

Real-time imaging of Microcrystal Growth and Dynamics by Lensless Microscopy in a Cell

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Summary:

We present a lensless microscopy setup for real-time imaging of germanium dioxide microcrystals forming directly inside an incubator. The system enables simultaneous observation over a large detection area, allowing tracking of crystal motion. A variable tilt angle modulates crystal dynamics. Post-processing enables quantification of particle-substrate and particle-solution interactions.

Keywords: microscopy, lensless, microcrystals, crystallization, tracking

Background, Motivation and Objective

Lens-based in situ microscopy of crystals is a classical approach for studying their dynamics in a liquid environment, for example, the growth and dissolution of immobilized crystals, or the diffusion and directed motion of mobile crystals [1]. However, under non-standard conditions (such as variable sample tilt angles, simultaneous detection over a large area, or space-constrained and temperature-controlled settings inside an incubator) this type of microscopy may encounter significant challenges. Lensless, chip-based microscopy circumvents these difficulties and has already demonstrated considerable promise for in situ observation and characterization of both micron-sized particles and bacteria directly within an incubator [2], [3]. Building on these advances in lensless microscopy, we investigated its applicability to the detection of micron-sized crystals.

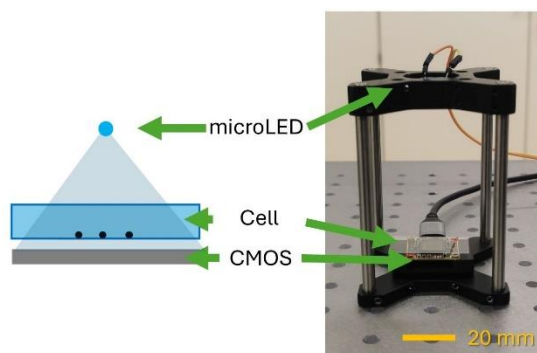


Fig. 1. The lensless microscope's streamlined architecture, comprising only a microLED, a CMOS sensor, and a sample holder, facilitates high-portability observations across diverse environments, including real-time monitoring inside an incubator.

The present work aims to observe the entire process, from the growth of the first detectable crystals in a solution, through their motion, to the accumulation at a preferred location. The study also focuses on the influence of temperature on the crystallization process, as well as on the effects of gravity represented by the tilt angle relative to the horizontal on crystal dynamics.

Description of the New System

Our setup consists of a lensless microscope in which a cell is placed between the microLED (75 μm size and $\lambda = 450 \pm 5$ nm) and the CMOS sensor, as shown in Fig. 1. The cell consists of two quartz glass windows separated by a PTFE spacer 2 mm in thickness. This portable configuration facilitates experimentation under both ambient conditions and regulated incubator environments, supporting real-time data acquisition through both high-frame-rate video and continuous capture modes.

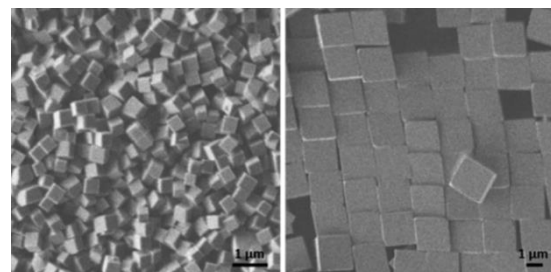


Fig. 2. SEM images of disordered and ordered assemblies of hexagonal GeO_2 cubes.

The cell contains a GeO_2 solution from which cubic-shaped crystals of hexagonal GeO_2 form, with sizes of approximately 0.5–2 μm (Fig. 2). The entire setup is mounted on a stand that allows the tilt angle to be varied from 0° to 90°, and

is placed inside an incubator in which the temperature can be adjusted from 5 °C to 40 °C.

