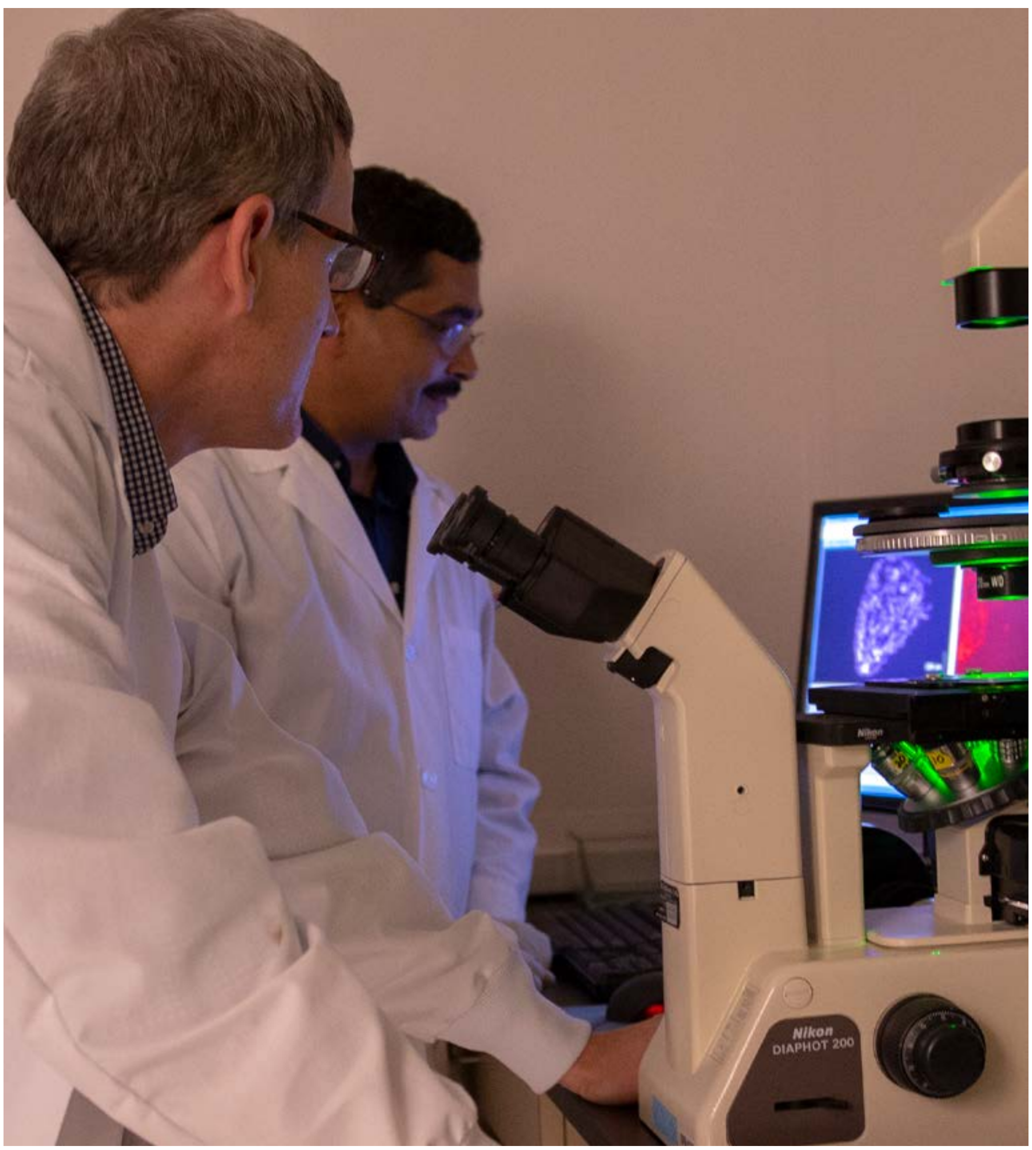
SHEDDING LIGHT ON THE NERVOUS SYSTEM

Researchers are harnessing infrared light to modulate, block and excite electrical signals that control organ function.

The first line of treatment for many diseases today, ranging from asthma to cardiac arrhythmias, is prescription drugs. But what if there was a better option?



“Drugs are pretty good at treating diseases, but they typically have lots of side effects,” says Michael Jenkins, PhD assistant professor of pediatrics and biomedical engineering at Case Western Reserve University School of Medicine. “Recently, it’s been shown that we may be able to treat diseases by modulating the electrical signals that control your organs and your autonomic responses.”

Last spring, a multidisciplinary team of researchers led by Jenkins received a four-year, $9 million grant from the National Institutes of Health (NIH) to develop enhanced infrared light technology for potentially treating a variety of diseases, including cardiac arrhythmias, high and low blood pressure, asthma and sleep apnea. Researchers from the Jenkins Lab, Vanderbilt University and the University of Pittsburgh have partnered to create new technologies to precisely send infrared light to nerves and ganglia in animals, watch the ensuing activity and map the molecular components in 3-D with high resolution.

