

The evolving portrait of a virus

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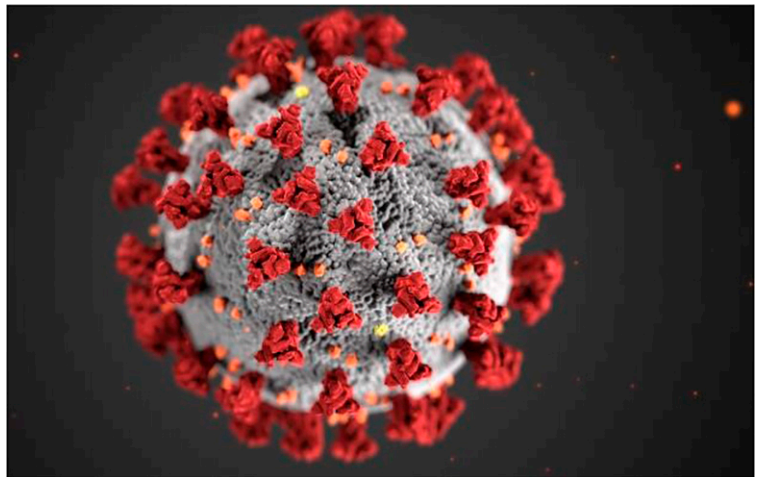
In late January 2020, as researchers began to gauge the public health threat posed by COVID-19, the Centers for Disease Control and Prevention (CDC) released an illustration of the virus. In that memorable three-dimensional depiction, the viral envelope appeared as a textured, almost carpeted, gray sphere. Spike proteins, which help the virus bind to and invade cells in a person's respiratory tract, emerged from the surface like a landscape of disquieting red shrubs. Other membrane proteins dotted the surface in yellow. The entire viral particle, or virion, floated before a charcoal gradient background as though it were sitting for a portrait (1). Just weeks after the release of the image, it had become the public face of a global menace.

Already, the image has become iconic, says Michael Rossi, an historian of medicine and science at the University of Chicago, IL. "We can see evidence of its iconicity in the most unexpected places," says Rossi. "I was hiking through these ruins with my daughters, and someone had graffitied the particle with the spikes and everything. It's instantly recognizable."

Rossi suspects no other microbiological image has ever become so popular or ubiquitous so fast; reports about the flu or flu shots, for example, only sporadically depict the virus (which bears a striking similarity to SARS-CoV-2). Other infamous viruses have fared much the same. "I don't think images of HIV got the same kind of traction," says David Jones, an historian of science at Harvard University in Cambridge, MA.

The CDC's portrait, however, became a visual touchstone for the public. It appeared not only in public health warnings but also media stories about all aspects of the pandemic. "That's what people associated with the virus," says Drew Berry, a biomedical animator at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. "And the science in it is very good, representing what we knew at the time."

Throughout 2020 and early 2021, artists and scientific illustrators continued to create new images, basing their works on increasingly sophisticated representations of emerging data. As microscopic and even molecular-level data emerged in the literature—about the virion's shape, or the geometry of its enclosed RNA, or the distribution of surface proteins—those illustrations evolved, too, offering updates on the state of research and the



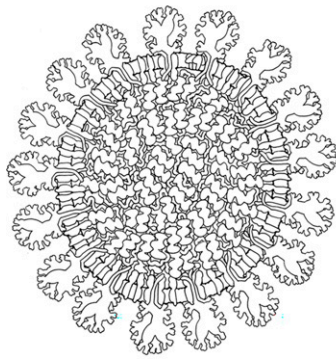
Over the course of a week—and based on knowledge about other coronaviruses—artists at the CDC produced this now-iconic image of the COVID-19 pathogen, the first to be widely distributed. It quickly became the face of the pandemic. Image credit: Centers for Disease Control and Prevention/Alissa Eckert, MSMI; Dan Higgins, MAMS.

mechanisms of transmission and infection—not to mention a way to communicate complicated information to a concerned public.

"These types of images are super-important," adds David Goodsell, a renowned illustrator and structural biologist who published his first watercolor of the virus in March 2020, just six days after the World Health Organization declared COVID-19 a pandemic. "This virus is not an abstract concept. It's something that is attacking you."

