Electronic Supplementary Material (ESI) for CrystEngComm.

Subsurface Nucleation of Supercooled Acetaminophen

Limin Shi and Changquan Calvin Sun*

Department of Pharmaceutics, College of Pharmacy, University of Minnesota, USA

Experimental Section

True density measurement

True density was measured at ambient temperature using a helium pycnometer (Quantachrome Instruments, Ultrapycnometer 1000e, Byonton Beach, Florida, USA). Acetaminophen supercooled liquid was prepared by heating acetaminophen crystals in an aluminium weighing pan at 185 ^{o}C on a hot stage. After all the crystals had melted, the pan was removed from the hot stage and exposed to room temperature undisturbed to form an amorphous film, the true density of which was immediately measured.

Sample surface imaging

Samples were coated with a thin layer of platinum (thickness ~50 Å) using an ion-beam sputter (IBS/TM200S; VCR Group Inc., San Clemente, CA) before SEM analysis. Images of the coated samples were obtained using either a scanning electron microscopy (JEOL 6500F, Tokyo, Japan) operated at 5 kV or a nanoindenter (Trioindenter, Hysitron Inc., Minneapolis, MN, USA) run in the scanning mode.

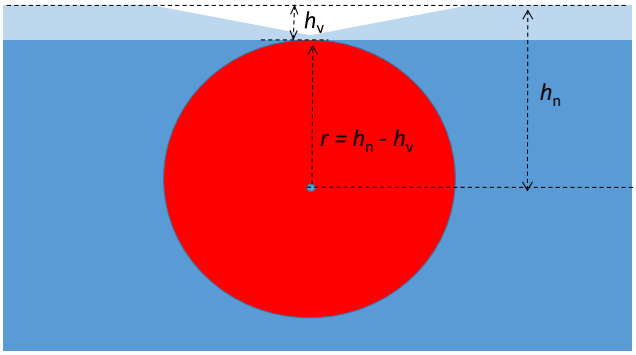
Derivation of equation (1)

For a spherical crystal, the mass, m, is expressed by equation S1

$$m = \frac{4}{3}\pi(h_n - h_v)^3\rho_c \qquad \text{(S1)}$$

For the crystallized mass, volume shrinkage from glass to crystal is equal to volume of the crater, V_v. Therefore, equation S2 can be written:

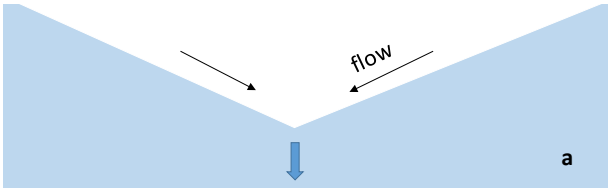
$$V_v = \frac{m}{\rho_g} - \frac{m}{\rho_c} \qquad \text{(S2)}$$



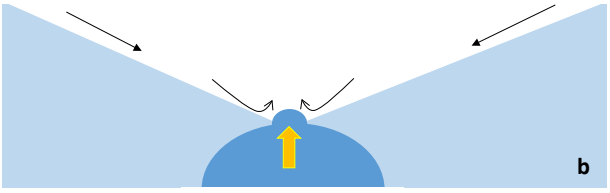
Substituting m in equation S2 with equation S1 and re-arrange terms, equation S3 is obtained

$$h_n = h_v + \sqrt[3]{\frac{3V_v \cdot \rho_g}{4\pi(\rho_c - \rho_g)}} \qquad \text{(S3)}$$

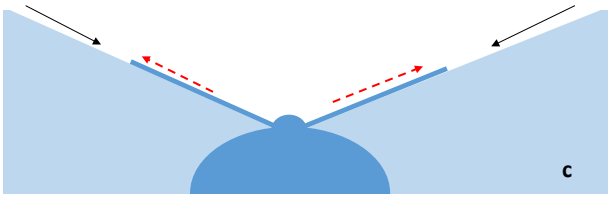
Graphic illustration of the mechanism of crater formation



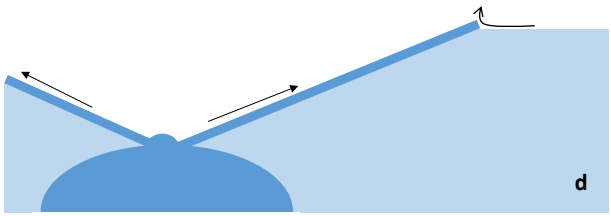
Mass is drawn downward to form a crater due to volume shrinkage associated with crystallization



Flow from either sides meet and crystallizes to form an island when the crystal emerges the surface



