

Screening Crystal Morphologies from Crystal Structure

Meenesh R. Singh,[†] Parul Verma,[‡] Hsien-Hsin Tung,[§] Shailendra Bordawekar,[§] and Doraiswami Ramkrishna^{*,†}

[†]School of Chemical Engineering, Purdue University, 480 Stadium Mall Drive, West Lafayette, Indiana 47907, United States [‡]Chemical Engineering Department, Indian Institute of Technology Bombay, Powai, Mumbai, Maharashtra 400076, India [§]Process Engineering, Global Pharamceutical R&D, AbbVie Inc., 1401 Sheridan Road, North Chicago, Illinois 60064, United States





ABSTRACT: Crystal morphology is a critical determinant of the physical properties of crystalline materials. Face-specific growth rates can be used to compute dynamic and steady-state morphologies of crystals growing in a specific environment. The synthesis of crystals with desired morphologies requires a framework to guide the selection of environmental conditions. The framework developed here utilizes combinatorics to generate a graph of different morphologies connected by edges describing morphology transformations. These edges collectively form a polyhedral cone containing domains of different morphologies in a crystal-state space. The face-specific growth rates of crystals allow the identification of accessible regions within the polyhedral cone using a generalized single-crystal model. Here, we introduce morphology domain as a fundamental property of crystals which can be used to screen crystallization conditions for the controlled synthesis of desired crystal morphologies that is both facile and readily usable. A user-friendly tool, MorphologyDomain, is presented that facilitates diverse applications.

1. INTRODUCTION

Crystal morphology has immense impact in determining the quality of products in food, pharmaceutical, catalyst, and semiconductor industries. Even after the historical development of crystal growth in over a century,¹ the complex phenomena of morphology transformations is a conundrum. Understanding of the dynamics of crystal morphology is essential for the synthesis of crystalline materials with advanced surface properties. It is well-known that a crystal grows in a faceted geometry dominated by slow-growing faces. The relative growth rates of crystal faces, which depends on environmental conditions, evokes transformations in crystal morphology due to appearance and/or disappearance of the faces. These transformations are owed to the geometric constraints imposed by the crystal structure. As the study of crystal morphology and morphology transformations are limited to a few crystal structures, a comprehensive framework is proposed to explicate morphology evolution in crystalline materials.

Crystal morphology can be classified as equilibrium morphology and kinetic morphology. The equilibrium morphology, as defined by J. W. Gibbs,² is the minimum

energy conformation of faces of a fixed-volume crystal, which can be directly identified from the Wulff construction³ on the polar plots of surface energies. It can be construed that the faceted geometry of crystals is due to the existence of a finite number of minima in the polar plots.⁴⁻⁶ Moreover, the appearance of shocks and fans in the characteristics of crystal shape evolution indicate the transition from smooth to faceted crystal shape.⁷ The potential faces to appear during growth are the low energy faces, the F faces, which can be estimated through the attachment energy calculation of the Hartman-Perdok theory.⁸⁻¹¹ The Miller indices of crystal faces and their perpendicular distances from the center can be used to draw a representative morphology of the crystal. Bond¹² and Dowty¹³ provided the necessary setup to enable the computer-assisted drawing of crystal shapes. Bond used the Matrix method for transforming Crystallographic frame to Cartesian frame and computing interfacial angles, interzonal angles, and clinographic

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projections. Successively, Dowty generated a FORTRAN program to draw crystal shape using Miller indices of faces and their perpendicular distances. If the perpendicular distances represent growth rates then the corresponding shape is a steady-state shape, and if they represent surface energies then the shape is the equilibrium shape of the crystal. Such programs are commercially available which are developed on different platforms; a few of them are Shape,¹⁴ JCrystal,¹⁵ CRYSTAL¹⁶ and WinXMorph.¹⁷ Our group has developed similar standalone software, CrystalShape,¹⁸ using Matlab that takes Miller indices and perpendicular distances to generate crystal morphologies.