The novelty of our system is threefold. First, we can detect the appearance of new crystals in real time and directly within the incubator, and investigate the dependence of this onset time on the liquid temperature. Second, simultaneous detection over a large area of approx. 35 mm² enables the study of particle dynamics driven by convective flows in the solution. Third, the variable tilt angle allows the crystal dynamics to be actively modulated. Together, these capabilities open new perspectives for in situ microscopy of microcrystal growth, as well as for investigating fundamental aspects of their dynamics governed by interactions with both the solution and the substrate. In addition, raw images are reconstructed via the angular spectrum method to enhance spatial resolution and overall image quality [2].

Results

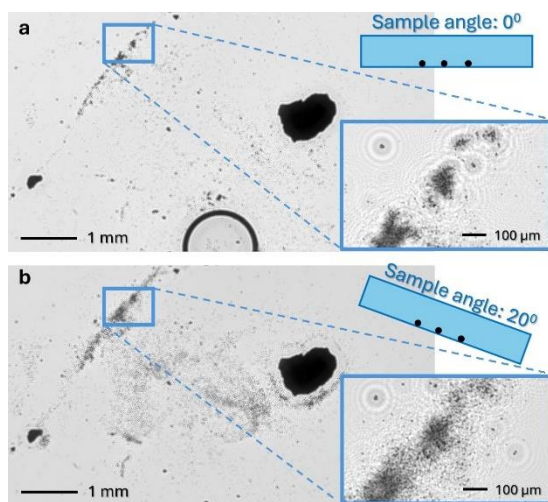


Fig. 3. The large dark spot is the region where particles accumulate due to convective flows in the liquid. Two different crystal densities are shown in the reconstructed images: (a) the cell is parallel to the floor, and in (b) it is slightly tilted to the right.

Over time, the number of newly formed GeO₂ crystals increases. As seen in Fig. 3, they are subject to convective flows and accumulate in a single region located approximately at the center of the cell. By varying the tilt angle of the cell relative to the floor, the crystal density and its spatial distribution can be influenced, as is clearly visible in Fig. 3a and 3b in the regions to the left and right of the cell. In post-processing, the full trajectory of an individual crystal can be reconstructed, and its displacement over a defined time interval calculated. This makes it possible to characterize numerically the interaction of a particle with the solution and the substrate through parameters such as the diffusion coefficient, friction coefficient, and hydrodynamic radius. These parameters depend on the cell tilt angle, as well

as on the material and surface properties of the substrate, which opens the possibility for broader systematic investigation.

By varying the distance between the sample and the CMOS sensor, the size of the detected diffraction patterns can also be adjusted. In Fig. 4a, this distance is 2 mm and the diameter of the outer ring is approx. 90 μm, while in Fig. 4b the distance is 17 mm and the diameter is approx. 350 μm. In both cases, the size of the patterns is about two orders of magnitude larger than the size of the microcrystals themselves (Fig. 2), which facilitates their detection.

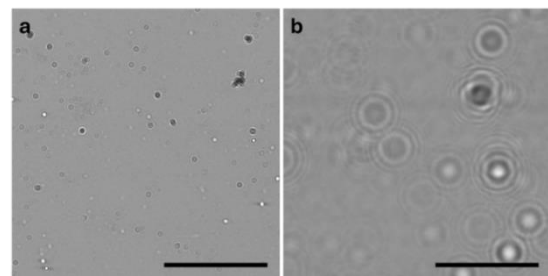


Fig. 4. Increase in diffraction pattern size as a function of distance between the crystals and the CMOS sensor: from 2 mm (a) to 17 mm (b). Scale bar: 500 μm.

Experimental results demonstrate that the lensless microscope maintains high-resolution imaging and an expanded field-of-view (FOV) even under harsh conditions, such as within regulated incubator environments. Furthermore, this approach introduces novel opportunities for in situ measurements, exceeding the technical limitations of conventional instrumentation. Current investigations are extending these findings by systematically modulating thermal parameters and illumination geometries as well as improving the resolution, to further enhance analytical precision and characterization accuracy.

Acknowledgement

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