of nearly 900 participants whose data they analysed, a higher prevalence of the Bact2 enterotype correlated with a higher body-mass index and obesity. However, the authors made the striking discovery that the pattern of enterotypes found in the population of obese individuals differed significantly depending on whether people were taking cholesterol-lowering drugs called statins (comprising about 12% of those studied). This result raised a surprising possible connection between statin intake and gut microbes. The obese participants taking statins had a significantly lower prevalence of the Bact2 enterotype (5.9% of the obese population) than did their obese counterparts not taking statins (17.7% of the obese population). Vieira-Silva and colleagues confirmed this phenomenon in an independent data set from the Flemish Gut Flora Project[11].

The use of statins is one of the great success stories of modern cardiovascular therapeutics. Originally derived from natural products of microbial denizens of the soil, these agents inhibit a rate-limiting enzyme in the pathway that makes cholesterol. By lowering cholesterol production, the treatment coaxes cells to boost the expression of receptors for low-density lipoprotein (LDL) that capture cholesterol-rich LDL particles, and this results in a robust decrease in cholesterol in the bloodstream. This LDL reduction substantially lowers the risk of cardiovascular events such as heart attack and stroke in a large swathe of the population at risk of such conditions, and many people use drugs of the statin class. Large meta-analyses of the effects of statin treatment reveal that it prolongs lifespan and that, on balance, the benefits outweigh any unwanted effects[12].

Independently of their effects on LDL, statins have anti-inflammatory actions that probably contribute to their clinical benefit through well-established molecular mechanisms[13]. However, no statin study has singled out obese individuals as targets for therapy, and no current guideline recommends considering obesity when making decisions about using statins for treatment.

Vieira-Silva and co-workers' unexpected findings therefore raise intriguing questions relating to the clinical use of statins. Yet interpretation of these findings warrants caution, in particular with regard to the risk of confusing correlation with causation. As the authors of this large and carefully executed study rightfully acknowledge, we should consider whether statin takers have had better access to health care or been more engaged in other health-promoting behaviours than have the individuals who were not taking statins. A large-scale clinical trial to determine whether statins lead to a reduced prevalence of the Bact2 enterotype in obese participants who would not otherwise receive statins could address this possibility, which is known as confounding by indication. Moreover, whether these findings apply across ethnic groups will require further study. In any case, following up on these provocative observations promises to provide new mechanistic insight into the complex relationships between obesity, metabolic status, gut microbes and cardiovascular disease.

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1. *Nature* https://doi.org/10.1038/nature.2016.19136 (2016).
2. Sender, R., Fuchs, S. & Milo, R. *PLoS Biol.* **14**, e1002533 (2016).
3. Qin, J. *et al. Nature* **464**, 59–65 (2010).
4. Vieira-Silva, S. *et al. Nature* **581**, 310–315 (2020).
5. Arumugam, M. *et al. Nature* **473**, 174–180 (2011).
6. Vieira-Silva, S. *et al. Nature Microbiol.* **4**, 1826–1831 (2019).
7. Costea, P. I. *et al. Nature Microbiol.* **3**, 8–16 (2018).
8. Graham, C., Mullen, A. & Whelan, K. *Nutr. Rev.* **73**, 376–385 (2015).
9. Tang, W. H. W., Bäckhed, F., Landmesser, U. & Hazen, S. L. *J. Am. Coll. Cardiol.* **73**, 2089–2105 (2019).
10. Baxter, N. T. *et al. mBio* **10**, e02566-18 (2018).
11. Falony, G. *et al. Science* **352**, 560–564 (2016).
12. Collins, R. *et al. Lancet* **388**, 2532–2561 (2016).
13. Oesterle, A., Laufs, U. & Liao, J. K. *Circ. Res.* **120**, 229–243 (2017).

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Applied physics

Artificial eye boosted by hemispherical retina

Hongrui Jiang

An artificial eye has been reported that incorporates densely packed, nanometre-scale light sensors into a hemispherical retina-like component. Some of its sensory capabilities are comparable to that of its biological counterpart. **See p.278**

Science fiction frequently features robots that have artificial eyes, as well as bionic eyes that interface with the human brain to restore the vision of people who are blind. Much effort has been made to develop such devices, but fabricating the spherical shape of a human eye – particularly a hemispherical retina – is an enormous challenge that severely limits the function of artificial and bionic eyes. On page 278, Gu *et al.*[1] report an innovative, concavely hemispherical retina consisting of an array of nanometre-scale light sensors (photosensors) that mimic the photoreceptor cells in human retinas. The authors use this retina in an electrochemical eye that has several capabilities comparable to those of the human eye, and that performs the basic function of acquiring image patterns.

