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Crystals in Light†

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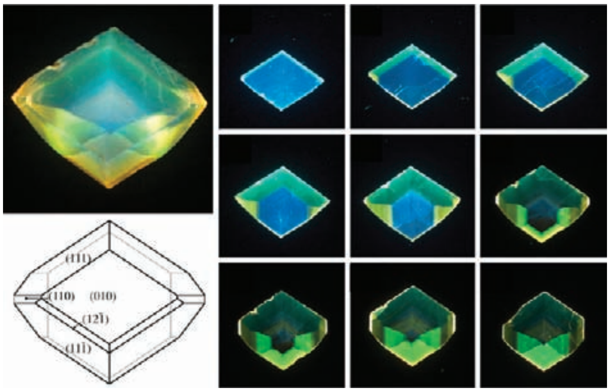

We have made images of crystals illuminated with polarized light for almost two decades. Early on, we abandoned photosensitive chemicals in favor of digital electrophotometry with all of the attendant advantages of quantitative intensity data. Accurate intensities are a boon because they can be used to analytically discriminate small effects in the presence of larger ones. The change in the form of our data followed camera technology that transformed picture taking the world over. Ironically, exposures in early photographs were presumed to correlate simply with light intensity, raising the hope that photography would replace sensorial interpretation with mechanical objectivity and supplant the art of visual photometry. This was only true in part. Quantitative imaging accurate enough to render the separation of crystalloptical quantities had to await the invention of the solid-state camera.

Many pioneers in crystal optics were also major figures in the early history of photography. We draw out the union of optical crystallography and photography because the tree that connects the inventors of photography is a structure unmatched for organizing our work during the past 20 years, not to mention that silver halide crystallites used in chemical photography are among the most consequential “crystals in light”, underscoring our title.

We emphasize crystals that have acquired optical properties such as linear birefringence, linear dichroism, circular birefringence, and circular dichroism, during growth from solution. Other crystalloptical effects were discovered that are unique to curiously dissymmetric crystals containing embedded oscillators. In the aggregate, dyed crystals constitute a generalization of single crystal matrix isolation. Simple crystals provided kinetic stability to include guests such as proteins or molecules in excited states. Molecular lifetimes were extended for the preparation of laser gain media and for the study of the photodynamics of single molecules. Luminophores were used as guests in crystals to reveal aspects of growth mechanisms by labeling surface structures such as steps and kinks.

New methods were adopted for measuring and imaging the optical rotatory power of crystals. Chiroptical anisotropies can now be compared with the results of quantum chemical calculations that have emerged in the past 10 years. The rapid determination of the optical rotation and circular dichroism tensors of molecules in crystals, and the interpretation of these anisotropies, remains a subject of future research.

Polycrystalline patterns that form far from equilibrium challenged the quantitative interpretation of micrographs when heterogeneities along the optical path and obliquely angled interfaces played large roles. Resulting “artifacts” were nevertheless incisive probes of polycrystalline texture and mesoscale chemistry in simple substances grown far from equilibrium or in biopathological crystals such as Alzheimer’s amyloid plaques.

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Polarized Light and Photography

Étienne Louis Malus (1775−1812) both discovered the polarization of light by reflection and constructed the first polarimeter with which he deduced his eponymous cosine-squared law, the law of Malus,[1] a quantitative statement involving polarized light. By application of the art of visual photometry, Malus established that the quantity of polarized light transmitted (I/I_0) by a crystalline analyzer was proportional to $\cos^2 \theta$, where θ is the angle between the plane of polarization and the pass direction of the crystal.

Malus witnessed how light polarized by reflection led to wholly new phenomena and strategies for the investigation of matter. His friend, François Arago (1786−1853), while passing polarized light along the optic axis of quartz, first observed the consequences of optical rotatory dispersion. Jean-Baptiste Biot (1774−1862), known best by chemists for detecting the optical activity of organic solutions, correctly interpreted Arago's observations, thus initiating a bitter dispute for priority.[2] Their rivalry would resonate in 1839 when two different techniques were claimed as the invention of photography. Arago championed iodine-sensitized silver plates or Daguerrotypes, while Biot promoted paper soaked in silver halide solutions introduced by Henry Fox Talbot (1800−1877). Both Arago and Biot set out to demonstrate that the Daguerro- and so-called Talbototypes, respectively, could be used as quantitative photometers in which the chemical action of light was proportional to intensity, thus transcending the limitations of Malus' visual photometry.[3]

