

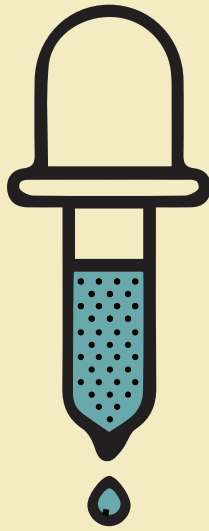
Caltech researchers are looking for



technological solutions to some of the most



common causes of blindness or vision impairment. ►



Though silent and usually painless, the onset of blindness is devastating. As the world slips away, blurs, or fades, the resulting loss of independence takes both an emotional and physical toll on an affected person's life.

For those facing the threat of blindness or whose vision is being compromised by age- or disease-related changes in their bodies, the promise of technologies that will prevent those changes or reduce that threat is about more than just a clear image. It is about being able to navigate through the world, relive the memories in a box of old photographs, or gaze upon a newborn grandchild.

Caltech scientists and engineers are working across disciplines—from biology to fluid dynamics, chemistry to electrical engineering—to develop technological solutions to vision-related issues that can affect the way in which the human eye takes in information and turns it into perception, into vision. They are considering the causes of blindness and their connection to common diseases. They are probing the eye's mechanics, optimizing treatments, and developing devices that can do what the eye itself no longer can.

Clearing the lens

Vision starts when light enters the eye through the cornea, the eye's outermost layer; the eye's colorful iris, the next structure the light encounters, then dilates the pupil to control the amount of light coming through. Next, the light passes through the eye's lens—a transparent, flexible membrane made of water and proteins. The lens focuses the light, allowing for a clear image to ultimately form.

At least, that is what the lens is meant to do.

Cataracts are caused by proteins that clump together in an eye's lens; the lens becomes cloudy and vision becomes blurred. The good news is that surgery to replace cataract-clouded eye lenses with artificial lenses is both

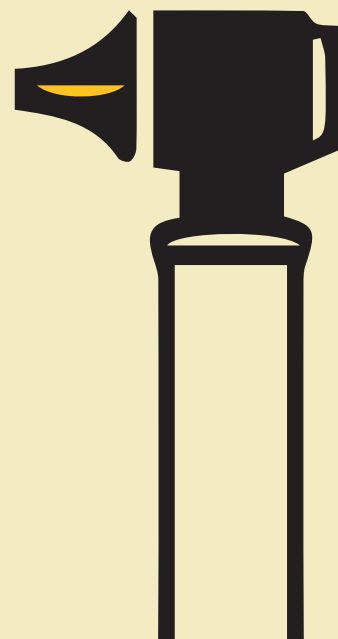
common and generally highly successful. In fact, it is one of the most frequently performed surgeries worldwide.

The less-good news? Traditionally, many patients have needed to wear glasses even after surgery, for a variety of reasons. It can be difficult, for instance, to predict exactly the shape an artificial lens will need to have in order to provide for perfect vision; also, implanted lenses can slip or shift subtly during the healing process, which will affect their ability to focus light.

That is why Caltech researchers and their colleagues created a new type of implantable intraocular lens that can actually be adjusted to a patient's eye and vision needs after surgery, ensuring that the patient ends up with 20/20 vision.

The idea for the lens started with UC San Francisco eye surgeon Daniel Schwartz, who was looking for a solution to these post-cataract-surgery vision problems. Schwartz looked to members of the Caltech faculty including Julie Kornfield, professor of chemical engineering, and Robert Grubbs, the Victor and Elizabeth Atkins Professor of Chemistry and a 2005 Nobel Prize winner in chemistry. Their collaboration ultimately led to the founding of a company that produces the adjustable lenses.

The lenses' ability to reshape themselves after implantation—and after enough time has passed that the eye has healed from the surgery—is made possible by molecules in the lens called macromers. (Macromers are the basic structural units that comprise polymers—the chemicals that make up plastics and other chemical compounds.) The macromers in these particular lenses were chosen because they will reshape themselves in predictable ways in response to beams of focused ultraviolet light. The lenses are so responsive to the UV light that



each can be reshaped and refined until it produces the desired individualized visual results.

