UNIT 12: ORGANIC CHEMISTRY

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ANESTHESIA

Chemistry in the Operating Room

By Claudia M. Caruana

Until the mid-1800s, undergoing surgery was excruciatingly painful because people would be awake during the operation. Thanks to drugs called anesthetics, all this pain and suffering is gone. How were these "miracle" drugs discovered and how do they work?

Throughout history, people have sought ways to relieve suffering. Many substances that control pain were found serendipitously, sometimes by trial and error. As early as 4200 B.C., people discovered natural substances—often plants and plant roots—that could cause unconsciousness in animals and people, so they used them to relieve pain.

But it is only during the first half of the 19th century that people started testing chemical substances on patients for their use in medical surgery. Over the years, various substances were identified, and their effectiveness was compared. This work has led to an array of medicines that can numb pain locally or cause unconsciousness and decrease pain over the entire body.

Scientists and health professionals now have a good understanding of which anesthetics work best on patients, but they are still trying to uncover how these drugs operate at the cellular and molecular level.

Local and general anesthetics

Anesthetics can be applied either to one area of the body—such as the skin, teeth and gums, or the spinal cord—or to the entire body. These two types of anesthetics, called local and general anesthetics, work by preventing nerves from carrying pain signals to the brain. This way, the brain does not perceive pain.

Local anesthetics can be given by injection to numb parts of the body during surgery and dental procedures. They can also be used to numb the eye before certain eye examinations—typically, when eye doctors measure eye pressure or remove stitches or foreign objects from the eye.

Other local anesthetics are available as ointments, sprays, or lotions to relieve itching, sunburn, insect bites, and minor cuts. They can even be taken orally to relieve throat pain or canker sores.

General anesthetics are used during medical and surgical procedures that would be too painful to endure while awake. In addition to suppressing pain, as local anesthetics do, general anesthetics also induce a loss of consciousness that may feel like deep sleep. But unlike sleep, in which parts of the brain work by forming dreams and processing information, this loss of consciousness does not form dreams nor does it store memories.

Over the past centuries, people searched far and wide for substances with anesthetic properties. A substance that would shut down the entire body was the most sought-after type of anesthetic. The pain from surgery and other medical procedures was often more excruciating than that from the local treatment of a wound or a dental procedure. So, medical personnel tested many different substances on patients, sometimes with unexpected side effects.

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Nitrous oxide

One of the most well-known and most successful general anesthetics is nitrous oxide (N_2O). It was discovered at the end of the 18th century and is still being used in surgical anesthesia.

Nitrous oxide is a colorless, almost odorless gas that was first discovered in 1793 by an English scientist and clergyman named Joseph Priestley. Following Priestley's discovery, British chemist Humphry Davy realized that nitrous oxide had physiological effects. He noticed that people who inhaled it started laughing for no reason, and he called it "laughing gas."

Davy realized the anesthetic effect of the gas, but for the next 40 years, the main use of nitrous oxide was in traveling medicine shows and carnivals. People would pay for inhaling small amounts of the gas and would laugh and act silly until the effect of the drug wore off. Nitrous oxide found a more scientific use as an anesthetic in dentistry and medicine in the early 1840s.

Other general anesthetics

Nitrous oxide is still used as a general anesthetic in combination with other chemicals. But its main use is as a mild sedative and a pain reliever, because nitrous oxide can cause the lungs to collapse and can lower the oxygen content of tissues.

Most of the other general anesthetics used today are administered through the lungs and thus are called inhalation anesthetics. The first widely used inhalation anesthetic was diethyl ether ($C_2H_5OC_2H_5$), a highly flammable liquid, especially in the presence of oxygen. Diethyl ether increases the risk of fires, or even explosions, in operating rooms during surgeries, so this compound has fallen out of favor.

Today, halogenated ethers have replaced most other compounds for use as inhalation anesthetic. An ether is an organic molecule that contains an oxygen atom connected to two organic groups. Its general formula is R-O-R', where R and R' are the organic groups. A halogenated ether is an ether in which one or more hydrogen atoms are replaced with halogen atoms (fluorine, chlorine, bromine, or iodine).

