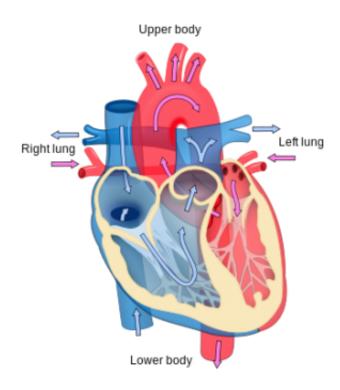


## Blue light sets the beat in biological pacemaker

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Heart diagram. Credit: Wikipedia

Israeli researchers have successfully established a new approach for pacing the heart and synchronizing its mechanical activity without the use of a conventional electrical pacemaker. This novel biologic strategy employs light-sensitive genes that can be injected into the heart and then activated by flashes of blue light.



More than 3 million people worldwide have had electronic pacemakers implanted. The most common indication for a pacemaker is the treatment of a slow heart beat which can put patients at risk for fainting, heart failure, and even death. Pacemakers work by sending electrical signals to the heart to regulate the heart beat. Pacemakers can also be used for cardiac resynchronization therapy (CRT), an approach aiming to synchronize the contraction of the heart's two ventricles in order to improve heart function, symptom status and decrease mortality in some patients who suffer from <a href="heart failure">heart failure</a>.

The new optogenetic approach for cardiac pacing and resynchronization was developed by Prof. Lior Gepstein and Dr. Udi Nussinovitch of the Technion-Israel Institute of Technology's Rappaport Faculty of Medicine, and Rambam Medical Center.

"Our work is the first to suggest a non-electrical approach to <u>cardiac</u> <u>resynchronization therapy</u>," Gepstein said. "Before this, there have been a number of elegant gene therapy and cell therapy approaches for generating biological pacemakers that can pace the heart from a single spot. However it was impossible to use such approaches to activate the heart simultaneously from a number of sites for resynchronization therapy."

If the biological pacemaker can be adapted for humans, it could help patients avoid many of the drawbacks of electrical pacemakers. These include the surgical procedure needed to implant the device, the risk of infection, the limitation on the number and locations of the pacing wires used, the possible decline in cardiac function resulting from the change in the normal electrical activation pattern, and the limitations on implantation in children.

"This is a very important proof-of-concept experiment, which for the first time, demonstrates a mechanism to pace the heart without the need



for wires and allows for simultaneous pacing from multiple sites," said Dr. Jeffrey Olgin, chief of the Division of Cardiology and co-director of the Heart and Vascular Center at the University of California, San Francisco. "The most common site of failure of current pacemakers are the leads or wires that connect the heart muscle to the electrical impulse. The approach demonstrated in this paper has the potential to eliminate these wires or have a single lead excite multiple sites simultaneously."

Pacing the heart with light is part of the emerging field of optogenetics, which has gained considerable momentum in the field of brain research. Researchers working in the field have been taking light-sensitive genes from algae and placing them in cells where they act like a switch, turning certain behaviors on or off when the cells are exposed to pulses of light.

As they report in the journal *Nature Biotechnology*, the Technion researchers injected one of these algae genes (channelorhodopsin-2) into a specific area of rat heart muscle. The scientists then showed that the light-sensitive protein expressed at this site could be turned on with flashes of <u>blue light</u> and drive the heart muscle to contract. By altering the frequency of the flashes, Gepstein and Nussinovitch could control and regulate the heart rate. They went on to deliver the gene to several places in the heart's pumping chambers, and demonstrated the ability to simultaneously activate the <u>heart muscle</u> from many places in an effort to synchronize the heart's pumping function.

Scientists will need to do more research for this optogenetic-based pacemaker strategy to become a reality in human health, Gepstein said. For instance, the gene injected in the rat experiments is sensitive to blue light which has poor tissue penetration potentially limiting its utility in large animals or humans.

"This means that the affected cells have to be relatively superficial—near the surface of the <a href="heart">heart</a>—and that an optical fiber



should be implanted bringing the illumination beam as close as possible to the cells," Gepstein said. "A potential solution in the future may be the development of similar light-sensitive proteins that will be responsive to light in the near-red or even infra-red spectrum, which penetrates tissue much better, allowing illumination from a long distance."

**More information:** "Optogenetics for in vivo cardiac pacing and resynchronization therapies." *Nature Biotechnology* (2015) DOI: 10.1038/nbt.3268

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