“The key thing we've learned out of this is that you need to have both doctors and scientists or engineers involved from the very beginning,” says Grubbs. “Otherwise—if you're a scientist or an engineer—you may not have all the clinical information you need, and you'll solve the wrong problem. And if you're a clinician, you may not have the expertise and the resources to be able to do the science and prove your concept.”

Lighting up the retina

Once they have been optimized, these newly unclouded, well-shaped lenses—like the lenses in the eyes of people without cataracts—send the now-focused light to the back of the eyeball. There it hits the retina, a thin layer of tissue containing millions of light-sensing nerve cells—the very nerve cells that are needed to convert light into electrical impulses for their journey to the brain.

Those nerve cells can be put at risk by a number of disease conditions, including diabetes. Hundreds of millions of people suffer from diabetes worldwide, and each of them may become susceptible to a type of creeping blindness, called diabetic retinopathy, that is associated with the disease in its more advanced stages.

High levels of glucose in the blood—like that caused by diabetes—is known to lead to damage to blood vessels; diabetic retinopathy is the consequence of such damage in the tiny blood vessels in the eye, which reduces blood flow and thus restricts the oxygen supply getting to the nerve cells in the retina, resulting in their eventual death.

As the disease progresses, the body attempts to counteract the effects of the damaged blood vessels by growing new ones within the retina. But these vessels tend to develop imperfectly and often bleed into the clear fluid inside the eye, obscuring vision; the body then repairs the damage these bleeds can cause by building scar tissue on the retina, rather than new light-sensing cells. Over time, diabetic retinopathy leads to a patient's vision becoming blurry and patchy, before fading away completely. Existing treatments, though effective, are painful and invasive, involving lasers and injections into the eyeball.

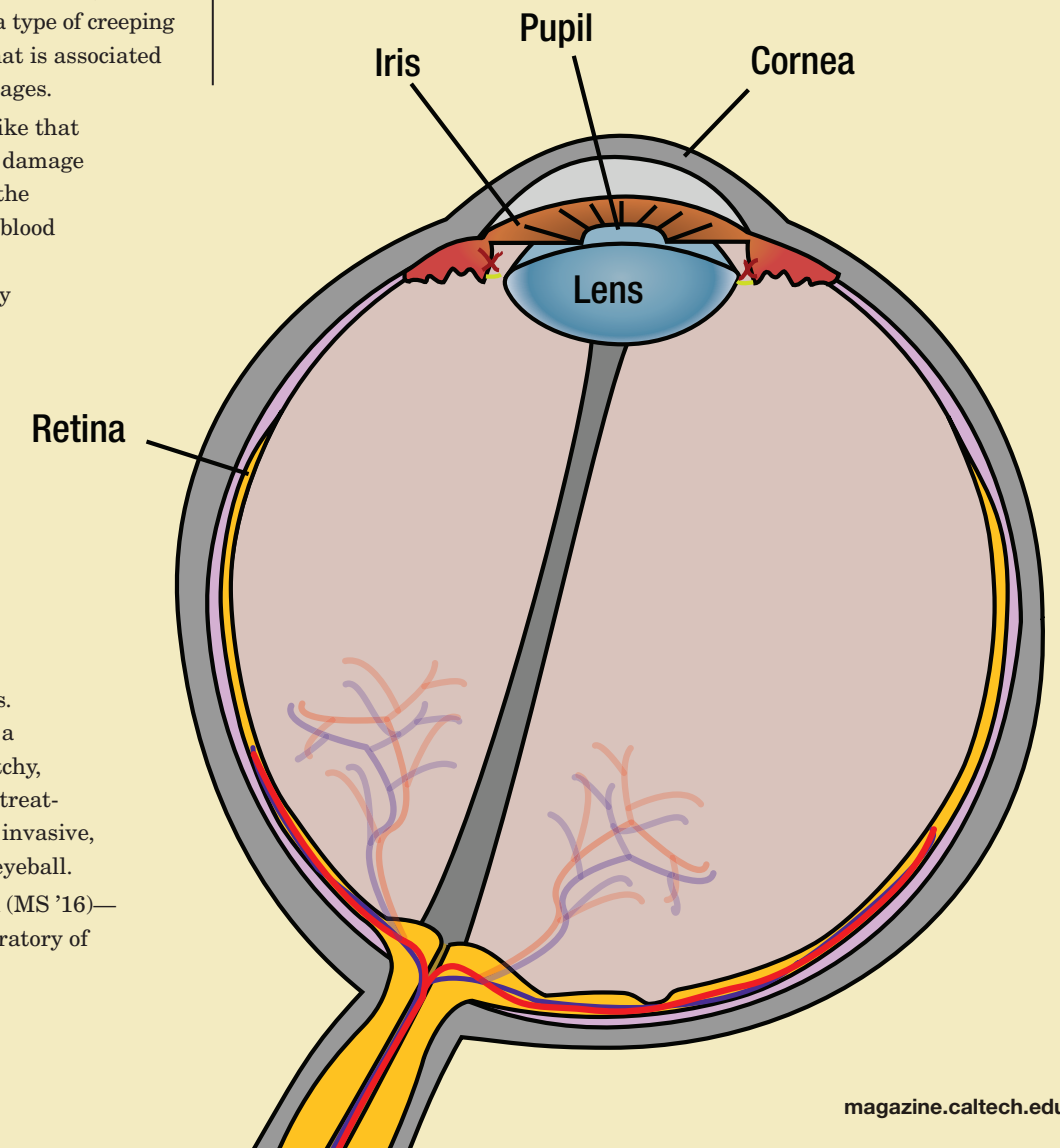
Caltech graduate student Colin Cook (MS '16)—along with other researchers in the laboratory of