Virus Visuals Evolve

CDC illustrators Alissa Eckert and Dan Higgins have a long history of visualizing viruses. But on January 21, 2020, they received perhaps their most important assignment to date: Image the SARS-CoV-2. "We knew what needed to be done to complete it in such a short time," recalls Eckert. They spent about a week hammering out aesthetic details about the viral shell, the shape of proteins, and the color scheme. Their research was rigorous: Because no one had yet imaged the new pathogen up close, they consulted with researchers and learned that the new pathogen was closely related



Artist David Goodsell depicted the SARS-CoV-2 particle in various ways based on his aims, his audience, and the emerging data. Based on his initial interpretation of the virus particle, which had the spike proteins evenly distributed around the edge, Goodsell created a coloring book page (left), which became a vehicle for public outreach, as well as a colored illustration (center). A few months into the pandemic, Goodsell revisited his interpretation, depicting the particle as more oblong and the spike proteins as having less structure, while being spaced asymmetrically about the surface. Image credit: David Goodsell, licensed under [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/).

to the SARS coronavirus. “We borrowed everything that was available for the SARS virus,” Eckert says.

They pored over scans of other similar coronaviruses captured with cryogenic electron microscopy (cryo-EM). They downloaded data from GENBANK, the National Institute of Health’s collection of genetic sequences, and the online RCSB Protein Data Bank.

“We downloaded protein data and put them together like a puzzle piece,” Eckert says. With the molecular details in place, the artists chose textures, light patterns, and depth of field to give the image a three-dimensional, photographic look that would communicate the urgency of this emerging viral threat. The image would soon become ubiquitous.

Over the next few months, new data changed researchers’ understanding of the virus—and changed artists’ interpretations. “The pictures changed entirely over one year,” says Goodsell, at Scripps Research in La Jolla, CA.

During the first year of the pandemic, Goodsell found himself revisiting his own image of the virus multiple times, each one updating and improving on the one before, by drawing surface proteins with stalks that bend and structures that better matched emerging data, for example. He also created paintings that depict scenes in the infection process. As he tracked the deluge of information, he often found himself planning for the next iteration even before the paint had dried on his work-in-progress. “I follow the information as it comes out,” he says. “I always joke that the pictures become obsolete the second I finish them.”

Goodsell is known for his lush watercolor paintings that often depict the inner lives of cells and microbes—whether a near-psychedelic rendering of *Escherichia coli* in cross-section or a snapshot of autophagy, during which a cell digests its own broken parts. His work has graced the walls of science museums and covers of scientific journals. He was ready to bring the virus particle to life on canvas.

The first of Goodsell’s SARS-CoV-2 watercolors depicted the coronavirus embedded in respiratory

mucus (2). Within the round viral envelope, a tangle of genomic RNA and its associated proteins crowded together in shades of purple. Membrane proteins spiked outward from the envelope like magenta trees. Mucus proteins in the surrounding space took on the appearance of green, sinewy vines; immune cells became yellow, leaflike structures. It was a striking image seen mostly by researchers who followed Goodsell or Scripps news releases online. An updated version of it would later appear on the cover of *Nature* (3).

He also released a simpler image: A coloring-book style page showing only the black-and-white outline of the virion, or viral particle, from the first image—and inviting people to color as they saw fit. Goodsell specifically rendered it to reach a different, broader audience of people who like to color. Within days, he received feedback on social media and in his inbox. “Thanks! Kids and I were talking today about how it is NOT an invisible enemy, just requires the right tools to see,” tweeted a pediatric neurologist and mom in Chicago. The images helped a 6-year-old learn about viruses, wrote another parent who “sent him to school today with copies of this for his whole class.” Adults reported that coloring the image was “relaxing” and “meditative.”

“People were actively using the pictures to gain agency at a time when we were all scared,” Goodsell says. Many people reached out to him with stories about how the image jumpstarted conversations about this then-unknown menace.

Seeing the Science

Of course, images often have to be more than beautiful—they have to be scientifically accurate. Goodsell continued to monitor newly published studies that coupled imaging technologies with computational techniques. He would produce six distinct portraits of the coronavirus in the first year.