Targeting Sensory Fibers

Modulation of the nervous system often utilizes electrodes for stimulation of large fibers. Jenkins’ group uses infrared neuromodulation (IRN) applied to peripheral structures, such as the nodose ganglion in the first cervical vertebra, to induce unique patterns of physiological responses that can’t be elicited by electrical current or drugs.

“Our infrared light targets small-diameter fibers preferentially, whereas electrical stimulation tends to target the large fibers,” says Jenkins. “Electrical currents are decent for eliciting movement – your arms and legs, for instance. But a lot of sensory fibers that control organs are actually small fibers, so there’s an advantage to being able to more easily get at those fibers.”

Recent work conducted by Jenkins and his peers indicates that IFN can affect collections of nerve cells that control autonomic function, such as heart rate, respiration, digestion and other visceral functions.

“Essentially, we take infrared light, shine it into the tissue and try to specifically target regions of the nodose ganglia,” says Jenkins. “We’ve discovered we can do things like lower blood pressure and affect the breathing rate. At this point, we are just starting to build tools to more accurately map what’s going on. But it’s exciting to get these different types of responses.”

Deciphering how the Technology Works

“The ganglion is like a little brain in the periphery structures, controlling certain autonomic functions,” says Jenkins. “If we can control those functions, it could be very valuable both as a tool for learning how the circuitry works, but also as a therapeutic tool.”

The goal of the NIH grant is four-fold:

- To create new devices that efficiently and precisely deliver infrared light to nerves and ganglia.
- To assess the safety, selectivity and repeatability of IRN.
- To map the spatial organization of the ganglionic function.
- To develop a deeper understanding of how IRN works.

Because the work is in its infancy, the group will spend time studying exactly how IRN affects autonomic functions. “The electromagnetic spectrum includes visible light and infrared light, which has longer wavelengths than visible light,” says Jenkins. “We have chosen to use wavelengths that have higher water absorption properties, and we think some of the responses we’re getting are due to transiently heating the tissues.”

One of the interesting things about the project, says Jenkins, is that the team has gotten different effects when stimulating the nodose ganglion depending upon the parameters they use. Electrode stimulation typically provokes one response no matter where the electrode is placed on the fiber. “But when we use the

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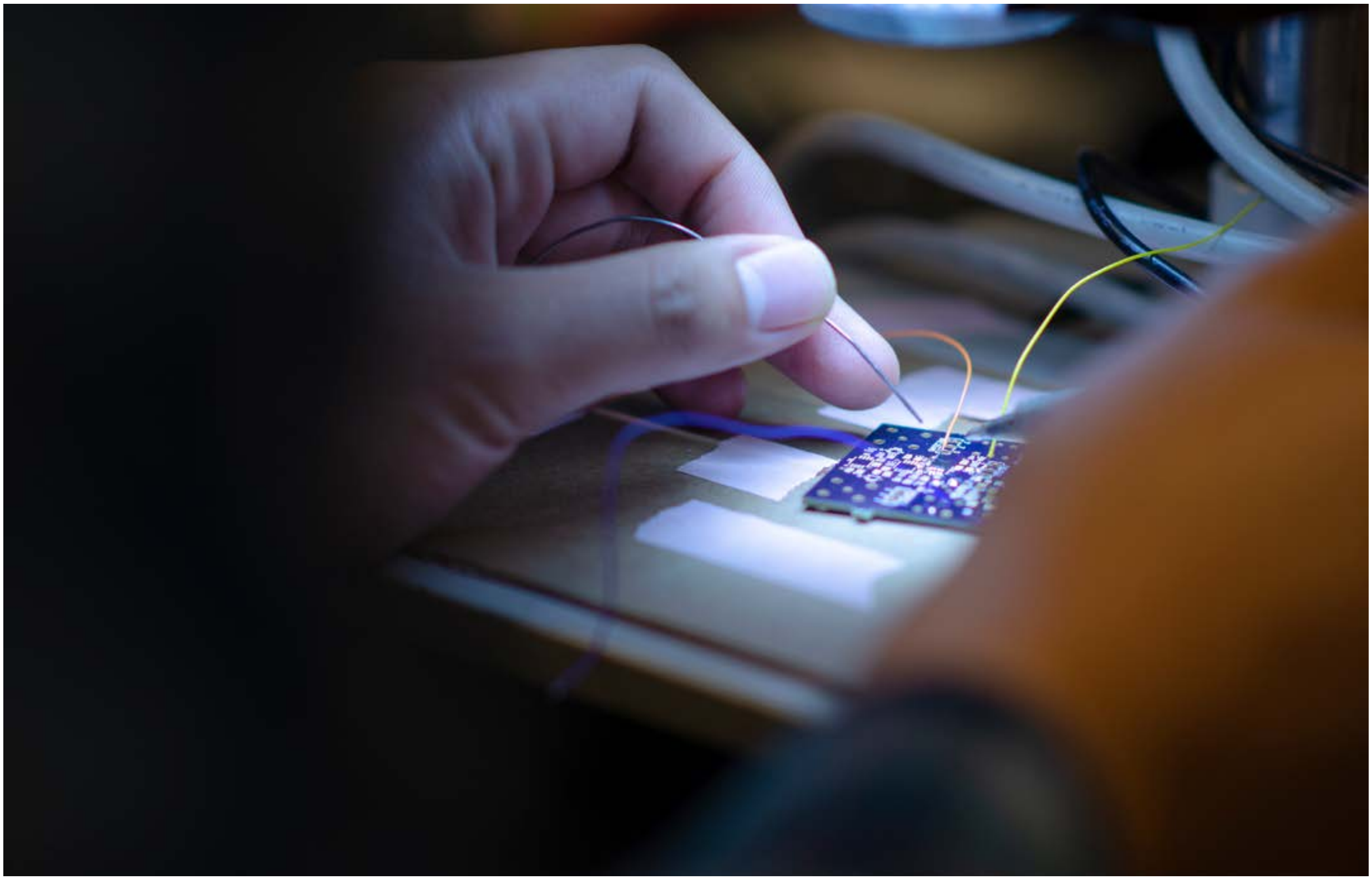