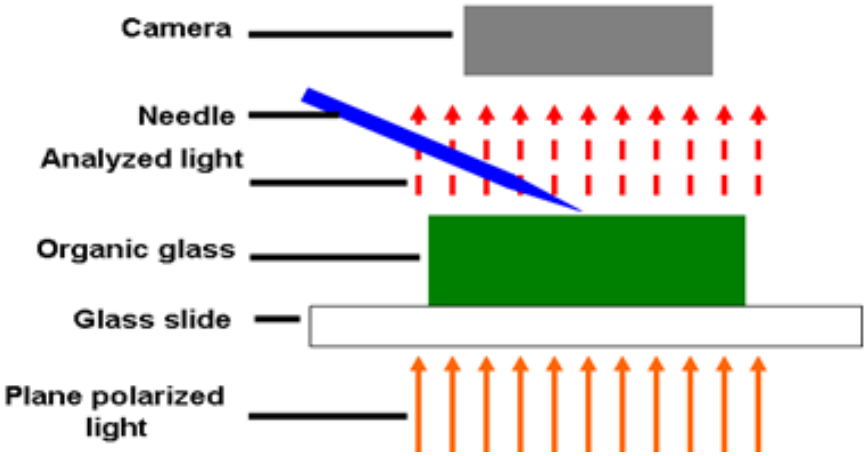
Fast crystal surface growth towards the edge of the crater as flow from edge of the crater continues.



Horizontal flow is thrust upward when meeting the fast growing surface crystalline layer to form a rim around the crater.

Setup for induce and observe fast surface crystallization

In the set up the needle is used to indent the sample to induce fast surface crystallization. The cross-polarized light allows direct observation of birefringent crystalline domains against a dark non-crystalline background.



Calibration of depth measurement using a microscope

A needle placed on top a stack of glass slides. The assembly was put under the microscope which was focus on the needle tip. After removing a glass slide with known thickness (measured by a micrometer), the needle tip was refocused and the dial reading was recorded.

This was repeated several times to construct a calibration curve of moved distance of the lens as a function of dial reading

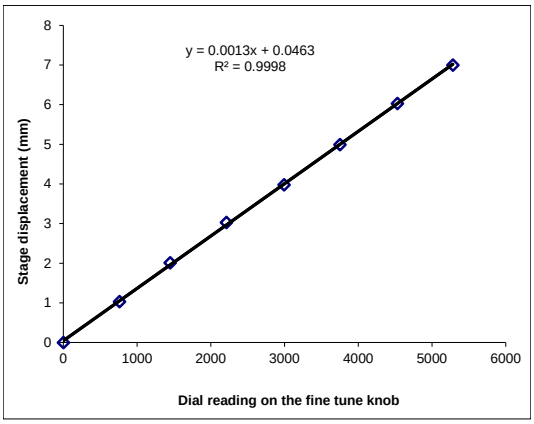


Figure S1. Calibration curve for the z-axis height measurement. Accuracy of this measurement is about 1 μm.

Measuring depth of nuclei from side

A small acetaminophen crystal was placed on a clean glass slide and covered with a clean cover glass. The crystal was heated to 5 °C above melting temperature and the cover glass was pressed slightly to form a thin layer of liquid. Then the slide was removed from the hot stage to allow cooling at ambient conditions. The samples were periodically observed for nuclei.

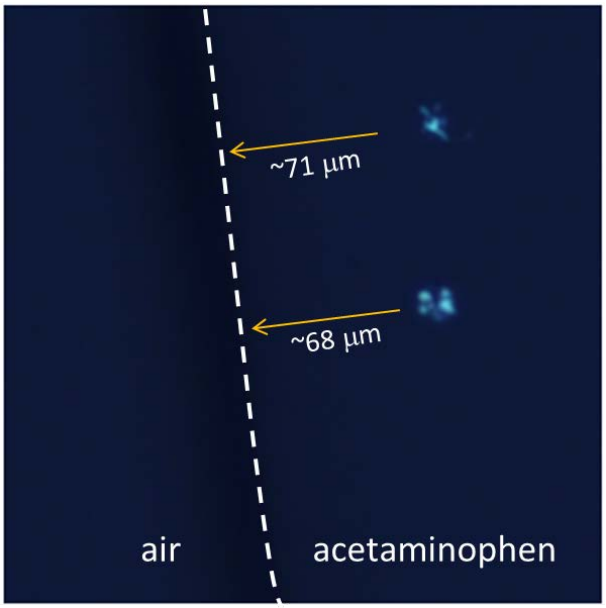


Figure S2. Nucleation of supercooled acetaminophen sandwiched between a glass slide and a cover glass at room temperature. Two crystals mark the nucleation sites that are ~ 60 μm below the surface. The sides of the image are 200 μm.