tasks. At the end, seeing your lab full of students, equipment and work is no less than a miracle. The first few years were extremely slow. There is a saying that 80% of the work is done in only 20% of the time, and this is very, very true as a PI. The combination of looking for funding, teaching, sitting in committees, mentoring students, writing papers, building the lab and dealing with human resources was extremely challenging. In retrospect, many of the choices that I made in the beginning were wrong. For example, I had startup fund money, so I invested a lot in an untested virtual-reality setup for awake, freely moving rats, and in retrospect this turned out to be too cumbersome to set up properly, such that the first successes in the lab occurred in very different directions. In the first few years in the lab, I also faced a terrible tragedy, when a visiting student from Nigeria, Alqasim Abdullahi, who had only been in the lab for three weeks, drowned and passed away during a lab trip. This was the moment when I understood that being a PI is a grave responsibility.

What brings you to the lab every day? This is an easy question to answer: the joy of discovery brings me to the lab every day. We are taught, in philosophy of science, that we should make hypotheses, and that these hypotheses should lead us to design specific experiments, which can potentially refute our hypotheses. However, reality is very different to that. From my experience over the years, I would say that we indeed ask questions, which lead us to perform scientific experiments. However, these experiments seldom answer the questions that we initially asked. Instead, new findings arise that raise new questions, which lead to surprising new findings, which lead to new unexpected experiments. I believe that one of the most important traits of a scientist is flexibility. The ability to understand the consequences derived from data, and how they lead to new paths and directions, is pivotal to good science. I am a great fan of the analysis of data. There is much joy in understanding something new about the world that has never been understood before. As a word of caution to new researchers: 90% of the time, what you discover are artifacts. However, this should not deter you from looking more deeply, as new exciting facts about the world will arise 10% of the time. One should be sceptical about one's findings; however, one should not throw the baby out with the bathwater. Golden eggs are there to be found.

I also really like to teach my graduate students. It is a joy to see them grow and mature as scientists. When a student of mine shows creative thought, and knows what to do better than I do, I feel I have succeeded. I am happy to see my former students as postdocs in very good labs around the world.

Whose studies have influenced you? When I teach graduate students about neuroscience, I usually start by reading texts from the following three researchers: Santiago Ramón y Cajal, Donald Hebb and David Marr. There are many others, but these are three of my heroes.

What do you think are the biggest problems that neuroscience is facing today? Too much technology. Too much data. Not enough insights. Not enough good questions.

What do you do to remain balanced? That's the hardest question of all. Time is a tricky asset, and it is much, much too easy to fill your time with lots of tedious and unnecessary errands. Now that my children are older (27, 21 and 17) and I have more time, I try to devote some of it to hobbies. I practice yoga and meditation, which I started after the drowning tragedy. In addition, I had a sabbatical last year and started getting interested in writing Hebrew poetry. Many new opportunities for writing groups on the internet were created following the pandemic, and I became very active with that. I am actually now in the process of editing my first poetry book.

If you could ask an omniscient higher being one scientific question, what would it be? Why do we die?

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Quick guide

Foveal vision

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What is the fovea? Vision begins in the retina, which houses the sensory receptors — rods and cones — that convert light into neural signals, and neurons that process those signals before they are relayed to the brain. In humans, the *fovea centralis* (hereafter referred to as the *fovea*, from the Latin for 'pit') is a morphologically distinct region of the retina named for its excavated appearance (Figure 1). It samples a circular region of the visual field about 1° in diameter — only twice the diameter of the image on the retina of the full moon. Despite its small field-of-view, less than 1% of the complete visual field, the fovea plays an outsize role in shaping our everyday visual experience.

Do all eyes have a fovea? In fact, most eyes do not. A true anatomical fovea can only be found in the eyes of select reptile, fish, bird and primate species, usually in those that lead life as a hunter. If a fovea is present, its location, size, shape and even quantity varies between species, but a unifying feature is the optimization of its neural sampling density to encode and transmit detailed spatial information in ecologically relevant portions of the visual environment. For example, the crocodile retina contains a foveal streak that courses along the equatorial midline, providing relatively uniform spatial resolving capacity across a broad section of the horizon; this organization may facilitate prey detection as it cruises along surreptitiously just beneath the water's surface. Some birds have two foveae, one pointing forward to facilitate binocular vision, one pointing out laterally for wide-angle monocular vision. But even in species without an anatomical fovea, or that lack a singular retina altogether, functional homologies to an area with heightened resolving power can be found, like the *visual streaks* of cats that contain smaller and more densely packed ganglion cells than in other parts

