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To see the Invisible

Scientists are curious by nature and often look where they should not. From such looking, discoveries are born that literally broaden the horizons. Working jointly, researchers from Professor Wojtkowski's team at IPC PAS, Nicolaus Copernicus University, Baltic Institute of Technology and their US collaborators from UC Irvine have recently managed to make practical use of infrared vision and by designing devices based on this phenomenon improve diagnosis of retinal diseases.

It started with scientific astonishment. Why is there a green glow when looking at an infrared emitting device? "Such a strange phenomenon was observed by my colleagues when they installed an imaging device at the Nicolaus Copernicus University in Toruń," says Prof. Wojtkowski. "They came to me sharing this interesting observation that although they use infrared, which should no longer be visible, they still see something; such a weak, greenish light. And why did they look into the assembled device? "Well," laughs the professor, "such human nature and curiosity. Every time you assemble something, you look inside. It's true that it's always risky to look in such device, because the infrared source is the laser, but it's safe to do so while maintaining the laser's power in accordance with the standards.

The scientists' first thought was that the laser was broken and, in addition to infrared (light wavelength similar to that used in old TV remote controls) generated green light. So they dismantled the laser and meticulously checked what could have broken down. They found nothing. Then someone came up with the simple but ingenious idea to put a filter in front of the eye of the observer, which would cut off visible light. They found the correct filters, put them between the laser and the eye and ... to their surprise the effect remained. "Our jaws dropped a little because that meant that the device was fine, but something strange was happening in the eye," says the professor. "Fortunately, there was another, very good laser at hand that generated ultra-short pulses of light and could be used to adjust the wavelength, of course in the infrared range. We started to change this length and it turned out that each one evoked a different colour effect in the eye - we could perceive various colours! What's more, not weakly, but very clearly." As it happens with such discoveries, it turned out that people had observed it before, but nobody had any idea how to explain it, or they couldn't interpret it correctly.

This unexpected colour vision turned out to be two-photon vision. "Luckily, at that time we were being visited by Professor Krzysztof Palczewski, who is a biochemist working in the USA and dealing with vision processes," recalls Professor Wojtkowski. "He was very interested in our discovery. So much so, that he organized a group of experts in various fields (including our team) to explain the mechanism of this vision. Tests were performed on mice, including genetically modified ones. Kasia Komar and Patryk Stremplewski from my team carried out tests on people, because our main expertise is in measurements on living eyes," explains the professor. "After collecting all the results, it turned out that we were dealing with two-photon vision." This involves the retina receiving a portion of energy half as low as the minimum required for the reaction of photosensitive cells, but very concentrated in time and space; and if the impulse is delivered, then the subject, e.g. a human, sees it as if it were twice as high. It's a bit like throwing small plasticine balls onto a board twice, in the same place and time. The imprint of both balls merges on the board into a larger, visible one. You can also imagine being hit on the head with these sorts of balls. We wouldn't feel any one of them singly, but a double portion could give us a bruise. This is what happens in the quantum world, the condition being that you have to throw these balls close enough to themselves and appropriately close to one another in time - so that they basically stick together into larger blobs. Physicists call this the optical non-linear effect. Such effects are known for many materials, but it is not obvious that they can occur in doses that are safe, e.g. for the eye. "Until we'd dealt with this ourselves, I myself had thought that two-photon absorption in the eye could occur only once (in principle, once in one eye, once in the fellow eye)," laughs the professor, "After which it wouldn't be possible to see anything . Fortunately, I was wrong."

On the other hand, in the eye there are a lot of intermediaries between what absorbs photon energy (i.e. retinal cells) and what introduces the image in our brain. Photon absorption in itself does not guarantee that we see something. A number of proteins must react. However, it turns out that this process called phototransduction does take place.

And what can it be useful for?- For instance, to check if the eye breaks down. With age or at the outset of a disease, say, macular degeneration (AMD), the effect is poorer. Hence the idea for a new generation of machines for microperimetry, i.e. checking whether we see and what we see at various points on the retina. Researchers thought that perhaps thanks to the two-photon effect, the sensitivity of such devices could be improved, or the threshold of infrared light could be measured. "Thanks to AM2M - a company that is a spinout from the Nicolaus Copernicus University in Toruń, we have already started to produce new microperimetry machines," the professor says with pride. "There are three in the world right now, and the fourth and fifth and sixth in our country.

What speaks in favour of the new discovery and the devices based on it is also that with age, the human eye becomes more and more turbid and disperses light waves more. Meanwhile, the principle of physics says that the longer the wave, the less it disperses. Infrared will therefore allow for a more thorough examination of the fundus also in people with advanced cataracts or vitreous floaters. Scientists hope that thanks to their device we will detect functional retinal changes, mainly AMD earlier on, but also better understand the process of vision. Indeed, these are the goals of the new IRA (International Research Agenda) working to improve the eyesight of older people.

"As part of our MAB we will try to objectify this process, i.e. move from a little subjective perimetry to objective ophthalmoscopy," the professor advances to the future, "Using holographic optical tomography. We will analyse functional signals on a principle similar as in tympanometry. This will allow us to determine whether the patient sees and what he sees, without feedback from him, even when he is unconscious or unable to communicate, e.g. after a stroke."

"Thanks to the work of Dr. Katarzyna Komar, we have noticed something that we cannot yet explain," adds Professor Wojtkowski. "Namely, infrared vision is different from normal vision. Cones appear to react differently to rods - they seem to be more sensitive. Now we are trying to understand what this results from." We, the potential patients, can only support the researchers, so that thanks to their discoveries our eyes serve us better and for longer.

Professor Maciej Wojtkowski is head of the CREATE ERA project.

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SCIENTIFIC PAPERS:

1. "Two-photon microperimetry: sensitivity of human photoreceptors to infrared light"
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Biomedical Optics Express Vol. 10, Issue 9, pp. 4551-4567 (2019)
DOI: 10.1364/BOE.10.004551

LINKS:

http://www.ichf.edu.pl/
The website of the Institute of Physical Chemistry of the Polish Academy of Sciences.

http://www.ichf.edu.pl/press/
Press releases of the Institute of Physical Chemistry of the Polish Academy of Sciences.

IMAGES:

IChF191129b_fot01s.jpg **HR:** http://ichf.edu.pl/press/2019/11/IChF191129b_fot01.jpg
Working together scientists from the Institute of Physical Chemistry PAS in Warsaw, Nicolaus Copernicus University in Toruń, Baltic Institute of Technology in Gdynia and American co-researchers succeeded in improving the diagnostics of retinal diseases. Posing for the photo presenting the issue of two-photon vision is the co-author of the research - Professor Maciej Wojtkowski.
(Source: IPC PAS, Grzegorz Krzyzewski)