Crystal Growth

Rate-Controlled Separations in Fine Chemistry Crystallization
Topics

1. Crystal growth: definition
2. Crystal surface
3. Crystal-fluid interface
4. Crystal growth: a 2-step process
5. Growth mechanisms: Continuous growth, Birth & spread (surface nucleation), Spiral growth (BFC)
6. Growth kinetics: experimental methods and parameter estimation
Crystal growth: single crystal (video)

Naphthalene in ethanol: single crystal growth
the fastest growing facet disappears immediately and the crystal grows to a regular shape
Crystal growth: definition

- **The linear growth rate** is the rate of growth of a face in the direction normal to the face: *velocity in the internal coordinate*
  
  \[ G = \frac{dL}{dt} \quad \text{[m/s]} \]

- Growth is a *kinetic* phenomenon driven by supersaturation \((S > 1)\), that is determined by the thermodynamic data.
  
  \[ S = \frac{c}{c^*(T)} \]

- Growth occurs *independently for each face* in layer-by-layer fashion.

- The relative growth rates of the faces determine the *crystal shape*. 
Crystal surface

- The ability of a surface to capture and integrate growth units into the crystal lattice depends upon the **strength and number of interactions** that can form between the surface and the growth unit.

- In a 2-D structure: the molecules are nodes of the structure, and a new molecule connects expanding the regular structure:
  - Case A: 1 bond is formed
  - Case B: 2 bonds are formed. Favoured, since the system gains more energy.

- The sites on the growing crystal surface can be classified as follows:
  - **Kink** (K-face): when 3 bonds are possible
  - **Step** (S-face): when 2 bonds are bonds possible
  - **Flat** (F-face): when 1 bond is possible

  With linear growth rate, $v$, proportional to the total binding energy:

  $$v_K > v_S > v_F$$

  Molecules tend to bond at locations where they have the maximum number of nearest neighbours.
Crystal-fluid interface

- Described by the “multilayer” model (Temkin, 1966): solid and fluid divided into blocks of equal size

*Energy change ($\Delta E$) occurring when a perfectly flat surface is roughened by removing one block (molecule) from the surface and start a new layer.*

$$\Delta E = \text{new bonds} - \text{broken bonds}$$

$$= (3 - 1)\phi_{ss} + (2 - 6)\phi_{sf} + (3 - 1)\phi_{ff}$$

**$\alpha$-factor:** indicates how easy a surface can form sites with multiple binding interactions (how easy a surface can grow).

$$\alpha = \frac{|\Delta E|}{kT}$$

- $\alpha < 3$: Rough surface, fast growth
- $3 < \alpha < 5$: Intermediate
- $\alpha > 5$: Flat surface, slow growth
Crystal growth: a 2-step process

1. **Mass transfer**: desolvation and diffusion from the bulk solution to the interface (faster mass transfer, faster growth).

2. **Surface integration**: inclusion in the crystal lattice: the more defects (inclusion sites), better integration.
Growth mechanism: **continuous growth** (or rough growth)

- The energy for the formation of a step is low: surface with many kink and step sites (rough)
- Diffusion is the limiting step, since every unit reaching the surface will find a growth site.

\[
G = k (c_{i,\infty} - c_i^*) = k c_i^* (S - 1)
\]
Growth mechanism: **birth and spread** (surface nucleation)

\[ 3 < \alpha < 5 \]

- Roughness decreases
- Mass transfer is fast, but some units do not find an inclusion site:
  - they return to the fluid
  - Or join adsorbed growth units to form surface **islands**, disks or nuclei, binding to the surface, and forming more step and kink sites, that promotes the growth of a new layer.

\[
\Delta G(D) = \Delta G_A + \Delta G_E = -\alpha' D^2 + \beta' D
\]

\[
G \propto \exp\left(-\frac{B}{\ln S}\right)
\]

*Similar to the equation for homogeneous primary nucleation, since the formation of critically sized 2D nuclei is needed*
Growth mechanism: **spiral growth**

- **Surface is flat**
- **Growth can occur only if built-in lattice defects (dislocations) provide energetically “cheap” processes for new molecule to be included in the crystal and start a new layer**
- **Phenomenon may be controlled either by diffusion from the bulk solution directly into the kink sites, or by two-dimensional diffusion across the crystal surface (Burton, Cabrera and Frank 1951).**
- **Each crystal can have its own growth rate determined by its specific dislocation structure.**

\[ G = c_{SD}g_{SD} = c_{SD} \ln^2 S \tanh \left( \frac{B}{\ln S} \right) \]

**Concentration of dislocation**

**Unitary growth of a single disk**


Growth mechanism: **spiral growth (video)**

Spiral growth of cysteine (oxidized dimer form of the amino acid cysteine)