Examples of halogenated ethers include isoflurane ($CF_3CHClOCHF_2$), desflurane ($CF_3CHFOCHF_2$), and sevoflurane ($CF_3CHCF_3OCH_2F$). Halogenated ethers have the advantage of being nonflammable and less toxic than earlier general anesthetics.

But not all halogenated ethers have an anesthetic effect. For example, flurothyl ($CF_3CH_2OCH_2CF_3$) has the opposite effect, by inducing convulsions and epileptic seizures. Flurothyl was previously used in psychiatric medicine for shock therapy, but this practice has been discontinued.

It's all in the chemistry

So, how do anesthetics work? When a painful sensation occurs—due to, say, a wound or a teething pain—nerve cells send a message of pain to the brain. This message is carried by small electrical currents through adjacent nerve cells. For these currents to flow from one nerve cell to the next, the nerve cells exchange ions, such as sodium ions (Na^+). A nerve cell will release these ions—through openings on the cell surface—and another nerve cell will capture them. Then, this nerve cell will do the same with another nerve cell, and so on.


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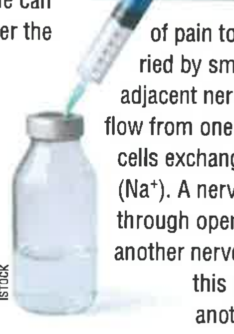
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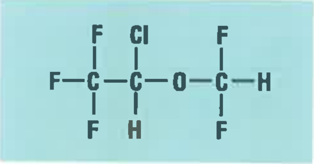
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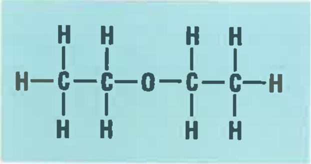
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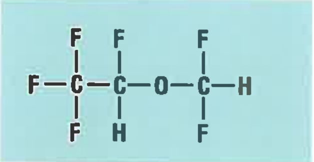
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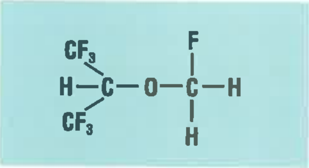
Sevoflurane

Anesthetics work by preventing sodium ions from going from one nerve cell to the next. But the details of how this is done are not well known. An easy explanation would be that the anesthetic molecules bind to a nerve cell and block the openings through which the sodium ions are released. But this is not what happens.

Scientists have observed that the anesthetic molecules do not bind to nerve cells, so the sodium ions are released. But somehow, these ions are not captured by other nerve cells, preventing them from carrying the pain signal to the brain.

The way general anesthetics work is even more mysterious. Not only do these anesthetics prevent pain signals from reaching the brain, but they also cause unconsciousness and memory loss. Scientists hope to find answers by comparing what happens at the cellular level during general anesthesia, actual loss of consciousness (say, due to a stroke) and amnesia (a medical condition that causes memory loss).

"It's still a black box," says John Stork, a pediatric anesthesiologist at Babies and Children's Hospitals, Cleveland, Ohio, and a professor of anesthesiology at Case Western Reserve Medical College in Cleveland. "But there is considerable research going on to help anesthesiologists understand how anesthetics affect the body at the cellular level."

General anesthetics also cause side effects, such as nausea and pain, so doctors provide antinausea drugs and painkillers to patients. But how these side effects happen is not well understood. What physicians know is that during surgery, stomach acids build up because of the many drugs given. Physicians and scientists are investigating what this build-up of stomach acids does to the body; they are also looking at other changes in the body that could cause nausea and pain.

Anesthesia has relieved surgery patients from all the pain and suffering that they would feel otherwise during surgical procedures. The next step will be for scientists to unravel the details of how anesthetics work at the cellular level and to find ways to prevent their side effects from happening.