Yu-Chong Tai, Caltech's Anna L. Rosen Professor of Electrical Engineering and Medical Engineering and holder of the Andrew and Peggy Cherng Medical Engineering Leadership Chair—has developed a much less invasive solution: a glow-in-the-dark contact lens.

The idea behind the lens is that if insufficient oxygen causes much of the retinal damage in diabetics, reducing the retina's oxygen demands should slow or stave off further eyesight loss. In laser treatments, for instance, burning away nerve cells in the peripheral parts of the retina allows the available oxygen to be used by the more important cells in the retina's center.

The new lens also reduces the metabolic demands of the retina, but it does so by concentrating on the retinal rod cells, the cells that allow us to see in low-light conditions. The less light the rod cells are exposed to—for instance, while we sleep—the harder they work and the more oxygen they need.

“Your rod cells, as it turns out, consume about twice as much oxygen in the dark as they do in the light,” Cook says.



Glow-in-the-dark contact lenses, on the other hand, reduce the retina's nighttime oxygen demands by giving its rod cells the faintest amount of light to look at while the wearer sleeps. The illumination comes from tiny vials—the width of just a few human hairs—filled with tritium, a radioactive form of hydrogen gas that emits electrons as it decays. The electrons are then converted into light by a phosphorescent coating. The vials in the lens are laid out like the rays of a cartoon sun, creating a circle just big enough to fall outside of a wearer's view when their pupils constrict, as when exposed to sun or artificial light. In the dark, however, the pupils expand enough that the faint glow from the vials can illuminate the retina.

Early testing of the lenses conducted in collaboration with physicians at the University of Southern California shows promising results, with the lenses reducing rod-cell activity in the dark by as much as 90 percent. Next will come testing to see if the lenses' ability to reduce retinal metabolism will translate into the prevention of diabetic retinopathy. Says Tai: "This is an innovative solution with a potentially huge impact on diabetic retinopathy."