Despite the advent of photography, Arago was unable to detect the effect of optical rotation (OR) in any crystal direction other than the high symmetry axis, a consequence of the confounding effects of the much larger linear birefringence (LB) in off-axis directions. Photography could not hope to capture the changes in light intensity that result from chiroptical perturbations to the state polarization in anisotropic media, consigning measurements of OR and electronic circular dichroism (CD) to isotropic solutions for two centuries. John Herschel (1792−1871), who coined "photography" and introduced hyposulfites for fixing the latent image, understood the chemical limitations of Biot-like solution studies of OR. He recognized that there may exist in some molecule directions in which the rotatory power is positive, and others in which it negative. In liquids, the measured OR must be a mere average.[4]

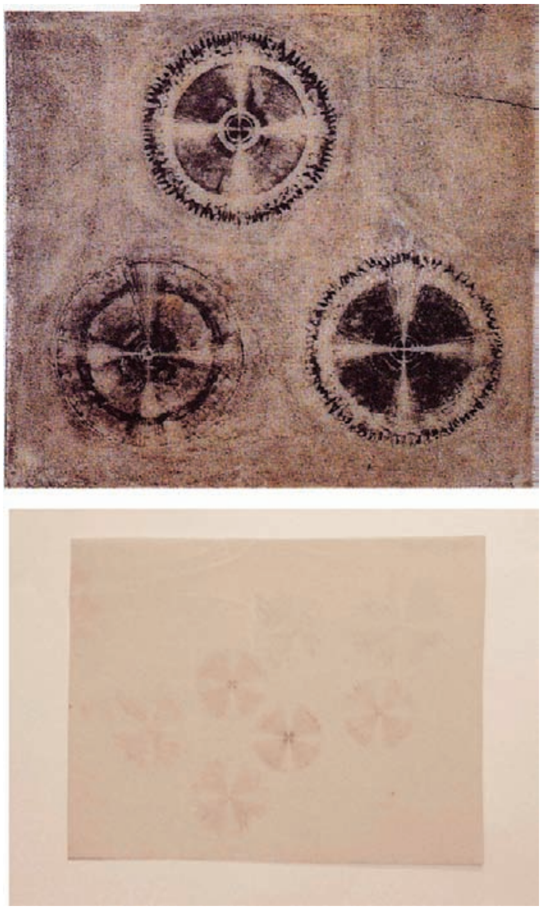

FIGURE 1. (a) W. H. F. Talbot. Talbototype negative (ca. 1840−42) of spherulite drawings. (b) W. H. F. Talbot. Boric acid (presumably) crystals through crossed polarizers (ca. 1848). Talbototype negative. National Museum of Photography, Film & Television, Bradford, and courtesy of K. Dowlatshahi.[7]

Polarized light and photography fared better in the characterization of LB as opposed to circular birefringence (CB, a synonym for OR). David Brewster (1781−1868), a champion of the cheap Talbototype over the costly Daguerrotype, showed that the interference that occurs by recombination in an analyzer of light transmitted through weakly linearly birefringent crystals could be used to establish crystal symmetry; Biot made similar correlations.[5] Brewster befriended Talbot who invented, in addition to photography, the polarized light microscope that Brewster used and developed to great effect in studies of crystal symmetry. Talbot later confounded Brewster's classification when he prepared "circular" crystals of boric acid (H_3BO_3),[6] detected only with the great resolving power of his newly invented microscope. Talbot copied drawings of these formations, spherulites in today's terminology, with photosensitive paper. Shown in Figure 1a are the first photographs of crystals, albeit photographs of drawings of crystals.[7] The black, so-called Maltese extinction crosses are now a familiar characteristic of any radial anisotropic body between crossed polarizers. Later, Talbot succeeded in impressing images of the spherulites directly to photosensitive paper through the agency of the microscope, the first bona fide photographs of crystals to the best of our knowledge.

Brewster and Talbot discussed crystal optics at Talbot's estate, Lacock Abbey, a subject of some of the very first photographs. This scientific conversation saved Talbot from melancholy,[8] but friendship notwithstanding Brewster claimed priority for the discovery of circular crystals[9] and published many subsequent examples despite confusion by their form. In fact, mechanisms of the growth of spherical crystals are only now just coming into focus.[10]

In large measure, Talbot's polarizing microscope, fitted with crossed Nicols or tourmaline gemstones, changed little throughout the generations. One exception was the introduction of conoscopic illumination, as opposed to orthoscopic illumination.[11] Using a cone of light, crystallographers could examine the properties of anisotropic media in many directions of incidence simultaneously. William Crookes (1832−1919) was the first to capture the effects of conoscopy on film. He started his scientific life in the chemistry of photography. By the 1850s, he had a secure reputation in London photography circles and was invited to testify in a failed patent infringement suit brought by Talbot.[12] During this period, he photographed anomalous conoscopic interference rings of potassium nitrate.[13] The confusing progression of these rings in his photo captured the attention of George Gabriel Stokes (1819−1903). "The circumstances which determine the rings [on film] are so different," wrote Stokes, "it is no wonder that the character of the rings seen on a photograph should differ... from that of the rings seen directly."[14] The eye was most sensitive to hue, the film to intensity, albeit at particular frequencies.