The evolution of a faceted crystal can be described using the rate of advancement of faces, known as growth rates.^{19,20} The growth rate functions, which can be determined from either surface energetics^{11,21-24} or diffusion mechanisms,²⁵ are crucial for the prediction of kinetic morphology. The evolving morphology often undergoes transition caused by appearance or disappearance of faces. Johnsen²⁶ classified the crystal faces as "real" if they are present on a crystal and "virtual" if they can appear later. He also provided the sufficient condition for the virtual face becoming real. Borgstrom²⁷ and Alexandru²⁸ considered the effect of growth rates and the angle between the surface normals on the disappearance of the faces. They introduced the concept of critical growth rates essential for real to virtual face transitions. Similar conditions were also derived for two-dimensional (2D) crystals by considering the lateral length of each face as a function of growth rates and angle between their normals.^{29,30} Prywer extensively studied the face transitions on three-dimensional (3D) crystals³¹ and developed the conditions for disappearance of rectangular faces³² and more general conditions for arbitrary-shaped faces.³³ Doherty and co-workers formulated the dynamic model for 2D crystal morphologies showing the steady state to be independent of seed morphologies¹⁹ and the dynamic model for 3D crystal morphologies considering the multifurcation of vertices into edges or faces.²⁰ There are some other recently developed methods to evaluate crystal morphologies and their transformations using the set-theoretic approach,³⁴ Minkowski additions,³⁵ and vertex multifurcations.³⁶ Ramkrishna and coworkers³⁴ were the first to introduce the idea of constructing a morphology domain in h space and address the issue of morphology transformation using the set-theoretic approach. Reinhold and Briesen³⁵ take a different and interesting route to describe morphology evolution of faceted and nonfaceted crystals using the Minkowski sum of elementary polyhedra. Subsequently, Borchert et al.³⁶ performed a detailed study of the behavior of edges and vertices of crystals during morphology transformations to derive morphology domains. This article presents a set-theoretic approach to evaluate morphology transformations, which does not involve specific calculations of edges and vertices to identify all possible morphologies of crystalline materials.

The morphology transformations can be difficult to identify for complex geometries of crystals and thereby posing some practical challenges regarding: (1) prediction of different growth morphologies possible for a crystalline material, (2) screening of operating conditions such as solvent, additives, and supersaturation to obtain desired morphologies, and (3) targeting and control of crystal morphologies.

The foregoing issues are addressed in this article by constructing a state-space for crystal morphology, referred to here as morphology domain, toward studying the dynamics of crystal growth. The morphology domain is the property of a crystal that can give insight into morphology transformations and assist in targeting specific morphologies. In laying out the contents, we include the description of crystal morphology, morphology graph, morphology domain and single-crystal model, screening of crystallization conditions, and control of crystal morphologies.

2. CRYSTAL MORPHOLOGY

As a crystal grows in a faceted form, its morphology can be described by a convex polyhedron. The most likely faces to be present on a crystal are the low energy faces (F faces and may be some S faces) and the faces that already exist. In accordance with the Hartman-Perdok theory, the F faces are those faces with more than one periodic bond chain and the S faces are those with exactly one periodic bond chain. This criterion provides a reasonable limit on the number of faces (n) to be considered in this framework. The Miller indices of likely faces can be converted to the unit normal vectors in the Cartesian frame, using the transformation matrix such that

$$\mathbf{N} = \mathbf{M}\mathbf{K} \tag{1}$$

The face normals and Miller indices are arranged as the rows of **N** and **M**, respectively. The transformation matrix **K** in eq 1 corresponds to the specific relative orientation of Crystallographic and Cartesian frames of references [i.e., the *c* axis (Crystal) is parallel to the *z*-axis (Cartesian), and the *b* axis (Crystal) is in the y-z plane (Cartesian).