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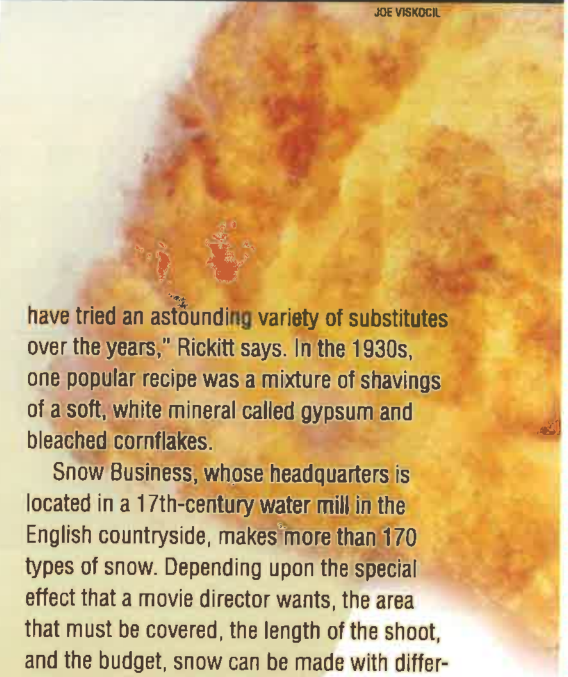
Claudia M. Caruana is a medical and science writer who lives in New York, N.Y. This is her first article in *ChemMatters*.

HOLLYWOOD'S SPECIAL EFFECTS

How Did They Do That?

By Diana Lutz



JOE VISKOCIL

Special effects in movies are not all done with computers. Fake snow, articial skin, and big explosions: They can look like the real thing!

These days, many special effects are done with computers. The fire-spewing Balrog that the wizard Gandalf fights in *The Lord of the Rings*, the Watcher in the Water, Gollum and the Orc armies at the Battle of Helms Deep are all computer-generated. But computer-generated effects have limitations and many films still mix old-fashioned physical effects with the trendy computer-generated ones.

Physical effects are usually based upon one simple idea: A material or event is substituted for another, usually one that is less messy, expensive, or dangerous than the real thing. Snow that won't melt might be made out of paper and creature skin that sags like real skin out of latex. Small blasts might substitute for full-scale explosions. But the basic fiddle, or cheat, is only part of the story. The illusion is helped by tricks of the trade, often ones known only to practitioners, and it is this unique knowledge that gives physical effects their sometimes astonishing realism.

Special effects experts use a wide range of chemicals. Snow blanketing the ground might be made of paper or wood pulp, and falling snow from ash or foam. Makeup experts combine either liquid latex or silicone with other chemicals to create a patch of skin that is either thick and leathery or soft and wrinkly. To make explosions or fires, they use miniature models, which they blow up or burn.

Fake snow

One of the paradoxes of fake snow is that it is better than the real thing. According to Richard Rickitt, author of *Special Effects: The History and Technique*, once snow is trampled, it can't be restored, so snow shots can be repeated just once or twice, after which a movie crew needs to move to a new location.

Darcey Crownshaw, founder and managing director of Snow Business, one of the leading suppliers of movie snow, says that real snow is unpleasantly cold and wet. His company sometimes covers real snow with "warm artificial snow that actors can snuggle into like being in a down quilt," he says.

But snow is also one of the hardest of all natural substances to fake. "Movie makers have tried an astounding variety of substitutes over the years," Rickitt says. In the 1930s, one popular recipe was a mixture of shavings of a soft, white mineral called gypsum and bleached cornflakes.

SNOW BUSINESS

Snow technicians use dry foam for this falling snow effect that will be part of a commercial for Waitrose, a supermarket company in the United Kingdom.

Snow Business, whose headquarters is located in a 17th-century water mill in the English countryside, makes more than 170 types of snow. Depending upon the special effect that a movie director wants, the area that must be covered, the length of the shoot, and the budget, snow can be made with different types of materials, including paper, rice or potato starch, plastics, foam, and Epsom salts (magnesium sulfate).

In all these cases, the final product must look like snow and, if necessary, must drift, clump, and melt like snow. This is sometimes tricky and not always done successfully. In one recent movie, Crownshaw noticed snow with "edges," which was actually cheap cotton wadding that was laid down "straight off the roll;" and, in another movie, a car was sliding through "wet snow" that clearly looked like detergent suds. "Bad snow"—as Crownshaw describes it—calls attention to itself, distracting the viewer from the story the movie is telling.