For a brief period, synthetic crystals that absorb light anisotropically were considered as inexpensive linear polarizers for microscopes. Hope was focused on single crystals of an iodide salt of quinine sulfate, called herapathite, accidentally precipitated from the urine of a dog laboring in the service of antimalarial toxicology.[15] Brewster wished for such crystals to adapt to his invention, the kaleidoscope.[16] Remarkably, in hindsight, Stokes interrupted his discovery of the cause of fluorescence ("change in refrangibility") and his formulation of the powerful description of polarized light, now known as the Stokes vector, in order to investigate the metallic reflectivity of herapathite.[17] Only with the invention of Polaroid, microcrystals of herapathite oriented in cellulose acetate, did polarized light become something for the masses, and only in the last year did we finally show how the first plastic polarizers really functioned.[18]

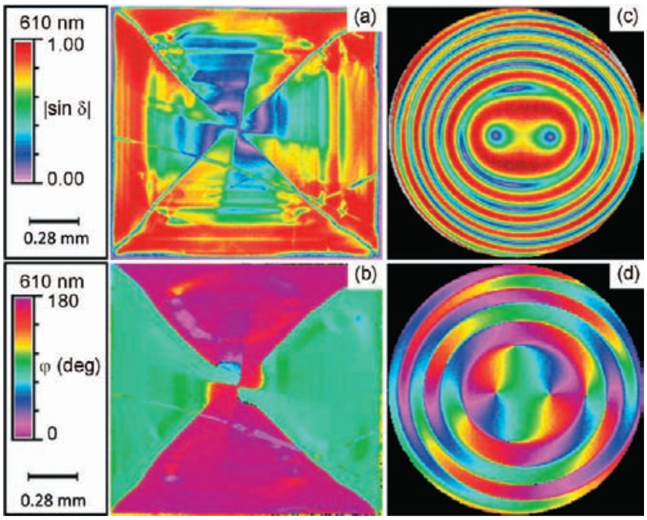

FIGURE 2. Micrographs of 1,8-dihydroxyanthraquinone made with the rotating polarizer method. (a,b) Orthoscopic illumination. (c,d) Conoscopic illumination. (a,c) |sin δ|, where $\delta = 2\pi L\Delta n/\Delta$; (b,d) φ (deg) is the extinction angle plotted counterclockwise from the horizontal. By K. Claborn, reproduced with permission of The Royal Society of Chemistry.[51]

Linear Birefringence

The polarized light microscope was transformed in the 1990s with the introduction of quantitative LB imaging systems fitted with solid-state cameras. By collecting intensity data as a function of the mechanical rotation of a plastic linear polarizer as did Glazer et al.,[19,20] or as a function of electro-optically modulated polarization as did Oldenbourg and Mei,[21] accurate false color maps of optical properties were generated through Fourier analysis of the transmitted signal.

The aforementioned techniques are forms of differential polarization imaging wherein images made with different polarization state generators or analyzers are compared. The intensity expression for a linearly birefringent medium between a variable polarizer and a circular analyzer, derived using the Jones calculus, is $I/I_o = 1/2\{\cos^2(\alpha - \varphi) + \sin^2(\alpha - \varphi) - \sin(\alpha - \varphi)\cos(\alpha - \varphi)[\exp(2i(\delta/2 + \pi/4)) + \exp(-2i(\delta/2 + \pi/4))]\}$, where α is the position of the rotating polarizer, φ is the angle between the slow direction of the crystal and the polarizer, and δ ($=2\pi\Delta nL/\lambda$) is the phase difference of the two eigenmodes propagating through the crystals (Δn is the LB, L is the path length, and λ is the wavelength). The law of Malus is embodied in the first two terms, whereas the effect of the interference in the crystal is expressed by the third term.