One of the first changes that Goodsell incorporated focused on the spike proteins. “Initially people drew these pictures with a whole bunch of very symmetrical spikes, giving it that beautiful and uniform

crown shape," he says. But cryo-EM scans revealed fewer spikes, scattered haphazardly on the surface (4). "And they're really wobbly. So they end up looking much more drunk."

He also started to see new analyses that focused on the interior. Inside the viral envelope, Goodsell says, illustrators initially drew RNA and proteins as a mess of twisty rope. "But it looks more like a bunch of blobby complexes, which I suppose is going to affect the way that it assembles when it enters the cell." For him, getting the picture right wasn't just a matter of accuracy; it also became a way to explain cellular processes.

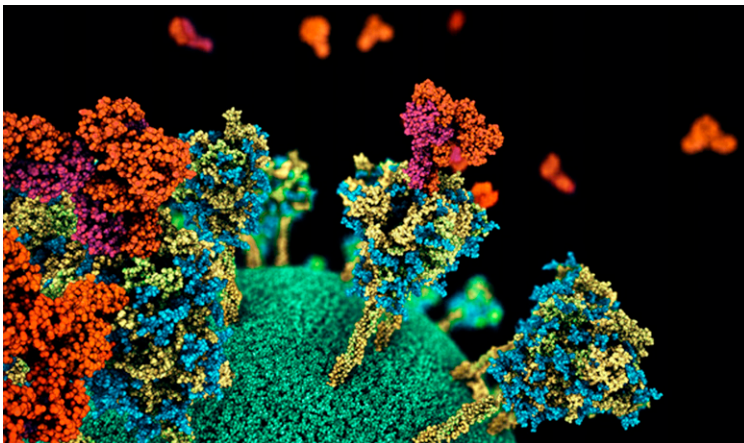
Over time, he expanded his gallery to include vivid scenes from the cycle of infection. In July, Goodsell published a piece called *Coronavirus Life Cycle*, which captures many moments in the replication of a coronavirus inside a cell. It reads like a story with pivotal moments, such as when viral RNA directs the production of spike proteins or when replicase complexes make new copies of the viral genome. "This is right in the middle of when it's replicating in a cell," he explains.

Researchers had found that the virus reorganized the endoplasmic reticulum of the host cell, but they had only a tenuous grasp of the cellular mechanisms that allowed the viral RNA to escape. So Goodsell offered his best guess and sketched the RNA inside these newly found membrane structures. Two months later, researchers found the secret to the process: It escaped through pores in the membrane. Goodsell plans an update (5).

Other artists likewise kept busy tracking the rapidly evolving virus visuals. In his lab in Melbourne, Berry specializes in designing dramatic, three-dimensional animations of the cellular world in motion. He has illustrated enzyme activities and the life cycle of the parasite that causes malaria; he has even projected giant virus visualizations on the sides of buildings. As Berry tracked the incoming science around COVID-19, he realized that he had the tools to show the virus in a new light—in three dimensions, and in motion. He and his colleagues had recently developed a new framework, built on the kinds of fast processors used for video games, to create high-resolution images of molecular detail.

Berry saw animations as a way to promote outreach efforts based on more accurate depictions of the SARS-CoV-2 cycle. "I wanted to create a dynamic, flexible virus with all the spikes and everything else being driven by dynamics," he says.

So in early 2021, Berry released a series of animations showing a jittery, squishy viral particle attacked by orange antibodies that approach it like a flock of butterflies. In those videos, the virus isn't firm; the spikes aren't menacing. The whole system looks nervous. Like Goodsell with his coloring book page, Berry began to hear from people who appreciated the depiction. "There were these delightful, little, small, fluttery little butterflies, and yet, they were attacking the virus," he says. "And I was really delighted by that aspect. It also made it more emotional."