light, we actually get different responses depending upon where we place our optical fiber," says Jenkins. "The idea is that perhaps we can get more spatial precision with this technique and target certain types of cells."

The collaborators also will study how long you need to shine infrared light on sensory fibers to achieve results. Some effects occur only when the laser is on, while other responses last for hours after applying IRN for only a few seconds.

Working Toward Real-World Applications

Discovering what IRN is capable of doing, creating models for how it works and developing advanced optical systems to facilitate the technology requires a multidisciplinary approach. The research team includes collaborators in seven labs across three universities. The primary biomedical engineers are Jenkins, who earned his PhD in biomedical engineering from Case Western Reserve University in 2008, and E. Duco Jansen, professor of biomedical engineering at Vanderbilt University and one of the inventors of IRN. Other researchers include Hillel Chiel, a biology professor at Case Western Reserve University with a secondary appointment in biomedical engineering, and Stephen Lewis, professor of pediatrics at Case Western Reserve University's School of Medicine.

"One of the exciting things about working in larger groups to solve problems is that you bring together expertise from a number of different areas," says Jenkins. "It's imperative to get a lot of viewpoints if you want to move your science along quickly." And advancing the science of IRN has the potential of helping millions of people with an array of conditions. Consider just two possibilities:

- Diarrheal diseases account for one in nine child deaths worldwide, making diarrhea the second leading cause of death among children under the age of five, according to the Centers for Disease Control and Prevention. Using IRN, clinicians may be able to target the part of the nodose ganglion that controls peristalsis, which pushes ingested food through the digestive tract toward its release at the anus. "By slowing peristalsis down, we can stop diarrhea from taking a fatal tool on people, especially young children in less developed countries, who are particularly susceptible to death from dehydration," says Lewis.

- More than 4 million Americans suffer from recurrent arrhythmias, according to the American Heart Association. Some undergo cardiac ablation to prevent abnormal electrical signals from entering the heart, thereby stopping the arrhythmia. However, there can be unwanted side effects. “Ablation can lead to other problems because no ganglion control just one thing. So people may develop a droopy half of their face or other significant side effects,” says Jenkins. “What if you could modulate the signal with infrared light instead of ablating it?”

While these real-life applications remain on the horizon, Jenkins is excited by the potential for IRN. “With this grant, we’ll learn how it works and map the types of responses we are getting. In the future, we’ll move toward better ways to deliver the light to the tissue,” he says. “Overall, we have a real chance to learn something new about how the biology [of sensory fibers] work and create therapeutic interventions for treating diseases.”

Michael Jenkins, PhD studies images created using infrared neuromodulation.

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info@FEScenter.org | www.FEScenter.org | (216) 231-3257

About the Cleveland FES Center

The Cleveland FES Center is a consortium of the Louis Stokes Cleveland VA Medical Center, MetroHealth Medical Center, Case Western Reserve University, University Hospitals, and the Cleveland Clinic Neurological Institute. With their support, researchers, engineers and clinicians collaborate together to develop innovative solutions that improve the quality of life of individuals with neurological or other muscular skeletal impairments. Through the use of neurostimulation and neuromodulation research and applications, the Cleveland FES Center leads the translation of this technology into clinical deployment.

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