The rotating polarizer technique was used to measure anomalous LB in high symmetry crystals such as tetragonal crystals of 1,8-dihydroxyanthraquinone (Figure 2), shown clearly as biaxial in micrographs made with orthoscopic (Figure 2a,b) and conoscopic (Figure 2c,d) illumination.[22] Brew-

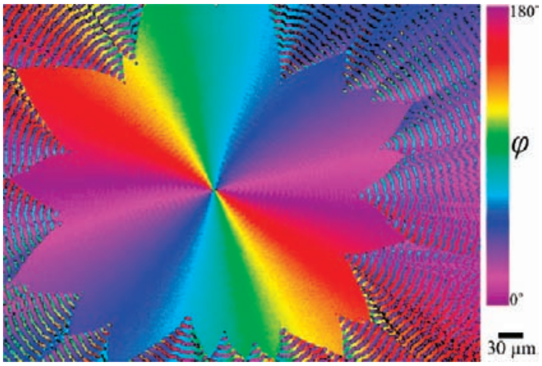

FIGURE 3. Linear extinction map of mannitol and 10 wt % polyvinylpyrrolidone grown from the melt. The angle φ (deg) indicates the larger refractive index (at 572 nm) of the linearly birefringent medium plotted counterclockwise from the horizon. Two polymorphs are evident; the "sunburst" on the inside is the δ form and on the outside the α form.[27] By E. Gunn.

ster first detected so-called optically anomalous crystals in 1815.[5] He was as interested in the violations to his correlations between form and optical properties as he was to the rules themselves. The study of crystals with optical symmetries incompatible with their shapes waxed and waned for two centuries.[5,23]

The etiology of the anomalous birefringence in 1,8-dihydroxyanthraquinone can be attributed in part to twinning.[22] More prominent among the causes of anomalous LB in crystals is the kinetic ordering of molecules and ions at dissymmetric sites on a crystallographic surface thereby breaking the symmetry that would relate the sites in the bulk.[24] This mechanism operates in mixed crystals of simple salts such as $Ba(NO_3)_2$ and $Pb(NO_3)_2$,[25] as well as $NaClO_3$ and $NaBrO_3$.[26] Ideal solid solutions with statistical distributions of one component within another are rarer than previously thought.

One of Brewster's circular crystals, mannitol, was recently rediscovered.[27] We analyzed it by the rotating polarizer method.[19] Mannitol, grown from the melt with a polymeric additive, showed a radial, sunburst structure (Figure 3) that strikingly illustrates quantitative differential polarization imaging. Brewster's comment that spherulites "form, in the estimation of all who have seen them, one of the finest objects for the polarizing microscope" hardly seems dated. The optical texture of mannitol spherulites is complex, yet from digital intensity data a micrograph is derived that shows the direction of the larger refractive index at each point in the dimorphous sample, clearly indicating a rhythm as growth proceeds along radii. Periodic crystallization of this kind is common in systems grown far from equilibrium; however, mechanisms for rhythmic optical contrast are far from settled.[28] Accurate optical measurements over broad, patterned fields are necessary for discriminating competing mesoscale structures.

In this Account, we emphasize the important roles that solid-state cameras and digital computers have played in the analysis of the linear optical properties of crystalline materials. However, it would be unfair to slight the eye and human brain as devices for detecting light and processing images, respectively. Indeed, even with old-fashioned, Talbot-like microscopes, there remain questions in crystallography that can be answered. For instance, we quelled the roiling debate about the existence of high-temperature phases of KH_2PO_4 by merely taking pictures made from silver halide crystallite dispersions (film).[29]

Linear Dichroism

The literature is replete with examples of crystals that show not only anomalous LB but also anomalous linear dichroism (LD), polarization dependent differences in the imaginary part of the complex refractive index. Most any transparent crystal may become linearly dichroic by orienting and overgrowing anisotropic, colored additives: dyes. The subsequent, intermittent[37] study of dyed crystals[30] mimicked the sporadic analysis of optical anomalies. Curiously, the dyeing of crystals never developed as a craft at any time in human history, and this general and often beautiful aspect of supramolecular chemistry never became a sustained scientific inquiry, despite the ease[32] and integrity[33] with which simple crystalline substances can be colored with both natural and synthetic dyes.[34]

Dyes were used to selectively recognize different phases of a given compound (polymorphs),[35] symmetry independent facets of a given crystal,[30] and even enantiomorphous faces when the additive is chiral.[30,31,36] Optically responsive molecules were used as probes of local interactions with distinct crystallographic surfaces. For instance, crystals grown in the presence of luminophores with varying protonation states showed distinct luminescence energies depending upon the electrostatic potentials of the surfaces of the growth sectors to which they were associated.[37] Dyes distinguished vicinal facets of emergent growth hillocks[30] as in Figure 4. In this way, every growth active hillock of some crystals can be identified and ordered in space and time.[38] Dyes have even selectively recognized symmetry independent kinks on a given step.[39] Reciprocally, distinct crystal faces recognized dyes in specific conformations[40,41] or tautomeric states.[42]