$$\mathbf{K} = \begin{bmatrix} a\omega_1 & 0 & 0 \\ a\omega_2 & b\sin\alpha & 0 \\ a\cos\beta & b\cos\alpha & c \end{bmatrix}^{-1}$$

where

$$\omega_{1} = \frac{\sqrt{1 - \cos^{2} \alpha - \cos^{2} \beta - \cos^{2} \gamma + 2\cos \alpha \cos \beta \cos \gamma}}{\sin \alpha},$$
$$\omega_{2} = \frac{\cos \gamma - \cos \alpha \cos \beta}{\sin \alpha}$$

a, *b*, *c*, α , β , and γ are the lattice parameters. The crystal morphology is described as follows:

$$\mathbf{Nr} \leq \mathbf{\tilde{h}}$$
 (2)

Here, \mathbf{r} is the position vector and $\mathbf{\tilde{h}}$ is the vector of perpendicular distances of faces from the center. The inequality sign in eq 2 implies its component-wise validity. The symmetry of the crystal allows faces with identical growth rates and geometries to behave in an identical manner. The crystallographic family (also referred to as crystal form) is the set of faces with identical molecular arrangements and therefore growth rates. They can be further classified based on face geometries. Two faces in a form can be geometrically different if their angular patterns with respect to all other faces are different.³⁷ For example, (001) and (100) of acetaminophen are kinetically similar (belonging to the {100} form) but geometrically different. The dynamics of crystal morphology can now be represented by the h vector, given as $h \equiv$ $[h_1, h_2, ..., h_m]$, corresponding to *m* groups of identical faces (kinetically and geometrically similar faces).

2. MORPHOLOGY GRAPH

A growing crystal can have, at most, *m* kinds of faces characterized by their perpendicular distances $[h_1,h_2,...,h_m]$. Different combinations of faces can create different morphologies which collectively form a morphology set. The morphology set is a power set of $[h_1,h_2,...,h_m]$, where each subset represents a closed convex polyhedron. For example, potassium acid phthalate (KAP) has three families of F faces $\{010\}, \{110\}, and \{111\}$ with perpendicular distances h_1,h_2 , and h_3 respectively. The power set of (h_1,h_2,h_3) has 2^3 elements; however, only four subsets such as $(h_1,h_2,h_3), (h_1,h_3), (h_2,h_3)$, and (h_3) form closed polyhedra and constitute the morphology set of KAP.

A morphology graph is a bidirected graph of the morphology set, such that each set is connected with its subsets. Figure 1 shows the morphology graph of KAP connecting the (a) morphology set and (b) their representative morphologies.



Figure 1. Morphology graph of KAP connecting (a) morphology set and (b) different kinds of morphologies representing each subset. The edges connecting i^{th} and j^{th} node or set are denoted as e_{ij} . The color codes are h_1 : blue, h_2 : green, and h_3 : red.

Each set in a morphology set represents a collection of morphologies (different values of h's) of the same kind. The bidirectional edges of the morphology graph represent the morphological transformations due to the appearance or disappearance of faces.

3. MORPHOLOGY TRANSFORMATION

Crystal morphology undergoes transformation if the faces (or groups of identical faces) appear or disappear during growth. The crystal faces are classified as "real" if they are present on a crystal and "virtual" otherwise.²⁶ The appearance and disappearance of faces are therefore virtual-to-real and real-to-virtual face transitions, respectively. Since vertices define edges of a closed convex polyhedron, a face transition can only occur at vertices. The necessary condition for face transitions is that the neighboring faces must converge to a vertex. The sufficient condition for disappearance of a face is that the real growth rate must be greater than the virtual growth rate of a face and for appearance of a face requires its real growth rate to be less than its virtual growth rate. Besides the strict positive values of *h*'s, the necessary conditions provide the upper and lower limit on *h* with respect to other *h*'s.

