Ultrasound has potential to damage coronaviruses, study finds

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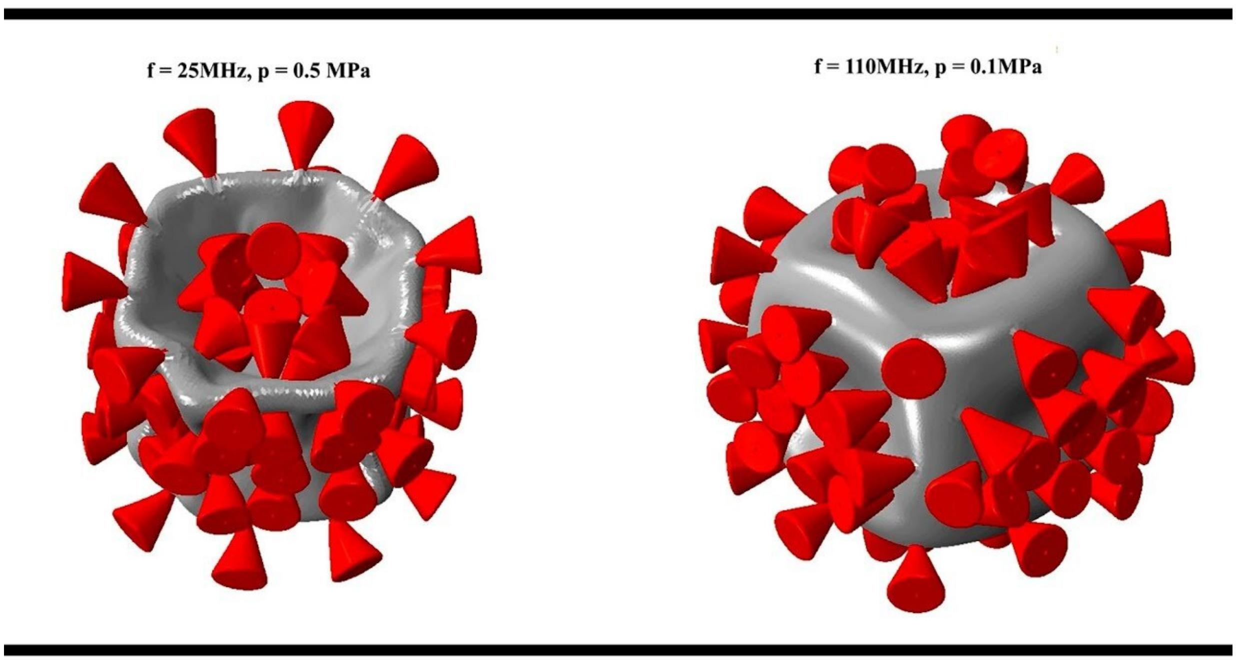

Credit: Massachusetts Institute of Technology

The coronavirus' structure is an all-too-familiar image, with its densely packed surface receptors resembling a thorny crown. These spike-like proteins latch onto healthy cells and trigger the invasion of viral RNA. While the virus' geometry and infection strategy is generally understood, little is known about its physical integrity.

A new study by researchers in MIT's Department of Mechanical Engineering suggests that coronaviruses may be vulnerable to ultrasound vibrations, within the frequencies used in medical diagnostic imaging.

Through computer simulations, the team has modeled the virus' mechanical response to vibrations across a range of ultrasound frequencies. They found that vibrations between 25 and 100 megahertz triggered the virus' shell and spikes to collapse and start to rupture within a fraction of a millisecond. This effect was seen in simulations of the virus in air and in water.

The results are preliminary, and based on limited data regarding the virus' physical properties. Nevertheless, the researchers say their findings are a first hint at a possible ultrasound-based treatment for coronaviruses, including the novel SARS-CoV-2 virus. How exactly ultrasound could be administered, and how effective it would be in damaging the virus within the complexity of the human body, are among the major questions scientists will have to tackle going forward.

"We've proven that under ultrasound excitation the coronavirus shell and spikes will vibrate, and the amplitude of that vibration will be very large, producing strains that could break certain parts of the virus, doing visible damage to the outer shell and possibly invisible damage to the RNA inside," says Tomasz Wierzbicki, professor of applied mechanics at MIT. "The hope is that our paper will initiate a discussion across various disciplines."

