



## ENGINEERING

# Universal pictures: A lithophane codex helps teenagers with blindness visualize nanoscopic systems

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People with blindness have limited access to the high-resolution graphical data and imagery of science. Here, a lithophane codex is reported. Its pages display tactile and optical readouts for universal visualization of data by persons with or without eyesight. Prototype codices illustrated microscopy of butterfly chitin—from *N*-acetylglucosamine monomer to fibril, scale, and whole insect—and were given to high schoolers from the Texas School for the Blind and Visually Impaired. Lithophane graphics of Fischer-Spier esterification reactions and electron micrographs of biological cells were also 3D-printed, along with x-ray structures of proteins (as millimeter-scale 3D models). Students with blindness could visualize (describe, recall, distinguish) these systems—for the first time—at the same resolution as sighted peers (average accuracy = 88%). Tactile visualization occurred alongside laboratory training, synthesis, and mentoring by chemists with blindness, resulting in increased student interest and sense of belonging in science.

## INTRODUCTION

Approximately 253 million people currently have blindness or low vision, including 1.4 million children with blindness (1, 2). People with blindness face barriers accessing the tools and information of science (3–8), especially within the “central” science of chemistry (9–16). Chemistry, blind persons have been told, is too difficult, too dangerous, and too visual (14, 15). Current research laboratories are not accessible to people with complete blindness. However, advances in machine vision and learning (17, 18) and robotic trends toward total laboratory automation (19, 20) have the potential to make future laboratories accessible and safe.

Ultimately, the total inclusion of persons with blindness into chemistry—the classroom, the laboratory, the data, and research literature—will require development of new assistive technology. These tools must be developed and implemented “along the way” in real time to permit inclusion of blind persons into science being done now. This work is part of the broader field of accessibility and inclusion science. The resulting boost in diversity within a scientific group—made of people who think differently because their lived experiences are different—can increase the impact of science produced by the group (21, 22).

Nearly all graphical information and imagery in chemistry textbooks, journal articles, research notebooks, theses, and data repositories remain inaccessible to people with blindness (3, 13). Instead, people with blindness rely on word descriptions (such as the infamous 298-word description of a porphyrin) (10), simplified molecular-input line-entry system (SMILES), Braille, or low-resolution tactile graphics (some of which are “homemade” by tracing printed pictures with a hot glue gun) (14, 23–26).

The principal investigators of this study are chemists and biochemists who wish to create a single universal (shareable) graphic that can be used by both sighted and blind persons presently in chemical research groups and classrooms, and those in high school or college wishing to matriculate to or join chemistry laboratories. The goal is to develop and popularize small, compact, durable, high-resolution universal graphics that will allow everyone to sit around a table at a weekly group meeting and visualize, interpret, and discuss the same imagery and data—equally—at the highest possible resolution. There is a need for long-lasting two-dimensional (2D) tactile graphics that can be taped inside a research notebook or passed out during presentations at research conferences.

The two most common benchmark methods for making tactile graphics are (i) plastic or paper embossing and (ii) swell form printing, also known as thermoform printing or “pictures in a flash” (Fig. 1) (27). These two graphic types are invaluable to people with blindness but have limited use in science because of low resolution, low maximum protrusion ( $\leq 0.7$  mm), and low durability (Fig. 1). Prior studies demonstrate that swell form printing—unrivaled in its speed and convenience—is inadequate for high-resolution data in science (6). For example, swell form printing produces distorted forms of common data such as electron micrographs, SDS–polyacrylamide gel electrophoresis (SDS–PAGE) gel electropherograms, and mass spectra (6). In particular, the unpredictable malformations and low, inconsistent resolution of swell form graphics (millimeter at best, centimeter at worst) make swell form graphics unable to accurately project high-resolution complex imagery of electron microscopy (6). This poor resolution is not acceptable in science [or science publishing, per the 300 dots per inch (DPI) requirements of imagery].

While there is a need to create universal graphics that can incorporate Braille, it is also important to create graphics that do not necessarily need Braille to function. Braille is an essential component of literacy for persons with blindness (28). However, the use of Braille can complicate data sharing and group study, as most sighted peers (or tutors) will not be able to read Braille, and only 10% of blind persons can read

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Braille or are being taught Braille in the United States. (28). Likewise, some persons lose vision suddenly and must continue their education while learning Braille. Last, while Braille is essential for text, it can be ambiguous if not used properly in chemistry. The lone electron pair, indicated with a vertical or horizontal colon, is similar to Braille characters for “b” and “c,” and an unpaired electron is similar to the letter “a.” For these reasons, there is a separate style of Braille for chemistry, where a lone electron pair is indicated by Braille dot positions 1, 4, 5, and 6, and an unpaired electron radical is indicated by dot positions 1 and 6 (29).

Two new types of tactile graphics (that use universal design) were recently reported to make high-resolution 2D and 3D imagery accessible and shareable between persons with blindness and eyesight (6, 9). For 2D imagery, thin tactile graphics can be 3D-printed from translucent polymers to use the “lithophane” effect (6). A lithophane is a thin, translucent engraving or embossing of an image (Fig. 2A). The tactile image can be interpreted by touch. However, lithophanes also scatter light when backlit, producing a video-like image for sighted people or those with low vision who need a hybrid tactile-visual image (Fig. 2A). In the case of lithophane forms of SDS-PAGE gels—the most common data in biochemistry—the protrusion of a protein band scales linearly with its optical intensity, allowing tactile and visual integration (6). The ability to interpret lithophane data equally with fingers or eyesight allows blind and sighted researchers to share and analyze the exact same piece of data, down to the signal-to-noise ratio of a mass spectrum (6). This method also uses low-cost commercial printers operating at 20- to 100- $\mu\text{m}$  resolution, with each print costing a few dollars. Micrometer-scale resolution will be useful in high-resolution tactile graphics, as fingertips can detect nanometer-scale differences in surface roughness (30).

For 3D imagery, micro-models can now be 3D-printed at the millimeter-scale from food-safe resin (Fig. 2, B and C) (9). These micro-models increase portability, lower cost, and facilitate tactile

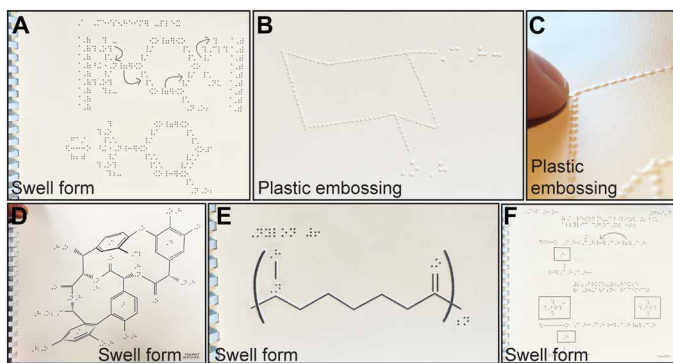
visualization by manual or oral stereognosis or by eyesight (9, 30). A side-by-side comparison of lithophane tactile graphics to current tactile graphics (swell form graphics) illustrates the greater resolution and protrusion of lithophanes (Fig. 3). Scaling up the size of a swell form graphic would not improve resolution, affect their failure to swell, or reduce the effect of “popcorning,” and any increase in image contrast or darkness (to induce swelling) is inappropriate with scientific data (Fig. 3) (31).

To date, there have been no reports of students with blindness being introduced to lithophane or micro-model prototypes as a form of outreach or for educational research. For example, the efficacy of lithophane graphics on high school students with blindness has not been assessed (6), and the efficacy of the micro-models have never been assessed on any persons with blindness (prior studies involved sighted college students who were blindfolded) (9). Moreover, lithophane graphics have not been applied to organic chemistry or electron microscopy. Last, there is also no report of a lithophane codex (a bound, tactile book or rotary file) to make graphics organizable in a sequence and portable. These four gaps are addressed in this current study.