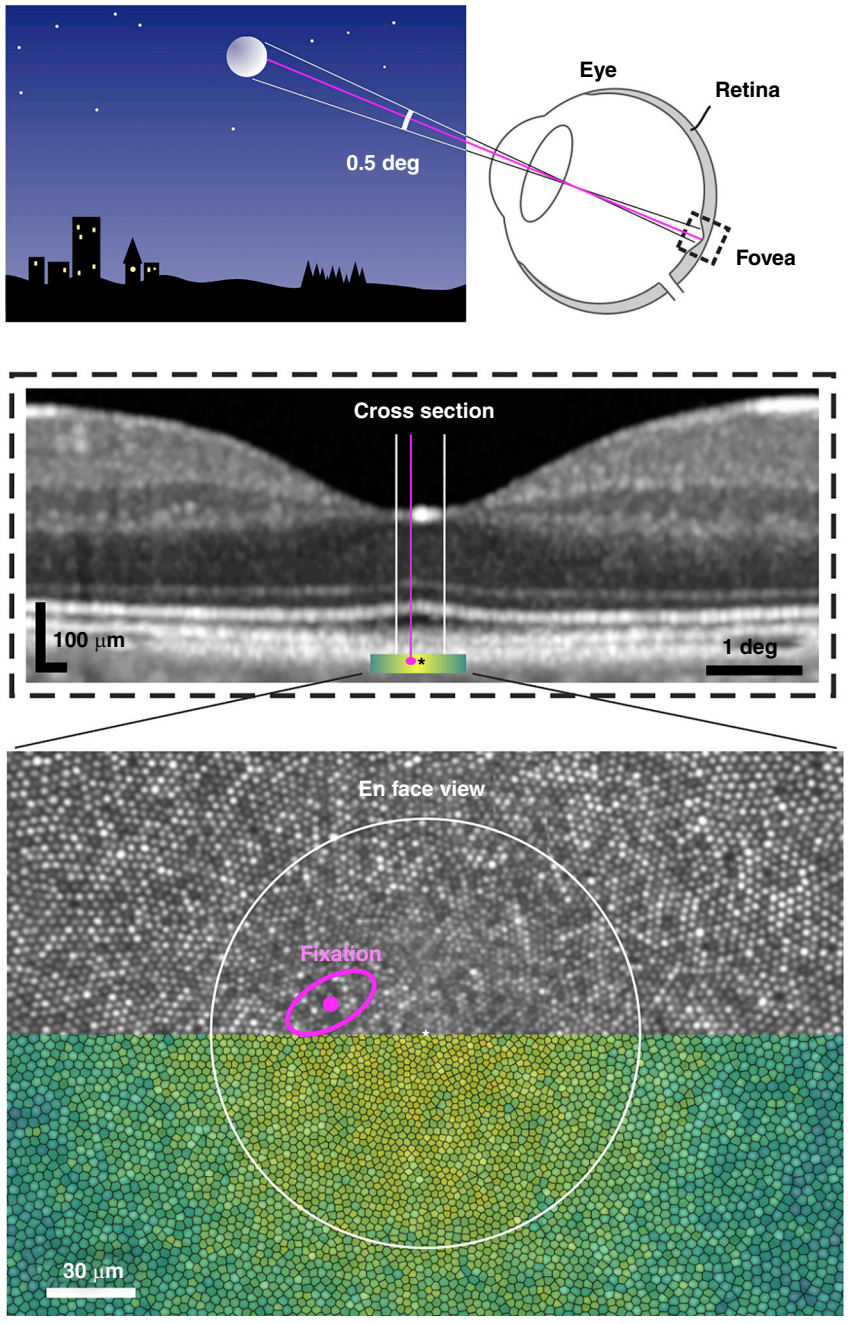

Figure 1. Humans use parts of their fovea for fixation.
The human fovea comprises only cone photoreceptors that can be visualized and studied in relationship to their visual function in the living eye with adaptive optics ophthalmoscopy. (Mosaic image from Wang *et al.* (2019; CC BY 4.0).)

of their retina, or the *love spots* in the compound eyes of some insect species.

