



# QnAs with Jeffrey S. Moore

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The most recent report card from the American Society of Civil Engineers provides a sobering analysis of the state of the transportation infrastructure in the United States (1). The findings detail the many repairs needed to strengthen bridges, roadways, railways, and other vital components of public networks. However, consider a scenario in which materials used in infrastructure could fix themselves: What if bridges could sense and seal cracks and roads could fill potholes without the need for costly intervention? Jeffrey Moore, a professor of chemistry and of materials science and engineering at the University of Illinois at Urbana-Champaign, has been studying molecules called mechanophores, which respond to force, and developing polymeric materials with self-healing properties. Moore envisions a future in which such materials are used not only in our environment but also in ourselves. Such polymers would either regenerate or harmlessly break down when their life cycles are complete. PNAS recently spoke to Moore, who was elected to the National Academy of Sciences in 2017, about his current research.



**Jeffrey Moore.** Image courtesy of Thompson-McClellan Commercial Photographers.

**PNAS:** Your Inaugural Article (2) describes a method that employs ultrasound to activate mechanophores—molecules that respond to force by changing color or generating light. What does your work reveal about their activation and potential for further use?

**Moore:** We were able to demonstrate that the acoustic field from high-intensity focused ultrasound produces enough force to drive chemical change. The beauty of ultrasound is that it has deep tissue penetration. So, the research opens the prospect of using mechanophores for noninvasive medical intervention in interesting ways. We're not there yet, but we're getting there.

**PNAS:** In using ultrasound, how can you ensure that the response is a result of the pressure or force and not the heat generated by friction caused by the sound waves?

**Moore:** The short answer: We ran a lot of control experiments! The long answer is that while we undoubtedly see a rise in temperature, it's very minor, about 2 °C. The mechanophores we used are thermostable

at 50 degrees or higher than the ultrasound-induced temperature elevation. Furthermore, the system we developed will not activate if the mechanophore is not coupled to the polydimethylsiloxane polymer network, which you would expect if it were truly a thermal response. While the mechanophore exists in the same thermal bath as the polymer, it's only activated through the mechanically responsive network.

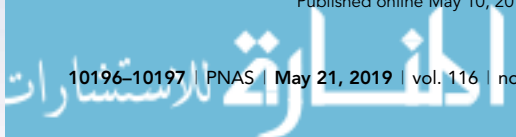
**PNAS:** How do you envision this technique expanding into biomedical investigation or therapeutics?

**Moore:** Biological systems are notoriously complicated and interconnected. So, it's especially useful to have an indirect means of interrogation, where you are targeting one specific molecule or pathway while not

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interfering with anything else. A truly orthogonal method of interrogation, like the use of mechanophores, could be very powerful. It's a niche angle, and it's quite uncommon.

I feel that mechanophores could be used, for example, for the targeted release of small-molecule therapeutics. The idea is that we could trigger on-demand doses in localized regions by applying a specific amount of force. Mechanophore-based probes and mechanosensors could also be used for imaging diagnostics. Whether or not such systems employed ultrasound, biologically compatible sensors could report out what their mechanical environment was experiencing.

**PNAS:** The article mentions optogenetics as a potential technique that could benefit from this approach. How do you see that working?

**Moore:** One of the reasons why we used two different mechanophores in this paper was that we wanted to see if ultrasound could trigger both a colorimetric indicator with which we had a lot of familiarity, naphthopyran, and one that might be useful in an optogenetic system, a luminescent dioxetane. Our results clearly put us on the pathway to the localized generation of visible light at a focal spot, which would be necessary to trigger a cellular response.

But before we get to optogenetics, our next big step is to increase the photon flux of the mechanophore. We've demonstrated proof of concept, and we're within an order of magnitude of optogenetic triggering.

This use of mechanophores for optogenetics spun out of discussions with my collaborators as well as coauthor King Li. At the Beckman Institute for Advanced Science and Technology, where I serve as director, we thrive off these kinds of collisions, and I'm very much appreciative of them.

**PNAS:** How do you see this system evolving in the future?

**Moore:** We would love to be able to mimic the luminescent system of a firefly, which regenerates its luminophore with enzymes and biological fuel. Our material right now is "one and done": It is stoichiometric, not catalytic. In other words, once a mechanophore generates light, it is no longer active. A combination of optogenetics plus an engineered capability to do biosynthesis of the luminophore—that's our Holy Grail.

From a synthetic materials standpoint, we're truly inspired by what biology can do and recognize how rudimentary our current material systems are relative to biology. We are interested in the full life cycle of polymers and composites: from manufacturing them in more energy efficient ways to building resiliency into materials, ensuring that they age healthily, and to reusing rather than disposing of them. Biology does a beautiful job of this.

**PNAS:** Where does this work fit into the trajectory of your career as a chemist and materials scientist?

**Moore:** I have built my career around working with others, and the article was a great example of a new collaboration—this time with medical ultrasound experts.

I have been developing the mechanophore hypothesis for almost 14 years, and this research both evolved from that concept and put it into practice. It fits into my interests at the intersection of chemistry and mechanical input as well as on self-healing polymers.

From a basic science perspective, this work addressed the question of "How can we employ a force that drives a reaction forward, over the activation barrier?" The broader picture is one of stimuli-responsive materials that respond to mechanical input. Most of my research is in structural materials for the built environment, not for biomedical efforts. So, this was really a first: bringing a mechanically sensitive polymer to problems that will show up in living systems.

<sup>1</sup> American Society of Civil Engineers (2017) Infrastructure Report Card. Available at <https://www.infrastructurereportcard.org/>. Accessed April 10, 2019.

<sup>2</sup> Kim G, et al. (2019) High-intensity focused ultrasound-induced mechanochemical transduction in synthetic elastomers. *Proc Natl Acad Sci USA* 116:10214–10222.