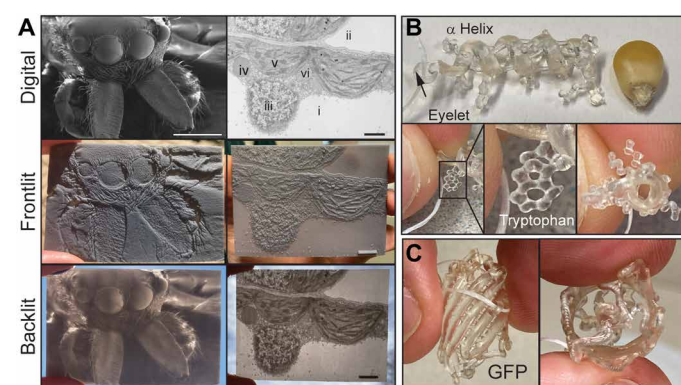
## RESULTS AND DISCUSSION

This project involved human subjects and received approval from an Institutional Review Board at Baylor University. Informed consent was obtained for subjects before enrollment in this study. Members of the community of people with blindness were involved in the design of this intervention study, i.e., elements of stakeholder theory and stakeholder engagement were incorporated (32–34). Four of the co-authors of this paper are people with blindness.

The primary goal of the project is to perform outreach to students with blindness in the local community and not to necessarily perform research on students with blindness. The goal is to demonstrate to students with blindness that they can easily visualize complex,



**Fig. 1. Conventional tactile graphics used to teach organic chemistry to a student with blindness.** These graphics are Braille transcriptions from *Organic Chemistry* by Brown, Foote, and Iverson, 4th Edition. (A) Swell form (thermo-form) tactile graphics depicting a Meisenheimer complex. (B) Plastic embossing graphic depicting (1*R*, 3*S*)-3-methylcyclohexan-1-ol. (C) Magnification of a chemical structure in plastic embossing. (D) Partial structure of a cyclic compound (the rest of the structure was continued on a next page due to size constraints). (E) Hybrid bond-line and Braille structure of nylon. (F) Resonance of an allylic carbocation structure. Note that although graphics are from the same textbook, three different indicators are used for a single covalent chemical bond (e.g., a raised line or Braille positions 1, 2, and 3). The plastic embossing uses a third indicator for single bonds: a string of dots.



**Fig. 2. Lithophanes and 3D models of microscopic and nanoscopic imagery made with an inexpensive 3D printer.** (A) Top row: digital images of electron and fluorescence micrographs; middle row: frontlit lithophanes of micrographs from the top panel; bottom row: backlit lithophanes of micrographs. From left to right: scanning electron micrograph of a jumping spider (scale bar, 500  $\mu\text{m}$ ), transmission electron micrograph of a plant cell showing chloroplast and mitochondria (scale bar, 1  $\mu\text{m}$ ). Labels for plant cell: (i) vacuole, (ii) intracellular space, (iii) nucleus with DNA, (iv) peroxisome, (v) chloroplast, and (vi) mitochondria. (B) 3D-printed cartoon micro-model of an  $\alpha$  helix from the NIH 3D print repository (indole side chain of tryptophan is shown). (C) 3D-printed micro-model of a  $\beta$ -barrel protein [green fluorescent protein (GFP)] from the NIH 3D print repository.

high-resolution graphics in chemistry at the same resolution as their sighted peers.

One hypothesis of this paper is that beginning high school students with blindness with little or no knowledge of chemistry (including ninth graders) will be able to visualize graphics at high resolution. In this project, the visualization of data by students is not assessed with functional magnetic resonance imaging (fMRI) or other techniques to assess activation of the visual cortex. Rather, visualization is assessed by quantifying the ability of the student to describe and recall quantitative and qualitative chemical and physical details of chemical systems depicted in the graphics (e.g., allosteric conformers of protein structures, small organic molecules, and micrometer-scale biomaterials).

Likewise, a key part of this study is to assess how the presentation of new visualization tools affects the attitudes of students with blindness, who are interested in learning chemistry. This assessment can inform researchers about the broader impact of new assistive technology on student interest, sense of belonging, and confidence in chemistry and science.

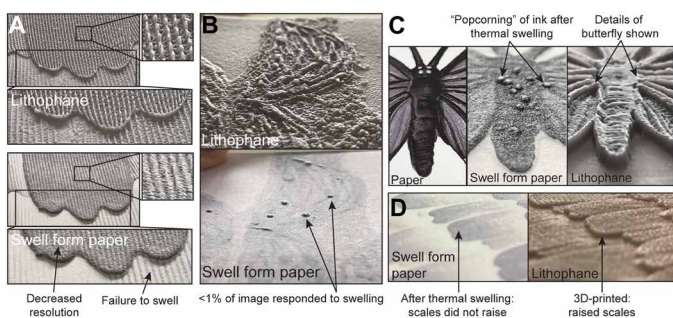
In this current study, 3D printing was used to manufacture and test approximately 120 lithophane graphics (eight copies of 15 different lithophanes). Approximately 70 molecular models were also 3D-printed from atomic coordinates deposited in the Protein Data Bank (PDB). 3D printing was carried out at ~100- $\mu\text{m}$  resolution.

These 2D and 3D graphics were ultimately used to teach and assess chemistry concepts and laboratory experiments to eight high school students with blindness or low vision from the Texas School for the Blind and Visually Impaired (TSBVI). Because of decades of systematic exclusion, it can be difficult to find large numbers of blind high schoolers who live in similar geographical regions (Texas), are interested in chemistry, and are learning at a grade level typical for their age. Thus, this cohort number is relatively large for this regional study

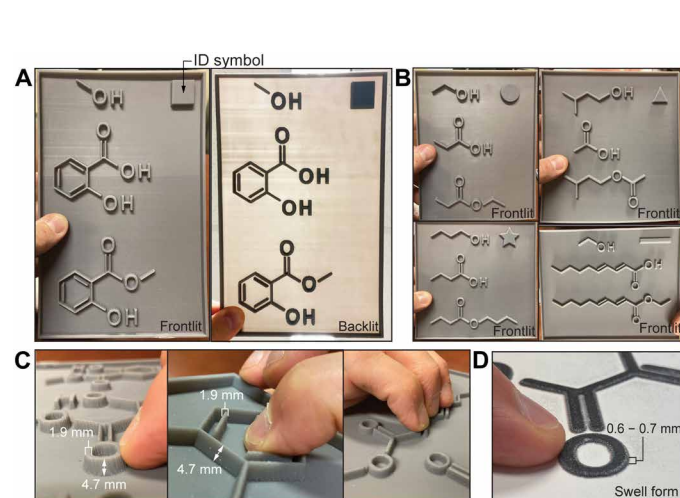
of secondary students with blindness. Students participated in a 3-day program, referred to as “In Your Element” by TSBVI staff. This 3-day program consisted of 1 day of “pre-laboratory” lectures at TSBVI (using pre-laboratory teaching materials shown in fig. S1) and 2 days of research experience inside research and core laboratories at Baylor University.

The cohort of students with blindness included four males and four females. Two of the students were residential students at TSBVI, while six others came from throughout the state of Texas for this short-term program at TSBVI (and were not educated at TSBVI during the regular school year). Each student had severe visual impairment requiring navigational assistance by a person, with all but one student using a white cane. The racial and ethnic background of students was 50% Hispanic and/or Latino, 25% Asian, and 25% white. Students were 9th to 11th graders: 50% freshmen, 25% sophomores, and 25% juniors. A total of 432 data points were collected from this cohort of students. Each of the eight students was asked 40 quantitative and qualitative questions regarding tactile graphics and 14 questions regarding interest, confidence, and sense of belonging in chemistry.

To begin, bond-line structures (35) of organic molecules were made universally accessible by 3D printing lithophane forms (6) of relevant structures and reactions. Five different lithophanes were printed depicting five different Fischer-Spier esterification reactions from alcohols and carboxylic acids (Fig. 4, A and B). Since these reactions were to be carried out with blind students, esters were chosen on the basis of their pleasant aroma. These consisted of isoamyl acetate (banana scent), ethyl decadienoate (pear scent), butyl butanoate (pineapple scent), ethyl propanoate (butterscotch scent), and methyl salicylate (wintergreen scent) (Figs. 4 and 5). The identity of each reaction was indicated with a unique tactile code in the upper right-hand corner; however, quick-response (QR) codes can also be printed into lithophanes (6).



**Fig. 3. Limitations of swell form graphics in portraying imagery from high-resolution electron microscopy compared to lithophane graphics.** (A) Lithophane (top) and swell form (bottom) graphics of a single butterfly scale micrograph captured with an SEM. Certain areas of chitin fibrils failed to swell. Further, the decrease in resolution of the swell form is apparent. While the lithophane depicts details in the chitin fibrils of the scale, the swell form paper melts it together, rendering it unresolvable. (B) Lithophane (top) and swell form (bottom) graphics of a plant cell capture with a TEM. The swell form paper shows a complete failure to swell, except for small spots of the chloroplast. The lithophane, in contrast, provides a high-resolution tactile and visual readout of all parts of the master image. (C) Paper (left), swell form paper (middle), and lithophane (right) graphics of a butterfly model. Upon thermal swelling, resolution was lost and the ink “popcorned” in the swell form image. (D) Swell form (left) and lithophane (right) graphics of a micrograph of chitin scales of a butterfly. After thermal swelling, chitin scales failed to swell completely.