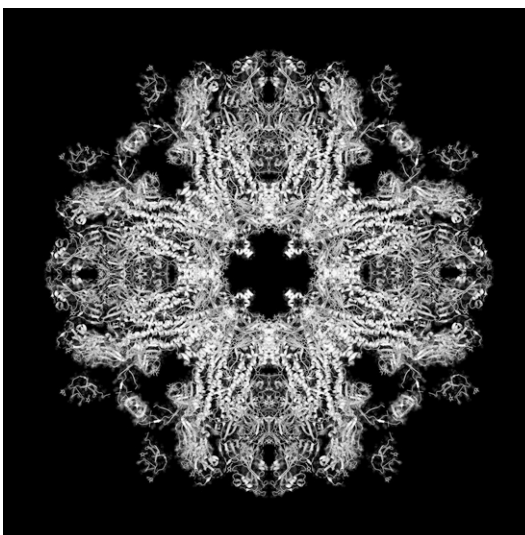


Animator and illustrator Drew Berry, in Australia, used high-resolution data to create precise three-dimensional animations depicting processes related to COVID-19 infection, including how antibodies (orange) attach to the spike proteins (blue and yellow). Image credit: Drew Berry (The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia).

Human Impact

These sorts of illustrations have helped enhance scientific literacy about viruses in recent months, says Laura Splan, a Brooklyn, NY-based artist who was inspired to create abstract representations of SARS-CoV-2. "Before the pandemic, this kind of work was still kind of niche; it only had a certain audience," she says. "I find myself having a lot less to explain about my work because of SARS-CoV-2." Splan sees the public's newfound ease with terms like "coronavirus" and "cell receptors" as an opportunity to "present a lot more information, and a new language, to people."

Goodsell notes the ability to image cells and molecules—and everything in between—has always been critical to advancing our understanding of biology;



Laura Splan's abstract, kaleidoscopic artworks in "Precarious Structures" are constructed with three-dimensional models of the SARS-CoV-2 spike protein. She combines molecular visualization software with digital imaging tools to create animations and prints. Image credit: ©2020 Laura Splan.

detailed visualizations can, for example, inform drug discovery efforts. And the same tools that fuel Goodsell's research as a computational biologist—many of which he's developed and shared with other researchers—can be used in education and outreach. He's now focusing on vaccine illustrations in an effort to address misconceptions among the public.

It's hard to predict how such images will shape the cultural history of the pandemic in the years ahead, says Rossi in Chicago. Before the availability of high-resolution microscope images, artists often depicted disease anthropomorphically, as an evil figure claiming human victims. In a 1912 illustration from *Le Petit Journal*, cholera becomes the grim reaper; a 16th century painting by Bruegel personifies the plague as a rank of murderous skeletons (6). For COVID-19, he says, the

menacing spiky ball has become synonymous with the disease. "It's nothing short of miraculous that we can visualize this thing that is literally not visible," he says, "that we can create images so faithful to the science."

But at the same time, Rossi and other historians note that this iconic image distances the virus from the deadly havoc it has wrought. "It signifies that science is on top of things," says Rossi, "but it has the disadvantage of not showing the human side."

Indeed, no matter how much scientific detail goes into an image of a viral particle, adds medical and biological historian Soraya de Chadrevian at the University of California, Los Angeles, those images still won't speak to the human experience. "Of course, it doesn't represent the epidemic in all its complexity," she says. "The epidemic is not the virus."

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- 1 Public Health Image Library (PHIL). <https://phil.cdc.gov/Details.aspx?pid=23311>. Accessed 1 February 2021.
 - 2 D. S. Goodsell, "Coronavirus." PDB-101. <https://pdb101.rcsb.org/sci-art/goodsell-gallery/coronavirus>. Accessed 15 February 2021.
 - 3 D. S. Goodsell, "SARS-CoV-2 and Neutralizing Antibodies." PDB-101. <https://pdb101.rcsb.org/sci-art/goodsell-gallery/sars-cov-2-and-neutralizing-antibodies>. Accessed 8 March 2021.
 - 4 D. Wrapp et al., Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science* **367**, 1260–1263 (2020).
 - 5 G. Wolff et al., A molecular pore spans the double membrane of the coronavirus replication organelle. *Science* **369**, 1395–1398 (2020).
 - 6 M. Rossi, "Visualising viruses." *London Review of Books Blog* (2020). <https://www.lrb.co.uk/blog/2020/april/visualising-viruses>. Accessed 28 May 2021.