Crystals with oriented, isolated luminophores are excellent media for the study of single molecules.[43] The extended lifetimes afforded to dyes buried within single crystals facilitated the observation of blinking dynamics with on and off times extending over nine decades in times.[44] This restricts mechanisms for blinking, an outstanding problem in single molecule photophys-

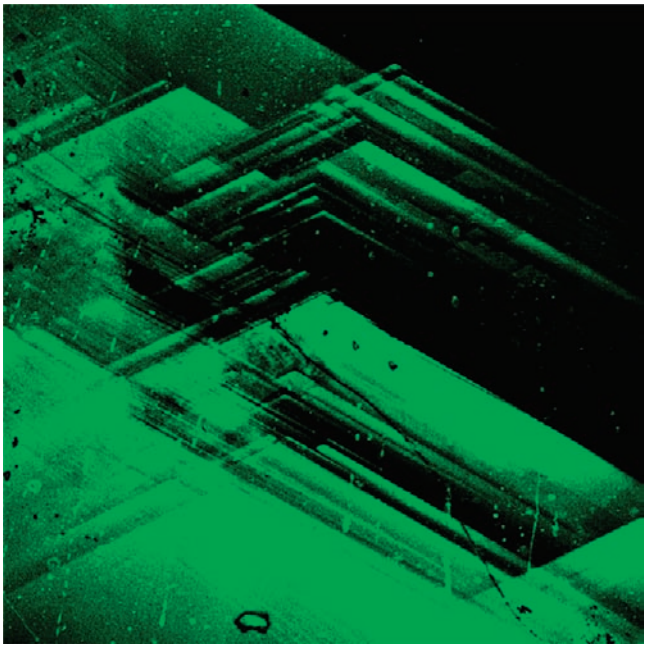

FIGURE 4. Confocal image of potassium hydrogen phthalate grown with 2,6-dichlorofluorescein showing details of luminescence (λ_{ex} = 488 nm) developed in the fast slopes of the (010) growth hillocks. [001] vertical, [100] horizontal. Vertices mark dislocation cores. Image size = 0.9 mm × 0.9 mm. Reproduced with permission of The Royal Society of Chemistry.[38] By T. Bullard.

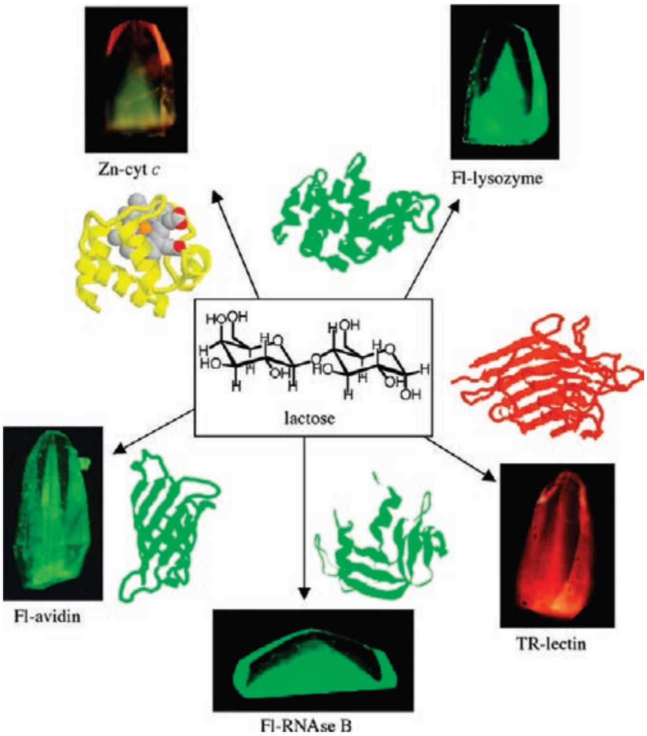

FIGURE 5. Crystals of α-lactose monohydrate containing luminescently labeled or intrinsically luminescent proteins (Zn-cyt c = zinc cytochrome c; Fl = fluoroscein; TR = Texas red). In each case, the mixed crystal shows a characteristic fluorescence from the (010) growth sector. Copyright Elsevier.[47] By H. Wang.

ics.[45] Crystals likewise have extended the lifetimes of molecules for the preparation of new laser gain media.[46] In the aggregate, it was clear that single crystal matrix isolation could be generalized for giving kinetic stability to a variety of analytes including excited states and proteins (Figure 5);[30,47] triplet states were extremely long-lived,[41,48] and green fluorescent protein was resistant to denaturation.[49]

In contrast to the process of dyeing crystals summarized above, the dyeing of organized structures found in tissues is a common practice in pathology and cell biology. Since the processes of both dyeing crystals and dyeing crystalline tissues are governed by the specificity of noncovalent interactions that lead to ordered arrays of visible chromophores, we considered whether our experience with the former might inform the latter. LB imaging was used to show that spherulitic amyloid plaques in Alzheimer's-diseased brain tissue contain disordered cores, providing clues to mechanisms of crystallization of in vivo.[50] At the same time, we clarified the orientation of the Congo red stain, a simple fact that had been confused when simulations of noncovalent interactions displaced direct observations of LD.