But looks aren't everything. Movie snow, particularly products used on location, must be environmentally friendly. Many of Crownshaw's snows are made of recycled materials, and the company is

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careful to use "self-clearing products" in sensitive outdoor locations, such as a cellulose powder that can be hosed down easily or a foam that evaporates within a few hours.

Crownshaw's signature product is paper snow. But there is more to it than you might think. If you try to make snow by cutting up paper, you get confetti. Because the paper "flakes" have straight edges, they don't fall right and, once on the ground, blow about like dry leaves. Snow Business's paper snow is torn rather than cut, so the edges are ragged. The torn edges make the snow flakes tumble as they fall, and, once on the ground, clump and drift like real snow.

ALL SNOW PHOTOS BY SNOW BUSINESS.

From the film *The Day After Tomorrow* (2004), this image shows frozen arctic effects.

Artificial snow used on movie sets.

Paper snow is made in huge machines called hammer mills—literally hammers attached to a rotating shaft—that expel the paper through fine screens, shredding it rather than cutting it. "On a typical run, we make 20 tons of snow, and we make about 500 tons of snow every year," Crownshaw says.

Another Snow Business product is a polymer similar to the one found in disposable diapers. A polymer is a large molecule made up of repeating small molecules known as monomers. The granules in a diaper are polymers called sodium polyacrylate that readily absorb water. Sodium polyacrylate is made of repeating units of the monomer [CH_2-CH(COONa)].

The sodium polyacrylate polymer is actually a combination of two polyacrylate polymers linked together like the rails of a railroad track (Fig. 1). Hanging off these "rails" are carboxyl groups (-COOH) in which the hydrogen atoms are replaced with sodium atoms (-COONa). When the polymer comes into contact with water, the sodium detaches, creating two ions, carboxyl (COO^-)—still attached to the chain—and a free sodium ion (Na^+).

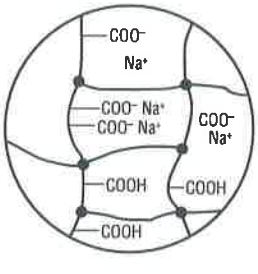

Figure 1. When sodium polyacrylate is in contact with water, it unravels, releasing sodium ions (Na^+).

Taken on the set of *The Chronicles of Narnia, The Lion, the Witch, and the Wardrobe* (2005), this shot shows winter effects created by the company Snow Business.

The carboxyl ions repel one another, widening the polymer coil. Water moves into the polymer from the outside to dilute the free sodium ions. Once the water is inside the polymer, it attaches to the chain by hydrogen bonding, where the hydrogen atoms in water are attracted to the oxygen atom in the carboxylate ions. The polymer swells, but the links between the two chains prevent it from dissolving; instead, it forms a stiff gel.

If you mix diaper granules with water, what you get looks more like ice than snow, Crownshaw says. So his team developed a polymer that swells even more, picking up 4,000 times its weight in water rather than the 800 times, which is more typical of diaper granules.

Artificial skin

The main problem with making artificial skin is that we are intimately familiar with how real skin wrinkles and moves, along with its translucency and flaws. Anything that is not quite right about artificial skin—such as a visible blend line at its edge—immediately tips us off and destroys the illusion.

High-quality skins and prosthetics—which can be anything from fake jowls to pointy ears—are custom-fitted to the actor who will wear them. The first step is to make an exact copy of the actor's face or body part, called a life cast. Then, the jowls or ears are sculpted in clay on the life cast. The clay parts are duplicated in a flesh-like material, such as whipped latex, that is then glued onto the actor to transform his or her appearance.

KNB EFX

Two mold makers from KNB EFX fill a silicone mold with fiberglass to make a life cast for an actor. Wrinkled skin or bite marks will be sculpted on this cast later.

Depending upon how the special effects artist wants the prosthetic to look and move, it can be made of whipped latex, gelatin, or silicone. *The Chronicles of Narnia*, a series of fantasy movies about Narnia, a place where animals talk, magic is common, and good battles evil, provides examples of special-effects work with all three materials.

The makeup for the films was done by KNB EFX, a special effects studio in Hollywood, Calif., famous for its work on horror and science-fiction movies. The studio won the 2006 Academy Award for makeup in the first *Chronicles of Narnia* movie, which included nearly every mythological creature ever invented.