The different kinds of face transitions can be identified from the edges of the morphology graph. Each edge connects a set with its subset and the difference in the cardinality of the connected sets determines the order of transition. In Figure 1a, $(h_1,h_2,h_3) \leftrightarrow (h_1,h_3)$ is a first order transition and $(h_1,h_2,h_3) \leftrightarrow$ (h_3) is a second order transition. Higher order transitions involve different kinds of faces disappearing or appearing simultaneously, which can also be interpreted as linear combinations of first-order transitions. The necessary condition for the real-to-virtual transition of ν^{th} face is given by

$$h_{\nu} = \mathbf{n}_{\nu}^{T} \begin{bmatrix} \mathbf{n}_{i}^{T} \\ \mathbf{n}_{j}^{T} \\ \mathbf{n}_{k}^{T} \end{bmatrix}^{-1} \begin{bmatrix} h_{i} \\ h_{j} \\ h_{k} \end{bmatrix}$$
(3)

where i_{ij} , and k are the indices of faces that are neighbors of the

 v^{th} face. The necessary condition for the virtual-to-real



Figure 2. (a) Morphology graph of KAP with the conditions for face transitions and (b) morphology domain of KAP, which is an open polyhedral cone with blue, green, and black faces. Crystals with all three families are located inside the cone, crystals with red and green faces are on the blue plane of the cone, crystals with red and blue faces are on the green plane of the cone, crystals with red faces are at the intersection of blue and green planes of the cone, and the black plane of the cone corresponds to $h_1 = 0$.

$$h_{\nu} < \mathbf{n}_{\nu}^{T} \begin{bmatrix} \mathbf{n}_{i}^{T} \\ \mathbf{n}_{j}^{T} \\ \mathbf{n}_{k}^{T} \end{bmatrix}^{-1} \begin{bmatrix} h_{i} \\ h_{j} \\ h_{k} \end{bmatrix}$$
(4)

Equations 3 and 4 provide conditions for face transitions corresponding to each edge in the morphology graph. The derivations of eqs 3 and 4 can be found in section 2.2 of Borchert et al.³⁸ These conditions for KAP are shown in Figure 2a.

The condition for the second-order transition in Figure 2a is given as the linear combination of first-order transitions, such that $e_{14} = e_{12} + e_{24} = e_{13} + 2.7549e_{34}$.

4. MORPHOLOGY DOMAIN

The inequalities associated with the edges of the morphology graph impose constraints on the \mathbf{h} vector that can be collectively written as

$$\mathbf{A}\mathbf{h} \le \mathbf{0} \tag{5}$$

Equation 5 represents a polyhedral cone in the positive orthant of *m*-dimensional space. Since different faces and edges of the polyhedral cone are the domains of different morphologies, it is referred to here as morphology domain. The morphology domain is the property of crystalline materials that elucidate their morphological behavior. It can be broader for some materials such as KAP enclosing wide varieties of morphologies, including needles and plates and narrower for materials like potash alum, which can never attain asymmetric morphologies. Figure 2b shows the morphology domain of KAP where every point inside the cone represents the size and morphology of the crystal.

The morphology domain of KAP can be further partitioned based on the general shapes such as fibers, needles, rods, prisms, strips, blades, plates, spheres, and bipyramids. Some of these shapes such as fibers, rods, and plates can show amazing properties at the nanometer scale and can also impose difficulties in downstream processing. Figure 3 shows the cross-sectional view of Figure 2b along the (111) direction, where regions are identified for different kinds of general shapes. The most symmetric crystals, the preferred ones in pharmaceutical industries, lie near the space diagonal of the morphology domain.

It is also possible to target crystals in Figure 3 based on their surface properties. The benzene rings of KAP molecules are arranged parallel to the $\{010\}$ faces with a high density of K⁺ ions. The $\{111\}$ and $\{11\overline{1}\}$ faces have different chemical activities due to the presence of hydroxyl ions and oxygen ions, respectively. The KAP crystals away from the blue plane of the morphology domain have more fraction of $\{010\}$ surfaces, crystals away from the green plane have more $\{110\}$ surfaces, and crystals toward the intersection of the green and blue planes have more $\{111\}$ surfaces.

The Morphology Domain of any crystalline material can be identified from the F faces and lattice parameters using the tool MorphologyDomain.³⁹ The morphology domain of potash alum, shown in the Appendix, is relatively narrower than KAP and allows only symmetrical shapes. It is therefore practically impossible to produce needles and plates of potash alum. The morphology domain is the remarkable property of crystalline materials that can guide in preparation of the next generation materials.