Circular Extinction

A microscope with mechanically modulated circular polarization states can image the differential transmission of left and right circularly polarized light (CPL).[22] Intensity expressions for such a device and others introduced herein were derived with the Jones calculus and can be found in ref 51. In favorable circumstances, an instrument modulating circular inputs will record CD. More generally, the instrument records circular extinction (CE), whether or not a consequence of absorption. In organized media, CE can occur by mechanisms involving only the electric dipole and as such are larger than CD.

$LiKSO_4$ crystals are enantiomorphously twinned with mirror image related faces that potentially incorporate conformationally chiral guest molecules selectively during growth. An instrument sensitive enough and sufficiently free of artifacts could be used with such crystals to measure anisotropies of a dye's induced chiroptical properties. Although mirror image related domains in the twinned $LiKSO_4$ crystals displayed marked CE, the signal changed sign with inversion of the sample with respect to the light path, a transformation inconsistent with natural CD. The anisotropy of the host generates elliptical states that will differentially interact with the absorbing sublattice of rodlike dipoles so long as the electric dipole transition moments are twisted in the same sense from the eigenmodes of the crystal.[52] A bias therefore becomes manifest in the interaction of dyes and the two elliptical light forms. Unlike intrinsic CD, this so-called anomalous CE does

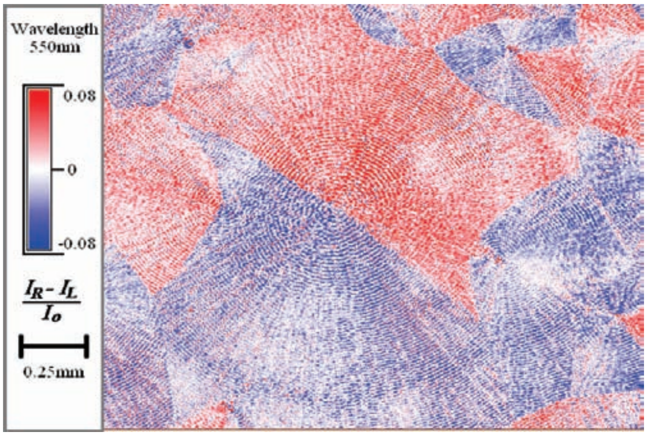

FIGURE 6. Circular extinction micrograph of a phthalic acid spherulite. Reprinted with permission from ref 54. Copyright 2006 American Chemical Society. By E. Gunn.

not convey absolute configuration but may be used instead to determine the *absolute orientation* of adsorbed dye molecules and thereby resolve an ambiguity present in polarized absorption measurements.[53]

When orthogonal circular polarization states enter an anisotropic medium, the exiting light is in orthogonal elliptical states. If the exiting surface is not normal to the wave vector, Fresnel reflection at the interface will discriminate between left and right circularly polarized input. A dramatic example of such an effect is seen in rhythmic precipitates of phthalic acid.[54] Ostensibly radial bodies were bisected into heterochiral halves, one of which preferentially scattered right CPL while the other preferentially scattered left CPL (Figure 6). This was shown to be a consequence of mesoscale chiral texture wholly consistent with the C_{2h} symmetry of the initial phthalic acid nucleus.

It is well-known that CD measurements of anisotropic media may contain artifacts that result from mixed linear anisotropies. Such artifacts are generally considered a nuisance. However, artifacts, carefully measured, may contain valuable information. Dyed polycrystalline sorbitol spherulites[55] developed strong apparent OR and CD signals at the boundaries between the polycrystalline bodies. The signs and magnitudes of these signals were sensitive to the angle of overlapping fibrils (Figure 7) and their relative heights along the optical path.[56] Systematic chiroptical artifacts should not be dismissed reflexively; in the aforementioned example they are comprehensible effects that serve to define mesoscale structure.

CD, as well as LD, can be imparted to transparent crystals through dyeing during growth from solution.[57] Our analysis of chiral $NaClO_3$ crystals stained with a textile dye, a propeller-shaped triarylmethane cation, revealed a confluence of properties, CD as well as anomalous CE described above. The relative magnitudes of these effects depended upon the orientation from which the dye in the crystal was analyzed.