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{S} & \quad \text{S} \\
\text{H}_3\text{N}^+ & \quad \text{O} \\
\end{align*}
\]
Crystal growth kinetics

Correlation between supersaturation and crystal growth can be incorporated in process models for process design:

\[ G = k_g(c - c^*)^{n_g} \]

The growth rate can be measured as:

- **Length/time**: linear crystal growth. It is facet specific
  \[ k_g^L = \frac{m}{s \left[ \frac{kg_{\text{solute}}}{kg_{\text{solvent}}} \right]^{n_g}} \]

- **Mass/area time**: mass rate of crystal growth
  \[ k_g^m = \frac{kg}{sm^2 \left[ \frac{kg_{\text{solute}}}{kg_{\text{solvent}}} \right]^{n_g}} \]

**Temperature dependence**

- **Arrhenius equation**:
  \[ k_g = a \exp\left(\frac{E_g}{RT}\right) \]
  Activation energy of growth: it informs about the rate-limiting step (diffusion or surface integration)
  - diffusion-limited growth  \[ E_g = 8 - 20 \text{ kJ/mol} \]
  - integration-limited growth  \[ E_g = 40 - 60 \text{ kJ/mol} \]

Measurement of crystal growth rates

The experimental methods for growth rate estimation can be classified as:

- **Direct methods**
  - Single crystal growth: length- or mass-based rate
  - Growth of suspension of crystals: mass-based rate

- **Indirect methods**
  - Concentration monitoring over time

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Different growth mechanisms as a function of $S$


Direct methods: single crystal experiments

- Monitoring over time the growth of a *large single crystal* in supersaturated conditions with *optical microscopy* techniques or *atomic force microscopy* (AFM).
- The growth mechanism and rate can be estimated for each facet.

*Theoretical predictions* are compared to experimental kinetic measurements in a range of supersaturations.

Alternatively, a *mass-based rate* can be computed by weighing the crystal before and after the experiment.

![Succinic acid](image)

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**Salicylamide**

<table>
<thead>
<tr>
<th>In Acetonitrile at $\sigma = 0.82$</th>
<th>Length: 361 $\mu$m</th>
<th>Width: 149 $\mu$m</th>
<th>0 min</th>
<th>Length: 539 $\mu$m</th>
<th>Width: 285 $\mu$m</th>
<th>12 min</th>
<th>Length: 696 $\mu$m</th>
<th>Width: 424 $\mu$m</th>
<th>36 min</th>
</tr>
</thead>
</table>


![Graph](image)

Single crystal experiments: devices

- Constant temperature
- Large volume of solution to ensure *constant supersaturation*
- *Not stagnant solution* in order to prevent diffusion from controlling the crystal growth rate
  - Stirred solution
  - Pumped solution: increase chance of nucleation
  - Rotating disk: the crystal is fixed on a disk that moves instead of the liquid

To minimize the effect of bulk diffusion, the growth rate is measured as a function of flow rate (or stirring speed, at constant S). The growth rate increases with increasing flow rate, if mass transfer is controlling, until a constant value. A flow rate is chosen in the range where constant rate is detected (no mass-transfer controlled).
Direct methods: crystal suspension

Conditions more similar to an industrial environment:

- Fluidized-bed crystalliser: solution is recirculated and seeds suspended in the vessel.
  - Constant temperature and supersaturation

- MSMPR operating at steady state: growth rates obtained based on population balance concepts.
Indirect methods: desupersaturation experiments

- **Batch seeded isothermal** experiment
- Monitoring over time the *concentration profile* of the bulk solution with spectroscopical techniques, at conditions where **only growth occurs** (nucleation is avoided).
- A model (no nucleation) is fitted to the experimental data for the estimation of the growth rate.

Procedure:

1. Equilibration of the saturated solution of known concentration, cooled to the desired supersaturation.
2. Addition of the seeds to the clear solution at constant temperature: they will grow until reaching the solubility concentration.
3. Monitoring the desupersaturation with IR (or densitometer, sampling) in the presence of the FBRM (counting the crystal number to detect nucleation and discard the experiment in case it occurs).
Parameter estimation

- Growth experiments are run at conditions at which nucleation is negligible.
- A PBE model is used to describe the process and solved assuming that nucleation is not occurring.
- Several models can be used to fit the experimental desupersaturation data, and the appropriate one should be chosen.

For example:

- **Isothermal case** [length or mass based G rate]
  \[ G = k_g(c - c^*)(n_g) \]

- **Temperature dependent** growth rate
  \[ G = k_{g,0} \exp\left(-\frac{B}{RT}\right)(c - c^*(T))^{n_g} \]
  Arrhenius type \(T\)-dependence