Howard Berger—the "B" in KNB—says that the studio relied heavily on latex for *The Lion,* *the Witch, and the Wardrobe* (the first installment in the series), then shifted to gelatin for *Prince Caspian* (the second installment) and is planning to rely mainly on silicone for the third installment, *The Voyage of the Dawn Treader.*

The basic ingredient in latex foam is liquid latex, the milky white sap of the rubber tree that is a dispersion of long-chain polymers in an aqueous medium. A foaming agent and a curing agent are mixed into the latex. The foaming agent is essentially a soap that helps the latex form bubbles, and the curing agent is a mix of chemicals that links the polymer chains in the latex. When heated, the curing agent transforms the liquid latex into a flexible solid.

After all of the ingredients are added, the syrupy latex is tipped into a mixer and whipped into a foam. The amount of time spent whipping the foam greatly affects its consistency, Rickitt says.


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Special effects are used to create a virus appearance on hands.

Small bubbles produce dense and heavy foam, while large bubbles create light and flexible foam. A heavy foam might be used for a large creature, such as a Minotaur—a mythical monster with the head of a bull and the body of a man—whose skin is thick and leathery. Light foam would be used to create a facial appliance or a skin that looks soft and wrinkly.

Once the latex is whipped, a gelling agent is added to the mix, which clears the soap from the latex before the foam is cured. The latex is injected into a mold, which is then left to sit for 15 minutes so that the gelling agent can set the foam, and then the mold is baked in an oven for 1–2 hours to turn the gel into a sponge.

The oven's heat activates the curing agent, which allows the latex molecules to bind with each other. As a result, the latex molecules cannot move independently anymore, and the latex goes from liquid to solid.

Latex is an ideal material for artificial skin because it has a fine enough structure to reproduce frown lines and wrinkles, and is pliable enough to pick up movements of the facial muscles. But its color on film depends upon the lighting conditions on set, a complication that led Berger and his team to switch to silicone for the upcoming movie, *The Voyage of the Dawn Treader.*


KNB EFX

An employee of KNB EFX prepares molds that will be filled with silicone. Once the silicone sets, it is peeled from the molds and glued to an actor's face.

Silicone is a polymer that has a silicon-oxygen backbone (…-Si-O-Si-O-Si-O-…) with organic side groups—such as methyl $[-CH_3]$, ethyl $[-C_2H_5]$, and vinyl $[-CH=CH_2]$—attached to the silicon atoms.

"Silicone comes in the form of a greasy cream like soft petroleum jelly," Rickitt says. "Unlike foam latex, you don't bake silicone to solidify it. Instead, you use a chemical catalyst that hardens the silicone by linking the silicone polymer molecules together."

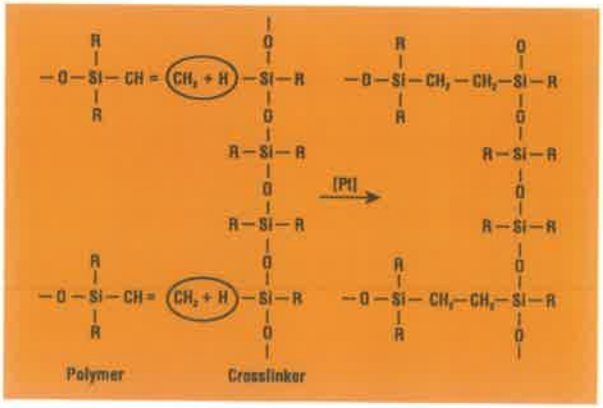

Figure 2. Curing of silicone by attaching silicon-hydrogen (Si-H) groups.

The catalysts speed up the curing of silicone by quickly building bridges between silicone molecules. Transition metals such as platinum and tin tend to be good catalysts because they readily accept and release electrons, which are then available to participate in chemical reactions.

For example, if the polysilicone has vinyl groups, then a small molecule with at least two silicon-hydrogen (Si-H) groups is added and the platinum catalyst catalyzes the addition of the silicon-hydrogen groups across the carbon-carbon double bonds ($CH = CH_2$) (Fig. 2).