Circular Birefringence

The difficulties associated with the measurement of optical activity in crystals have caused confusion evident in persistent misstatements of the necessary condition for OR and CD.[58] For this reason, we determined the optical rotatory power of a simple, achiral molecule, pentaerythritol ($C(CH_2OH)_4$), sitting on an improper rotation axis in an achiral crystal and compared these data to the results of quantum chemical calculations of single molecules.[59] The difficulty of measuring the optical activity of crystals is a consequence of the fact that the much larger LB has the effect of damping the measurable azimuthal rotation by a factor of $\sim(\sin \delta)/\delta$, causing the optical activity to oscillate in sign[60] (not to mention the up-front lapidary work (drudgery) required to obtain large, cut, polished thin sections).

Homochiral, isomorphous $NaClO_3$ and $NaBrO_3$ crystals have been long known to have opposite signs of rotation,[26] underscoring the extent to which we struggle to understand the rotatory power of organized media. Mixed crystals showed anomalous LB as described above, complicating observations of OR. We used a scanning stage to image the optical activity of mixed halate crystals.[51] Dextro- and levorotatory islands coexist in crystal sections, indicating a composite structure of chlorate and bromate rich domains as opposed to a homogeneous mixed crystal.

To characterize these domains with greater resolution, we turned to Mueller matrix microscopy (MMM),[61] a technique naturally suited to problems we have previously encountered because it permits the simultaneous analysis of linear and circular anisotropies. The Mueller calculus owes its power to the general description of polarized light as introduced by Stokes. Here, the polarization properties of a sample are analyzed in terms of the transformation of an input Stokes vector ($S_{\text{in}} = [E_x^2 + E_y^2, E_x^2 - E_y^2, 2E_xE_y \cos \delta, 2E_xE_y \sin \delta]$) via the Mueller matrix (M): $S_{\text{out}} = MS_{\text{in}}$. E_x and E_y are orthogonal electric field components, and δ is the phase shift between them. A MMM generates 16 images, each representing one of the elements of the 4 × 4 Mueller matrix, expressed in terms of measurable input and output polarization state intensities.

Unfortunately, the 16 images are not simply related to the fundamental optical constants of interest. To achieve the separation of linear and circular anisotropies, we implemented a differential analysis:[62] $S_{\text{out}} = e^{mz}S_{\text{in}} = MS_{\text{in}}$ where, z is the distance of propagation and m is the differential Mueller matrix describing the transformation of the Stokes vector for some infinitesimally small path Δz. The process of deriving m

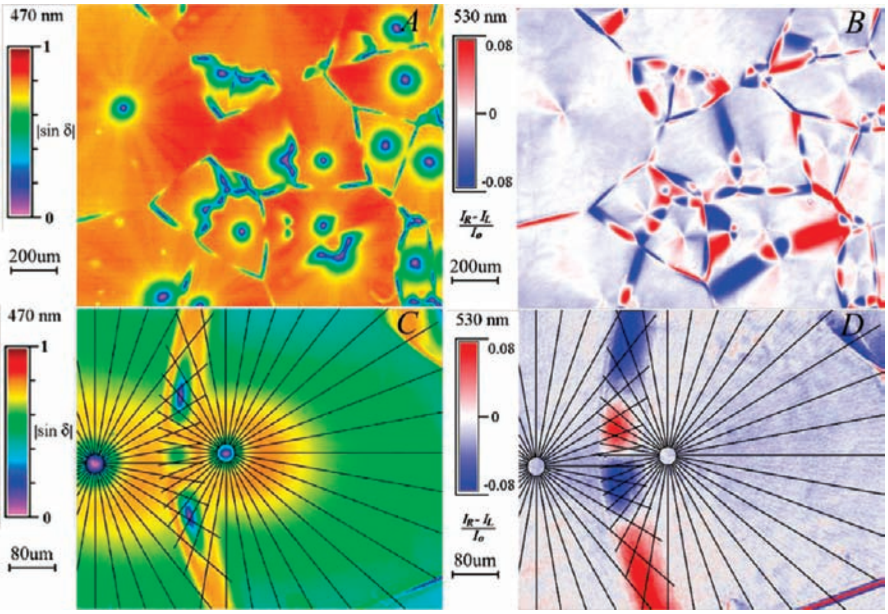

FIGURE 7. (A,B) Images of |sin δ| for 1 wt % amaranth doped D-sorbitol spherulites made with LB imaging system. (C,D) Corresponding images of circular extinction. Nuclei overlaid with radial grids that indicate directions of fibril growth. Null signals where grid lines are parallel or perpendicular. Here, the medium behaves as if it were homogeneous. Reproduced with permission of Wiley-VCH.[56] By E. Hollis.