The human eye, with its hemispherical retina, has a more ingenious optical layout than, say, that of the flat image sensors in cameras: the dome shape of the retina naturally reduces spreading of light that has passed through the lens, thus sharpening the focus. The core component of Gu and colleagues' biomimetic electrochemical eye is the high-density array of photosensors that serves as the retina (Fig. 1). The photosensors were formed directly inside the pores of a hemispherical membrane of aluminium oxide (Al_2O_3).

Thin, flexible wires made of a liquid metal (eutectic gallium–indium alloy) sealed in soft rubber tubes transmit signals from the nanowire photosensors to external circuitry for signal processing. These wires mimic the nerve fibres that connect the human eye to the brain. A layer of indium between the liquid-metal wires and nanowires improves electrical contact between the two. The artificial retina is held in place by a socket made from a silicone polymer, to ensure proper alignment between the wires and nanowires.

A lens combined with an artificial iris is placed at the front of the device, just as in the human eye. The retina at the back combines with a hemispherical shell at the front to form a spherical chamber (the 'eyeball'); the frontal hemispherical shell is made from aluminium lined with a tungsten film. The chamber is filled with an ionic liquid that mimics the vitreous humour – the gel that fills the space between the lens and the retina in the human eye. This arrangement is necessary for the electrochemical operation of the nanowires. The overall structural similarity between the artificial eye and the human eye confers on Gu and colleagues' device a wide field of view of 100°. This compares with roughly 130° for the vertical field of view of a static human eye.

The structural mimicry of Gu and colleagues' artificial eye is certainly impressive, but what makes it truly stand out from previously reported devices is that many of its sensory capabilities compare favourably with those of its natural counterpart. For example, the artificial retina can detect a large range of light intensities, from 0.3 microwatts to 50 milliwatts per square centimetre. At the lowest intensity measured, each nanowire in the artificial retina detects an average of 86 photons per second, on a par with the sensitivity of photoreceptors in human retinas. This sensitivity derives from the perovskite material used to make the nanowires. Perovskite compounds are extremely promising materials for various optoelectronic and photonic applications[2]. The perovskite used by Gu *et al.* is formamidinium lead iodide, and was chosen for its excellent optoelectronic properties and good stability.

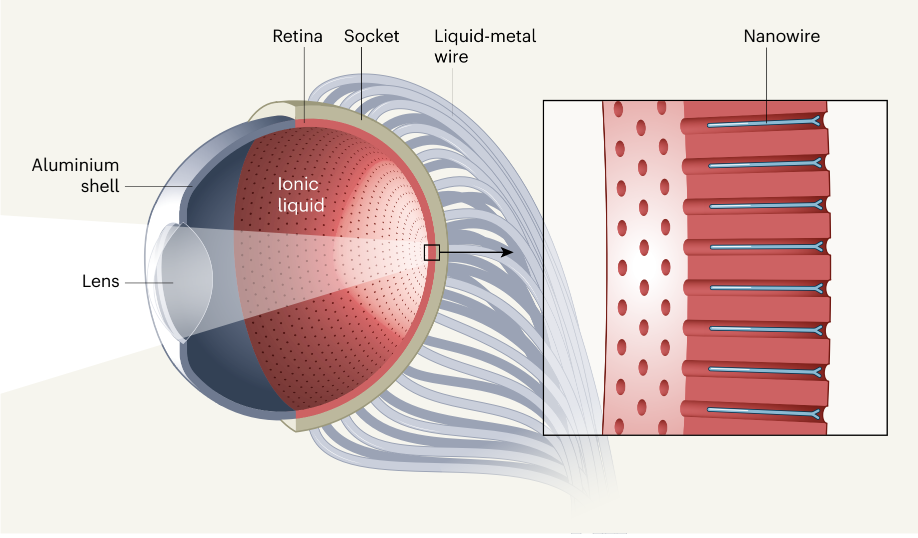

Figure 1 | A biomimetic artificial eye. Gu *et al.*[1] report an artificial visual system that mimics the human eye. A lens is fixed over an aperture in an 'eyeball', which consists of a metal shell at the front, an artificial retina at the back and an ionic liquid in the middle. The key advance is the hemispherical retina: a dense array of light-sensitive nanowires held in the pores of an aluminium oxide membrane. The nanowires mimic the photoreceptor cells in biological retinas. A polymeric socket holds the retina, ensuring electrical contact between the nanowires and liquid-metal wires at the back. The liquid-metal wires mimic the nerve fibres by transmitting signals from the nanowires to external circuitry for signal processing.