The team's results appear online in the *Journal of the Mechanics and Physics of Solids*. Wierzbicki's co-authors are Wei Li, Yuming Liu, and Juner Zhu at MIT.

A spiky shell

As the COVID-19 pandemic took hold around the world, Wierzbicki looked to contribute to the scientific understanding of the virus. His group's focus is in solid and structural mechanics, and the study of how materials fracture under various stresses and strains. With this perspective, he wondered what could be learned about the virus' fracture potential.

Wierzbicki's team set out to simulate the novel coronavirus and its mechanical response to vibrations. They used simple concepts of the mechanics and physics of solids to construct a geometrical and computational model of the virus' structure, which they based on limited information in the scientific literature, such as microscopic images of the virus' shell and spikes.

From previous studies, scientists have mapped out the general structure of the coronavirus—a family of viruses that s HIV, influenza, and the novel SARS-CoV-2 strain. This structure consists of a smooth shell of lipid proteins, and densely packed, spike-like receptors protruding from the shell.

With this geometry in mind, the team modeled the virus as a thin elastic shell covered in about 100 elastic spikes. As the virus' exact physical properties are uncertain, the researchers simulated the behavior of this simple structure across a range of elasticities for both the shell and the spikes.

"We don't know the material properties of the spikes because they are so tiny—about 10 nanometers high," Wierzbicki says. "Even more unknown is what's inside the virus, which is not empty but filled with RNA, which itself is surrounded by a protein capsid shell. So this modeling requires a lot of assumptions."

"We feel confident that this elastic model is a good starting point," Wierzbicki says. "The question is, what are the stresses and strains that will cause the virus to rupture?"

A corona's collapse

To answer that question, the researchers introduced acoustic vibrations into the simulations and observed how the vibrations rippled through the virus' structure across a range of ultrasound frequencies.

The team started with vibrations of 100 megahertz, or 100 million cycles per second, which they estimated would be the shell's natural vibrating frequency, based on what's known of the virus' physical properties.

When they exposed the virus to 100 MHz ultrasound excitations, the virus' natural vibrations were initially undetectable. But within a fraction of a millisecond the external vibrations, resonating with the frequency of the virus' natural oscillations, caused the shell and spikes to buckle inward, similar to a ball that dimples as it bounces off the ground.

As the researchers increased the amplitude, or intensity, of the vibrations, the shell could fracture—an acoustic phenomenon known as resonance that also explains how opera singers can crack a wineglass if they sing at just the right pitch and volume. At lower frequencies of 25 MHz and 50 MHz, the virus buckled and fractured even faster, both in simulated environments of air, and of water that is similar in density to fluids in the body.

"These frequencies and intensities are within the range that is safely used for medical imaging," says Wierzbicki.

To refine and validate their simulations, the team is working with microbiologists in Spain, who are using atomic force microscopy to observe the effects of ultrasound vibrations on a type of coronavirus found exclusively in pigs. If ultrasound can be experimentally proven to damage coronaviruses, including SARS-CoV-2, and if this damage can be shown to have a therapeutic effect, the team envisions that ultrasound, which is already used to break up kidney stones and to release drugs via liposomes, might be harnessed to treat and possibly prevent coronavirus infection. The researchers also envision that miniature ultrasound transducers, fitted into phones and other portable devices, might be capable of shielding people from the virus.

Wierzbicki stresses that there is much more research to be done to confirm whether ultrasound can be an effective treatment and prevention strategy against coronaviruses. As his team works to improve the existing simulations with new experimental data, he plans to zero in on the specific mechanics of the novel, rapidly mutating SARS-CoV-2 virus.

"We looked at the general coronavirus family, and now are looking specifically at the morphology and geometry of COVID-19," Wierzbicki says. "The potential is something that could be great in the current critical situation."

More information: Tomasz Wierzbicki et al. Effect of receptors on the resonant and transient harmonic vibrations of Coronavirus, *Journal of the Mechanics and Physics of Solids* (2021). DOI: 10.1016/j.jmps.2021.104369

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