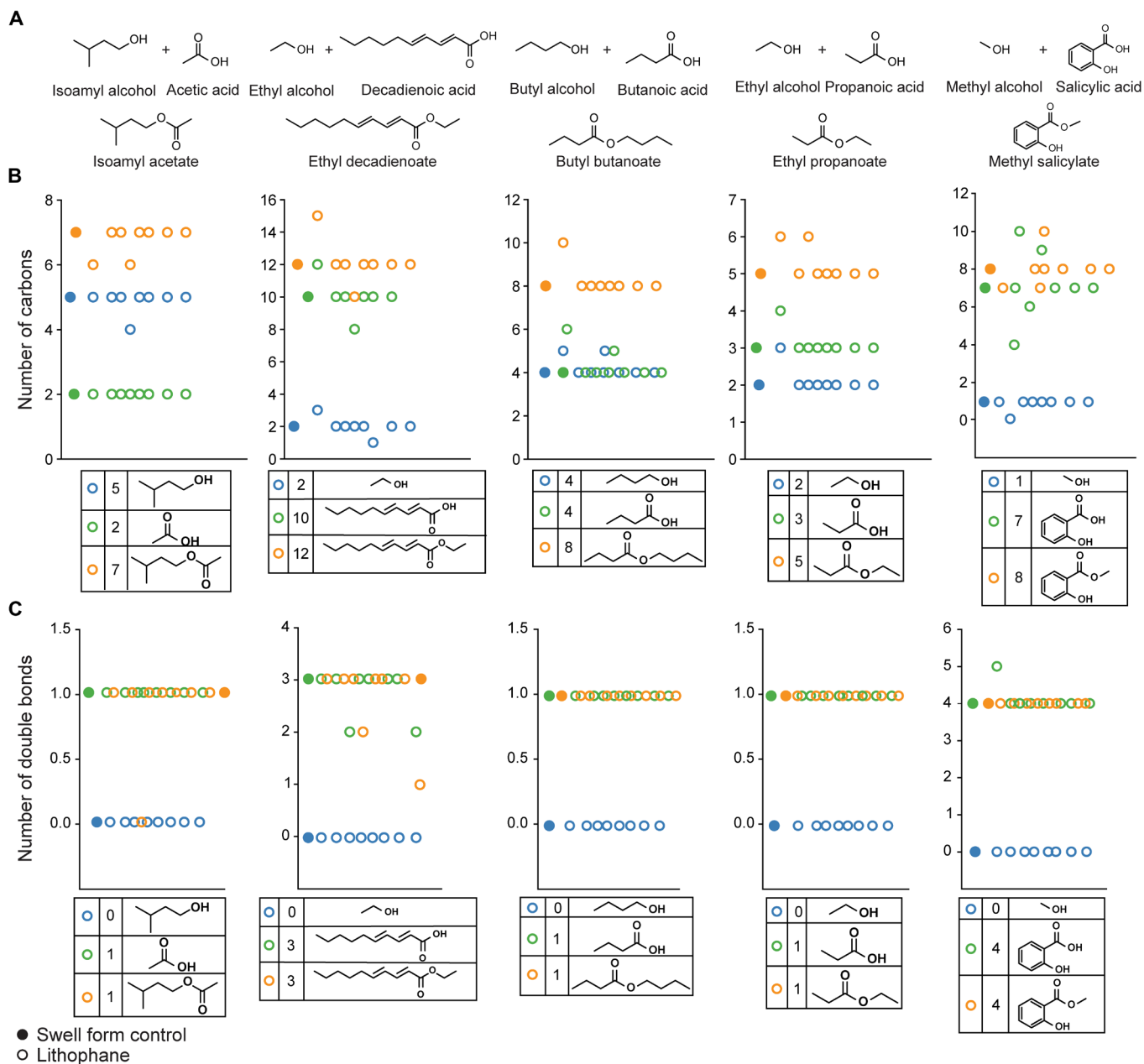


**Fig. 4. Lithophane graphics of five Fischer-Spier reactions between alcohol and carboxylic acid reagents and their ester products.** (A) Lithophane showing frontlit (left) and backlit (right) esterification of methanol and salicylic acid. (B) Frontlit lithophanes of reactions for ethyl propanoate (top-left), isoamyl acetate (top-right), butyl butanoate (bottom-left), and ethyl decadienoate (bottom-right). (C) Tactile dimensions of lithophane graphics. (D) In contrast, swell form graphics of the same image present with shallow maximal protuberance (i.e., 0.6 to 0.7 mm off the surface of the paper).

After trial and error of printing different sizes of lithophanes, a final size was used with physical dimensions of 13.3 to 14.4 cm in width and 13.6 to 21.0 cm in length. The tactile protuberances were 4.7 mm high and 1.9 mm wide (Fig. 4C). These dimensions were chosen after incorporating feedback from an undergraduate student of chemistry with total blindness. Lithophanes permit universal sharing of information so long as the shapes of alphabet letters are known. This universal format is contrary to Braille-based graphics or video-based graphics/video screens, where information cannot be shared easily between sighted and blind persons (24, 29, 36). These lithophanes do

have greater resolution and an unlimited range of protuberance compared to swell form graphics, which only project ~0.7 mm off surface (Fig. 4D). While both are useful for large chemical structures, the polymeric lithophanes are more durable and explicit than swell form graphics. Several blind users in this study reported—without solicitation, prompting, or inquiry—that they enjoyed the explicit, crisp feel of lithophane graphics compared to soft, dull swell form graphics.

High school students with blindness were able to accurately interpret lithophanes of esterification reactions despite little or no prior training in chemistry or experience with lithophanes (Fig. 5). Here,



**Fig. 5. Visualization of bond-line structures from lithophanes in Fig. 4 by high school students with blindness or low vision.** (A) Fischer-Spier esterification products and reactants for each ester synthesized. (B) Student answers to counting queries for the number of carbons and (C) the number of double bonds in each molecule. Closed circle denotes control data, carried out by an undergraduate chemistry student with blindness using swell form images of each lithophane in Fig. 4.

students with blindness were asked to use manual tactile senses to interpret the five different lithophanes. Students were then asked six questions related to each lithophane (30 questions total). They were asked to count the number of carbons in each of the 15 molecules, followed by how many double bonds were in each molecule. The average accuracy for all students and all questions was 86% (table S1). The main point that was demonstrated to these students is that small changes in the number or arrangement of carbon atoms in a molecule can lead to profound changes in its properties, such as its smell.

As a control, identical graphics were produced using conventional swell form printing. The control cohort (that used conventional swell form tactile graphics, and later, 3D micro-models of allosteric proteins) consisted of an undergraduate student with blindness (who had completed two semesters of organic chemistry) and three PhD-level chemists with blindness. A “two-by-two” analysis was not used to test these swell form graphics on TSBVI high schoolers with blindness, where half the students analyze lithophane graphics of one structure, and then analyze swell form graphics of the same structure (while the other half performs the same test in reverse order). These practices follow a planned core design feature of this outreach activity, which was to minimize testing and assessment on high school students with blindness from TSBVI. Such a two-by-two design could yield trans-graphic priming effects, wherein one graphic type is interpreted with the assistance of prior knowledge from sensing the other graphic type. Different molecules were not used to test each graphic type (which could mitigate trans-graphic effects) as the study design was to focus on the 15 molecules being used in laboratory (without including 15 additional carboxylic acids, alcohols, and esters, and 30 additional questions). Both these minimizations of testing on TSBVI students were considered ideal to (i) ethically minimize testing on this vulnerable group (37) and (ii) prevent boredom and low engagement related to excessive testing (38–40).