Figure 3. The cross-sectional view of Figure 2b along the (111) direction with identified regions for different kinds of shapes. The boundaries separating different regions are marked qualitatively and are rather diffused.

5. SINGLE CRYSTAL MODEL

A point (or h vector) in the morphology domain represents the state (size and morphology) of a single crystal. Growth of the crystal can be described by movement of this point in the morphology domain. The growth rates of crystal faces govern the velocity field in the morphology domain, which is a function of supersaturation, temperature, solvent, cosolvent, and additives. The availability of advanced experimental tools and theoretical models provide reliable means to predict face-specific growth rates. The dynamics of crystal morphology in *m*-dimensional morphology domain (a polyhedral cone) bound by *l* number of faces is given as

$$\frac{d\mathbf{h}}{dt} = \alpha(\mathbf{h}, \dot{\mathbf{H}})\mathbf{P}(\mathbf{h}, \dot{\mathbf{H}})\dot{\mathbf{H}}(\mathbf{h}, \mathbf{c})$$
(6)

where **h** is the *m*-dimensional **h** vector, $\dot{\mathbf{H}}$ is the vector of facespecific growth rates that may depend on **h** and **c** (crystallization conditions such as temperature, supersaturation, solvent, and cosolvent), α is the scaling factor to change the magnitude of $\dot{\mathbf{H}}$ after projection, and **P** is the *m*-dimensional projection matrix that projects $\dot{\mathbf{H}}$ onto the faces of the morphology domain. The projection matrix is an identity matrix inside the morphology domain:

$$\mathbf{P} = \mathbf{I} \quad \text{if } \mathbf{A}\mathbf{h} < \mathbf{0} \tag{7}$$

Otherwise,

....

$$\mathbf{P} = \sum_{i} \nu_{i} \nu_{i}^{T} + \sum_{j} \boldsymbol{\mu}_{j} \boldsymbol{\mu}_{j}^{T}, \quad \boldsymbol{\nu}_{i} \in N(\mathbf{B}), \quad \boldsymbol{\mu}_{j} \in N(\mathbf{G})$$
(8)

where \mathbf{v}_i are the ortho-normal basis vectors of the null space of **B** which is a submatrix of **A**, such that $\mathbf{Bh} = 0$ and $\mathbf{B\dot{H}} \ge \mathbf{0}$, and $\boldsymbol{\mu}_j$ are the ortho-normal basis vectors of the null space of **G**, such that $\mathbf{G\dot{H}} = 0$. The equation $\mathbf{G\dot{H}} = 0$ is the symmetric

equations of line relating growth rates of real faces, and the equation $\mathbf{B}\dot{\mathbf{H}} = 0$ relates the growth rates of virtual faces with real ones.

At fixed growth rates of the crystal faces, the eq 6 would simplify to $\mathbf{h}(t) - \mathbf{h}(0) = \dot{\mathbf{H}}t$ inside the morphology domain, which at longer time scales would yield the condition for the steady-state morphology,⁴⁰ given as

$$\mathbf{h} \propto \dot{\mathbf{H}}$$
 (9)

In general, the steady-state solutions of eq 6 under fixed operating conditions are given as $\mathbf{h} \propto \alpha \mathbf{P} \dot{\mathbf{H}}$. The stability of these steady states is extensively studied by Lovette et al.⁴¹ The important result from their analysis is that steady-state morphologies are asymptotically stable because the associated eigenvalues are negative. Therefore, the trajectories of crystal morphologies given by eq 6 will unanimously converge to the steady-state morphology (eq 9), irrespective of their initial morphologies. This also implies that all steady-state morphologies can be attained and maintained at fixed operating conditions. Figure S1 of the Supporting Information shows the steady-state trajectory at fixed growth rates pulling the morphologies toward the region of plates. The steady-state trajectory is a straight line along the direction of $\alpha P\dot{H}$, which will change with the crystallization conditions. This provides a handle to screen crystallization conditions to obtain desired crystal morphologies.

