langer, H. Offermann, On the solubility of sodium chloride in water, J. Crystal Growth 60 (1982) 389–392.
[13] I.N. Tang, H.R. Munkelwitz, An investigation of solute nucleation in levitated solution droplets, J. Colloid Interface Sci. (1984) 430–438.
[14] M. Hayashi, T. Shichiri, Theoretical and experimental study of the growth of perfect crystals, J. Crystal Growth 21 (1974) 254–260.
[15] P.R. Ten Wolde, D. Frenkel, Enhancement of protein crystal nucleation by critical density fluctuations, Science 277 (1997) 1975–1978.
[16] P.G. Vekilov, Dense liquid precursor for the nucleation of ordered solid phases from solution, Crystal Growth Des. (2004) 671–685.
[17] D. Kashchiev, P.G. Vekilov, A.B. Kolomeisky, Kinetics of two-step nucleation of crystals, J. Chem. Phys. 122 (2005) 244706-6.