The accurate interpretation of organic structures by blind high school students is noteworthy because six students had never taken a full chemistry course in high school (one had taken a course in basic chemistry, and another was enrolled in chemistry for less than 2 months at the time of testing). Likewise, six of the eight students reported having “some knowledge” of chemistry, with two stating that they had no knowledge. The goal of this activity was not to test the ability of a student to learn a chemical structure and recall it, but rather to test their ability to examine or interpret (in real time) a tactile structure in the same way a sighted student would examine the structure printed or written on a piece of paper, or displayed on a computer screen. Therefore, each student was given a 10-min “crash course” on bond-line structures 1 day before testing. This primer course did not use lithophanes but used tactile graphics made with conventional swell form paper (fig. S1) (23). These graphics illustrated an atom with protons, electrons, and neutrons; the basic logic of bond-line structures; and a visual explanation of how light interacts with a surface (fig. S1).

Second, imagery of electron microscopy was also made universally accessible via lithophane. Making electron microscopy accessible to children is centrally important because imagery can be an initial source of interest in science for young people. Showing students with blindness that they can visualize the micro- and nanoscale world, as well as students with eyesight, might increase interest, confidence, and sense of belonging (and mitigate bias from peers and instructors).

Tactile diagrams of different electron microscopes were also created to show the students the position and path of the electron beam.

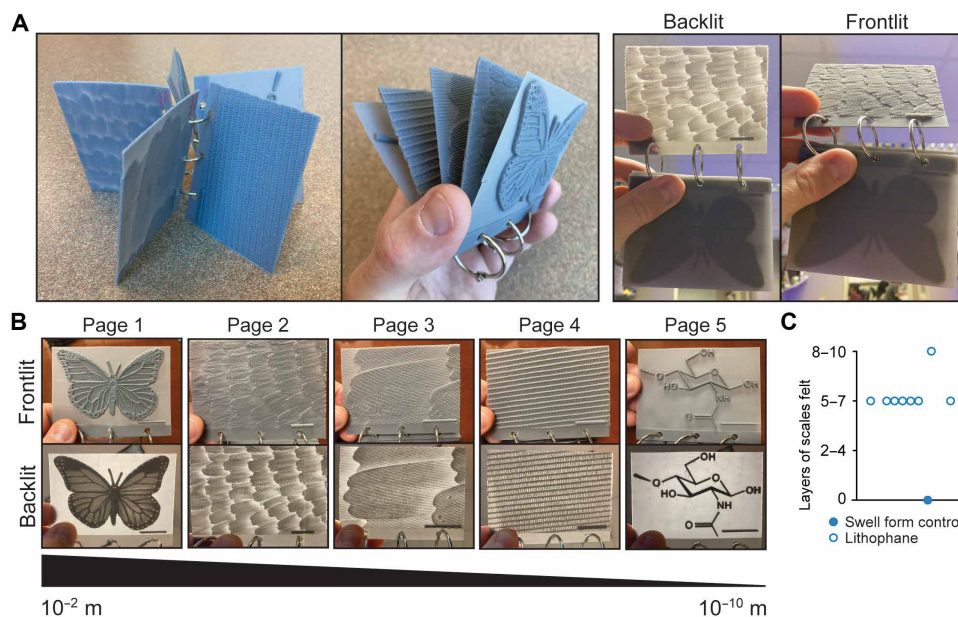
This lithophane diagram depicted the same microscope that students were able to observe and examine by touch. The tactile diagrams included both a scanning electron microscope (SEM) and a transmission electron microscope (TEM), the latter of which was produced in lithophane format. The lithophane diagrams were anywhere from 8.0 to 8.4 cm in width and 12.6 to 15 cm in length, with tactile protrusions up to 2.1 mm (fig. S2). These lithophanes illustrate (in a universal format) the path and focusing of electron beams for detection in SEMs and TEMs. As these graphics were Braille-free, the orientation of the lithophane and type of microscope were indicated with a tactile shape in the upper right-hand corner (fig. S2).

After students were taught about the inner workings of SEM and TEM, they were given lithophane forms of electron micrographs of butterfly wings to determine how effectively they could visualize and interpret these micrographs (Fig. 6). These electron micrographs were presented to students as a lithophane codex (Fig. 6A). The codex displayed three different micrographs with progressively higher magnifications of chitin wings, with scale bars from 100 to 10  $\mu\text{m}$  (Fig. 6B). A tactile image of a full butterfly (Fig. 6B, page 1) and a tactile bond-line structure of a single *N*-acetylglucosamine monomer that comprises chitin were included (Fig. 6B, page 5). Each page of the five-page lithophane codex (Fig. 6A) was approximately 100 mm in length and 74.5 mm in width, with tactile protrusions up to 1.8 mm. The spatial scale of the tactile features ( $\sim 0.5$  to 2 mm, at 100- $\mu\text{m}$  resolution) is on the same order of magnitude of tactile acuity of the fingertips ( $\sim 0.9$  mm) (41–43) and the resolution of the human eye (i.e.,  $\sim 1$  arc min) at typical reading distances (44).

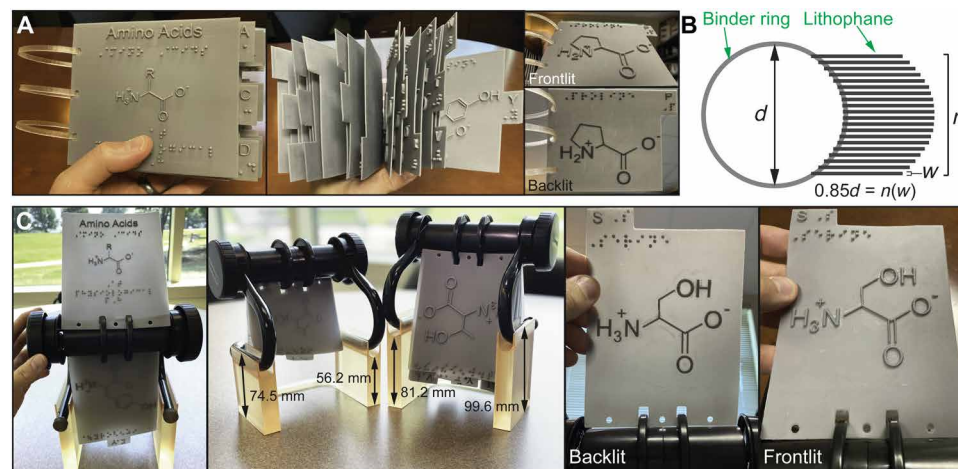
High school students were asked how many layers of chitin scales they could visualize by tactile sensing on page 2 of the lithophane codex (Fig. 6C). It is essential to point out that this book was given to the students with no information other than it contained progressively magnified images of a butterfly from insect to chitin monomer. Thus, students were required to use the booklet to tactilely discern the appearance of a single scale from a layer of scales, from a parallel array of chitin fibrils, as they had never visualized or learned about the shape of chitin scales or fibrils. The tactile page with a single scale (shown in Fig. 6B) was used by students to visualize and calibrate the size of a single scale, from which they were able to estimate the number of feathered layers on the subsequent page. The possible answers provided were (i) 2 to 4 layers, (ii) 5 to 7 layers, or (iii) 8 to 10 layers. Despite never visualizing any type of microscopic image before, seven of the eight students answered this question correctly (88% accuracy; Fig. 6C). In addition, the students were able to visualize and interpret details of the microscope diagrams (fig. S2, A and B). When asked whether electrons were reflected (i) or transmitted (ii) in one diagram or the other, the students responded with 100% accuracy (fig. S2C).

As a benchmark control, the same micrograph of layers of chitin scales was printed using conventional swell form paper (Fig. 3D). The scales failed to swell or protrude. An internal evaluation of this uninterpretable graphic was performed with an undergraduate chemistry student who is completely blind (Fig. 6C). When asked how many layers they could feel on the swell form paper, they responded: “Zero layers. I don’t know what’s going on here actually.”

As a proof of concept of the scalability of the lithophane codex, a prototype lithophane codex was printed with large numbers of pages (Fig. 7A). Here, a 22-page lithophane codex demonstrating all 21 amino acids was made to show how compact reference guides can be



**Fig. 6. Lithophane codex depicting chitin in butterflies: From chitin monomer to complete insect.** (A) The lithophane booklet [pages shown in (B)] bound with binder rings, containing scanning electron micrographs of butterfly wings in lithophane format. (B) Page 1: frontlit (top) and backlit (bottom) lithophane of a butterfly; scale bar, 2 cm. Page 2: frontlit (top) and backlit (middle) lithophane of scales of a butterfly wing; scale bar, 100  $\mu$ m. Page 3: frontlit (top) and backlit (bottom) lithophane of a single scale of a butterfly wing; scale bar, 40  $\mu$ m. Page 4: frontlit (top) and backlit (bottom) lithophane of chitin fibrils; scale bar, 10  $\mu$ m. Page 5: frontlit (top) and backlit (bottom) lithophane of a chitin monomer; scale bar, 2  $\text{\AA}$ . (C) Number of layers of chitin scales from page 2 detected by high schoolers with blindness or low vision. Closed circle denotes control carried out by an undergraduate chemistry student with blindness using swell form images.



