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## Contact lenses Look into my eyes

**Biotechnology: Smart contact lenses exploit the unusual characteristics of the eye to diagnose disease, deliver drugs and more besides**

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EYES can reveal an awful lot about somebody. Look into someone's eyes and you can tell if he is happy or sad, truthful or insincere, sober or drunk. By peering deeper still, ophthalmologists are even able to gauge a person's health, spotting far more than just conditions that affect the eye itself: hypertension and brain tumours can also be diagnosed by examining the retina. Eyes are in many respects windows on the body, even if they are not quite windows on the soul.



And now contact lenses, normally used to bring the outside world into focus, are making it possible to peer back in through these windows. The idea of "smart" contact lenses that can superimpose information on the wearer's field of view has been around for a while, but contact lenses are also being developed that use embedded sensors and electronics to monitor disease and dispense drugs. Such devices may eventually be able to measure the level of cholesterol or alcohol in your blood and flash up an appropriate warning.

The technology has huge potential, says Babak Parviz, a researcher at the University of Washington, in Seattle, who is one of the pioneers of smart contact lenses. Such lenses could act as both sensors and displays, providing new ways for data to pass in and out of the body. By adding tiny light-emitting elements to contact lenses, it is becoming possible to map digital images directly onto the wearer's field of vision to create a head-up display or augmented-reality overlay that requires no glasses, screen or headset. "The ultimate goal would be to have a fully fledged display," says Dr Parviz.

The first smart contact lenses are already on the market. The Triggerfish, created by Sensimed, a spin-off from the Swiss Federal Institute of Technology in Lausanne, is a wirelessly powered contact lens designed to help people with glaucoma manage their treatment. It does this by continuously measuring the curvature of the eye over a 24-hour period using a tiny strain gauge built using micro electromechanical system (MEMS)

If it isn't treated correctly this can irreversibly damage the patient's vision, says Jean-Marc Wismer, Sensimed's chief executive. But determining the correct drug treatment depends upon first knowing when during the day the intraocular pressure (IOP) peaks.

The profile of this pressure is believed to follow characteristic circadian patterns. But at the moment there is no technology that can measure it continuously. "The standard today is to place patients in a laboratory for 24 hours," says Mr Wismer. During this time a patient's IOP can be measured every few hours using a standard machine called a Goldmann tonometer. But although this approach can measure the IOP very effectively, it is unable to do so continuously.

### An eye for an eye

By measuring the changes in the curvature of the eye caused by a build-up of intraocular pressure, Sensimed's Triggerfish lens can build up a much more accurate profile. In addition to the strain gauge, all the electronics required to handle the signal-processing and communications are embedded within the silicone lens (pictured).

An induction loop is used to power the device and to relay data from the lens to a receiver worn by the patient. (Induction loops are also used to power hearing-aid implants without the

need for troublesome wires.) Since the end of 2010 the technology has been available in eight European countries, and approval in America is expected by the end of this year, according to Mr Wismer. "We currently have about 200 patients in total," he says.

The device does have one significant drawback, however. The short range of the induction-loop antenna in the lens means the external antenna has to be very close to the eye: taped around the eye socket, in fact. Wearing a small chip in your eye (normal vision is not impaired) looks strange enough, but having a giant monode taped to your head looks stranger still.

It is less than ideal, Mr Wismer admits, but his firm's device is not meant to be worn continuously. Instead, the idea is that it would be worn for 24 hours once every six months or so. The hope is that this device will help to improve the treatment of glaucoma by illuminating the relationship between variations in the IOP and the progression of the disease.

Another smart contact lens is, however, designed to be worn continuously. Although still under development, this lens is aimed at treating diseases rather than monitoring them. It has been developed by Daniel Kohane, a professor of anaesthesiology and director of the Laboratory for Biomaterials and Drug Delivery at the Children's Hospital in Boston. His smart lenses are designed to release drugs slowly into the eye over a long period.