How is the fovea specialized for spatial vision? In humans, three anatomical characteristics distinguish the fovea from the rest of the retina, all of which reflect optimizations for high-acuity daytime vision. First, cone photoreceptors are distributed to sample space finely, with packing densities peaking around 15,000 cells/deg^2. Second, rod photoreceptors, highly sensitive cells that function under low light conditions, are absent from the central most fovea. And third, inner retinal structures — bipolar and retinal ganglion cells, and retinal blood vessels — are displaced centrifugally from the foveal center, resulting in the fovea's hallmark dimpled profile (Figure 1).

Leveraging this unique morphology for high-acuity vision requires that the spatial information encoded by the densely packed foveal cone mosaic is preserved in ascending neural pathways. In primates, midget retinal ganglion cells are presumed to mediate spatial vision in the fovea because they receive excitatory input from just one foveal cone via one midget bipolar cell. The lack of crosstalk in this 'private-line' circuit ensures that spatial information is not lost in the signal transmitted to the brain. Psychophysical experiments in which optical aberrations — another factor that can limit resolution—are corrected with adaptive optics show that foveal visual acuity is ultimately limited by photoreceptor spacing, reaching values of 20/10 or better — twice as good as the clinical benchmark of 20/20. These results suggest individual foveal cone signals remain segregated up to the locus of perception.

Why does the foveal pit form? It seems plausible that the foveal pit evolved for optical reasons: in most lens eyes, the photoreceptors must 'view the world' through the inner retinal layers, as they sit at the very distal end of the retina. In the fovea, those layers are pushed aside during development, and the foveal cone lattice samples a retinal image that is less perturbed than it otherwise might be. Direct experimental evidence supporting an optical advantage conferred by the fovea is scant. Normal foveal development can be disrupted in individuals born prematurely and in conditions such as albinism; some individuals in these groups can have clinically normal visual acuities despite lacking a foveal pit altogether.

How does the fovea shape our experience of the visual world? Decades of controlled laboratory experiments confirm that, with some exceptions mentioned below, visual

performance quickly degrades away from the line of sight. When we are situated in more naturalistic environments, however, we tend to perceive our visual world as mostly uniform in quality. How can we reconcile this paradox? There is emerging consensus that humans use the fovea for active vision: by moving our head and eyes, we direct our gaze to obtain detailed glimpses of objects in our environment. In addition to facilitating performance on detailed tasks, such as threading a needle, these high-resolution foveal representations may continue to inform the appearance of previously fixated objects as the fovea is directed elsewhere, creating a visual experience that is more homogenous than the underlying neurosensory apparatus. Fovea-centric active vision strategies likely work in concert with other perceptual constancy mechanisms traditionally associated with peripheral vision, such as those that compensate for losses in contrast sensitivity and increases in image blur away from the line of sight, to improve the appearance of our visual field.

What happens when we lose foveal vision? Retinal diseases such as age-related macular degeneration can cause irreversible central vision loss. Transient blind spots, known as scotomas, can emerge during the aura phase of migraines. In either case, scotomas that encroach on the fovea lead to impairments in reading speed, facial recognition, and navigation. That these fundamental visual abilities are so closely linked to the integrity of the fovea underscores its central role in our everyday vision. By comparison, we are rarely, if ever, conscious of vision loss at the physiological blind spot, despite it being many times larger than the fovea and located fewer than 20 degrees from the line of sight.

In what ways is foveal vision inferior to peripheral vision? The optimization of the fovea for high-acuity vision is not entirely without cost. Compared to the peripheral retina, human visual performance along the line of sight is, in some instances, worse than in the periphery. For example, the absence of rods in the fovea means that under nighttime conditions, our ability to detect dim lights is better in the periphery where rods predominate. Likewise, the displacement of postreceptoral neurons in the foveal pit produces foveal cones with elongated axons; this distinct morphology slows down their signaling kinetics, placing a limit on our ability to detect rapid flicker near the center of gaze. Finally, humans with normal color vision have three cone types. These cone types can be found throughout the retina except for the central most fovea, where short-wavelength-sensitive cones are absent, impairing our ability to discriminate certain colors when stimuli are confined to the central 1/3rd of a degree.