**Fig. 7. A universal lithophane codex and Rolodex depicting amino acid structures at physiological pH.** (A) A codex of lithophanes depicting structures and names of all essential amino acids with  $pK_a$  (where  $K_a$  is the acid dissociation constant) values and physiological protonation states. (B) The maximum number ( $n$ ) of lithophanes in a codex can be expressed as  $0.85d = n(w)$ , where  $d$  is the diameter of binder and  $w$  is the lithophane width. (C) A rotary file (i.e., "Rolodex") of lithophanes depicting chemical structures of amino acids. Custom legs were added to this commercially available Rolodex to accommodate larger lithophanes. These codices are intended not only to make print or digital data accessible but also to organize data that are presented in sequence such as during a research presentation or lecture.

made and handled. Each page is small (128 mm  $\times$  115 mm  $\times$  3.0 mm), with chemical notation similar in magnitude to the ester lithophanes.

The theoretical limit to the number ( $n$ ) of lithophane plates that can be bound in a lithophane codex can be expressed with the following equation:  $0.85d = n(w)$ , where  $d$  is the diameter of the ring binder and  $w$  is the maximum width of each plate (Fig. 7B). This equation

predicts that  $\sim 42$  pages can be fit in a codex with binder loops of 10 cm diameter (assuming that the thickness of each plate is 2 mm). Such a lithophane codex could display  $\sim 170$  lithophane images if each plate displayed 4 images (i.e., four quadrants of a page with dimensions of 8 inches  $\times$  11 inches). This image capacity far exceeds the requirements of a conventional research seminar. Multiple codices

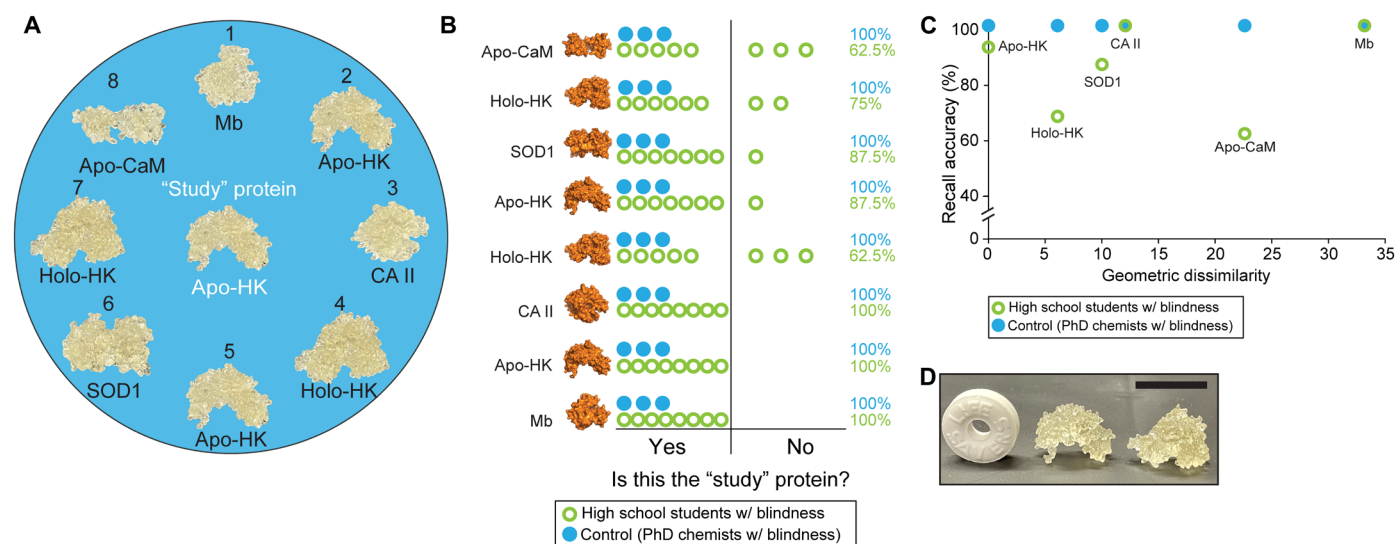
would be needed to display all graphical images in a chemistry or biochemistry textbook. For example, a 42-page codex with an 8 × 11 inch layout (203.2 mm × 279.4 mm) is capable of displaying all of the graphical imagery contained in the first six chapters of *Fundamentals of Biochemistry*, 5th Edition (Wiley) by Voet, Voet, and Pratt. Five of these codices would be needed to display all 912 numbered figures in the 28 chapters of this textbook.

A prototype rotary file was also created for lithophane storage using a commercially available Rolodex file (Fig. 7C). This rotary system can function as a stable reference guide (to be kept on a desk). Each page was 103 mm wide, 145 mm long, and 2.0 mm high. To increase the size of the lithophane prints that can be accommodated by a Rolodex rotary file, a platform riser was 3D-printed for the Rolodex (Fig. 7C). The lithophane codex and Rolodex provide a convenient means for organizing lithophanes in a portable manner that could be useful for studying or for following along and assessing critical data presented during a visual PowerPoint presentation. The Rolodex can be easily unloaded and reloaded.

The tactile Rolodex or codex prototypes are not as dynamic as a refreshable tactile display (45–49). However, the resolution of the lithophane images is higher than current tactile displays. Refreshable Braille or tactile displays hold great promise but currently produce imagery at low resolution compatible with Braille (i.e., approximately 10 to 15 DPI by our estimate). This low-resolution display is not useful for visualizing 2D scientific data and imagery or complex molecular structures. A lithophane or micro-model, in contrast, can project >1200 DPI when printed at 20- $\mu$ m resolution (and >200 DPI when printed at 100- $\mu$ m resolution). Tactile displays can also be expensive (>\$3000). The lithophane sheets used in this study cost \$1.50 to 5.00 per piece, are low in mass (5 to 70 g per sheet), and can be easily transported to (and function within) resource-limited settings.

A central paradigm of protein biochemistry is “structure equals function.” To illustrate shape and structure to students with blindness, different 3D structures of folded proteins were demonstrated with micro-models (millimeter-scale models 3D-printed at micrometer resolution). Here, three points were conveyed and illustrated: (i) the bulbous van der Waals surface features of protein structures, (ii) the geometric diversity of proteins, and (iii) protein allostery. Students were provided with 3D-printed micro-models of proteins from the PDB (Fig. 8). These atomically accurate renderings were made to be millimeter-scale to (i) improve portability (so that a student can have models of dozens of molecules in a backpack), (ii) enable use of the mouth as a tactile sensor for visualization (the mouth is ~2-fold more sensitive than fingers) (30, 50), and (iii) lower cost of production and transport. In this study, students used manual stereognosis to visualize protein structures. The development of these types of tiny “micro-models” was previously reported, but they were never provided to high school students with blindness to test utility and likeability (9).

To test how well high schoolers with blindness could discern one molecular shape from another, each student was given a single model of an allosteric globular protein, Apo-HK, denoted as the “study” protein. Students were informed about various structural details of the protein being modeled. Then, following a previous protocol reported by Baumer *et al.* (9), each person was given a series of eight protein structures consisting of two replicas of the study structure, two replicas of an alternate allosteric conformer of the study protein, and four completely different globular protein structures (Fig. 8A). Each time a student was given a new model, they were asked: “Is this protein the same protein as the protein you were first given?” Students no longer had access to the original study protein but were required to remember its shape from tactile sensing (9). This test was also carried out on three blind PhD chemists, who are listed as coauthors on this paper but did not contribute to the fabrication of these models or the test



**Fig. 8. Tactile recall of allosteric (shape-shifting) proteins by high schoolers and PhD chemists with blindness or low vision.** (A) Micro-models of atomic structures from the PDB. Eight micro-models provided to test manual tactile distinction from the central study protein (i.e., recall accuracy in identifying the study protein). The control cohort consisted of PhD chemists with blindness, examining the same model structures. (B) List of student response to the question: Is this protein the study protein? Recall accuracy is listed on the right for each protein query. (C) Recall accuracy for protein models and their geometric dissimilarity compared to the study protein. Closed circle denotes scores for PhD chemists with blindness (who scored 100% on each model regardless of its geometric dissimilarity). (D) Relative size of the micro-models; scale bar, 20 mm.

design; these PhD chemists with blindness served as mentors and teachers to the high school students from TSBVI.