6. SCREENING OF CRYSTALLIZATION CONDITIONS

The face-specific growth rates are crucial for targeting crystal morphologies. These growth rates can be determined either experimentally using microscopes or theoretically using mechanistic models and computer models. With the situations when experimental measurements on single crystals are difficult to perform for certain crystallization conditions, the theoretical models can be very useful for reliable estimation of relative growth rates. The dependence of growth rates on the crystallization conditions can be extended to the steady-state morphologies using eq 9. For example, the morphology of KAP crystals growing in aqueous solution is strongly dependent on the supersaturation and the concentration of additives such as ethylene glycol and PEG-200. Figure S2 of the Supporting Information shows the growth rates of KAP as a function of supersaturation and concentration of additives obtained experimentally by Kuznetsov et al.⁴² These additives promote growth rates at low concentrations and impede at higher concentrations. It is interesting to note that the resulting steady-state morphologies occupy different regions in the morphology domain, depending on the range of operating conditions. The region containing steady-state morphologies, specific to a chosen range of operating conditions, is referred to as steady-state domain. This steady-state domain can be determined from the face-specific growth rates such that $\mathbf{h} \propto$ $\alpha P\dot{H}$.

The effect of ethylene glycol and PEG-200 on steady-state morphologies is shown in Figure 4. The span of steady-state morphologies increases tremendously in the presence of additives. The steady-state domains, shown as a closed dotted line in Figure 4, are established by collecting steady-state morphologies for a chosen range of operating conditions such as 1% to 5% supersaturation, 0-0.267 mol % ethylene glycol, and 0-0.09 mol % polyethylene glycol. The trajectories in Figure 4a move from plates to needles and back to plates with an increase in ethylene glycol concentration. Similarly, the



Figure 4. Trajectories of steady-state morphologies at different concentrations of (a) ethylene glycol and (b) PEG-200. Each trajectory starts from 1% supersaturation (\bullet) and ends at 5% supersaturation (\bigcirc). The space diagonal is marked as with a × symbol, and the dotted line shows the steady-state domain.

trajectories in Figure 4b move from plates-to-prisms-to-plates with an increase in the PEG-200 concentration. The more symmetric crystals can be obtained using 0.01 mol % PEG-200 in 1.7% supersaturation of the KAP solution. The crystals with the minimum area of {010} faces can be obtained with 0.267 mol % ethylene glycol and 1.9% supersaturation. The crystals with the minimum area of {110} faces can be obtained with 0.04 mol % PEG-200 and 5% supersaturation. It is clear that only the steady-state domain in the morphology domain can be attained and maintained at fixed operating conditions. This steady-state domain decides the degree of freedom in targeting crystal morphologies. These examples show that the screening of crystallization conditions for desired morphologies can be performed readily with the help of the morphology domain.

7. CONTROL OF CRYSTAL MORPHOLOGIES

The targeting of crystal morphologies, as shown in the previous section, can be very helpful in determining the best operating conditions for crystallizers. Such operating conditions will drive every crystal, with **h** nonparallel to $\dot{\mathbf{H}}$ in the morphology domain, asymptotically toward the targeted morphology. Since the time to reach a target depends on its distance from the initial morphology, the operating conditions corresponding to the target morphologies are not the best ones to implement. One of the strategies could be the two-step control of crystal morphologies, which involves directing crystals toward the target followed by maintaining them near the target. Directing crystals toward the target will help in attaining the desired morphology and maintaining them near the target will control their sizes. If the target is inside the steady-state domain, every crystal can be readily steered to and maintained at the target. With the start from an initial morphology, any steady-state morphology can be attained within the operating conditions used to determine the steady-state domain. Prior to entering the steady-state domain, the path from the initial morphology must necessarily pass through a region not containing steady states. We define this region as transient domain, which is given by the transient solutions of eq 6, starting from the initial morphology X (in Figure 5). Clearly, morphologies in the transient domain can be attained but cannot be maintained. Hence, a morphology in the transient domain can serve as a