Reaching the macula

The retina's peripheral rods surround the nerve cells, called cones, that are concentrated in an area at the center of the retina called the macula. The macula is responsible for sharp central vision and detecting fine details. When the macula is damaged or begins to break down, as it does in a condition known as macular degeneration, vision disturbances and loss of vision can follow.

UCSF's Schwartz—who worked with Kornfield and Grubbs on the lens for use in cataract surgery—has also



been concerned with finding a better way to treat macular degeneration. One such treatment involves the use of a medication that works to stop the growth of new blood vessels that causes most of the macular damage in what is known as the "wet" form of the disease.

The problem with this treatment, however, is that the medication does not always make it to the right spot in the right concentration to do the job well.

And so Schwartz contacted Caltech's Morteza Gharib, the Hans W. Liepmann Professor of Aeronautics and Bio-inspired Engineering, whose research focuses (in part, at least) on fluid dynamics. Since the eye itself is essentially a bag of fluid, Gharib thought he could discern what was stopping the medication from making its way to the macula.

"When we started to do experiments, we found that the movement of the fluid within the eye may actually prevent this medication from getting to where it needs to be," Gharib says. "There are certain flow loops in the eye due to the movement of the eyeball itself, and if you happen to inject the drug into a wrong position within these loops, the drug may stay in that loop and never get to the desired location."

The next step is for Gharib and Schwartz to create a way to avoid the vortexes during treatment, and then to test that concept. "Basically," Gharib says, "we're figuring out how and where to best inject the medicine."

Protecting the optic nerve

The connection between the eye's retina and the brain's vision center is the optic nerve. It is, in many ways, the last bridge that the incoming light—now an electrical impulse—must cross on its way to becoming a perceptible image.

Glaucoma can collapse that bridge. The second-most-common cause of blindness, after cataracts, glaucoma affects 65 million people worldwide. It is the result of fluid buildup in the eye putting pressure on the million or so nerve fibers that make up the optic nerve, ultimately damaging or destroying them.

For patients with glaucoma, knowing what their intraocular pressure is—and, especially, when it is elevated and for how long—can be essential when trying to preserve vision. That's why people with glaucoma make regular visits to an ophthalmologist, where a device called a tonometer is used to measure eye pressure. The problem is that eye pressure fluctuates throughout the day, and thus even regular office-visit measurements may not detect dangerous pressure spikes.

The need for even more precise tracking of the state of a glaucoma patient's eyes led to a collaboration between Yu-Chong Tai and Azita Emami, Caltech's Andrew and Peggy Cherng Professor of Electrical Engineering and Medical Engineering and a Heritage Medical Research Institute Investigator. The result: an implantable pressure sensor

that can reside in the human eye for years at a time and wirelessly transmit data about that eye's health to a patient or their medical professionals.

"With our wireless implanted device, a patient could read their eye pressure any time," says graduate student Abhinav Agarwal (MS '14), co-author of a 2018 paper describing the implant. "Catching elevated eye pressure early would allow the doctor to modify the therapy if necessary to prevent further loss of vision."

The device is a little smaller than a dime and is implanted in a spot on the white of the eye where it will not interfere with vision. It consists of a pressure sensor, control circuitry, and an antenna. The implant has no battery, making it long lasting. During a reading, radio waves from a handheld scanner are received by the antenna and generate a small voltage that temporarily powers up the device, which takes a pressure reading and sends the signal back to the reader using the same antenna. By encapsulating their device in a specialized coating that consists of a silicone-oil bubble surrounded by a biocompatible polymer called parylene, the Caltech team projects that its device could last up to four years.

The device might even be modified to provide treatment by adding a valve that would release small amounts of the excess fluid as tears. "We would create a 'smart' glaucoma-drainage device in which a single implant could measure eye pressure and relieve excessive pressure," says graduate student Aubrey Shapero.

Their goal—like that of the other Caltech research groups that are focusing in on the eye—is to collaborate in human testing of their device within the next several years, and ultimately to get FDA approval for its use in patients. 📺