Overall, both the high school students and PhD chemists with blindness did well in recall and recognition of the protein models (Fig. 8B). Students scored an average recall accuracy of 84%, and PhD chemists with blindness each scored a recall accuracy of 100% (Fig. 8B). The recall accuracy of protein structures, by all 11 blind participants (89%), was similar to the recall accuracy of blindfolded-sighted undergraduate biochemistry students in a previous study ( $n = 41$ ; 91.8%) and sighted college biochemistry students using computer graphics ( $n = 24$ ; 92.2%) (9). When determining the difference between distinct conformers of identical proteins (Apo-HK versus Holo-HK), the recall accuracy for all the blind participants was 77% (i.e., a 69% recall accuracy for the blind students and a 100% recall accuracy for the blind PhD chemists). The recall accuracy of HK conformers in this small cohort of high schoolers is similar to the recall accuracy of models in the larger cohort of blindfolded-sighted college students from a previous study (85.4%) and the recall of sighted college students using computer graphics (95.8%) (9).

The recall accuracy was also compared with the geometric dissimilarity between the study protein and the test protein (Fig. 8C). Here, geometric dissimilarity of each protein pair—the study and the test protein—was calculated previously (9). Larger numbers express greater differences in shape (i.e., dissimilarity). Students and PhD-level scientists with blindness were able to discriminate similar shapes more effectively than previous cohorts of sighted and blindfolded-sighted students using manual stereognosis and eyesight (9).

Although the micro-models that were prepared and given to students were space-filling models, it was also found that micro-models of cartoon diagrams of  $\alpha$ -helical and  $\beta$ -sheet proteins could be 3D-printed and were mechanically robust (Fig. 2, B and C). The model shown in Fig. 2 was printed from .STL files deposited in the 3D print repository of the National Institutes of Health (NIH). Note the high resolution and small size of the single  $\alpha$  helix (including side chains) and green fluorescent protein (with the fluorophore structure included) (Fig. 2, B and C). An eyelet was attached to each model for the attachment of a tether or lanyard (Fig. 2B).

Students were also given lithophanes of microscopic images of mammalian and plant cells. These cells included bovine pulmonary artery endothelial cells and a tobacco plant cell (*Nicotiana tabacum*) (Fig. 2A). Images were collected in the microscopy core facility using fluorescence and electron microscopes. Students were given a short lesson on the parts of the cell while exploring lithophane graphics depicting cell shapes and organelles. As many of the students had taken a biology course (or were enrolled in one), they had knowledge of the mitochondria and the nucleus but had never been able to visualize actual examples of these organelles. Students expressed enthusiasm and amazement at finally being able to visualize the appearance of cells and how difficult it can be to identify organelles. Identifying sub-cellular structures in these types of images is not self-evident but requires high-level training and years of experience (Fig. 2A).

### Visualization of 2D and 3D tactile graphics during manual stereognosis

It is well established that the tactile manipulation and somatosensory perception of objects can activate regions of the visual cortex in blind and sighted persons, according to regional cerebral blood flow imaging, blood oxygen level-dependent imaging using positron emission tomography (PET), and fMRI (51–55). Visual impairment results in

reorganization of the visual cortex, with early-blind persons exhibiting cross-modal recruitment of occipital areas during tactile sensing (55). Likewise, disruption of the visual cortex in sighted persons and those with early blindness [using focal transcranial magnetic stimulation (TMS)] also impairs the tactile discrimination of sighted and blind persons (56, 57). The brain activity of teenagers with blindness was not assessed in this study using fMRI, PET, or TMS. Whether these students are using their visual cortex to analyze, describe, and recall 2D and 3D tactile graphics cannot be known. It is important to remember that the molecular models are noncognitive structures. That is, they are not known shapes, symbols, letters, or numbers. The students with blindness had never perceived these structures before but were able to analyze, describe, and recall them via manual stereognosis.

### Evaluation of outreach experiences using mixed methods

It must be remembered that the primary focus of this research paper is outreach to a severely marginalized group in science, that is, the aim is to make different types of images and graphics that are accessible to high schoolers with blindness (which were previously unobtainable). An evaluation of the effectiveness of these outreach activities was performed. This assessment is also required by the Science Education Partnership Award (SEPA) program of the NIH that funded this outreach activity.

Mixed methods were used to assess how these outreach activities (tactile visualization, laboratory training, and organic synthesis) affected high schoolers with blindness. These methods involved focus groups, observations, and retrospective post-survey assessment to triangulate quantitative and qualitative data on student experiences and outcomes (58). Pre-survey analysis—using only post-survey assessment—was not used. This post-survey analysis was done to (i) ethically minimize data collection on this highly vulnerable population (37) (whom would ultimately answer 54 queries each), particularly given the short time period they would participate in the activities; (ii) prevent boredom, annoyance, or survey fatigue due to the data collection, which can negatively affect motivation and engagement (38–40); and (iii) mitigate threats to validity of assessment [e.g., priming effects of exposure to pre-survey items affecting responses on post-survey items (59–62) and ceiling effects on attitudinal items with highest scale of response selected on pre- and post-surveys (63–66)]. The full evaluation report, including methodology and all observational data, focus group data, and retrospective survey assessment, is included as a PDF report in the Supplementary Materials.

The retrospective post-survey was carried out at the end of the 3-day outreach experience (Fig. 9). According to the survey—the results of which are summarized in Fig. 9—all students expressed an increased sense of confidence in chemistry (100%), and most students reported an increased interest in chemistry (87%), learning science in college (75%), sense of belonging in chemistry (75%), and self-perception as a scientist (75%). A student's sense of self perception (seeing oneself as a scientist) and belonging in science, technology, engineering, and mathematics (STEM) can positively affect success (67–70). Interestingly, 87% of students reported that they learned how to visualize pictures with their hands. This high number does not necessarily suggest a low prior exposure to tactile graphics per se, but perhaps that students had never experienced tactile graphics at high resolution ( $<100 \mu\text{m}$ ).



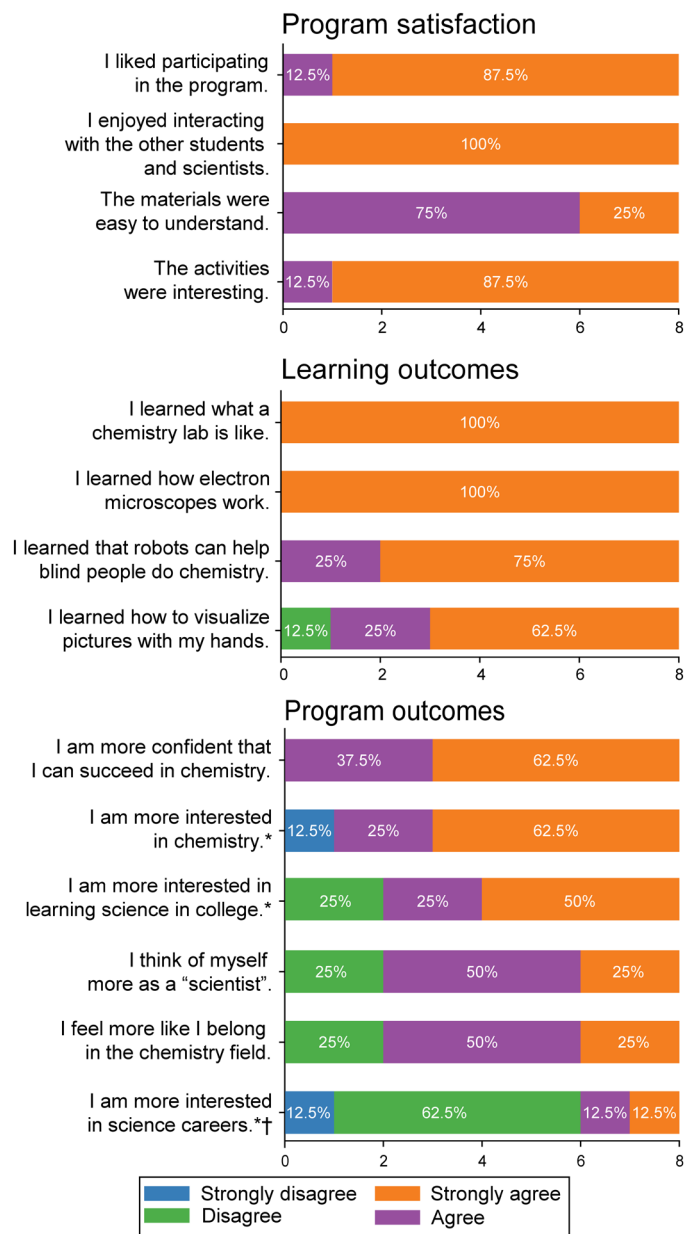
Interviews with students during a focus group (after completion of the survey) helped explain some of the survey findings (see evaluation report in the Supplementary Materials), including possible ceiling effects regarding the level of increased interest after participating in the outreach activities. For example, it was found that some students did not express an increased interest in pursuing a science career as a result of the outreach experience because they already had a very high level of interest in pursuing a science career, and it was impossible to have more interest. This type of ceiling effect has been reported in out-of-school STEM programs (65).

