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Jamin-interferometer-setup for the determination of concentration and temperature dependent face-specific crystal growth rates from a single experiment

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ABSTRACT

An interference technique that permits the investigation of the crystal growth from a temperature controlled solution is presented. Contrary to Mach–Zehnder- or Michelson-type interferometers, the Jamin-interferometer applied in this work is characterized by improved thermal and long-time stability. In consequence a single experiment may comprise several temperature steps leading to significant changes in the bulk concentration. A procedure for the automated analysis of the acquired sequence of interference patterns is presented. Within this evaluation procedure the position of the selected crystal face, the bulk concentration and the vertical concentration distribution above the crystal are determined simultaneously. Long-term single crystal growth experiments in the range from 20 to 60 °C with sucrose and lactose crystals are used to test the method. The exact bulk concentration is determined by the interferometer. The obtained results for the growth rate of sucrose are consistent with values given in the literature. The vertical concentration distribution above the two saccharide crystals differs clearly indicating that the diffusion strongly limits the sucrose growth but not the growth of the lactose crystal. The major benefit of the described setup is that the data of a single experiment are sufficient to deduce the parameters of the model equation for the growth rate as a function of temperature and supersaturation.

1. Introduction

Crystallization from solution is a process widely used in research and industry [1–3]. The process design is usually based on the crystal growth rate depending on temperature and bulk concentration. Besides this, crystal growth is also affected by further experimental parameters such as flow conditions. Dincer et al. [4] presented a survey of different experiments dealing with the growth of lactose as a function of supersaturation. They attribute the apparent differences in growth rate mainly to size dependent growth. However, additionally they mentioned changed concentrations of growth retarding ions and varying flow conditions. We hypothesize that the variations in the flow field and consequently in mass transport are another important contribution to the observed differences in growth rate of crystals with similar size. The influence of flow regimes on apparent crystal growth rates has been shown for KDP crystals by Srivastava et al. [5]. In this work we try to present a direct way of differentiating between diffusion- and integration-controlled growth, in which the transport of solute molecules to the crystal surface and the integration of such molecules in the crystal lattice are the rate-limiting steps, respectively [6].

This concept corresponds well to the modeling of crystal growth from solution with molecular dynamics (MD) simulation [7–9]. However, by MD only the processes directly at the crystal-solution-interface can be investigated due to the small time and length scales accessible. The computational modeling of crystal growth for process design is particularly gaining importance if the ingredients, such as some active pharmaceutical ingredients (API), are only available in very limited quantities. Nevertheless, the validation of the MD simulation requires an experimental setup that provides access to the solute concentration at the crystal-solution-interface and demands a minimum of solute.

For resolving the solute concentration directly at the crystal-solution interface interferometric methods that measure the concentration field surrounding the growing crystal seem to be promising. A comprehensive review on this topic is given by Verma and Shlichta [10] or by Srivastava et al. [11]. Generally, the experiments presented in the literature are aiming for optimizing the crystallization process in order to grow perfect mono-crystals and not for obtaining supersaturation dependent growth rates. Such crystals are important for nonlinear optics [12–15] or are necessary for the structure determination of proteins [16–21]. Usually,

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Notation

c	solute concentration [g/g H_2O]
c_s	saturation concentration [g/g H_2O]
D	position of the crystal surface [m]
g	order of the growth process [–]
G	growth rate [m/s]
h	chip height [m]
i	number of image [–]
k	reaction constant [m/s]
m	shift of interference fringes [–]
n_{meas}	refractive index in growth chamber [–]
n_{ref}	refractive index in reference chamber [–]
N_y	number of vertical pixels [–]
R	universal gas constant (R=8.3144621 J/(mol K))
s	geometric path length, layer thickness [m]
t	time [s]
T	temperature [K]
V	magnification of the camera lens [–]
X	optical path length difference [m]
y	number of the pixel row of the crystal surface [–]
ΔE	activation energy [kJ/mol]
Δn_1	change in refractive index causing a shift of one fringe [–]
λ	wavelength [m]