JOE VISKOCIL

By igniting black powder in the presence of gasoline, special effects artist Joe Viskocil makes it seem like a fireball is engulfing a house.

Explosives and fires

When it comes to explosions, flames, or other similar effects used in the entertainment industry—also called pyrotechnic special effects—the problem is to create an illusion of towering fires and shattering explosions by the safest possible means. One of the best ways to do this is to blow up a miniature building or truck rather than a full-sized one.

Special effects expert Joe Viskocil, who has spent nearly 40 years blowing up miniatures, is not a fan of big explosions. Sometimes, he says, directors who are trying to outdo one another ask him for bigger, more dramatic explosions. He says, "I have two words for you: *Twilight Zone.*" During filming in 1983, a big pyrotechnic effect caused a low-flying helicopter to spin out of control and crash, killing an actor and two child

actors. "No movie is worth a life," Viskocil says.

One of his best known special effects is the explosion of the Death Star in *Star Wars Episode IV: A New Hope*. Producer and director George Lucas planned to animate the explosion; in fact, the cartoons for the animation had already been drawn. "It looked cool, very colorful, very weird, but still like an animation," Viskocil says. So, he decided that a physical effect would work better. But what would an explosion in space look like?

RICHARD RICKITT

Joe Viskocil prepares a scene from the movie *True Lies* (1994) in which a bridge explodes. The bridge and the truck were actually miniatures, and the explosives were set off by the truck as it crossed the 40-feet long bridge. The resulting explosion is shown on the cover of the magazine.

He reasoned that since there is no air and no gravity in space, the explosion should be perfectly spherical and not lopsided or squashed. To get a perfectly symmetric effect, he put the camera on the ground and filmed straight up.

A cardboard container of black powder mixed with titanium shavings was suspended from the studio's ceiling. Black powder is a mixture of sulfur, potassium nitrate (KNO_3), and charcoal—a black substance made mostly of carbon, along with other chemicals, and resulting from the heating of wood. When the black powder ignited, sparks and debris were propelled toward the camera as if travelling outward in the vacuum of space. The technique was so successful that it has been copied many times since then.

In 1997, Viskocil won the Academy Award for the special effects in *Independence Day*, a science-fiction film about an alien invasion of Earth. When the death ray from the alien spaceship hits the White House, a fireball rips downward through the building, which then explodes. The White House in the movie was a plaster model 6 feet high by 12 feet wide. "Many movie miniatures are plaster, because plaster shatters into nice chunks that are believable as masonry or concrete," Viskocil says.

Viskocil emphasizes that he has licenses to work with and transport explosive materials; that he prepares all special effects carefully, conducting many tests and checks; that he has a crew of people who watch his back; and that he calls off shots if anything seems even slightly amiss. He would be devastated, he said, if anyone were to be injured trying to imitate an effect he had described.

RICHARD RICKITT

Joe Viskocil's Death Star explosion for *Star Wars* (1977). The camera is on the floor, looking up at the explosion.

The end of film?

Viskocil and other special effects experts say that they are living on borrowed time. "We're dinosaurs," Viskocil says. "The computer has taken over the movie business. Eventually there won't be any film, which is an incredibly sad state of affairs for an art form that is now more than 100 years old."

Perhaps not surprisingly, Viskocil says he is not impressed by computer-generated effects. "The first *Star Wars* was all done with models with real explosions, and none of those were color corrected or computer enhanced," Viskocil says. "What you saw, is what we actually shot. The last three *Star Wars* used a minimum amount of special effects. So, a lot of the explosions and other effects look to me like cartoons." After a moment, he adds, "The old movies had heart, and the computer-generated ones are sterile. That's the way I see it, at least. There is no magic to it any more."

Might he be right? Viskocil makes this observation about his craft, "Commercials on TV are now so saturated with color they look completely fake. The grass is unnaturally green and the sky artificially blue. The producers just take crayons out, in essence, and color everything as brightly as possible." Once Viskocil points this out, you begin to understand—at least a little—what he means by heart. ▲

RICHARD RICKITT

Joe Viskocil (extreme right) prepares a miniature version of the White House for destruction in *Independence Day* (1996).

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Diana Lutz is a science writer in Madison, Wis. This is her first article in *ChemMatters*.