The responsivity of the nanowires, which measures the current produced per watt of incident light, is almost the same for all frequencies of the visible spectrum. Moreover, when the nanowire array is stimulated by regular, rapid pulses of light, it can produce a current in response to a pulse in just 19.2 milliseconds, and can then take as little as 23.9 ms to recover (return to its inactive state) when the pulse has ended. The response and recovery times are important parameters, because they ultimately determine how quickly the artificial eye can respond to a light signal. For comparison, the response and recovery times of photoreceptors in human retinas range from 40 to 150 ms.

Perhaps most impressive is the high resolution of the imaging achieved by Gu and colleagues' artificial retina, which results from the high density of the nanowire array. In previous artificial retinas, the photosensors were first fabricated on flat, rigid substrates; after that, either they were transferred onto curved supporting surfaces[3] or the substrate was folded into a curve[4]. This limited the density of the imager units, because space had to be left between them to allow for the transfer or folding.

By contrast, the nanowires in Gu and co-workers' device are formed directly on a curved surface, which allows them to be packed together more closely. Indeed, the nanowire density is as high as $4.6 \times 10^{8}\ \mathrm{cm}^{-2}$, much greater than that of photoreceptors in the human retina (about $10^{7}\ \mathrm{cm}^{-2}$). The signal from each nanowire can be acquired individually, but the pixels in the current device were formed from groups of three or four nanowires.

The overall performance of Gu and colleagues' artificial eye represents a leap forwards for such devices, but much still needs to be done. First, the photosensor array is currently only 10 × 10 pixels, with roughly 200-µm gaps between the pixels; this means that the light-detecting region is only about 2 mm wide. Moreover, the fabrication process involves some costly and low-throughput steps — for example, an expensive process known as focused-ion-beam etching is used to prepare each pore for nanowire formation. High-throughput fabrication methods must be developed in the future to produce larger photosensor arrays, at drastically reduced cost.

Second, to improve the resolution and scale of the retina, the size of the liquid-metal wires will need to be reduced. The outer diameter of the wires is about 700 µm, but this should ideally be comparable to the nanowire diameter (a few micrometres). It is currently challenging to reduce the diameter of the liquid-metal wires to that size.

> **"Perhaps most impressive is the high resolution of the imaging achieved by the artificial retina."**

Third, more testing is needed to establish the operational lifetime of the artificial retina. Gu *et al.* report that there is no obvious reduction in its performance after nine hours of operation, but the performance of other electrochemical devices can deteriorate over time. Lastly, the authors note that the response and recovery times of their device are reduced at higher concentrations of the ionic liquid, but at the expense of light transmission through the liquid. Further optimization of the ionic-liquid composition is needed to address this problem.

Nevertheless, Gu and colleagues' work adds to the breakthroughs that have been made in the past few decades[3–9], which have been achieved by mimicking not only camera-like eyes (such as those of humans), but also compound eyes similar to those of insects. Given these advances, it seems feasible that we might witness the wide use of artificial and bionic eyes in daily life within the next decade.

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1. Gu, L. *et al. Nature* **581**, 278–282 (2020).
2. Stranks, S. D., Snaith, H. J. *Nature Nanotechnol.* **10**, 391–402 (2015).
3. Ko, H. C. *et al. Nature* **454**, 748–753 (2008).
4. Zhang, K. *et al. Nature Commun.* **8**, 1782 (2017).
5. Jung, I. *et al. Proc. Natl Acad. Sci. USA* **108**, 1788–1793 (2011).
6. Liu, H., Huang, Y., Jiang, H. *Proc. Natl Acad. Sci. USA* **113**, 3982–3985 (2016).
7. Floreano, D. *et al. Proc. Natl Acad. Sci. USA* **110**, 9267–9272 (2013).
8. Huang, C. C. *et al. Small* **10**, 3050–3057 (2014).
9. Jeong, K. H., Kim, J., Lee, L. P. *Science* **312**, 557–561 (2006).