Mach–Zehnder- [12,14,17,22,23] or Michelson-type configurations [24,25] are applied for the visualization of the concentration field surrounding the crystal. If the crystal growth is diffusion-controlled, the concentration at the phase boundary is the solubility. Furthermore, the amount of mass transport can be deduced from the concentration gradient. Some authors also calculated the crystal growth rate from a sequence of images [18,21,26–29]. There are few experiments where a significant change in solute concentration occurs during run-time and where this change is measured from the shift of the interference fringes. Garcia-Ruiz et al. [30] observe the time evolution of salt concentration at various points in a protein chamber. Zhao et al. [29] describe the solute concentration during the growth of NaCl crystals by evaporation whereas Yin et al. [28] and Zhang et al. [16] present the measurement of the absolute protein concentration in different regions of the growth cell. In the last three articles it is also pointed out that there are many environmental influences that may cause errors of the absolute concentration measurement by the fringe shift in the case of long-term processes. The authors minimize these errors by a numerical compensation using the fringe shift observed in a region of the interference pattern that is not affected by the solution. Whereas the concentration measurement in the above studies was limited to isothermal conditions, Yin et al. [17] report the successful concentration measurement in a temperature-varying process using the temperature dependence of the refractive index additionally to the compensation of environmental influences mentioned above.

Here we present an experimental setup with immanent compensation of environmental influences. The parallelism of the two beams of the proposed Jamin-type interferometer [31] is fixed per construction. Due to the small beam distance, environmental influences affect both beams to the same extent and cause no fringe shift. The fringe shift caused by temperature changes can be eliminated if the reference beam passes a layer of liquid with the same temperature dependence of the refractive index as the sample solution.

Experiments with sucrose and lactose are used for validation. In a single experiment with various temperature steps in which the holding time is long enough to generate a significant change in concentration, growth rate, bulk concentration and concentration gradients next to the growing crystal surface are investigated in the whole concentration and temperature range relevant for process design.

2. Materials and methods

2.1. Interferometer setup

The core of the experimental setup (Fig. 1) is the Jamin-interferometer. The beam of a polarized red HeNe-laser (Qioptiq: Laser Head HeNe 633-15P) is expanded by a laser beam expander (Qioptiq: beamexpander 10 ×) to a beam diameter of about 10 mm. A fused silica flat (Edmund Optics: 2” Dia. 1/4λ fused silica dual surface flat) with a thickness of 12.7 mm acts as a beam splitter. The distance between axis of the two resulting parallel beam is 12 mm. The beams are recombined by a second identical fused silica flat. In order to achieve vertical interference fringes a

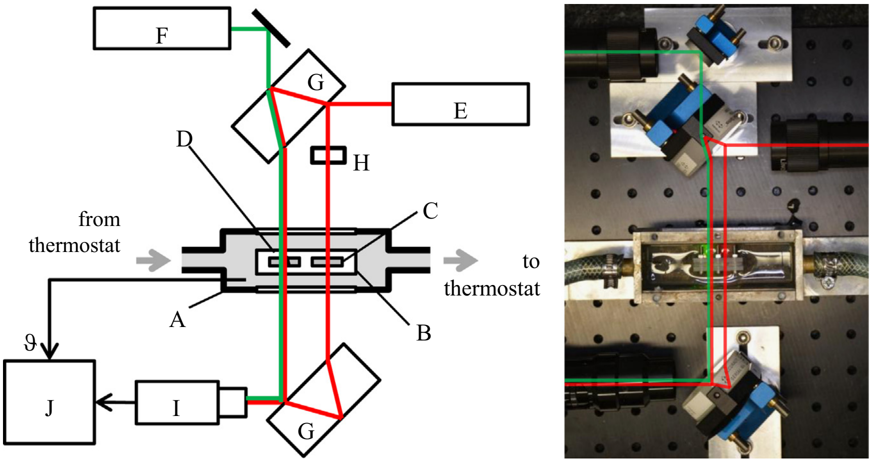

Fig. 1. Experimental setup with flow-through cell (A), measurement cell (B) containing reference chamber (C) and growth chamber (D). The red laser (E) is used for the Jamin-interferometer composed of two fused silica flats (G), a permanent phase shifting element (H) and a CCD-camera (I) connected to a PC (J). The green laser (F) passes only the measurement but not the reference chamber.