Figure 5. Operating conditions at A', (B',B''), and C' to steer crystal morphology (X) to three different targets A, B, and C, respectively. The closed dotted line shows the steady-state domain. The region enclosed between solid lines and the steady-state domain shows the transient domain.

target, only if the crystallization is terminated upon reaching it. Figure 5 shows three kinds of targets: A inside the steady-state domain, B inside the transient domain, and C neither in the steady-state domain nor the transient domain. The domain of accessible morphologies is made up of the steady-state domain and the transient domain. With a start at X, target A can be attained and maintained, B can be attained but not maintained, and the target C can neither be attained nor maintained because it is not an accessible morphology under the chosen conditions.

There can be many ways to attain the target based on the criteria such as crystallization time and operability. For example, controlling the seed crystal X to the target A with a minimum addition of mass will require operating the crystallizer at A' until X reaches A. Notice that X can also be maintained at A to obtain any desirable size. The control of seed morphology X to the target B can be achieved by operating anywhere on the line segment $\overline{B'B''}$. As X cannot be steered along B, there is a limited access to the sizes at B. The morphology of X can never attain the target C; however, it can be brought closer to C by operating at C'. Clearly in a crystallizer, the initial morphology distribution would be represented by a spatial distribution of points; their navigation to a target distribution can be described by the morphological population balance model.⁴³

8. SUMMARY

This article presents a generalized framework for modeling crystal morphology, screening crystallization conditions, and targeting and control of crystal morphologies. The framework utilizes the groups of kinetically and geometrically similar F faces that can be identified for any crystal structure and characterized by the **h** vector. A set of different morphologies, called the morphology set, is developed from different combinations of h's in the **h** vector, such that each set forms

a closed polyhedron. A bidirected graph of the morphology set is produced, such that every set is connected with its subsets. The edges of the morphology graph represent the conditions for morphology transformations. These conditions form a polyhedral cone known as the morphology domain in the space of h vectors. Different faces and edges of the polyhedral cone are the domains of different morphologies. The morphology domain is the property of crystalline materials that originates from the energetics of the crystal structure. The morphology domain spans all possible morphologies of crystals where the regions of general shapes such as fibers, needles, rods, plates, and prisms can readily be identified. The steady-state domain containing steady-state morphologies in the morphology domain can be determined from the growth rate functions alone. The targeting of crystal morphologies followed by the screening of crystallization conditions is shown for KAP-EGwater and KAP-PEG-water solutions. It is also shown that the ability to control crystal morphology depends on the location of the target with respect to the accessible regions. The twostep strategy to control crystal morphology is proposed. The first step quickly direct crystals toward the target, and in the second step crystals are maintained near the target.

A user-friendly tool called MorphologyDomain³⁹ is developed to generate the morphology graph and morphology domain for any crystalline material. For example, one of the surprising results obtained from the software is that Form I of acetaminophen can attain 96 different morphologies. It can also give information on the accessible morphologies in the morphology graph from the growth rate data. This framework is envisaged to provide guidelines for the synthesis of crystals of desired morphologies.

APPENDIX: MORPHOLOGY DOMAIN OF POTASH ALUM

Potash alum has three families of *F* faces {100}, {110}, and {111} that can be characterized by their perpendicular distances h_1,h_2 , and h_3 , respectively. The morphology set consists of 7 different morphologies such as (h_1,h_2,h_3) , (h_1,h_2) , (h_1,h_3) , (h_2,h_3) , (h_1) , (h_2) , and (h_3) . The morphology graph and morphology domain of potash alum are shown in Figure S3 and S4 of the Supporting Information. The morphology domain of potash alum is narrower than that of KAP and hence does not allow any asymmetric shapes such as needles and plates.

ASSOCIATED CONTENT

Supporting Information

This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: ramkrish@purdue.edu.

Notes

The authors declare no competing financial interest.

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