The greater interest (and confidence) expressed by students might be due to their positive opinions about the curriculum. All students reported finding the tactile materials easy to understand (100%), and all students expressed becoming knowledgeable of chemistry laboratories (100%; Fig. 9). Students stated, “I’ve always liked chemistry, but I’ve never really had the chance to really get into it [until this program]” and “I’ve always wanted to [have] a science career ... this course has helped me feel like it’s slightly more possible, like there’s possibilities.” Social effects might have contributed to the increase in interest. Previous reports have shown that social quorums can increase interest in STEM and that a person’s interest in STEM can be “infectious” to peers (71). Students with blindness expressed that they strongly enjoyed interactions with each other and with PhD scientists with blindness (100%; Fig. 9), even exclaiming that “[It was] nice that we had [mentors] who were blind like us who we could relate to.”

### Chemistry and inclusion science

A top priority in inclusion science is to make the graphical imagery and information of science accessible to all students at the earliest age. Showing off the imagery produced by science—a galaxy from the Webb telescope or a plant cell from an electron microscope—is important for sparking interest, regardless of whether the individual understands all the technical details of how the image was captured. In particular, the nanoscale and microscale imagery achievable with electron microscopy represents a convenient opportunity to spark interest in multiple areas of science, at almost any age (72). Visual images are important in STEM learning and content knowledge, wherein levels of scientific literacy (i.e., the ability to communicate scientific ideas) are linked to visual literacy (i.e., the ability to understand, create, and use images) (73–77). Students with blindness can now use lithophanes and micro-models to experience high-resolution imagery. This type of 3D printing can make data and imagery more accessible than ever before. However, the experimental science laboratory still remains stubbornly inaccessible, especially chemical and biochemical research laboratories.

The customized, technical (and sometimes dangerous) nature of a chemistry research laboratory suggests that chemists might be—in some cases—the most qualified people for increasing accessibility in their field (in consultation with experts in special education, safety, occupational therapy, and accessibility). Chemists are already excellent tool makers who build (or repurpose) devices to detect things that cannot be seen or directly visualized with eyesight. They are creative pedagogists who use models, pictures, and diagrams to analyze and illustrate systems that cannot be seen with eyesight. Chemistry has been always recognized for its central role in modern science (78). It has the potential to play a central role in inclusion science too.



**Fig. 9. Attitudes of high schoolers with blindness toward chemistry after a 3-day program on learning tactile visualization and laboratory tools.** \*During the focus group, some students mentioned that their interest in chemistry, in learning science in college, or in pursuing a science career could not increase as they already had a very high interest in chemistry, in learning science, or in having a career in science before attending the program. †During the focus group, some students expressed that they did not have an increase in interest for having a science career since they were already maximally interested in having a science career (“ceiling” effect), already knew of a different career path they wanted to follow (and then stated that this program still made them more interested in chemistry), or felt like it was too soon to know what careers they would be interested in pursuing.

## MATERIALS AND METHODS

Additional materials and methods can be found in the Supplementary Materials. This study involved human subjects and received approval from an Institutional Review Board at Baylor University. Informed consent was obtained for all subjects before enrollment and data collection. The cohort was composed of four males and four females enrolled in high schools throughout Texas. Students were in 9th to 11th grade: 50% freshmen, 25% sophomores, and 25% juniors. Two students were residential students at TSBVI, and six came from throughout the state of Texas (i.e., were not educated at TSBVI during the regular school year). Seven of the eight students used white canes. The ethnic and racial background of students was 25% Asian, 25% white, and 50% Hispanic and/or Latino.

### Design of lithophanes depicting Fischer-Speier esterification

Bond-line structures corresponding to reactants and products of the five esterification reactions were initially drawn in ChemDraw and then exported to Adobe Illustrator. The two reactants and one product for each of the five reactions were included into a single image file for production into a single lithophane. The layout for each lithophane involved placing the alcohol molecule at the top, the carboxylic acid in the middle, and the ester product at the bottom. This layout and orientation (to be orally described to students with blindness) was denoted by including a shape in one corner of the image (to designate “upper right-hand” corner). These symbols were added in Adobe Illustrator and were a triangle for isoamyl acetate (banana), rectangle for ethyl decadienoate (pear), circle for ethyl propanoate (butterscotch), five-point star for butyl butanoate (pineapple), and square for methyl salicylate (wintergreen). Each master image was exported as a .PNG for conversion into lithophane format (.STL).

### Design of lithophanes of scanning electron micrographs of insect biomaterials

Lithophane images of chitin polymers at various magnifications were made as follows: scanning electron micrographs of butterfly wings (Gulf fritillary, *Argaulis* sp.) were collected as previously described using a Versa 3D FIB-SEM (FEI, OR, USA) (79). A scale bar was added to the bottom right-hand corner of each to indicate the relative size of each image. The fabrication of a chitin polymer was made in ChemDraw; a scale bar was added to the bottom right-hand corner in Adobe Illustrator based on measurements taken in PyMOL. The lithophane image of the whole insect was made by collecting a digital image of an anatomic replica of a butterfly; a scale bar was added to the bottom right-hand corner based off the average size of the butterfly. Each image was converted into .PNG format before conversion to .STL format. The lithophanes resulting from these images were eventually bound into a tactile picture book (described below).

### 3D printing lithophane graphics

Each .PNG file of the image to be transformed into a lithophane was converted into a .STL using free software (available online at 3dp.rocks/lithophane). This software is designed to generate lithophanes from 2D images. The .STL files were uploaded to either PreForm software or Ultimaker Cura software. An example of a lithophane fabricated in this method using PreForm software is depicted in fig. S3. Lithophanes were made using two different types of small commercially available 3D printers: an Ultimaker S3 printer from Dynamism or a Form 3B+ printer from Formlabs.

For the models constructed from the Form 3B+ printer, 3D prints were fabricated in the same method as previously described by Koone *et al.* (6). All models were made using the Form 3B+ printer; however, for the SEM diagram, an Ultimaker S3 was used. For the construction of tactile graphics by the Ultimaker S3, polylactic acid filament was used, and the adhesive was removed.

### The lithophane picture book

A tactile “flip book” depicting electron micrographs of insect chitin scales at different levels of magnification was created from the lithophane pages whose creation is described above. This book also included an image of the whole insect and a bond-line structure of a monomer of chitin (*N*-acetylglucosamine). Each image that was used to make the lithophane butterfly booklet was processed in a free online 3D digital design maker (Tinkercad) to add a physical pane surrounding the lithophane (as a mechanical reinforcement to prevent breaking). Each reinforcement consisted of a rectangular pane of 1 mm in height, 10 mm in width, and 100 mm in length. Three holes (5 mm in diameter) were added to each page to allow three-ring binding. The pages were bound together by three 25.4-mm binder rings to allow page turning without one page crushing other pages and to allow for the lithophane effect to be viewed page-by-page (for people with eyesight or low vision).

### The lithophane amino acid codex and Rolodex

Amino acid structures were drawn in ChemDraw before they were exported to Adobe Illustrator. Braille and text were added to each structure, and then the image was exported as a .PNG. Images were converted into a .STL as described above before being processed in free online 3D design software (Tinkercad), where the tab for each page and holes (three for the book, approximately 5 mm in diameter; three holes, approximately 5 mm in diameter, plus two square slits, 8 mm at its widest and 14 mm at its longest, for the Rolodex) were added before printing. The binder rings (74 mm diameter and 1.5 mm thick) and risers (56.2 to 81.2 mm high and 137 mm wide) were constructed in Onshape and printed using surgical guide resin. The caps added to the Rolodex, upon being cut, were constructed in Tinkercad and then printed using an Ultimaker S3 with acrylonitrile butadiene styrene filament.