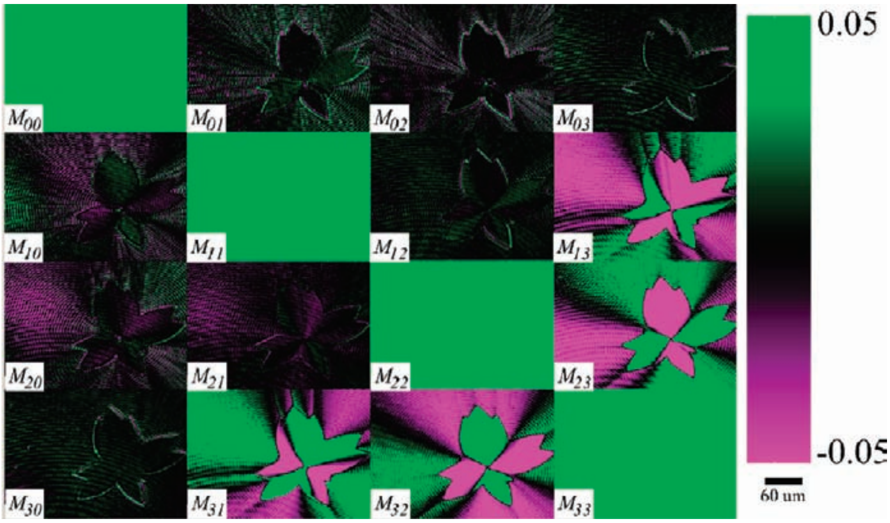

FIGURE 8. Raw Mueller matrix, *M*, of mannitol spherulites with 10 wt % polyvinylpyrrolidone of the type grown in Figure 3. Image taken at 532 nm. Scale refers to values of the matrix operator *M*. By J. Freudenthal.

unfolds the convolution of linear and circular anisotropies so that each fundamental quantity has a unique place in the matrix. Recently, an MMM was operated under conoscopic illumination so as to derive dielectric tensors from a single image.[63] The same technique holds promise for measuring chiroptical tensors for small crystals quickly. Mueller matrix polarimetry has been applied to Arago's old problem, the determination of off-axis OR in quartz.[64]

Figure 8 shows the raw Mueller matrix *M* of a mannitol sample of the type shown in Figure 3. One differential matrix element, m_{02}, is described below.

Outlook/Lookback

Talbot wrote that the dance of color and light from growing spherulites seen with his newly invented polarized light microscope resembled the "coruscations of a firefly".[6] He went no further. Even with better tools, trying to pin down the complex optical properties of polycrystalline patterns can still sometimes seem like chasing fireflies. Mannitol, while nonabsorbing, gives a strong LD signal (m_{02}) by MMM. This is undoubtedly a consequence of differential linear light scattering (as opposed to differential CPL scattering as in Figure 6, though mannitol does this too). Apparent dichroism from transparent media was long ago debated under the banner of *pseudopleochroism* and was considered as a mechanism for the synthesis artificial polarizers before the invention of Polaroid.[65] The mannitol image is further problematic because it changes character with focus, suggesting that some of the contrast is a consequence of interference from its grating-like structure. In other words, part of what is seen is a chimerical phase image rather than an amplitude image.[66] Optical diffractometry must be coupled with microscopy to further parse convolutions of this kind. These future challenges are raised here to impress upon the reader that linear crystal optics has been, is, and will remain a vital subject.[67]

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BIOGRAPHICAL INFORMATION

Bart Kahr was born in New York City in 1961. He studied chemistry with I. D. Reingold at Middlebury College, with Kurt Mislow at Princeton University (Ph.D. 1988), and with J. M. McBride at Yale University. He was a faculty member at Purdue University from 1990 to 1996 and at the University of Washington, Seattle from 1997 to 2009. He is currently professor of chemistry in the Molecular Design Institute at New York University.

John Freudenthal was born in Thermopolis, Wyoming in 1982. He earned his bachelor degree in chemistry from University of Idaho and a masters degree in Seattle, and he is currently completing his doctorate at New York University. John is analyzing the properties of crystals with differential polarization imaging techniques.

Erica Gunn was born in Plymouth, Massachusetts. She earned a bachelor degree at Simmons College in Boston and a Ph.D. under the supervision of B. Kahr in Seattle in 2009 for a study of polycrystalline growth. Erica is currently a postdoctoral fellow with Lian Yu, in the School of Pharmacy at the University of Wisconsin, Madison.

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FOOTNOTES

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