Compared with the simplicity of eye drops this may seem a bit over the top, but there are very good reasons to develop this sort of technology, says Dr Kohane. "Eye drops are not very efficient—only a small fraction actually gets into the eye," he says. "But the bigger problem is compliance." A common problem with ophthalmic diseases is that patients fail to apply their eye drops as prescribed. "Things that should work don't work, and that leads to an escalation of the disease and the therapy."



A sight for sore eyes, perhaps

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Tears contain charged atoms which interfere with the operation of a smart lens's built-in antenna

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## **A new perspective on drug delivery**

Dr Kohane's solution is to create a type of contact lenses that has encapsulated within it a pouch containing a drug. "It's a flat toroid or doughnut made out of a permeable polymer that contains the drug," he says. "As the film degrades it releases the drug, leaching out slowly." The payload could be almost anything, such as a painkiller, an antibiotic or an anti-inflammatory drug. In vitro experiments have showed that such a lens could continue to release ciprofloxacin, an antibiotic, in a controlled manner for more than 100 days.

The current design is purely passive, but Dr Kohane is now working on a version that can be triggered in response to a particular stimulus. If his lens were to be combined with sensors like those found in the Triggerfish, for example, it would be possible to monitor the IOP and deliver glaucoma drugs when it peaks. But there are other things that have to be taken into account. "If I cough, my IOP goes up," says Dr Kohane. A smart contact lens would have to be clever enough to cope with this.

An additional concern is the effect his therapeutic lens may have on the wearer's vision. "A concern is that as the drug is released, the change in shape will alter the focus of the patient," says Dr Kohane. This is one reason why the pouch is doughnut-shaped, so that it wraps around the pupil without obscuring the wearer's vision. "As far as we can tell that doesn't change it much," he says.

Smart contact lenses don't just have to focus on monitoring or treating the eyes. Dr Parviz has been developing a different type of lens intended for monitoring glucose levels in people with diabetes. The eye is a surprisingly good place to do this non-invasively, because glucose levels in tear fluid correspond directly to those in the blood, he says. This means levels can be continuously gauged without so much as a pinprick.

To measure the glucose level Dr Parviz uses a technique called amperometric sensing that involves measuring the changes in tiny currents between sets of electrodes. Like the Triggerfish, the lens is powered and communicates wirelessly. But his design has a greater range, so no induction loop around the eye is needed.

Tests on rabbits have showed that the lenses work and can detect even very low glucose levels, says Dr Parviz. But there is a problem with using amperometric sensing: the electrodes are not sealed within the lens, and therefore are exposed. Proteins then build up on the sensors, affecting their operation and reducing the useful lifespan of the lens. It is possible that cleaning the lens regularly could reduce this problem, but it is unclear what effect lens-

lens's built-in antenna.

As with Sensimed's device, all the electronics and sensors in Dr Parviz's contact lens are located outside the central area of the lens, to avoid interference with the wearer's vision. But Dr Parviz wants to add display elements, in the form of tiny embedded light-emitting diodes (LEDs), to his lenses so that they can overlay information on the wearer's field of view.

Dr Parviz has already demonstrated that red and blue dots, or pixels, can indeed be embedded in lenses, though green will also be required to create a full-colour display. He has shown that the pixels can be powered wirelessly and he has demonstrated that he can shrink the optics required to bring these dots of light into focus, even when they are so close to the eye. So far, however, the closest Dr Parviz has come to creating an actual display is a lens containing a grid of just eight pixels.

Given the ubiquity of high-definition screens containing millions of pixels this may not seem very impressive. But it is worth remembering that this is much more difficult than creating normal displays. Quite apart from the challenges of powering such a small device and bringing the pixels into focus, the small size of a contact lens means that the pixels will have to be much smaller than those in a typical computer monitor or mobile-phone display in order to provide a similar resolution. "Our smallest ones are about 50 microns across," he says. "We can definitely make them smaller." He will have to: a pixel on a high-resolution iPhone screen, by comparison, is about 80 microns (millionths of a metre) across.

It is still early days for this new field. Dr Parviz's immediate goals are to build simple, low-resolution displays, and to develop other types of biosensor, such as one capable of measuring lactic-acid levels in athletes during training. As he and other researchers develop smart contact lenses with new capabilities, this is a technology that is worth keeping an eye on.

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