### 3D printing of micro-models of folded proteins

The fabrication of the protein micro-models was conducted as previously described, using atomic x-ray coordinates deposited in the PDB (9). The PDB codes of the atomic coordinates used were 1V4T (apo-HK; apo-hexokinase), 3RGK (Mb, myoglobin), 5A6H (CAII, carbonic anhydrase II), 3IDH (holo-HK, holo-hexokinase), 2C9V (SOD1, superoxide dismutase-1), and 1CFD (apo-CaM, apo-calmodulin).

### Fabrication of conventional tactile graphics using thermoform printing

Conventional tactile graphics from swell form or thermoform paper were prepared to teach students about basic chemistry concepts before introduction of lithophanes and micro-models. The graphics were printed using a laser printer (Hewlett Packard Color LaserJet Enterprise M653) at default settings onto swell form paper (Zytex2 Swell Paper). Pages were then fed through a swell form machine (ZY-Fuse) on a heat setting of 7 to 9 to produce the conventional tactile graphics. Images were made in ChemDraw, Adobe Illustrator, or GoodNotes. Swell form graphical renderings of each lithophane were

also made, to be used as a control, to compare the resolution and relief of swell form versus lithophane graphics. Here, we did not alter the contrast or brightness of the image to optimize results but used the same images used to create lithophanes.

### Fischer-Speier synthesis of esters with high school students with blindness

Five different esters were synthesized by graduate students in a fume hood. High school students with blindness were standing next to these graduate students at the fume hood, examining the structures of alcohols, carboxylic acids, and resulting esters (via tactile sensing) during the synthesis. Products and reagents in each reaction were isoamyl acetate (banana scent), isoamyl alcohol, acetic acid; ethyl decadienoate (pear scent), ethanol, decadienoic acid; butyl butanoate (pineapple scent), 1-butanol, butanoic acid; ethyl propanoate (butter-scotch scent), ethanol, propanoic acid; methyl salicylate (wintergreen scent), methanol, salicylic acid. Each alcohol and carboxylic acid were combined in a 1:1 molar ratio in a test tube and mixed. Two drops of concentrated sulfuric acid were added to the tube and placed in a hot water bath with simmering water. This reaction proceeded for 10 min before a drop of the solution was pipetted onto a Kimwipe for the students to smell and identify. Before synthesis, the high school students were provided candy pertaining to these scents (banana, pear, and pineapple jellybeans, butterscotch hard candies, and wintergreen LifeSavers) to smell or eat (in a food-safe environment outside of the laboratory).

### Logistical details and schedule of outreach activities

A full description and schedule of all activities carried out during the 3-day outreach program can be found in the Supplementary Materials. The first day of the program occurred at the TSBVI, with the second and third days occurring at Baylor University.

Briefly, students from the TSBVI traveled by bus from TSBVI (Austin) to Baylor University (Waco) for each day of the consecutive 2-day laboratory experience. Informed consent was obtained for all students, including from parents/legal guardians of minor subjects, before enrollment and data collection. One day before the arrival of TSBVI students at Baylor University, a seven-member team of professors, graduate students, and postdoctoral fellows from Waco (Baylor) visited TSBVI to provide students with a half-day introductory lesson on some basic concepts in chemistry, including bonding, nuclear structure, organic shorthand, and carbohydrate structures. This lesson involved conventional tactile materials such as molecular models and swell form graphics shown in fig. S1. Throughout the entire program, three PhD-level chemists with blindness were present to provide insight into being a chemist with blindness, to offer career and educational advice, and to provide technical explanations of scientific materials and concepts being discussed throughout the program.

All eight of the students were white cane users, except for one student. During their 2-day immersion in wet laboratories at Baylor University, the students were equipped with laboratory coats, safety goggles, and gloves to ensure proper laboratory safety measures. Voice recorded talking buttons were used to label various laboratory instruments and tools with the recording “this is the [insert name of object],” e.g., for the 3D printing area of laboratory, there were three buttons, which were for the printers themselves, the wash station, and the curing station. This allowed the students to identify laboratory equipment independently. The students were broken into two groups of four to tour two different laboratory spaces (after which the tour

switched). The first group learned about a chemical robotic device (capable of weighting solids, dispensing them into reaction vessels, delivering solvent, mixing, stirring, and purifying reaction products) and 3D printers. The second group learned how to use analytical micro-pipettes and pipetted water from one beaker into another. The groups then switched spaces, allowing students to have the same experience.

During the experience in organic synthesis, all TSBVI students remained in the same groups, with each group of four surrounding an organic chemistry graduate student synthesizing esters at the fume hood. The graduate student conducted each of the five reactions in succession. During each synthesis, the students were given the lithophanes of each ester being synthesized to simultaneously feel the structure of the lithophane while also being able to smell the aroma of the ester after it was synthesized (a process that required ~10 min for each ester).

During the tour of the microscopy core facility, TSBVI students were able to feel three different types of microscopes: a light microscope, an SEM, and a TEM. Students were able to feel both the inner and outer components of the SEM and the outer portion of the light microscope and TEM. Because of the height and placement of the TEM, a stepladder was used to ensure that the students were able to feel even the top of the microscope. Lithophane diagrams of electron microscopes were given to students (who were later quizzed on details of their layout).

At the beginning of the 3-day outreach experience, students received boxes containing the lithophanes graphics. At the end of the 3-day outreach experience, students also received laboratory kits (to keep and take home) that contained a molecular model kit, a laboratory coat, and Bose audio sunglasses (with frame-integrated Bluetooth speakers) to double as safety goggles and an audio device for the student's screen reader.

### Technical quizzes of lithophane graphics and protein micro-models

Students were asked to use lithophanes to count the number of carbon atoms and double bonds in various molecules depicted on the five lithophanes. These assessments were carried out in the laboratory. Again, students were present at the fume hood (with goggles and a laboratory coat), holding lithophanes while the molecules depicted in the lithophanes were being reacted to produce the ester, i.e., students were tactilely examining the structure of esters while simultaneously being able to smell the ester. When carrying out assessments of ester lithophanes, students responded with their answer by holding up the number of fingers that corresponded to their answer. For binary “yes or no” responses, participants submitted answers via an extended hand (for “yes”) or closed fist (for “no”). The full list of specific questions that were asked of each student for each tactile material is included in the Supplementary Materials.

### Assessment of outreach activities using mixed methods

A full description of the assessment of the outreach activities can be found in the full assessment report, provided as PDF in the Supplementary Materials. The primary goal of the assessment of the outreach program was to determine efficacy at increasing (or maintaining high levels of) student interest, confidence, and sense of belonging in chemistry and science. A critical design element of the assessment (and technical assessment of graphics) was to minimize direct testing

and surveying of minors with blindness to minimize testing on vulnerable populations and to prevent fatigue and boredom.

Two external evaluators were continually present during the 3-day outreach activity to assess the outreach program using mixed methods of direct observation of students and mentors, a retrospective survey of students from TSBVI, a focus group of students from TSBVI, and a review of tactile materials. We chose to use a post-survey (retrospective assessment) to ethically minimize research on a vulnerable population (37) and to mitigate boredom, priming effects (59–62), and ceiling effects (63–66). A full description of evaluation methodology (and results of assessment) is included as a PDF report in the Supplementary Materials.

At the end of the 3-day research program, all eight TSBVI students with blindness/low vision participated in an orally administered survey. Here, one evaluator read the questions while the other evaluator recorded students' responses (see full evaluation report included in the Supplementary Materials for survey protocol). Students answered survey questions by holding up the number of fingers that corresponded with a response option (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = strongly agree). To provide demographic information (including grade level), students were asked to raise their hands if they identified with a response option. All eight students then participated in a focus group in which they were asked about their experiences in the research program, e.g., how the program affected their interest in chemistry, their confidence and ability to learn chemistry, and their sense of belonging in chemistry.

## Supplementary Materials

This PDF file includes:

Supplementary Materials and Methods

Quizzes

Figs. S1 to S3

Tables S1 to S3

Full description of outreach program and external assessment report

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