What remains unexplored about foveal vision in humans? Two features that make the fovea optimized for spatial vision also pose difficulties for visual psychophysicists aiming to establish firmer links between foveal structure and function. First, the size and spacing of foveal cones are smaller than the magnitude of the optical blur produced by the eye's imperfect optics. Ocular aberrations hamper our ability to obtain images of foveal anatomy and make it difficult to estimate the shape of the stimulus landing on the foveal array. Second, the eye is continuously moving, even during fixation, which lends uncertainty about the region of the retina that samples the stimulus from one moment to the next. Although studies employing gaze-contingent visual displays have begun to unravel the relationship between eye movements, top-down factors like attention and saccadic suppression, and visual performance in and around the fovea, the connection to the underlying anatomy remains opaque.

Recent advances in retinal imaging have enabled *in vivo* characterization of single-cell photoreceptor structure at the foveal center; an example image obtained from a human eye is shown in the bottom panel of Figure 1. Consistent with histological observations, cone topography changes markedly across this region, and the peak packing density can vary widely between individuals. Interestingly, the preferred retinal locus used for fixation tends to be displaced from the location of peak density. It remains to be seen if this dissociation is simply the acceptable outcome of a complex-but-imperfect developmental process, or if the displacement of the preferred retinal locus confers some advantage in another visual domain, for example, stereopsis. Adaptive optics stimulation platforms, where the stimulus can be visualized directly on the photoreceptor mosaic and its location and trajectory on the retina can be controlled experimentally with single-cell precision, may provide one approach for resolving these questions.

Where can I find out more?

Cohen, M.A., Botch, T.L., and Robertson, C.E. (2020). The limits of color awareness during active, real-world vision. Proc. Natl. Acad. Sci. USA *117*, 13821–13827.

Harmening, W.M., Tuten, W.S., Roorda, A., and Sincich, L.C. (2014). Mapping the perceptual grain of the human retina. J. Neurosci. *34*, 5667–5677.

Intoy, J., and Rucci, M. (2020). Finely tuned eye movements enhance visual acuity. Nat. Commun. *11*, 795.

Ko, H., Poletti, M., and Rucci, M. (2010). Microsaccades precisely relocate gaze in a high visual acuity task. Nat. Neurosci. *13*, 1549–1553.

Nagloo, N., Collin, S.P., Hemmi, J.M., and Hart, N.S. (2016). Spatial resolving power and spectral sensitivity of the saltwater crocodile, *Crocodylus porosus*, and the freshwater crocodile, *Crocodylus johnstoni*. J. Exp. Biol. *219*, 1394–1404.

Poletti, M., Listorti, C., and Rucci, M. (2013). Microscopic eye movements compensate for nonhomogeneous vision within the fovea. Curr. Biol. *23*, 1691–1695.

Poletti, M., Rucci, M., and Carrasco, M. (2017). Selective attention within the foveola. Nat. Neurosci. *20*, 1413–1417.

Provis, J.M., Dubis, A.M., Maddess, T., and Carroll, J. (2013). Adaptation of the central retina for high acuity vision: Cones, the fovea and the avascular zone. Prog. Retin. Eye Res. *35*, 63–81.

Ratnam, K., Domdei, N., Harmening, W.M., and Roorda, A. (2017). Benefits of retinal image motion at the limits of spatial vision. J. Vis. *17*, 30.

Sinha, R., Hoon, M., Baudin, J., Okawa, H., Wong, R.O.L., and Rieke, F. (2017). Cellular and circuit mechanisms shaping the perceptual properties of the primate fovea. Cell *168*, 413–426.

Victory, N., Segovia, Y., and García, M. (2021). Foveal shape, ultrastructure and photoreceptor composition in yellow-legged gull, Larus michahellis (Naumann, 1840). Zoomorphology *140*, 151–167.

Wang, Y., Bensaid, N., Tiruveedhula, P., Ma, J., Ravikumar, S., and Roorda, A. (2019). Human foveal cone photoreceptor topography and its dependence on eye length. eLife *8*, e47148.

Zhang, C., Kim, Y.J., Silverstein, A.R., Hoshino, A., Reh, T.A., Dacey, D.M., and Wong, R.O. (2020). Circuit reorganization shapes the developing human foveal midget connectome toward single-cone resolution. Neuron *108*, 905–918.

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